



**UNIVERSIDAD
DE GRANADA**

Programa de Doctorado en Psicología

Tesis Doctoral

**Eficacia de la Terapia Cognitivo-Conductual en el Manejo
del Estrés Prenatal e Impacto en el Cortisol y Desarrollo
Infantil**

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Granada, 2023

Editor: Universidad de Granada. Tesis Doctorales
Autor: José Antonio Puertas González
ISBN: 978-84-1117-992-8
URI: <https://hdl.handle.net/10481/84439>

*A mis queridos padres y a mi hermana,
por el apoyo y la confianza*

AGRADECIMIENTOS

“No es una gran cosa mostrarse fuerte en una situación próspera, en la que la vida avanza con un curso favorable: tampoco un mar tranquilo y un viento propicio ponen de manifiesto el arte del piloto, conviene que irrumpa alguna adversidad que pruebe el ánimo.”

Lucio Anneo Séneca (4 a. C. – 65 d. C.)

En primer lugar, me gustaría expresar mi más sincero agradecimiento a mi directora de tesis, la Dra. María Isabel Peralta Ramírez, por ser un referente para mí en el mundo académico, por enseñarme que la ciencia es trabajo en equipo, humildad y pasión. Por acoger mis propuestas con una actitud inmejorable y por acompañarme en cada paso de la presente tesis. Por todo esto y por mucho más, gracias.

Quiero dar las gracias a Miguel, director del grupo de investigación CTS-581 “Neuropsicología y Psiconeuroinmunología Clínicas (PNinsula)” en el que se ha desarrollado la presente tesis. Gracias por su compromiso con la ciencia y con las personas, por crear un entorno de trabajo basado en el compañerismo y por todo su trabajo y gestión.

I would also like to thank Dr. Carolina de Weerth, my supervisor during my research stay at the Donders Institute for Brain, Cognition and Behaviour. Thank you for the warm welcome in the research group and for making me feel at home.

Me gustaría agradecer a todas las mujeres y bebés que han participado en los estudios que compila la presente tesis, sin más motivación que ayudar altruistamente al desarrollo de la ciencia. Sin su colaboración esta tesis no podría haberse llevado a cabo. También me gustaría agradecer a todo el personal sanitario que ha colaborado en los

distintos estudios, gracias a Milagros, Helen y Bemi. Gracias también a Raquel, por su ayuda en el análisis de cortisol y por su colaboración.

A mi equipo de trabajo, puesto que ha sido el pilar fundamental de esta tesis. Gracias a Borja por su confianza, sus sugerencias e ideas y por ser un reflejo de la humildad y del compañerismo. Gracias también a Carolina por su actitud, por su energía y por su ayuda y apoyo. Esta tesis ha incrementado en calidad indudablemente gracias a vosotros. Gracias también a Marta, Isis, Marie, Ana, Gracia y Aurora por su colaboración en los distintos estudios.

Extiendo mi gratitud a mis amigos y compañeros de PNinsula, quienes me han acompañado en este viaje académico y han contribuido al enriquecimiento de mi experiencia como investigador. Especialmente, quiero dar las gracias a Álvaro por su generosidad, su sentido del humor y por su amistad. A Carmen, Sofía y Haritini por hacer del grupo un lugar acogedor cada día y por contagiarme a diario de vuestra pasión por la ciencia. A Agar por todo su cariño y por su apoyo. A María y Raquel por toda la energía que aportan al grupo.

Gracias también a Inma y Juanma por la cooperación aportada y por contar con una espléndida disposición. A Ismael por su amistad, bondad y su disposición a ayudar.

También me gustaría agradecer a mis amigos del grado, los cuáles ayudaron a promover mi entusiasmo por la ciencia. Gracias a Juan por el cariño inmenso, por su sentido del humor y por todas las bromas que hemos gastado juntos. A Yared y a Ana por la paciencia inmensurable para aguantarnos, por la amistad y la confianza. Gracias también a Jorge por contagiarme su pasión por el conocimiento y la ciencia.

A Pablo por llenar mi ocio, gracias por acompañarme sobre ruedas y también online. A Sara y Marta por acogerme en su rinconcito durante mis idas y venidas, por los ratos de escalada y por enseñarme el apasionante mundo del buceo.

Gracias también a Natalia y a Luis, por seguir siempre mis pasos desde distintos puntos de la península.

A Alberto, Domingo, Luis y a los Ferreiras, mis amigos de toda la vida, los cuales permanecen aún con el paso del tiempo y me hacen sentir como en casa en cada reencuentro.

También deseo dar las gracias a Miguel, Vero, Begoña, Marta, Lucía y a las Andreas, las personas que hicieron que mi estancia en los Países Bajos fuera tan divertida y placentera. A Mauricio por su altruismo y por todos los *tips* recibidos para adaptarme a la cultura neerlandesa. *Bedankt*.

También quiero agradecer a las personas que han aparecido en la última parte del proceso y han conseguido enseñarme mucho en poco tiempo. Gracias a Juanpe, María, Jorge y Antonio, por acogerme con cariño en mi nueva etapa laboral en el mundo del dato.

A Cassandra, quiero agradecerle por ser mi refugio en los momentos difíciles, por estar siempre dispuesta a escuchar y ayudar. Su amor, amistad y risas han sido el mejor antídoto contra el estrés y las preocupaciones. Su compañía ha sido un regalo invaluable.

Mi más sincero agradecimiento a mi hermana, que siempre ha estado a mi lado brindándome apoyo, consejos y amor incondicional. Sin duda ha sido un soporte esencial en esta travesía académica. Finalmente, me gustaría dedicar un sincero agradecimiento a mis padres, cuya fe en mí y amor inquebrantable han sido una fuerza motriz en mi camino.

En definitiva, gracias a todos y a todas por enseñarme conocimientos y valores en este proceso.

Esta Tesis Doctoral se presenta como un compendio de 7 artículos publicados, los cuales responden a los objetivos de la misma. A continuación, se desglosan los estudios que la componen:

Artículo 1

- **Título:** Hair cortisol levels in pregnancy as a possible determinant of fetal sex: a longitudinal study.
- **Autores:** Borja Romero-Gonzalez, Jose A. Puertas-Gonzalez (corresponding author), Raquel Gonzalez-Perez, Marta Davila, Maria Isabel Peralta-Ramirez.
- **Revista:** Journal of Developmental Origins of Health and Disease.
- **Factor de impacto por *Journal Citation Report*:** 3.034.
- **Categoría:** Public, Environmental & Occupational Health
- **Posición en la categoría:** 117/210.
- **Cuartil:** Q3.
- **Año de Publicación:** 2021.
- **Referencia:** Romero-Gonzalez, B., Puertas-Gonzalez, J. A. (corresponding author), Gonzalez-Perez, R., Davila, M., & Peralta-Ramirez, M. I. (2021). Hair cortisol levels in pregnancy as a possible determinant of fetal sex: a longitudinal study. *Journal of Developmental Origins of Health and Disease*, 12(6), 902-907. <https://doi.org/10.1017/S2040174420001300>

Artículo 2

- **Título:** Can we influence the neurological development and hair cortisol concentration of offspring by reducing the stress of the mother during pregnancy? A randomized controlled trial.

- **Autores:** Jose A. Puertas-Gonzalez, Borja Romero-Gonzalez, Carolina Mariño-Narvaez, Raquel Gonzalez-Perez, Isis O. Sosa-Sanchez, Maria Isabel Peralta-Ramirez.
- **Revista:** Stress and Health.
- **Factor de impacto por *Journal Citation Report*:** 3.454.
- **Categoría:** Psychology.
- **Posición en la categoría:** 30/80.
- **Cuartil:** Q2.
- **Año de Publicación:** 2023.
- **Referencia:** Puertas-Gonzalez, J. A., Romero-Gonzalez, B., Mariño-Narvaez, C., Gonzalez-Perez, R., Sosa-Sanchez, I. O., & Peralta-Ramirez, M. I. (2023). Can we influence the neurological development and hair cortisol concentration of offspring by reducing the stress of the mother during pregnancy? A randomized controlled trial. *Stress and Health*. <https://doi.org/10.1002/smi.3222>

Artículo 3

- **Título:** The psychological impact of the COVID-19 pandemic on pregnant women.
- **Autores:** Jose A. Puertas-Gonzalez, Carolina Mariño-Narvaez, Maria Isabel Peralta-Ramirez, Borja Romero-Gonzalez.
- **Revista:** Psychiatry Research.
- **Factor de impacto por *Journal Citation Report*:** 11.225.
- **Categoría:** Psychiatry.
- **Posición en la categoría:** 9/143.
- **Decil:** D1.
- **Año de Publicación:** 2021.

- **Referencia:** Puertas-Gonzalez, J. A., Mariño-Narvaez, C., Peralta-Ramirez, M. I., & Romero-Gonzalez, B. (2021). The psychological impact of the COVID-19 pandemic on pregnant women. *Psychiatry Research*, *301*, 113978. <https://doi.org/10.1016/j.psychres.2021.113978>

Artículo 4

- **Título:** Giving birth during a pandemic: From elation to psychopathology.
- **Autores:** Jose A. Puertas-Gonzalez, Carolina Mariño-Narvaez, Borja Romero-Gonzalez, Maria Isabel Peralta-Ramirez.
- **Revista:** International Journal of Gynecology & Obstetrics.
- **Factor de impacto por *Journal Citation Report*:** 4.447.
- **Categoría:** Obstetrics & Gynecology.
- **Posición en la categoría:** 17/85.
- **Cuartil:** Q1.
- **Año de Publicación:** 2021.
- **Referencia:** Puertas-Gonzalez, J. A., Mariño-Narvaez, C., Romero-Gonzalez, B., & Peralta-Ramirez, M. I. (2021). Giving birth during a pandemic: From elation to psychopathology. *International Journal of Gynecology & Obstetrics*, *155*(3), 466-474. <https://doi.org/10.1002/ijgo.13803>

Artículo 5

- **Título:** Resilience, stress and anxiety in pregnancy before and throughout the pandemic: a structural equation modelling approach.
- **Autores:** Jose A. Puertas-Gonzalez, Carolina Mariño-Narvaez, Borja Romero-Gonzalez, Raquel Vilar-López, Maria Isabel Peralta-Ramirez.

- **Revista:** Current Psychology.
- **Factor de impacto por *Journal Citation Report*:** 2.387.
- **Categoría:** Psychology, Multidisciplinary.
- **Posición en la categoría:** 74/148.
- **Cuartil:** Q2.
- **Año de Publicación:** 2022.
- **Referencia:** Puertas-Gonzalez, J. A., Mariño-Narvaez, C., Romero-Gonzalez, B., Vilar-López, R., & Peralta-Ramirez, M. I. (2022). Resilience, stress and anxiety in pregnancy before and throughout the pandemic: a structural equation modelling approach. *Current Psychology*, 1-11. <https://doi.org/10.1007/s12144-022-03305-6>

Artículo 6

- **Título:** Stress and Psychopathology Reduction in Pregnant Women through Online Cognitive Behavioural Therapy during COVID-19: A Feasibility Study.
- **Autores:** Jose A. Puertas-Gonzalez, Carolina Mariño-Narvaez, Borja Romero-Gonzalez, Maria Isabel Peralta-Ramirez.
- **Revista:** Behavioral Sciences.
- **Factor de impacto por *Journal Citation Report*:** 2.286.
- **Categoría:** PSYCHOLOGY, MULTIDISCIPLINARY
- **Posición en la categoría:** 82/148.
- **Cuartil:** Q3.
- **Año de Publicación:** 2021.
- **Referencia:** Puertas-Gonzalez, J. A., Mariño-Narvaez, C., Romero-Gonzalez, B., & Peralta-Ramirez, M. I. (2021). Stress and Psychopathology Reduction in Pregnant Women through Online Cognitive Behavioural Therapy during COVID-19: A

Artículo 7

- **Título:** Online cognitive behavioural therapy as a psychological vaccine against stress during the COVID-19 pandemic in pregnant women: A randomised controlled trial.
- **Autores:** Jose A. Puertas-Gonzalez, Carolina Mariño-Narvaez, Borja Romero-Gonzalez, Gracia M. Sanchez-Perez, Maria Isabel Peralta-Ramirez.
- **Revista:** Journal of Psychiatric Research.
- **Factor de impacto por *Journal Citation Report*:** 5.250.
- **Categoría:** Psychiatry.
- **Posición en la categoría:** 41/143.
- **Cuartil:** Q2.
- **Año de Publicación:** 2022.
- **Referencia:** Puertas-Gonzalez, J. A., Marino-Narvaez, C., Romero-Gonzalez, B., Sanchez-Perez, G. M., & Peralta-Ramirez, M. I. (2022). Online cognitive behavioural therapy as a psychological vaccine against stress during the COVID-19 pandemic in pregnant women: A randomised controlled trial. *Journal of Psychiatric Research*, 152, 397-405. <https://doi.org/10.1016/j.jpsychires.2022.07.016>

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RESUMEN

1. RESUMEN

El objetivo general de la presente Tesis Doctoral fue investigar la eficacia de la Terapia Cognitivo-Conductual (TCC) para el afrontamiento del estrés en mujeres gestantes, aplicada en modalidad presencial y telemática. La tesis reúne siete estudios publicados en revistas indexadas en el *Journal Citation Report* (JCR), divididos en dos bloques de objetivos.

El primer bloque, titulado “Eficacia de la TCC en mujeres embarazadas y efectos en la descendencia” cuenta con dos objetivos específicos: 1) analizar si existe una relación entre los niveles de cortisol en el cabello y/o el estrés psicológico durante la concepción y las primeras semanas de embarazo con respecto al sexo del feto; y, 2) evaluar la eficacia de la TCC en la reducción del estrés en mujeres embarazadas a nivel psicológico y hormonal, y cómo dicha eficacia se relaciona con el neurodesarrollo y cortisol del bebé. Los estudios 1 y 2 abordan estos objetivos específicos.

Los resultados del estudio 1 mostraron una asociación entre niveles más elevados de cortisol en cabello el momento de la concepción y las primeras semanas de embarazo y una mayor probabilidad de tener un feto femenino. Sin embargo, no se halló relación entre el estrés psicológico de la madre y el sexo fetal. De este modo, los resultados de la investigación parecen respaldar las teorías explicativas que sugieren que las concentraciones de cortisol en el momento de la concepción tienen un papel importante en la determinación del sexo del feto.

El estudio 2, un seguimiento de un ensayo controlado aleatorio, incluyó dos grupos de mujeres embarazadas: uno que recibió TCC para controlar el estrés durante el embarazo y un grupo control que recibió los cuidados habituales. Los resultados

mostraron que, los bebés del Grupo de Terapia (GT) presentaron menor concentración de cortisol en cabello al nacer, pero no se encontraron diferencias significativas entre los dos grupos en relación con los niveles de cortisol a los 6 meses. Con respecto al neurodesarrollo, los resultados revelaron que los bebés de los GT presentaban un mayor nivel de neurodesarrollo cognitivo y motor a los 6 meses de edad.

A modo de conclusión del primer bloque, los estudios 1 y 2 revelan que existe una relación entre la concentración de cortisol de la madre durante el momento de la concepción y los primeros meses de embarazo y el sexo fetal. Por otro lado, la TCC para el afrontamiento del estrés es eficaz, aplicada durante el embarazo, en la reducción de estrés y síntomas psicopatológicos, y además, podría tener implicaciones en las concentraciones de cortisol de los bebés a corto plazo y en el neurodesarrollo motor y cognitivo a medio y largo plazo.

El segundo bloque de objetivos se titula “Eficacia de la TCC en gestantes implementada de manera telemática durante una crisis sanitaria” y aborda tres objetivos específicos mediante cinco estudios.

El primer objetivo específico del segundo bloque se enfocó en analizar la salud psicológica perinatal durante la pandemia, tanto en el transcurso del embarazo como después del parto. Para la consecución de este objetivo se llevaron a cabo los estudios 3 y 4. Por un lado, los resultados del estudio 3 mostraron que el grupo de mujeres gestantes durante la crisis sanitaria presentaban mayores niveles de sintomatología depresiva y de ansiedad fóbica, así como, mayores niveles de estrés percibido en comparación con aquellas mujeres gestantes antes a la misma. En esa misma línea, los hallazgos del estudio 4 revelaron que las mujeres que dieron a luz durante la pandemia presentaban niveles más altos de depresión, ansiedad, hostilidad, ansiedad fóbica, somatización, obsesiones y compulsiones, sensibilidad interpersonal y psicoticismo.

El segundo objetivo específico del segundo bloque, consistió en investigar la interacción de la resiliencia, estrés y ansiedad en mujeres embarazadas en dos situaciones de estrés diferentes: antes y durante la pandemia de COVID-19. Para abordar este objetivo se llevó a cabo el estudio 5, en el cual se estudió la relación entre la resiliencia psicológica, estrés percibido, estrés específico del embarazo y ansiedad, del mismo modo que en los dos estudios previos, a través de dos cohortes de mujeres gestantes: el primero evaluado antes de la pandemia; y, el segundo evaluado durante la misma. En ambos grupos, se observó que la resiliencia disminuía los niveles de estrés específico del embarazo y el estrés general percibido, así como la sintomatología de ansiosa. Asimismo, el estrés específico del embarazo y el estrés percibido presentaron correlación entre ambos y, éstos a su vez, predecían el aumento de los síntomas de ansiedad.

El tercer y último objetivo específico del segundo bloque se focalizó en estudiar la viabilidad y eficacia de la TCC para el control del estrés en mujeres embarazadas, aplicada telemáticamente durante la pandemia. Para alcanzar este objetivo se llevaron a cabo los estudios 6 y 7. A través de ambos estudios, se comprobó que la TCC para el control del estrés aplicada de manera telemática en mujeres gestantes es viable y eficaz en la reducción de los niveles de estrés y sintomatología psicopatológica de ansiedad, depresión y obsesiones-compulsiones, así como, en el incremento de la resiliencia.

A modo de conclusión del bloque 2, las situaciones de crisis sanitarias como las pandemias, que implican restricciones en la movilidad y el contacto social, desembocan en un aumento del estrés y los síntomas psicopatológicos en el periodo perinatal. No obstante, la resiliencia psicológica puede actuar como un factor protector contra el aumento del estrés y los síntomas ansiosos, tanto en situaciones de crisis como en contextos ordinarios. Por último, un programa de intervención psicológica basado en la TCC para el manejo del estrés, aplicado de manera telemática, puede aumentar los niveles

de resiliencia psicológica y reducir los niveles de estrés psicológico y los síntomas psicopatológicos en mujeres gestantes.

En resumen, los resultados obtenidos en los dos bloques de objetivos demuestran que la TCC es efectiva en la reducción del estrés y los síntomas psicopatológicos en mujeres embarazadas, tanto en modalidad presencial como telemática. Además, se encontró una relación entre las concentraciones de cortisol materno durante la concepción y los primeros meses de embarazo y el sexo fetal. La intervención con TCC también mostró implicaciones en las concentraciones de cortisol en los bebés a corto plazo y en su neurodesarrollo motor y cognitivo a medio y largo plazo.

Por otro lado, durante situaciones de crisis sanitaria, como pandemias, el estrés y los síntomas psicopatológicos en el periodo perinatal aumentan. No obstante, la resiliencia psicológica puede actuar como un factor protector contra el aumento del estrés y los síntomas ansiosos en contextos de crisis y situaciones ordinarias. En este sentido, la aplicación de un programa de intervención psicológica basado en la TCC para el manejo del estrés de manera telemática puede mejorar la resiliencia psicológica y reducir los niveles de estrés y síntomas psicopatológicos en mujeres embarazadas.

SUMMARY

2. SUMMARY

The general objective of this Doctoral Thesis was to investigate the efficacy of Cognitive-Behavioral Therapy (CBT) for stress coping in pregnant women, applied in face-to-face and telematic modalities. The thesis compiles seven studies published in journals indexed in the Journal Citation Report (JCR), divided into two blocks of objectives.

The first block, entitled "Effectiveness of CBT in pregnant women and effects on offspring" has two specific objectives: 1) to analyze whether there is a relationship between cortisol levels in hair and/or psychological stress during conception and the first weeks of pregnancy with respect to the sex of the fetus; and, 2) to evaluate the effectiveness of CBT in reducing stress in pregnant women at the psychological and hormonal level, and how this effectiveness is related to neurodevelopment and cortisol in the baby. Studies 1 and 2 address these specific objectives.

The results of study 1 showed an association between higher levels of cortisol in hair at the time of conception and the first weeks of pregnancy and a higher probability of having a female fetus. However, no relationship was found between maternal psychological stress and fetal sex. Thus, the research results appear to support explanatory theories suggesting that cortisol concentrations at the time of conception play an important role in determining the sex of the fetus.

Study 2, a follow-up of a randomized controlled trial, included two groups of pregnant women: one that received CBT to manage stress during pregnancy and a control group that received usual care. The results showed that, the babies in the Therapy Group (TG) had lower hair cortisol concentration at birth, but no significant differences were

found between the two groups in relation to cortisol levels at 6 months. With respect to neurodevelopment, the results revealed that the TG infants presented a higher level of cognitive and motor neurodevelopment at 6 months of age.

To conclude the first block, studies 1 and 2 reveal that there is a relationship between the mother's cortisol concentration during conception and the first months of pregnancy and fetal sex. On the other hand, CBT for stress coping is effective, applied during pregnancy, in the reduction of stress and psychopathological symptoms and, in addition, it could have implications on infant cortisol concentrations in the short term and on motor and cognitive neurodevelopment in the medium and long term.

The second block of objectives is entitled "Effectiveness of telematically implemented CBT in pregnant women during a health crisis" and addresses three specific objectives through five studies.

The first specific objective of the second block focused on analyzing perinatal psychological health during the pandemic, both during pregnancy and after delivery. In order to achieve this objective, studies 3 and 4 were carried out. On the one hand, the results of study 3 showed that the group of pregnant women during the health crisis presented higher levels of depressive symptomatology and phobic anxiety, as well as higher levels of perceived stress compared to those pregnant women before the crisis. Along the same lines, the findings of study 4 revealed that women who gave birth during the pandemic had higher levels of depression, anxiety, hostility, phobic anxiety, somatization, obsessions and compulsions, interpersonal sensitivity, and psychoticism.

The second specific objective of the second block consisted of investigating the interaction of resilience, stress and anxiety in pregnant women in two different stress situations: before and during the COVID-19 pandemic. To address this objective, study

5 was carried out, in which the relationship between psychological resilience, perceived stress, pregnancy-specific stress and anxiety was studied in the same way as in the two previous studies, through two cohorts of pregnant women: the first evaluated before the pandemic; and the second evaluated during the pandemic. In both groups, resilience was observed to decrease levels of pregnancy-specific stress and general perceived stress, as well as anxiety symptomatology. Likewise, pregnancy-specific stress and perceived stress correlated with each other and, in turn, predicted the increase in anxiety symptoms.

The third and last specific objective of the second block focused on studying the feasibility and efficacy of CBT for stress management in pregnant women, applied telematically during the pandemic. In order to achieve this objective, studies 6 and 7 were carried out. Through both studies, it was proven that CBT for stress management applied telematically in pregnant women is feasible and effective in reducing stress levels and psychopathological symptoms of anxiety, depression and obsessions-compulsions, as well as in increasing resilience.

To conclude block 2, health crises such as pandemics, involving restrictions in mobility and social contact, lead to increased stress and psychopathological symptoms in the perinatal period. However, psychological resilience can act as a protective factor against increased stress and anxious symptoms, both in crises and in ordinary contexts. Finally, a CBT-based psychological intervention program for stress management, applied telematically, can increase levels of psychological resilience and reduce stress levels and psychopathological symptoms in pregnant women.

In summary, the results obtained in the two blocks of objectives demonstrate that CBT is effective in reducing stress and psychopathological symptoms in pregnant women, both in face-to-face and telematic modalities. In addition, a relationship was found between maternal cortisol concentrations during conception and the first months of

pregnancy and fetal sex. The CBT intervention also showed implications on cortisol concentrations in infants in the short term and on their motor and cognitive neurodevelopment in the medium and long term.

On the other hand, during health crises, such as pandemics, stress and psychopathological symptoms increase in the perinatal period. However, psychological resilience can act as a protective factor against increased stress and anxious symptoms in crisis contexts and ordinary situations. In this way, the application of a CBT-based psychological intervention program for stress management in a telematic manner can improve psychological resilience and reduce levels of stress and psychopathological symptoms in pregnant women.

INTRODUCCIÓN

3. INTRODUCCIÓN

3.1 Estrés psicológico y sus consecuencias en el embarazo

Según el modelo teórico de Lazarus y Folkman (1986), cuando un individuo se enfrenta a una situación novedosa o amenazante, se produce una evaluación cognitiva en la que se analizan las demandas del ambiente y los recursos disponibles para enfrentar dicha situación. Así, la relación entre la persona y el entorno, así como, la evaluación cognitiva de la situación son los elementos clave en este modelo. De este modo, la evaluación cognitiva determina la respuesta de estrés y está influenciada por diversos factores individuales, tales como la genética, las experiencias previas durante el desarrollo, los patrones de pensamiento y las conductas aprendidas a lo largo de toda la experiencia vital.

La respuesta al estrés es altamente individual y varía entre las personas debido a la combinación única de estos factores. En este sentido, cada individuo presenta diferentes respuestas psicológicas y conductuales al estrés, lo que se traduce en una mayor o menor capacidad para afrontar situaciones adversas.

A nivel fisiológico, la respuesta al estrés se encuentra mediada por la activación de los sistemas alostáticos y los mediadores biológicos, como los glucocorticoides (Musillo y cols., 2022; Pilnik, 2010). Los sistemas alostáticos son mecanismos de adaptación que el organismo utiliza para mantener la homeostasis frente a cambios en el entorno, y su activación prolongada puede conllevar consecuencias negativas para la salud, conocidas como "carga alostática".

Los glucocorticoides, como el cortisol, son hormonas esteroides producidas por las glándulas suprarrenales y liberadas en respuesta al estrés. Su función principal es la

de regular el metabolismo energético y los procesos antiinflamatorios en el organismo. Sin embargo, una exposición crónica a altos niveles de glucocorticoides puede tener efectos perjudiciales en el sistema nervioso, el sistema inmunológico y el sistema cardiovascular, entre otros.

Por lo tanto, el impacto de la respuesta al estrés en la salud de un individuo no es solo el resultado de la activación de estos sistemas biológicos, sino también de cómo el individuo interpreta y afronta las situaciones estresantes. Por esta razón, es fundamental considerar la interacción entre los aspectos cognitivos, conductuales y fisiológicos en la comprensión de las respuestas al estrés y sus consecuencias para la salud y el bienestar de las personas.

En la sociedad contemporánea, el rápido ritmo de vida a menudo conduce a un aumento del estrés mental. En el caso específico de las mujeres embarazadas, estas deben enfrentarse no solo al estrés cotidiano, sino también a la agitación emocional causada por las transformaciones físicas y fisiológicas que ocurren durante el embarazo. Estos cambios incluyen la maduración del tejido placentario, el desarrollo fetal y su interacción, así como el estrés generado por las modificaciones en sus roles sociales y familiares (Davis y Narayan, 2020).

Como se ha comentado, el estrés activa respuestas fisiológicas y psicológicas esenciales para la supervivencia, sin embargo, cuando esta activación se mantiene durante períodos prolongados, puede resultar perjudicial. En este contexto, la carga alostática, producto de la respuesta al estrés crónico, puede tener efectos negativos en el desarrollo, el metabolismo, las respuestas inflamatorias e incluso neuroendocrinas (Cirulli y Berry, 2013; McEwen y cols., 2015; McEwen, 2017).

Esta situación de estrés crónico durante el embarazo puede aumentar el riesgo de complicaciones tanto para la madre como para el bebé en desarrollo. En particular, el estrés prolongado puede afectar la función placentaria, el desarrollo neurológico fetal y alterar el equilibrio hormonal en la madre. Además, puede contribuir a la aparición de trastornos del estado de ánimo, como la ansiedad y la depresión, lo que puede dificultar la adaptación de la madre a su nuevo rol y comprometer su capacidad para cuidar y establecer vínculos afectivos con el recién nacido

Las consecuencias del estrés perinatal son múltiples y están intrínsecamente relacionadas con la alteración del eje Hipotálamo-Hipófisis-Adrenal (HHA). Este eje es el encargado de regular la respuesta al estrés en el organismo, y su desregulación puede ocasionar perturbaciones en la producción de hormonas como la adrenocorticotrófica, la hormona liberadora de corticotropina y el cortisol, como se muestra en la Figura 1. Estas hormonas juegan un papel crucial en la respuesta del organismo al estrés y en el mantenimiento del equilibrio homeostático.

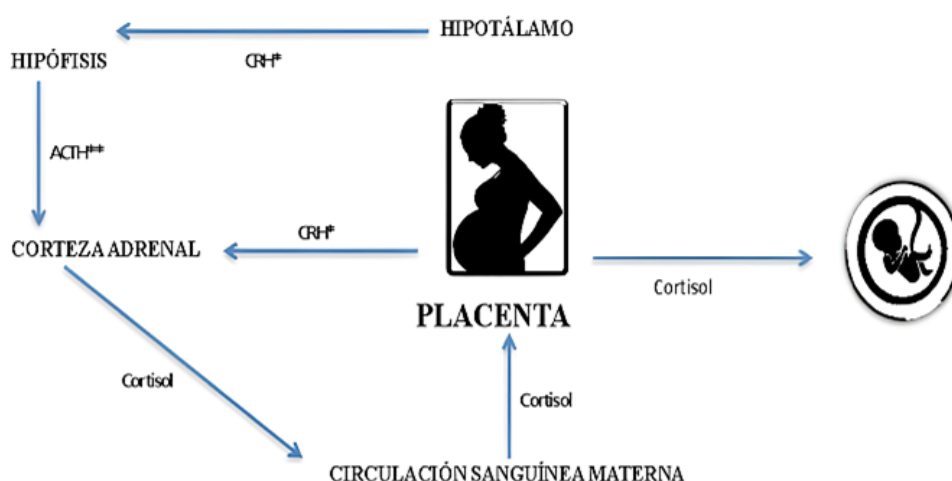


Figura 1. Desregulación del eje Hipotálamico-Hipofisiario-Adrenal durante el embarazo. Esta imagen está recogida del libro “Un villano llamado estrés” (Peralta-Ramírez, 2019,

pág. 271). **Nota:** * = Hormona Liberadora de Corticotropina (CRH); ** = Hormona Adrenocorticotropa (ACTH).

Cuando el estrés se mantiene en niveles altos durante el embarazo, se incrementa el riesgo de diversas complicaciones obstétricas. Entre estas, la preeclampsia es una de las más estudiadas (Pop y cols., 2022; Yu y cols., 2013; Zhang y cols., 2013), y se caracteriza por un aumento en la presión arterial y la presencia de proteínas en la orina. La hipertensión inducida por el embarazo también es una posible consecuencia del estrés perinatal, como lo indica Cardwell (2013). Esta condición puede aumentar el riesgo de complicaciones tanto para la madre como para el feto.

La diabetes gestacional es otra complicación relacionada con el estrés durante el embarazo. Horsch y cols. (2016) demostraron que el estrés perinatal puede contribuir al desarrollo de esta enfermedad, que se caracteriza por niveles elevados de glucosa en sangre. Además, la diabetes gestacional es un factor de riesgo para la aparición de diabetes tipo 2 en la madre después del embarazo.

El estrés perinatal también se ha asociado con un mayor riesgo de abortos espontáneos (Qu y cols., 2017), por lo que se produce una interrupción involuntaria del embarazo antes de que el feto alcance la viabilidad. Además, se ha observado que el estrés puede aumentar la incidencia de partos prematuros (Gilles y cols., 2018; Karakash y cols., 2016; Tanpradit y Kaewkiattikun, 2020), es decir, aquellos que ocurren antes de la semana 37 de gestación. Los bebés prematuros pueden enfrentar una serie de desafíos de salud a lo largo de su vida debido a su desarrollo incompleto.

Por último, destacar que el estrés perinatal se ha relacionado con un mayor riesgo de bajo peso al nacer (Bussières y cols., 2015; Lima y cols., 2018). Los bebés con bajo peso al nacer pueden ser más propensos a enfrentar problemas de salud a lo largo de su

vida, como infecciones, dificultades en el desarrollo neurológico y enfermedades crónicas en la edad adulta.

3.2 Estrés perinatal y sus implicaciones en la descendencia

Por otro lado, la activación del eje HHA y la liberación de cortisol perinatal no solo tienen implicaciones en la madre, sino que desempeñan un papel crucial en el desarrollo y maduración fetal (Benediktsson y cols., 1997). En términos de desarrollo, el período fetal es mucho más significativo que cualquier otro período de la vida, ya que la plasticidad es mayor durante el desarrollo temprano y los órganos se encuentran en proceso de maduración (Bock y cols., 2014; Faulk y Dolinoy, 2011). De esta manera, las características específicas del entorno temprano, comenzando en el útero o incluso antes, pueden generar factores de riesgo para problemas de salud futuros en el individuo (Hanson y Gluckman, 2011; Van den Bergh, 2011).

En esta línea, han surgido diversas hipótesis, como la hipótesis de programación del desarrollo (Barker, 2004; Langley-Evans, 2006, 2015), la hipótesis de programación fetal (Seckl y Holmes, 2007) y la hipótesis de los orígenes del desarrollo de la salud y la enfermedad (Barker, 1990, 2004). Estas teorías sugieren que las alteraciones en los factores ambientales uterinos durante los períodos críticos del desarrollo pueden tener un impacto duradero en los sistemas biológicos y en la plasticidad intrínseca para responder a las influencias ambientales. Siguiendo esta línea de investigación, varios estudios han encontrado una asociación negativa significativa entre el estrés prenatal y el neurodesarrollo posterior de la descendencia (Schechter y cols., 2016; Tarabulsky y cols., 2014; Van den Bergh y cols., 2020). Estos hallazgos pueden tener implicaciones a largo plazo, ya que un neurodesarrollo cognitivo deficiente en la infancia se ha asociado con

un mayor riesgo de psicopatología en la edad adulta (Koenen y cols., 2009). En la Figura 2 se presenta un resumen de las relaciones halladas entre el estrés prenatal y alteraciones posteriores en la descendencia.

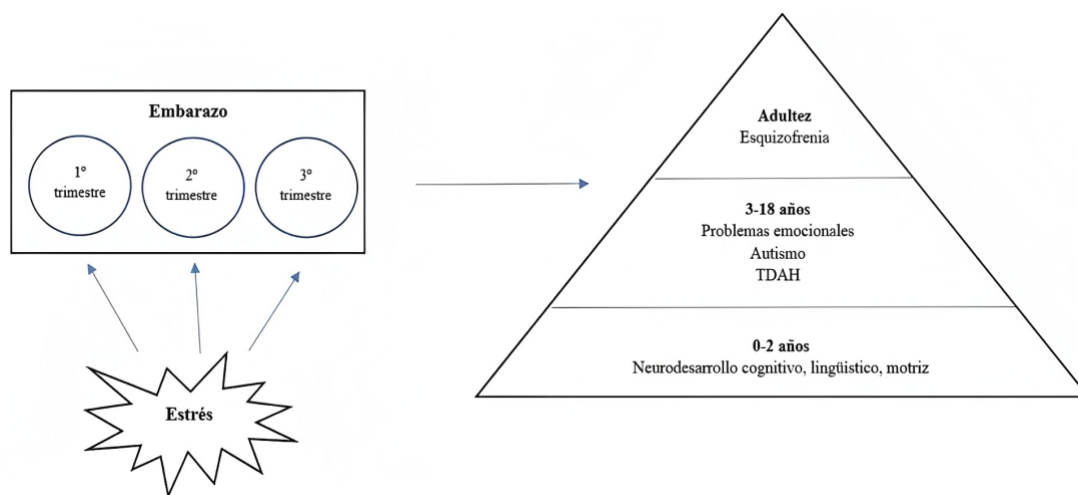


Figura 2. Relaciones entre el estrés prenatal y alteraciones en la descendencia. Esta imagen está recogida del libro “Un villano llamado estrés” (Peralta-Ramírez, 2019, pág. 298).

Por otro lado, también se han establecido asociaciones entre las concentraciones de cortisol materno durante el embarazo y el neurodesarrollo posterior del bebé, hallándose una relación positiva entre ambos durante el primer y segundo trimestre y, una relación negativa en el tercero (Caparros-Gonzalez y cols., 2019). Además, la relación entre el estrés prenatal, los niveles de cortisol materno y el bebé puede manifestarse incluso más temprano. En este sentido, es conveniente destacar los estudios previos que han encontrado un descenso de nacimientos varones en poblaciones que han experimentado un evento estresante, como un ataque terrorista (Bruckner y cols., 2010; Catalano y cols., 2005) un terremoto (Saadat, 2008), o situaciones económicas adversas (Catalano, 2003), acontecimientos marcados por un aumento significativo de los niveles de estrés en la población (Bourque y cols., 2002; Schuster y cols., 2001). Los resultados

de estos estudios sugieren que el estrés puede ser un factor relevante incluso en la determinación del sexo.

Aunque es necesario continuar investigando los mecanismos concretos implicados en este efecto, hipotetizamos que el estrés psicológico puede activar el eje HHA desembocando en un incremento en la secreción de cortisol, que a su vez puede tener impacto en diferentes tejidos incluido el sistema reproductivo. Por lo tanto, una hipótesis es que el estrés de los padres modifica la concentración de hormonas sexuales a través de la activación de dicho eje, presentando implicaciones en la asignación de sexos. Esta hipótesis parece ser respaldada por el estudio de Chason y cols. (2012), quienes investigaron el cortisol salival materno, el cual es una medida puntual del cortisol, de manera prospectiva en una cohorte de mujeres embarazadas durante el momento de la concepción. Encontrando que aquellas con niveles más altos de cortisol tenían mayores probabilidades de gestar fetos femeninos. Otros estudios han examinado la relación entre las concentraciones de cortisol materno y el sexo fetal en momentos posteriores a la concepción, obteniendo resultados contradictorios (Enlow y cols., 2019; Vrijkotte y cols., 2023).

Por lo tanto, es necesario estudiar la relación entre el cortisol materno y el sexo fetal utilizando medidas retrospectivas sólidas que no se vean afectadas por el momento de la extracción para profundizar en esta línea de conocimiento.

3.3 Terapias psicológicas para el control del estrés en el embarazo

Dadas las repercusiones del estrés en la madre y en la descendencia a corto y largo plazo, es fundamental abordar el estrés durante el embarazo tanto a nivel individual como

en el marco de políticas de salud pública y apoyo social. La detección temprana de factores estresantes y el acceso a intervenciones para reducir el estrés pueden marcar una diferencia significativa en el bienestar de las mujeres embarazadas y en la salud de sus futuros hijos. Por lo tanto, se han desarrollado diversas intervenciones con el objetivo de reducir el estrés en el periodo perinatal, entre las que destacan por ser las más estudiadas, las intervenciones de reducción del estrés basadas en la atención plena (MBSR, por sus siglas en inglés: *Mindfulness-Based Stress Reduction*) (Kabat-Zinn, 1982; Shi y MacBeth, 2017) y las basadas en la Terapia Cognitivo-Conductual (TCC) (Robles-Ortega y Peralta-Ramírez, 2010). Además, existen intervenciones centradas la aplicación de técnicas de relajación, como la respiración diafragmática o la relajación muscular progresiva de Jacobson (Alipour y cols., 2017; Jacobson, 1929), sin embargo, actualmente estas técnicas se suelen incluir como un módulo complementario de las intervenciones mencionadas anteriormente.

3.3.1 Mindfulness para la reducción del estrés psicológico

El propósito principal de los programas MBSR es enseñar a los participantes diversas prácticas de meditación, que pretenden fomentar el desarrollo de la atención plena. Aunque los distintos enfoques para el entrenamiento de la atención plena tienen protocolos ligeramente diferentes, todos comparten el objetivo de enseñar a las personas a ser más conscientes de los pensamientos y emociones, y a modificar su relación con los mismos. De este modo, se parte del supuesto de que las técnicas de meditación pueden promover una perspectiva de los pensamientos y sensaciones que permite separarlos de ser considerados partes del ser o representaciones precisas de la realidad. Así, la práctica regular de la atención plena pretende desarrollar la habilidad de distanciarse de los pensamientos y emociones en situaciones estresantes, en contraposición a la preocupación ansiosa u otros patrones de pensamiento negativos, que intensifican la

respuesta de estrés e incrementa el estrés emocional (Kabat-Zinn, 1982). Shi y MacBeth (2017) llevaron a cabo una revisión sistemática sobre la eficacia de las intervenciones basadas en la atención plena, incluyendo los estudios que analizaban los programas de MBSR, concluyendo que los mismos mostraban evidencia preliminar para la reducción de la ansiedad perinatal. Sin embargo, estos autores señalan la falta de rigor metodológico presentado en los estudios indicando la necesidad de realizar más investigaciones.

3.3.2 Terapia cognitivo-conductual para reducción del estrés psicológico

La Terapia Cognitivo-Conductual (TCC) ha demostrado ser una de las intervenciones más eficaces en una amplia variedad de trastornos psicológicos (Hofmann y cols., 2012) y en la reducción de estrés en población general (Butler y cols., 2006).

La TCC se basa en un modelo que sostiene que la disforia psicológica es provocada por distorsiones cognitivas y creencias irracionales que un individuo presenta ante una situación y que desembocan en comportamientos y emociones desadaptativas (Corey y cols., 2017). Una parte fundamental de este abordaje terapéutico está basado en la psicología cognitiva, donde autores como Beck (1963) y Ellis (1970), aplicaron estas ideas a la psicoterapia con el propósito de dar una explicación a las alteraciones conductuales y emocionales implicadas en los trastornos psiquiátricos.

A través de la terapia cognitiva de Beck se crearon una serie de técnicas para abordar las estructuras cognitivas problemáticas, conocidas como esquemas mentales, que albergan creencias fundamentales sobre el yo, los demás y el futuro. Estos métodos se centran principalmente en la transformación de emociones y conductas mediante la identificación y modificación de pensamientos, imágenes y recuerdos automáticos en situaciones específicas (Beck y cols., 1979).

En relación a los componentes fundamentales de la TCC para la reducción de estrés, destacan: la psicoeducación, con el fin de crear conciencia sobre la respuesta de estrés y la importancia de las cogniciones en distintas situaciones; las técnicas de desactivación o relajación, como la respiración diafragmática, la visualización temática o la relajación muscular progresiva; técnicas propias del modelo cognitivo-conductual, como la identificación de distorsiones cognitivas y creencias irracionales, así como, la reestructuración cognitiva con el fin de modificarlas por otras más adaptativas; entrenamiento en autoinstrucciones, con el propósito de abordar las tareas y situaciones en pasos desglosados; entrenamiento en habilidades sociales, ya que un déficit en las mismas puede ser una fuente de estrés; y, técnicas para el control y reducción de la ira (Peralta-Ramírez, 2019; Robles-Ortega y Peralta-Ramírez, 2010).

A pesar de que los resultados de las intervenciones para el manejo del estrés perinatal son prometedores, la revisión sistemática de Matvienko-Sikar y cols. (2021), que recopiló estudios publicados hasta marzo de 2019 e incluyó intervenciones como la TCC, atención plena, psicoeducación y relajación, biofeedback de la variabilidad de la frecuencia cardíaca y ejercicio físico (yoga), concluyó que las intervenciones para reducir y/o prevenir el estrés o la ansiedad perinatal eran inconsistentes. Aunque los autores no encontraron pruebas suficientes para apoyar la efectividad de las intervenciones perinatales dirigidas a reducir el estrés, sí destacaron una utilidad potencial para la TCC.

Con el fin de investigar la eficacia de un programa de control de estrés basado en TCC en mujeres gestantes, nuestro grupo de investigación llevó a cabo un ensayo controlado aleatorizado (Romero-Gonzalez y cols., 2020). El estudio aplicó una intervención presencial de 8 semanas basada en TCC en un grupo de mujeres embarazadas y comparó los resultados con un grupo control.

Esta intervención adaptó los principios y técnicas de la TCC al contexto perinatal, abordando temas específicos relacionados con el estrés durante el embarazo, como preocupaciones sobre la salud del bebé, cambios en las relaciones personales y miedo al parto. La adaptación de la TCC al embarazo permite ofrecer una intervención personalizada y específica para las mujeres embarazadas, aumentando así su relevancia y efectividad. La intervención aplicada fue adaptada del programa de control de estrés preexistente (Robles-Ortega y Peralta-Ramírez, 2010) y contó con los siguientes módulos y contenidos:

- **Psicoeducación** (1ª sesión): En esta primera sesión se presentan el objetivo general del programa, que es conseguir un mayor control sobre las respuestas que se generan ante los acontecimientos estresantes. Además, se comentan las normas del grupo: confidencialidad; puntualidad; asistencia; participación activa; respeto; y compromiso con la realización de las tareas para casa. Posteriormente, se conceptualiza el estrés y se explican sus características, así como, los tipos de estresores, respuestas y consecuencias. Finalmente, se enseña el uso de autorregistros para completar las tareas de casa.
- **Técnicas de desactivación** (2ª sesión): En esta sesión se desarrolla una justificación del uso y beneficios de las técnicas de desactivación, destinadas especialmente a reducir la reactividad propia del estrés. Se entrenan dos de ellas: la imaginación temática y la respiración diafragmática. Posteriormente, se realiza un ejercicio práctico con cada una.
- **Reestructuración cognitiva** (3ª y 4ª sesión): En la tercera sesión se conceptualiza la relación entre los pensamientos, las emociones y la conducta, a través del modelo cognitivo ABC (Ellis y Bernad, 1994). Además, se describen las principales distorsiones cognitivas, con el objetivo de aprender a identificarlas. En la cuarta

sesión se enseñan las principales creencias irracionales y cómo emplear la reestructuración cognitiva mediante los diferentes tipos de debate. Para afianzar estos conocimientos, se practica de manera colaborativa la reestructuración cognitiva con distintos ejemplos.

- **Estrategias alternativas de control de pensamiento** (5ª sesión): Dentro del paradigma cognitivo se trabajan otras dos habilidades complementarias. Esta sesión está destinada a que las participantes aprendan técnicas alternativas de control del pensamiento para afrontar las situaciones estresantes. Las técnicas que se practican en esta sesión son: el entrenamiento en autoinstrucciones (Meichenbaum y Goodman, 1971), para ayudar a controlar los pensamientos disfuncionales que provocan más estrés, y la parada del pensamiento, con el fin de bloquear pensamientos automáticos resistentes al cambio. Finalmente, se dan pautas para gestionar el tiempo de manera óptima.
- **Entrenamiento en habilidades sociales** (6ª sesión): El objetivo de esta sesión es aprender a gestionar las relaciones interpersonales de manera eficiente, reduciendo así posibles estresores. Para ello, se conceptualiza el término “asertividad” y se enseña a identificar comportamientos pasivos y agresivos. También se describen los derechos asertivos básicos y se practican distintas técnicas clave en la gestión del estrés, como son “decir no” sin sentir culpa y solicitar cambios de conductas a otras personas de manera asertiva.
- **Autorregulación emocional** (7ª sesión): La séptima sesión está dirigida a comprender la relación entre la ira y el estrés. El objetivo principal es aprender a detectar los primeros síntomas de ira en cuanto aparecen, tanto signos cognitivos como fisiológicos, y aprender gestionarlos adecuadamente para no responder desadaptativamente ante los mismos.

- **Optimismo, buen humor y recapitulación** (8ª sesión): La última sesión está dirigida a entender los beneficios del buen humor, trabajando al mismo tiempo distorsiones cognitivas del tipo “tengo que tomarme todo muy en serio para poder hacerlo bien”. Por último, en esta sesión se realiza una recapitulación y resumen de todo lo aprendido en las sesiones previas.

Además, al inicio de cada sesión las participantes cuentan con tiempo para comentar en grupo las dificultades encontradas con las tareas y recibir *feedback* sobre la realización de las mismas.

Los resultados del estudio en el que se aplicó el programa, mostraron una reducción significativa en los niveles de estrés específico del embarazo, estrés percibido, concentración de cortisol en pelo y menor sintomatología psicopatológica general en las mujeres que participaron en la TCC para el manejo del estrés durante su embarazo. Estos hallazgos respaldan la idea de que la TCC es una intervención efectiva en el contexto perinatal, que puede contribuir al bienestar de las mujeres embarazadas. De este modo, conociendo la eficacia de este tratamiento en la reducción del estrés psicológico y el cortisol capilar y, teniendo en cuenta las relaciones entre el cortisol materno y el neurodesarrollo de la descendencia, se hace necesario analizar si los efectos hallados en las madres presentan implicaciones posteriores en la descendencia.

Por lo tanto, se ha incluido como uno de los objetivos de la presente Tesis Doctoral analizar las concentraciones de cortisol y neurodesarrollo de los bebés de las madres que participaron en el programa, con el fin de profundizar en la comprensión de la influencia de la TCC en el bienestar de las madres y sus hijos a corto y largo plazo.

3.3.3 Terapia cognitivo-conductual online para el control del estrés en mujeres gestantes durante la pandemia

Asimismo, es bien sabido que la población ha enfrentado recientemente una crisis sanitaria de gran envergadura, la pandemia de COVID-19, causada por el virus SARS-CoV-2. Este evento estresante de alcance mundial ha generado miedo a las consecuencias de contraer la enfermedad, preocupación por la afectación en familiares, y ha llevado a medidas de confinamiento y consecuencias económicas adversas, resultando en un aumento del estrés, ansiedad y depresión en la población general (Wang y cols., 2020). La población gestante no ha estado exenta de las consecuencias de esta pandemia. Investigaciones en diversos países, incluyendo Estados Unidos, China, Canadá, Italia, Turquía y Grecia, han señalado un incremento en los síntomas de ansiedad y depresión en mujeres embarazadas durante la misma (Hessami y cols., 2020; Liu y cols., 2021; Wu y cols., 2020). Estos hallazgos resaltaron la necesidad de estudiar la salud perinatal en España y verificar el impacto psicológico en la misma, así como investigar qué variables podrían funcionar como factores protectores ante el aumento potencial del estrés y síntomas psicopatológicos. La resiliencia psicológica, que se define como el conjunto de habilidades o recursos que un individuo posee para enfrentar adversidades y eventos amenazantes (Fletcher y Sarkar, 2013; Newman, 2005), destaca como un factor clave a explorar en este contexto.

Dada la situación de crisis sanitaria y las restricciones al contacto social, los profesionales de la salud mental tuvieron que adaptarse a la nueva situación. De este modo, muchos de los profesionales clínicos comenzaron a llevar a cabo las intervenciones psicológicas de manera telemática, con el fin de evitar el contacto social, pero proporcionando al mismo tiempo la asistencia psicológica necesaria. En el caso de la TCC, antes de la pandemia se había mostrado que las intervenciones aplicadas en línea,

presentaban en adultos eficacia para reducir los síntomas depresivos, el trastorno de pánico con y sin agorafobia, los trastornos somáticos, la adicción al alcohol y los síntomas bulímicos (Carlbring y cols., 2018; Chipps y cols., 2020). Sin embargo, no se había estudiado la eficacia de la TCC aplicada en línea en mujeres gestantes, con el fin de reducir y/o prevenir los síntomas de estrés y psicopatológicos, en un contexto de pandemia donde la angustia psicológica es creciente en la población.

En este escenario, las intervenciones telemáticas de la TCC podrían ser una alternativa a las intervenciones presenciales tradicionales, ya que no requieren contacto social directo, lo que ayuda a prevenir contagios, y pueden llegar a personas en distintas ubicaciones, incluyendo áreas más desatendidas. La intervención telemática de la TCC se basa en los mismos principios fundamentales, descritos en apartados anteriores, de la intervención aplicada presencialmente. Del mismo modo, se incluyen sesiones estructuradas, donde se pone énfasis en las distorsiones y creencias irracionales y se espera que los participantes practiquen regularmente las estrategias aprendidas entre sesiones.

Por lo tanto, con el propósito de promocionar la salud psicológica perinatal que la situación requería, se hizo necesario adaptar a un formato telemático el programa de control de estrés estudiado anteriormente de manera presencial. El objetivo fue comprobar su viabilidad y eficacia en línea, lo cual también fue objeto de la presente Tesis Doctoral.

A modo de conclusión de la introducción presentada y dadas las implicaciones que el estrés y las concentraciones de cortisol pueden tener en el periodo perinatal, es necesario profundizar en la comprensión de la relación entre el cortisol materno durante la concepción y el futuro bebé, así como, estudiar los efectos de la TCC para el manejo del estrés prenatal sobre cortisol y el neurodesarrollo de la descendencia. Además, debido

a los efectos directos e indirectos que la pandemia de COVID-19 puede presentar en la salud mental, es conveniente estudiar el impacto de la misma en la salud psicológica perinatal española y analizar la eficacia de la TCC para el manejo del estrés prenatal aplicada de manera telemática. Los hallazgos de este trabajo podrían tener implicaciones clínicas importantes, proporcionando información valiosa para el desarrollo de estrategias de prevención y tratamiento para mejorar la salud mental de las mujeres embarazadas y, potencialmente, el neurodesarrollo de sus hijos.

OBJETIVOS

4. OBJETIVOS

El objetivo general de la presente Tesis Doctoral fue investigar la eficacia de la Terapia Cognitivo-Conductual (TCC) para el afrontamiento del estrés en mujeres gestantes, aplicada en modalidad presencial y telemática. Este objetivo general queda dividido en dos bloques de objetivos específicos.

El primer bloque de objetivos específicos se titula “**Eficacia de la TCC en mujeres embarazadas y efectos en la descendencia**” y cuenta con dos objetivos específicos:

1. Investigar si los niveles de cortisol en pelo y/o el estrés psicológico durante el momento de la concepción y las primeras semanas de embarazo presentan una relación con el sexo fetal (Artículo 1).

2. Comprobar la eficacia en la reducción del estrés de la TCC en las mujeres embarazadas, tanto a nivel psicológico como a nivel hormonal, y cómo se relaciona dicha eficacia con el posterior neurodesarrollo y cortisol del bebé (Artículo 2).

El segundo bloque se titula “**Eficacia de la TCC en gestantes implementada de manera telemática durante una crisis sanitaria**” y cuenta con tres objetivos específicos:

3. Estudiar la salud psicológica perinatal durante la pandemia a través de la evaluación de la sintomatología psicopatológica y el estrés psicológico, en el transcurso del embarazo y tras dar a luz (Artículo 3 y Artículo 4).

4. Investigar la interacción de la resiliencia, estrés y ansiedad en mujeres embarazadas en dos situaciones de estrés distintas: antes y durante la pandemia por la COVID-19 (Artículo 5).

5. Estudiar la viabilidad y eficacia de la TCC para el control del estrés en mujeres embarazadas, aplicada telemáticamente durante la pandemia (Artículo 6 y Artículo 7).

Esta división de objetivos en bloques puede consultarse también en la Figura 3.

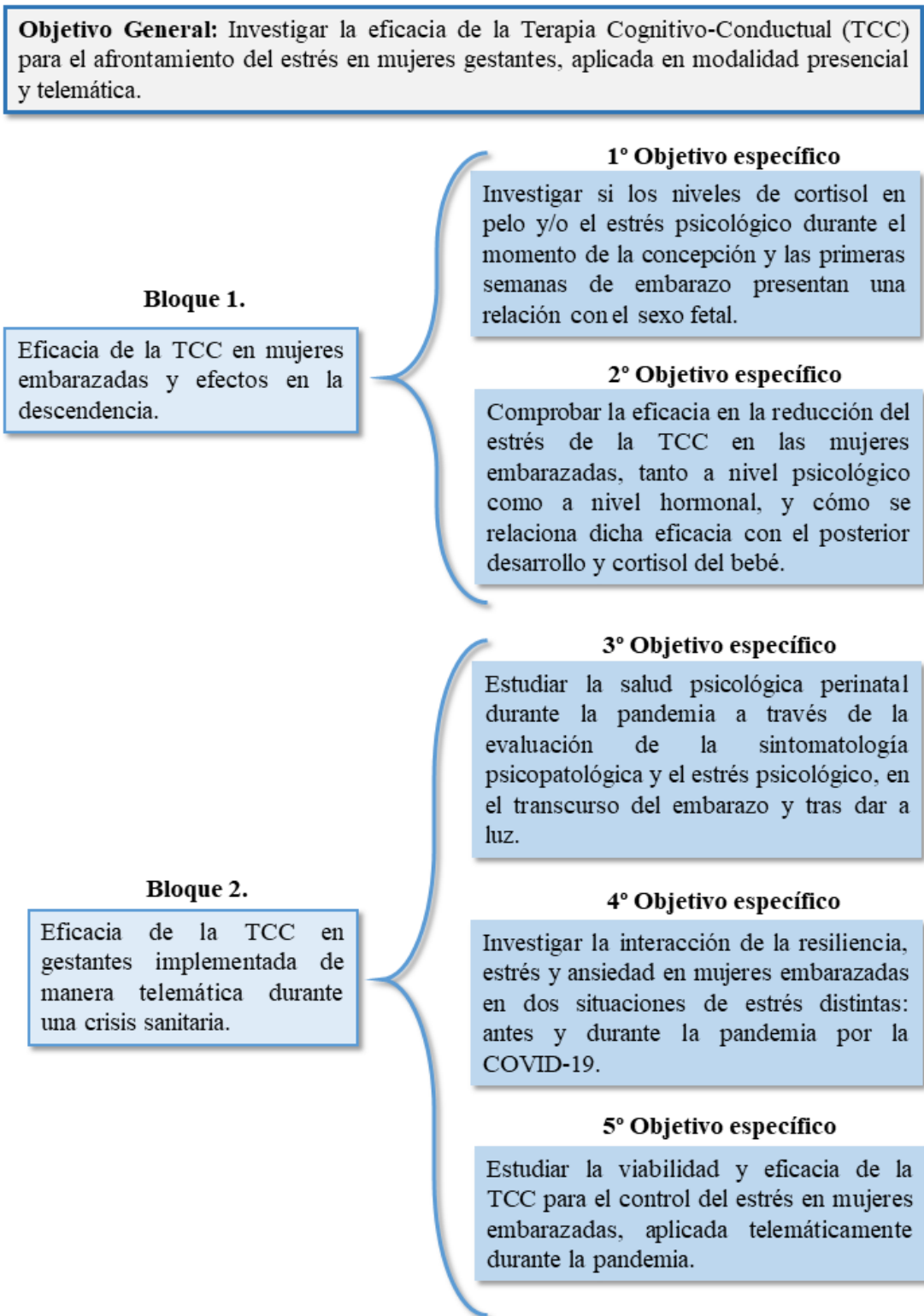


Figura 3. Objetivo general y objetivos específicos de la Tesis Doctoral.

**BREVE DESCRIPCIÓN DE LA
METODOLOGÍA DE LOS ESTUDIOS**

5. BREVE DESCRIPCIÓN DE LA METODOLOGÍA DE LOS ESTUDIOS

5.1 Metodología del Artículo 1

El primer estudio publicado en la *Journal of Developmental Origins of Health and Disease*, presenta un diseño de cohorte retrospectivo, para el cual se contó con un grupo de mujeres que se encontraban entre la semana 8 y 10 de embarazo. Las participantes fueron reclutadas de varios centros de salud de la provincia de Granada. Se obtuvieron los datos sociodemográficos y obstétricos de las participantes, y se emplearon la *Perceived Stress Scale*, el *Pregnancy Distress Questionnaire* y el *Stress Vulnerability Inventory*, para evaluar el estrés percibido, el estrés específico del embarazo y la vulnerabilidad al estrés de las participantes, respectivamente. Además, se obtuvo una muestra de pelo de las mismas para analizar la secreción de cortisol de los tres meses anteriores, a través del kit ELISA, periodo relativo al momento de la concepción y las primeras semanas de embarazo. Posteriormente, cuando las participantes dieron a luz fueron contactadas para recoger la información relativa al sexo de los bebés. Finalmente, las participantes fueron divididas en dos grupos con relación al sexo de los bebés y se compararon los niveles de cortisol en pelo y las puntuaciones de las medidas de estrés psicológico recogidas en el primer trimestre de embarazo.

5.2 Metodología del Artículo 2

La segunda investigación, publicada en la revista *Stress and Health*, es un seguimiento de un ensayo controlado aleatorio (ECA) registrado como ensayo clínico con el código NCT03404141. El ensayo contó con dos grupos de mujeres, que se encontraban

entre la semana 12 y 38 de embarazo, divididos de manera aleatoria. Un grupo recibió un programa de control de estrés basado en la Terapia Cognitivo-Conductual con una duración de 8 semanas, mientras que, el segundo grupo únicamente recibió los cuidados habituales del embarazo. Se evaluaron y compararon a las participantes de ambos grupos antes y después de la intervención, a través de sus niveles de cortisol en pelo, los niveles de estrés percibido, estrés específico del embarazo, vulnerabilidad al estrés, resiliencia y psicopatología, empleando los siguientes instrumentos, respectivamente: la *Perceived Stress Scale*, el *Pregnancy Distress Questionnaire* y el *Stress Vulnerability Inventory*, la *Connor Davidson Resilience Scale, abbreviated version* y el *Symptom Checklist-90-Revised*. Posteriormente, se recogieron muestras de pelo para analizar y comparar los niveles de cortisol de los bebés de ambos grupos en el momento del nacimiento y a los 6 meses de vida. Además, a los 6 meses, los bebés también fueron comparados a través de sus niveles de neurodesarrollo evaluados mediante la *Bayley Scales of Infant Development-III*.

5.3 Metodología del Artículo 3

El tercer trabajo ha sido publicado en la revista *Psychiatry Research*. En este trabajo se comparó la sintomatología psicopatológica, el estrés percibido y el estrés específico del embarazo de dos cohortes de mujeres durante su embarazo: el primer grupo evaluado antes de la pandemia por la COVID-19 (entre marzo y junio de 2019); y el segundo grupo evaluado durante la misma (entre marzo y junio de 2020). Asimismo, el grupo evaluado durante la pandemia también completó una escala destinada a evaluar los niveles de insomnio y respondió a un cuestionario que evaluaba diferentes dimensiones relacionadas con la pandemia y el confinamiento. Los niveles de insomnio y las

respuestas a este cuestionario, se emplearon para estudiar sus relaciones con las variables psicológicas evaluadas en las que se encontraron diferencias entre los grupos.

5.4 Metodología del Artículo 4

El cuarto estudio ha sido publicado en la *International Journal of Gynecology & Obstetrics*. En esta investigación se siguió una metodología similar al anterior, sin embargo, en este caso se compararon a los dos grupos de mujeres en el puerperio. Así, se evaluaron los niveles de depresión postparto, los síntomas psicopatológicos, el estrés percibido y la resiliencia de dos grupos de mujeres: el primero contaba con mujeres que habían dado a luz entre marzo de 2019 y febrero de 2020; y, el segundo estaba constituido por mujeres que dieron a luz entre abril y julio de 2020 (durante la pandemia y confinamiento). Ambos grupos fueron comparados con respecto a sus síntomas psicopatológicos y sus niveles de depresión postparto. Finalmente, para verificar qué variables psicológicas podían predecir los síntomas psicopatológicos en mujeres que dieron a luz durante la pandemia, se realizaron diferentes regresiones jerárquicas múltiples, siendo las variables dependientes las distintas dimensiones psicopatológicas. En el paso 1 se incluyeron las variables relacionadas con el parto (edad gestacional, primípara o no, parto vaginal o instrumental y satisfacción con el parto), y en el paso 2, las variables independientes fueron las puntuaciones de estrés percibido y resiliencia.

5.5 Metodología del Artículo 5

El quinto trabajo, publicado en la revista *Current Psychology*, tuvo como base explorar la relación entre la resiliencia y el estrés específico del embarazo, el estrés percibido y la ansiedad, en mujeres en periodo de gestación, tanto antes como durante la

pandemia. Así, se contó con un grupo evaluado entre finales de 2017 y principios de 2020, y otro grupo evaluado entre marzo de 2020 y marzo de 2021. En ambas muestras, se aplicó un modelo de ecuaciones estructurales para comprobar dos hipótesis. La primera hipótesis de los modelos fue que la resiliencia influía negativamente en el estrés relacionado con el embarazo, y también en el estrés percibido y la sintomatología de ansiedad. La segunda hipótesis consistió en que el estrés relacionado con el embarazo y el estrés percibido presentaban una correlación y éstos, a su vez, influían positivamente en la sintomatología de ansiedad. Por último, se compararon ambos grupos con respecto a las variables incluidas en los modelos.

5.6 Metodología del Artículo 6

El sexto estudio, publicado en la revista *Behavioral Sciences*, consistió en comprobar la viabilidad, a través un ensayo piloto, del programa de control de estrés basado en la terapia cognitivo-conductual aplicado de manera telemática, durante la pandemia y el confinamiento en España. Para ello, se aplicó el programa de manera telemática, con una duración de 8 semanas, a dos grupos de mujeres embarazadas. Las variables que se tuvieron en cuenta para la evaluación fueron: estrés percibido, estrés específico del embarazo, vulnerabilidad al estrés, sintomatología psicopatológica, y resiliencia. Se llevó a cabo la evaluación, tanto antes de comenzar el programa como al finalizar el mismo, y se compararon los resultados de ambas.

5.7 Metodología del Artículo 7

La séptima investigación fue publicada en la *Journal of Psychiatric Research*. Este estudio fue un ensayo aleatorio controlado (NCT03404141) en el que se comprobó

la eficacia de un programa de control de estrés, basado en la terapia cognitivo-conductual, aplicado de manera telemática durante la pandemia y el confinamiento en España. La variable independiente contaba con tres niveles: gestantes que recibieron el tratamiento; gestantes que recibieron apoyo psicológico; y, gestantes que recibieron los cuidados habituales del embarazo. Las variables psicológicas incluidas como variables dependientes, evaluadas antes y después del tratamiento, fueron: sintomatología psicopatológica, estrés percibido, estrés específico del embarazo, vulnerabilidad al estrés y resiliencia. Finalmente, se realizó un modelo lineal mixto de medidas repetidas con el grupo y el tiempo como efectos principales, y una interacción grupo x tiempo. Además, se especificó el participante como efecto aleatorio para tener en cuenta la naturaleza de medidas repetidas de los datos.

RESULTADOS

6. RESULTADOS

6.1 Artículo 1

Romero-Gonzalez, B., Puertas-Gonzalez, J. A. (*corresponding author*), Gonzalez-Perez, R., Davila, M., & Peralta-Ramirez, M. I. (2021). Hair cortisol levels in pregnancy as a possible determinant of fetal sex: a longitudinal study. *Journal of Developmental Origins of Health and Disease*, 12(6), 902-907. <https://doi.org/10.1017/S2040174420001300>

Hair cortisol levels in pregnancy as a possible determinant of fetal sex: a longitudinal study

Abstract

Stress during pregnancy has been widely studied and associated to different variables, usually with negative results for the health of the mother and the newborn, such as having a higher risk of suffering postpartum depression, premature birth, obstetrics complications or low birthweight, among others. However, there are not many lines of research that study the role that the sex of the baby plays on this specific stress and vice versa. Thus, the main objective was to analyze the relationship between the sex of the offspring and the stress of the mothers in the first trimester of pregnancy. In order to achieve this, 108 women had their biological stress measured (through hair cortisol levels) and psychological stress evaluated (the Prenatal Distress Questionnaire (PSS), the Perceived Stress Scale (PDQ) and the Stress Vulnerability Inventory (IVE)). The results revealed significant differences in maternal hair cortisol levels in the first trimester based on the sex of the baby they had given birth to ($t = -2.04$; $p < .05$): the concentration of the hormone was higher if the baby was a girl (164.36:54.45-284.87 pg/mg) than if it was a boy (101.13:37.95-193.56 pg/mg). These findings show that the sex of the future baby could be conditioned, among many other variables, by the mother's stress levels during conception and first weeks of pregnancy. Further research is needed in this area to support our findings.

Keywords: *cortisol; pregnancy; stress; fetus; sex*

Introduction

Pregnancy is a stressful period. Not only do expectant mothers undergo physical changes, they also fear childbirth and are preoccupied about the baby's health as well as their motherhood¹. They may suffer strains in personal relationships¹. The worries and stress experienced during pregnancy activate the hypothalamic-pituitary-adrenal axis (HPA), leading to the release of cortisol, a hormone with the ability to cross the placenta and condition fetal development^{2,3}.

Cortisol levels have traditionally been evaluated using blood, urine, saliva or amniotic fluid samples⁴⁻⁶. These measurements, however, are punctual and highly affected by the sleep-wake cycle. An alternative is the extraction of hair cortisol: indeed, hair cortisol is the only retrospective biomarker of chronic stress that is unaffected by contextual variables such as noise, temperature or social interaction. It enables retrieving cortisol measurements over the three months prior to the date of extraction^{7,8}.

During pregnancy, high concentrations of prenatal hair cortisol have been associated with preterm birth, childbirth complications, maternal psychological diseases and wellbeing, postpartum depression and the baby's neurological development⁹⁻¹⁴. Nevertheless, the relationship between cortisol at the time of conception and the baby's future sex has been scarcely studied. Studies conducted on the relationship between cortisol and the sexual predisposition of the fetus found high levels of salivary cortisol in the third trimester of pregnancy in women who gave birth to a girl¹⁵⁻¹⁸. In the same vein, other authors showed that women who had higher cortisol concentrations in their saliva before conception were less likely to have a male baby¹⁹.

These findings are in fact in line with numerous studies showing the decline of male births in the population following exposures to stressful stimuli such as earthquakes, murders, terrorist acts, stressful work or life-changing events²⁰⁻²⁸.

One hypothesis is that parents' stress modifies the concentration of sex hormones through the activation of the HPA axis and has implications regarding sex allocation. This approach is supported by several experimental studies that have found that the sex of the zygotes is influenced by the stress of both parents around the moment of conception: the higher the stress level, the more likely of giving birth to a girl^{19,28-31}.

However, other authors have failed to find such a relationship between cortisol and the baby's sex³². The studies linking stress to biological measures and the sex of future babies may be promising, but they are in fact few and far between.

Therefore, further tests are necessary to show whether cortisol concentrations during pregnancy influence the sex of the offspring and whether they do so during conception²⁸. In fact, to the best of our knowledge, no study, that is not merely punctual (cortisol in saliva, urine or blood), has yet been carried out using a retrospective measure (the mother's hair cortisol) on the relationship between cortisol and the baby's sex.

Therefore, the study's main objective was to check whether a relationship existed between the sex of the offspring and the cortisol secretion in the mother's hair before and during the baby's conception, as well as in the first weeks of pregnancy. In a complementary way, a second aim was to know whether psychological stress could be related to sex of the offspring, the levels of psychological and specific stress were evaluated in those weeks of pregnancy.

Methods

Sample size estimation

There are some studies which aim was to find out the relationship between salivary cortisol and sex of the fetus. Sample size estimation was calculated using this variable in Giesbrecht et al.¹⁷. G *Power³³ was used to calculate the sample size to achieve 80% power and contrast the null hypotheses $H_0 : \mu_1 = \mu_2$ at the 5% alpha level. Comparing two independent means (t -test) using mean scores and deviation standards of Giesbrecht et al.¹⁷ (2015) of two groups (male and female), the sample size required were 72 participants, 37 for each group (Cohen's $d = .77$).

Participants

The total sample was made up of 108 expectant women in weeks 8 and 10 of their pregnancy and there was 7 women who were pregnant using a fertility treatment. They were recruited in various health centres of the province of Granada (Spain).

The inclusion criteria were as follow: being an expectant woman in weeks 7 to10 of pregnancy; aged over 18 years; and having a minimum of an average level in Spanish. The exclusion criterion was: having a pre-pregnancy illness or taking corticosteroids.

Participation was voluntary, and an informed written consent document was read and signed by every participant. This study followed the guidelines of the Helsinki Declaration (AMM, 2008) and the Good Clinical Practice Directive (Directive 2005/28/EC) of the European Union; and was approved by the Human Ethics Research Committee of the University of Granada (reference 881).

Instruments

Sociodemographic and obstetric data were collected from the 2010 Pregnant Woman's Health Document³⁴, which is the official health record for pregnant women and their newborns. The included variables were: age, marital status, educational level, employment status, smoking or not, maternal body mass index, type of pregnancy,

number of children, number of previous abortions, whether or not the pregnancy was desired, as well as whether or not it was risky.

Psychological Assessment

- Perceived Stress Scale (PSS)^{35,36}. The PSS provides information on the perception of general stress during the preceding month. It consists of 14 items scores on a 5-point Likert scale (0 = never, 1 = almost never, 2 = once in a while, 3 = often, 4 = very often). Spanish reliability alpha's Cronbach coefficient is 0,81.

- Pregnancy Distress Questionnaire (PDQ)^{37,38}: this is a 12-item scale that measures pregnancy-specific stress related to maternal concerns about pregnancy, such as medical problems, labour and delivery, physical symptoms, bodily changes and the baby's health. Responses are given using a 5-point Likert-type scale where 0 = not at all and 4 = very much. The Cronbach's alpha reliability coefficient is 0.71.

- The Spanish version of the Stress Vulnerability Inventory (IVE)^{39,40}. It consists of 22 items that evaluate the person's predisposition to feel affected by perceived stress. It has a Yes/No answer format. Items receiving an affirmative answer add 1 point. The range of scores on the scale is 0 to 22, higher scores corresponding to greater vulnerability to stress. The scale is highly reliable, with a Cronbach alpha of .87.

Chronic stress biomarker: hair cortisol levels

- The cortisol evaluation consisted in taking a lock of hair containing approximately 150 strands from the rear corner of the skull, as close as possible to the scalp⁴¹. A maximum length of 3 cm was set for each sample to reflect cortisol levels during the preceding 3 months⁴². The samples were wrapped in aluminium foil to be adequately protected from light and humidity and were kept at room temperature until further analysis using the salivary kit ELISA. The analysis protocol was published in

Romero-Gonzalez et al.¹³ The lower detection limit was 12.5 pg/mg and the cross-reactivity reported by the manufacturer was as follows: Prednisolone 13.6%, corticosterone 7.6%, deoxycorticosterone 7.2%, progesterone 7.2%, cortisone 6.2%, deoxycortisol 5.6%, prednisone 5.6%, and dexamethasone 1.6%. No cross-reactions were detected with DHEAS or tetrahydrocortisone.

The intra- and inter-assay precision were analyzed on internal quality controls used for routine salivary cortisol measurement, measured in duplicate in eight consecutive assays. The intra-assay coefficients of variation (CV) were 2.7% at 10.7 ng/ml and 4.3% at 43.9 ng/ml. The inter-assay CVs were 4.4% and 6.3%, respectively¹³.

Procedure

Women were told about the study when they attended their first prenatal appointment with their midwife, 7 to 10 weeks into their pregnancy. Those who agreed to participate were given an information sheet and then signed the informed consent document. Each participant was assigned an identification code in order to ensure anonymity throughout the study. Subsequently, sociodemographic and obstetric information was collected, psychological questionnaires were completed in paper format (PDQ, PSS, IVE), and hair samples were then taken applying the established sample collection protocol⁴¹. Once they gave birth, they were contacted and asked the sex of their baby. This study followed the STROBE standards for cohort studies.

Data Analysis

The averages and percentages of the most relevant sociodemographic and obstetric variables (age, marital status, educational level, employment status, type of pregnancy, number of children, number of previous abortions and whether the pregnancy was desired, as well as whether it was risky or not) were calculated first.

The participants were then divided into two groups according to the sex of their babies (male or female). Subsequently, in order to check any differences regarding major sociodemographic and obstetric variables between both groups, the t-Student (quantitative variables) and chi-square (categorical variable) tests were performed.

The data met the assumptions of normality and uniformity of variances (tests of Kolmogorov-Smirnov and Shapiro-Wilk of normality $p > .05$; Levene test to evaluate the homogeneity of variances $p > .05$).

To verify the presence of significant differences in maternal hair cortisol levels between women who had given birth to a girl and those who had given birth to a boy, a comparison was made of independent samples using non parametric Mann-Whitney test. The variable "baby's sex" was the independent variable, with two levels (female and male). The dependent variables were maternal hair cortisol levels. Besides, to know whether psychological variables were different regarding baby's sex, a comparison was made of independent samples using the t-Student test. The variable "baby's sex" was the independent variable, with two levels (female and male) and dependent variables were the scores on perceived stress (PSS), vulnerability to stress (SVS) and pregnancy-specific stress (PDQ).

In addition, calculations were performed, using Cohen's d, to determine whether the differences between the groups were clinically relevant. We took into account the considerations regarding the interpretation of the effect size magnitudes: d .20: size of the small effect; (d) .50: medium effect size; d .80: large effect size⁴³. The analyses were conducted using the IBM SPSS Statistics for Windows version 25.0. (Armonk, New York).

Results

Sample Description

Initially, a total of 178 pregnant women were willing to take part in the study, of which 164 met the inclusion criteria. It was not possible to know the sex of the baby of 21 of them, another 12 decided to leave the study due to a lack of time, and 15 had a miscarriage. In the case of 8 babies (4 girls and 4 boys) of the remaining 116 mothers, the amount of baby hair was deemed insufficient for cortisol analysis, so they were removed from the sample. The final total sample consisted of 108 pregnant women in their first trimester of gestation, aged between 22 to 43 years ($M = 33.73$; $SD = 4.37$).

The participants were divided into two groups based on the sex of the baby they gave birth to (male or female). Thus, 46 women ($M = 33.41$ years of age; $SD = 3.83$) were included in the baby boy group and a total of 62 women ($M = 33.98$ years of age; $SD = 4.78$) were included in the baby girl group.

Table 1 shows the main sociodemographic and obstetric differences depending on the newborn's sex. No significant differences were found between the two groups in terms of age, marital status, educational level, employment status, type of pregnancy, number of children, number of previous abortions, pregnancy risk, or desired/non-desired pregnancy.

Table 1. Differences in sociodemographic variables and obstetric information between pregnant women who had a girl or boy baby.

		Girl baby (N=62) M(SD/%)	Boy baby (N=46) M(SD/%)	Test (χ^2/t)	p
<i>Sociodemographic variables</i>					
Age		33.98(4.78)	33.41(3.83)	.61	.55
Marital status	Married/cohabitant	60(96.8%)	46(100%)	2.46	.65
	Single/divorced/widow	2(3.2%)	-		
Level of education	Primary	4(6%)	3(7.1%)	2.42	.29
	Secondary	15(24%)	11(23.8%)		
	University	43(70%)	32(69.1%)		
Employment situation	Unemployed	14(22%)	7(15.4%)	1.78	.78
	Working	47(76%)	37(79.5%)		
	Student	1(2%)	2(5.1%)		
Smoking	Yes	9(14.5%)	6(13%)	.048	.827
	No	53(85.5%)	40(87%)		
Body Mass Index		23.40(4.46)	24.90(5.03)	1.41	.161
<i>Obstetric information</i>					
Type of pregnancy	Spontaneous	53(86%)	43(93.5%)	3.31	.19
	In vitro	4(6%)	3(6.5%)		
	Artificial insemination	5(8%)	-		
Previous children	0	28(45.2%)	21(45.7%)	1.64	.44
	1	28(45.2%)	17(37%)		
	≥2	6(9.7%)	8(17.4%)		
Previous miscarriages	0	36(58.1%)	29(63%)	1.41	.49
	1	18(29%)	9(19.6%)		
	≥2	8(12.9%)	8(17.4%)		
Pregnancy desired	Yes	53(85.7%)	44(95.7%)	3.94	.27
	No	9(14.3%)	2(4.3%)		

Note: Significance level at $p \leq .05$. Student t -test used for continuous variables and Chi-squared test for categorical variables.

Relationship between the baby's sex and hair cortisol levels representing the preconceptional period and the first trimester of pregnancy

Statistically significant differences in maternal cortisol levels were found in the first trimester, depending on the baby's sex ($U = 1097.50$; $p < .05$). The levels were higher in the case of baby girls (expressed in median: lower quartile - upper quartile) (164.36:54.45-284.87 pg/mg) compared to that of baby boys (101.13:37.95-193.56 pg/mg). Cohen's d reported an effect size of .40 (Figure 1).

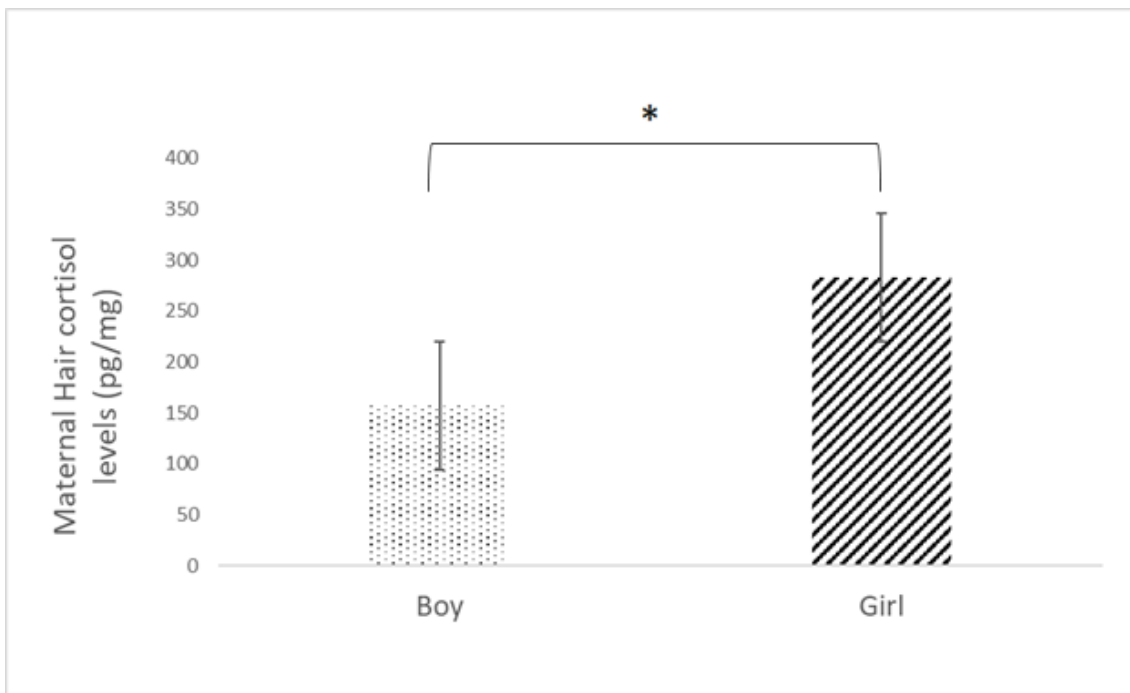


Figure 1. Hair cortisol levels among pregnant women who had a boy or girl baby. *Note:*

* significance at $p < .05$

Relationship between the Baby's Sex and Stress and Pregnancy Concerns during the First Trimester

There were no significant differences regarding the baby's sex based on the results obtained in the PDQ ($t = 1.46$; $p > .05$), nor were there any differences in the results of PSS ($t = .70$; $p > .05$) or in the IVE ($t = .08$ $p > .05$).

Discussion

The study's objective was to understand the relationship between the baby's sex and the level of cortisol in the mother's hair before conception and in the first weeks of the first trimester, as well as between the baby's sex and the psychological stress perceived by mothers in the first trimester of gestation.

The results showed differences in maternal hair cortisol levels in the first trimester of pregnancy among women who gave birth to a baby boy compared to those who delivered a baby girl. Specifically, cortisol levels were higher in the first trimester of pregnancy when the fetus was a girl. Therefore, the level of this hormone in the hair in the first trimester of pregnancy seems to be related to the baby's sex.

When interpreting the results of this study, we must remember that the hormone was extracted from women's hair between weeks 8 to 10 of their pregnancy. In this way, retrospective information on maternal cortisol levels was obtained during the conception and in the first weeks of pregnancy. Thus, maternal stress was shown to be higher over that period in mothers who later gave birth to a girl as opposed to those who gave birth to a boy.

Previous studies on links between maternal stress during conception and the baby's sex have produced similar findings: women who presented higher concentrations of cortisol in their saliva prior to conception were less likely to deliver a male baby¹⁹. Nevertheless, our study seems to contradict other results, such as those of Bosquet Enlow et al.⁴⁴ who have found that maternal hair cortisol levels were higher across the three

trimesters when mother have a boy. Future research should focus on this aspect in order to increase knowledge on this topic.

On the other hand, the results showed that there was no difference in perceived psychological stress in the first trimester between mothers who had a boy and those who had a girl. That is, neither the specific stress of pregnancy, nor the levels of perceived stress, nor the levels of vulnerability to stress influenced the sex of the baby. These results are in line with that of a previous longitudinal study, in which maternal stress was measured using a series of psychological instruments, and no significant differences were found between the scores of women who gave birth to a boy and those who gave birth to a girl¹⁷.

Thus, the results of the study seem to support the explanatory theories according to which this hormone plays an important role in determining the sex of the baby, both during conception and in pregnancy.

A possible explanation would be that the activation of the hypothalamus-pituitary-adrenal axis modifies sex hormone concentrations at the time of conception³⁰. However, the mechanisms underlying this modification are unclear. On the one hand, there is evidence that testosterone functions as a mechanism when determining the baby's sex, since the greater the prenatal stress levels, the higher the levels of female testosterone²⁹. Some studies have also focused on the role of the father's stress at the time of conception, although we did not take such research into account in the present study. Song et al.³¹ found that the proportion of sex chromosomes in ejaculated sperm may be altered by exposure to stress, reducing the viability of Y chromosomes, thus affecting the distribution of sexes at birth. Moreover, the X sperm are better at passing through cervical mucus, so when hormonal changes occur, caused by stress, these sperm are greater achievers than the Y sperm²⁸.

On the other hand, another possible explanation for the results is the theory according to which selective male miscarriages take place during pregnancy³⁰. Our sample, however, did not include pregnant women who subsequently aborted, so we were not able to learn more about this latter relationship.

What does seem clear—and this has been shown in a number of studies—is that fetuses are vulnerable and that stress plays a role. For example, it has been shown that Y fetuses mature more slowly than X fetuses⁴⁵; they tend to present pregnancy complications and preterm birth^{18,46-48}; and at birth, they are more likely to have shorter telomeres^{49,50}.

The study presented a number of limitations. For example, the role that fathers' stress may have at the time of conception, which seems relevant in determining the sex of the baby, was not taken into account. Therefore, it would be interesting to include measurements of cortisol in fathers' hair in subsequent studies. Besides, some authors have detected in older adults that hair cortisol levels are slightly higher in dark brown hair⁵¹, so it could be worth obtaining this information to know if this phenomenon could occur also in pregnant women.

It would also be relevant, in the future, to follow up female participants who were discarded because they aborted. Examining these cases would allow checking whether women expecting boys undergo more stress abortions than women expecting girls, as suggested by recent research. Including this data in future studies would thus lead to a deeper understanding of the mechanisms underlying deviations in the sex of the offspring.

Finally, a future line of research could also be that of reproducing the study with samples of women who present high-risk pregnancies (such as pregnancies resulting from in-vitro fertilisation or artificial insemination). Such populations experience high levels

of stress and would allow us to better understand the relationship between stress and the child's sex.

The findings of the present study suggest that a relationship exists between cortisol levels in mothers at the time of conception and in the first trimester of gestation and the sex of their future babies. Thus, giving birth to a girl would imply higher levels of maternal hair cortisol at the time of conception and in the first weeks of pregnancy. However, no relationship was found between the sex of the offspring and perceived psychological stress levels in the first trimester.

To conclude, the research presented here is pioneering to the extent that it links prenatal stress to the sex of newborns. This was done by measuring pregnant women's hair cortisol, the only longitudinal measure that is suitable for this purpose. Therefore, this work contributes to an open field of research which requires further studies to explain the role played by prenatal stress and cortisol on sex allocation.

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6.2 Artículo 2

Puertas-Gonzalez, J. A., Romero-Gonzalez, B., Mariño-Narvaez, C., Gonzalez-Perez, R., Sosa-Sanchez, I. O., & Peralta-Ramirez, M. I. (2023). Can we influence the neurological development and hair cortisol concentration of offspring by reducing the stress of the mother during pregnancy? A randomized controlled trial. *Stress and Health*. <https://doi.org/10.1002/smi.3222>

Can we influence the neurological development and hair cortisol concentration of offspring by reducing the stress of the mother during pregnancy? A randomized controlled trial

Abstract

The objective was to evaluate the effects of a stress management cognitive, behavioural therapy followed during pregnancy on subsequent childhood on hair, cortisol at birth and on neurodevelopment and Hair Cortisol Concentrations (HCC), at 6 months of age. The study sample included 48 pregnant women, divided into two, groups: 24 women in the Therapy Group (TG) and 24 women who received standard, pregnancy care (control group (CG); CG). To test the therapy efficacy, an evaluation, of the HCC and psychological stress, psychopathological symptomatology and, resilience was conducted before and after the treatment. The level of cortisol in, their hair was obtained during pregnancy and that of their babies at birth. Six, months after birth, a cortisol sample was taken from the hair and the babies', neurodevelopment was evaluated based on a Bayley-III test. The TG presented, reductions in psychological stress and psychopathological symptomatology after, treatment. On the other hand, the CG increased their cortisol concentrations between, the pre and post intervention, remaining stable in the TG. Moreover, results, showed that TG babies had lower cortisol concentrations at birth and obtained, significantly higher cognitive and motor development scores at 6 months. These, findings support that providing psychological care to pregnant women may not only, have a benefit on these women's mental state, but may also benefit the neurodevelopment, of their offspring.

Keywords: *cognitive behavioural therapy, CBT, cortisol in hair, neurodevelopment, prenatal stress.*

Introduction

Pregnancy brings about numerous changes in a woman's life at different levels and requires physical, psychological and hormonal adaptations (Alhusen et al., 2016). These psychological changes and adaptations, at the psychological level, can lead to increased stress in the mother, which may affect her health both psychologically (Puertas-Gonzalez, Mariño-Narvaez, Romero-Gonzalez, Vilar-López, & Peralta-Ramirez, 2022) and physically, for example, by increasing the likelihood of developing pregnancy-induced hypertension (Cardwell, 2013). Similarly, maternal stress has also been associated with adverse childbirth outcomes, such as the type of childbirth or preterm birth (Chiarello et al., 2018; Glynn et al., 2008; Romero-Gonzalez, et al., 2019). In addition, maternal stress has also been shown to affect the development of the foetus (Glover, 2015) and could have consequences such as low birth weight (Chiarello et al., 2018), sleep problems (O'Connoret al., 2007) and alterations in the baby's neurodevelopment (Caparros-Gonzalez et al., 2019a). Long-term effects could include an increased risk of ADHD, behavioural disorder (O'Connor et al., 2002) and an increased likelihood of neurodevelopmental disturbances in infants (Glover, 2015; Sandman et al., 2016).

On the other hand, it is well known that psychological stress is physiologically correlated with the modulation of the hypothalamic-pituitary-adrenal axis (HPA), in which cortisol's role as a mediator has been extensively investigated (Harris & Seckl, 2011; Moisiadis & Matthews, 2014). The activation of this axis involves the intervention of the hypothalamus, pituitary gland and adrenal glands. When perceiving a stressful situation, the hypothalamus secretes the corticotropin-releasing hormone (CRH), which activates the pituitary gland, producing the adrenocorticotrophic hormone (ACTH), which stimulates the release of cortisol in the supra-renal glands (Tsigos & Chrousos, 2002). The hypothalamus and placenta increase the concentration of the CRH especially during

pregnancy, which raises cortisol concentrations, passes through the placenta through blood circulation and reaches the foetus (Sandman et al., 2016). This increase in cortisol occurs naturally in pregnancy, and not especially due to stress.

However, increased in the mothers' cortisol has been found to be linked to changes in the offspring's cortisol concentrations, in studies both on animals and humans (Kapoor et al., 2016; Romero-Gonzalez et al., 2018). These studies show that when mothers show high cortisol concentrations during their first trimester of pregnancy, newborns present a low regulation of cortisol concentrations, which can jeopardise the maturation of certain organs, such as the lungs. In this sense, according to the Developmental Programming of Health and Disease Hypothesis (Barker, 1998; Seckl & Holmes, 2007) restrictive and adverse situations experienced during pregnancy may be likely to create unfavourable intrauterine environments. This could lead to long-term effects on the development of offspring. Therefore, both the mother's psychological stress during pregnancy and the mother's cortisol levels could have an influence on the subsequent neurodevelopment of her babies. On the one hand, a relationship has been found between an increase in perinatal stress and a greater likelihood of neurodevelopment alterations in babies (Glover, 2015; Sandman et al., 2016). On the other hand, several studies postulate cortisol levels play a key role in the formation and maturation of the foetal brain, thus being an important factor in cognitive, linguistic and motor development (Caparros-Gonzalez et al., 2019a; Kingston et al., 2012). Nevertheless, there is some controversy in this regard, as some studies have found a positive association between maternal cortisol levels and offspring development, while others have found an inverse association (Sandman et al., 2016; Van den Bergh et al., 2017).

Therefore, considering the critical role of cortisol levels and perinatal stress regarding the mother, foetus and future baby as described above, different strategies have been designed

to relieve stress, including stress management interventions based on Cognitive Behavioural Therapy (CBT). Although some studies have not found consistent results regarding the efficacy of CBT in reducing prenatal stress (Matvienko-Sikar et al., 2021), others have found through CBT a large reduction in maternal stress levels and psychopathological symptoms (Puertas-Gonzalez, Mariño-Narvaez, Romero-Gonzalez, Sanchez-Perez, & Peralta-Ramirez, 2022) and in the reduction of cortisol levels in saliva (Urizar & Muñoz, 2011; Zaheri et al., 2017). In addition, our research group discovered in the first part of the present study, that CBT is related to lower levels of cortisol in hair and psychological stress in pregnant women, supporting the efficacy of such evidence-based therapies on perinatal stress management (Romero-Gonzalez et al., 2020).

Therefore, given the impact of perinatal stress could have on child health, as postulated by the Developmental Programming of Health and Disease Hypothesis (Seckl & Holmes, 2007), and the effectiveness of CBT regarding stress management, the objective of this research was twofold.

On the one hand, we would like to test whether the benefits of CBT performed during pregnancy could have an impact on the infant's hair cortisol at birth and on neurodevelopment and Hair Cortisol Concentrations (HCC) at 6 months of age. For this purpose, we followed part of the participants of a previous study, where we found a reduction in HCC, perceived and pregnancy-specific stress, psychopathological symptoms and an increase in resilience in pregnant women through CBT (Romero-Gonzalez et al., 2020).

On the other hand, since this study is a follow-up of a previous study, we would like to check whether the results on CBT for stress management during pregnancy found in the full sample (reduction of psychopathology, psychological stress, HCC and increase in

resilience) (Romero-Gonzalez et al., 2020), are also found in the subsample used for the present follow-up.

Method

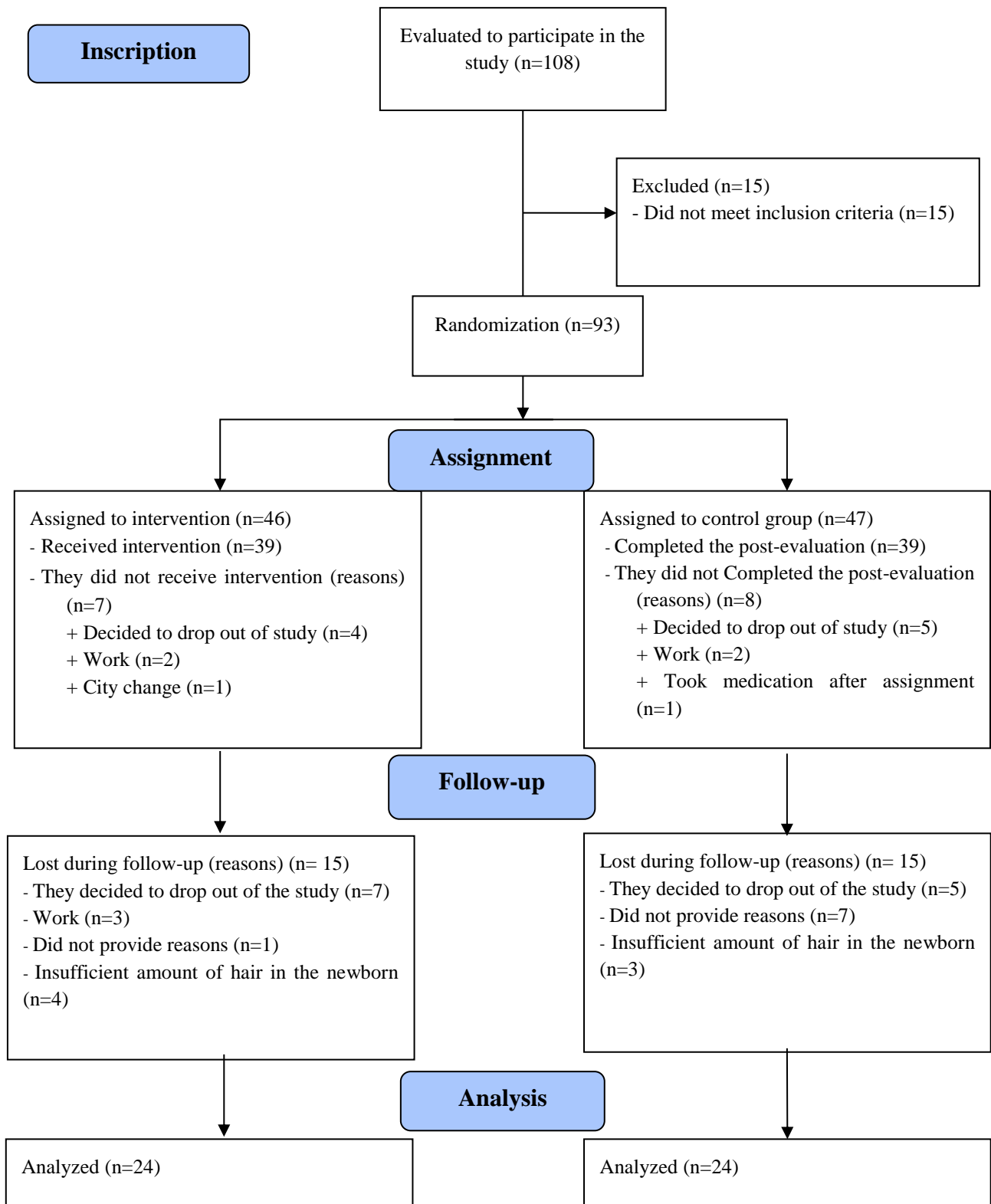
Design

The study was a follow-up to an individual level randomized controlled trial registered as a *Clinical Trial* with the code NCT03404141.

Participants

The study sample for the present follow-up consisted of 48 pregnant women aged between 19 and 39 years ($M = 32.65$ years; $SD = 4.26$) and their 48 babies aged 6 months ($M = 6.12$ months; $SD = 0.34$) (Figure 1). The women were recruited from the Góngora and Mirasierra health centres belonging to the Andalusian Health Service, in the province of Granada (Spain). The participants were enrolled between September 2017 and May 2019, the follow-up was conducted during the months that followed ending in February 2020.

Figure 1. CONSORT flow chart



The inclusion criteria were women between weeks 12-28 of their pregnancy, with a good command of both oral and written Spanish and be over 18 years old. Week 12 was

selected because at this stage of pregnancy the participant is at less risk of miscarriage. The 28th week of gestation was selected to ensure that participants would still be pregnant at the end of the intervention, so that they would have the necessary tools to face the last period of pregnancy, a period when they are usually more tired and have to start preparing for childbirth. The exclusion criteria were that of suffering from a medical or psychological illness (for example, having a diagnosis of clinical depression or anxiety) or following a corticosteroid treatment.

All the women who participated in the study read the information sheet and signed the informed consent document. This document certified the confidentiality of the data collected by the evaluator and guaranteed their freedom to leave the study whenever they wished.

The study was approved by the Human Research Ethics Committee of the University of Granada (reference 881) and the Biomedical Ethics Research Committee and the Ethics Research Committee of the Health Centres, and the hospital where this study was implemented. Moreover, this study followed the guidelines of the Helsinki Declaration (World Medical Association, 2013) and the Good Clinical Practice Directive (Directive 2005/28/EC) of the European Union.

Instruments

Firstly, socio-demographic and obstetric history variables that could be relevant were collected. Specifically, the following variables were collected: age, nationality, marital status, educational level, employment status, weekly hours of sport, smoking, week of gestation, first pregnancy, pregnancy planning, type of pregnancy and sex of the baby. In addition, birth weight and gestational age were also collected when the babies were born.

Subsequently, psychological and cortisol levels were assessed using the instruments described below.

Psychological evaluation

- *The Prenatal Distress Questionnaire (PDQ)* (Caparros-Gonzalez et al., 2019b): this is a 12-item self-report scale that measures pregnancy-specific stress related to maternal concerns about pregnancy, medical problems, labor and delivery, physical symptoms, bodily changes, parenting, interpersonal relations and the baby's health. Responses are given using a 5-point Likert-type scale where 0 = not at all and 4 = very much. It was used the Spanish version, which has adequate convergent validity (Caparros-Gonzalez et al., 2019b). In relation to reliability, the Cronbach's alpha was 0.73 in this study.

- *The Perceived Stress Scale (PSS-14)* (Cohen et. al., 1983; Remor, 2006): this is a 14-item scale that measures general stress. Responses are given using a 5-point Likert-type scale where 0 = never and 4 = very often. Scores range from 0 to 56, and the higher the score, the greater the perceived stress. In this study the Spanish version was employed, which has showed adequate concurrent validity and sensitivity (Remor, 2006). This instrument had a Cronbach's alpha of 0.92 in this study.

- *The Stress Vulnerability Inventory (IVE)* (Robles-Ortega et al., 2006). It consists of 22 items that evaluate the person's predisposition to feel affected by perceived stress. Therefore, it does not evaluate how much stress a person manifests, but how it affects them. The person is presented with a list of different situations and has to tick "Yes" if the situation occurs regularly or "No" if it does not. Items receiving an affirmative answer add 1 point. The range of scores on the scale is 0 to 22, higher scores corresponding to greater vulnerability to stress. Some of the items of this assessment tool include: "Finding yourself too indecisive; spending too much time making decisions, putting aside things

that need to be done” or “Not being able to concentrate at home or at work; easily distracted by irrelevant and unwanted problems”. This instrument has demonstrated concurrent validity (Robles-Ortega et al., 2006) and the Cronbach’s alpha was 0.72 in this research.

- *The Symptom Checklist-90-Revised (SCL-90-R)* (Caparrós Caparrós et al., 2007): this measures the subject’s perceived distress in nine primary dimensions (somatisation, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism) and three global indices of psychological distress (global severity index, positive symptom distress index and total positive symptoms). It is a 90-item self-report inventory and items are scored using a 5-point Likert-type scale, where 1 = never and 5 = very often. This instrument has demonstrated its construct validity in its Spanish version (Caparrós Caparrós et al., 2007). In addition, all dimensions showed an acceptable reliability, with a Cronbach’s alpha ranging from 0.69 to 0.95 for the four dimensions in this investigation.

- *The Connor Davidson Resilience Scale, abbreviated version (CD-RISC-10)* (Connor and Davidson, 2003, Notario-Pacheco et al., 2014). This instrument evaluates resilience, understood it as a person's ability to cope and adapt to their circumstances. It is composed of 10 items that are answered by a Likert-type scale with five response options ranging from 0 (“almost never”) to 4 (“almost always”), which had a single dimension. Some of the items it presents are: “I am able to adapt when changes occur” or “I think of myself as a strong person when dealing with life’s challenges and difficulties”. The scale provides a total score ranging from 0 to 40, and higher scores indicate a higher level of resilience. The Spanish version was used, which has high construct, divergent and convergent validity (Notario-Pacheco et al., 2014). It presents good reliability, with a Cronbach’s alpha was 0.87 in this study.

- *The Bayley Scales of Infant Development-III* (Bayley-III) (Bayley, 2006): the babies' neurodevelopmental evaluation was conducted using the Bayley-III instrument. The instrument is standardised and was administered individually. It measures the development levels of children aged between 16 days and 42 months. The main objective of the Bayley-III scale is to identify any developmental problems and to provide data that is useful to plan interventions. The test is structured into three main scales: the cognitive scale, the language scale (divided into expressive and receptive communication) and the motor scale (divided into fine and gross motor skills). The Spanish adaptation of the Bayley-III scales was employed and the direct scores were transformed into Spanish percentile scores (Bayley, 2006, 2015). All domains showed an acceptable reliability, with a Cronbach's alpha ranging between 0.70 and 0.77 in this research.

- *The Kaufman Brief Intelligence Test* (K-BIT) (Kaufman, 1990; Kaufman & Kaufman, 2009): the mothers' level of intelligence was evaluated using the K-BIT, since as has been shown, maternal intelligence is a determining factor in the early stages of infants' neuropsychological development (Forns et al., 2012). It consists of a screening test that lasts between 15 to 30 minutes and that aims at measuring verbal and non-verbal intelligence in boys and girls, adolescents and adults. It is divided into two subscales: vocabulary (divided into expressive vocabulary and definitions) and matrices. The Spanish version showed excellent concurrent and construct validity (Kaufman, 2009). In addition, all dimensions showed an acceptable reliability, with a Cronbach's alpha ranging from 0.70 to 0.73.

Hair cortisol concentrations

The cortisol evaluation consisted in taking a lock of hair containing approximately 150 strands from the rear corner of the skull, as close as possible to the scalp (Sauvé et al., 2007). A maximum length of 3 cm was set for each sample to reflect cortisol

concentrations during the preceding 3 months (Stalder and Kirschbaum, 2012). The samples were wrapped in aluminium foil to be adequately protected from light and humidity and were kept at room temperature until further analysis by the Department of Pharmacology of the Faculty of Pharmacy of the University of Granada. The analysis protocol was published in several studies (Caparros-Gonzalez et al., 2017; Romero-Gonzalez et al., 2018)

Procedure

Participants were recruited by their midwives during their pregnancy's quarterly examination at the health centre. They were informed of the study at that moment and were given a phone number to call if they wished to participate. After informing them and describing the study to them, those who agreed to participate read the information sheet and gave their consent to participate.

Participants were randomly divided into two groups: a Control Group (CG) and a Therapy Group (TG). Randomisation was performed using SPSS. A research assistant, who did not know the participants' data generated the random allocation sequences, registered the participants and assigned the interventions. Patients assigned to the CG received standard pregnancy care. Patients assigned to the therapy group attended 8 weekly, consecutive sessions of cognitive behavioural stress management therapy. Each group consisted of 4 to 5 participants lasted 1.5-2 hours and were led by two trained psychologists. The intervention and control groups had the same number of participants in each edition. Thus, after the initial evaluation, the programme was implemented for two months, followed by a post-intervention evaluation. Then, the recruitment period started again and when the necessary participants were available, a new randomisation, evaluation and implementation of the programme was carried out. The entire procedure has been published in the first part of the present research (Romero-Gonzalez et al., 2020).

The intervention was based on the adaptation of a pre-existing treatment programme (Robles-Ortega & Peralta-Ramírez, 2006). It was a cognitive-behavioural programme that has shown to be highly effective to control stress (Linares-Ortiz et al., 2014; Navarrete-Navarrete et al., 2010; Peralta-Ramirez et al., 2009; Santos -Ruiz et al., 2017). The main objective was to provide the participants with psychological tools to gain greater control over the different stressful situations they are exposed to throughout pregnancy, allowing them to develop optimal coping strategies. The programme consisted of eight sessions divided into seven modules: 1) Psychoeducation; 2) Deactivation techniques; 3) Cognitive restructuring; 4) Alternative thought control strategies; 5) Training in social skills; 6) Relationship between anger and stress; 7) Recapitulation. All sessions had a similar structure, at the beginning of each session the participants commented on how the week had gone and the difficulties encountered in applying the techniques seen in the previous session. In this way they received feedback from the therapists. Afterwards, the technique to be worked on that week was presented and explained, and a practical exercise was carried out. At the end, the participants received a behavioural self-report so that they could write down the moments during the week when they had applied the technique, their thoughts and the difficulties encountered. The contents of the eight sessions are presented in Table 1.

Table 1.*Intervention sessions and topics*

Session name	Topics
Session 1: Psychoeducation	<ul style="list-style-type: none"> • What stress is, characteristics, identification of stressors, responses and consequences
Session 2: Deactivation techniques	<ul style="list-style-type: none"> • Thematic imagination along with diaphragmatic breathing
Session 3: Cognitive restructuring	<ul style="list-style-type: none"> • Cognitive distortions
Session 4: Cognitive restructuring	<ul style="list-style-type: none"> • Irrational beliefs
Session 5: Alternative thought control strategies	<ul style="list-style-type: none"> • Self-instructional training and time organisation
Session 6: Training in social skills	<ul style="list-style-type: none"> • Assertiveness, basic assertive rights, saying no and asking for a change of behavior
Session 7: Relationship between anger and stress	<ul style="list-style-type: none"> • Emotional self-regulation
Session 8: Recapitulation	<ul style="list-style-type: none"> • Optimism and good humour, and recapitulation

On the other hand, the CC, who did not receive the intervention programme, did receive the usual care during the pregnancy process, such as attending medical check-ups with their midwife and gynaecologist or attending maternity education classes. The evaluation instruments described in the previous paragraph were delivered to both the TG and CG members at the same time. In addition, a hair sample was taken to obtain information about cortisol concentrations. Those assigned to the TG were informed of the starting date and time of their therapy. Participants of the CG were told to follow their standard routine care, which consists of three medical visits during the entire pregnancy with their midwives. At the end of the therapy, the assessment tools described above were re-administered to participants in both groups. During this second extraction of hair, only

the two centimetres closest to the root were used to avoid overlap between pre- and post-treatment samples.

On the other hand, the CC, who did not receive the intervention programme, did receive the usual care during the pregnancy process, such as attending medical check-ups with their midwife and gynaecologist or attending maternity education classes. The evaluation instruments described in the previous paragraph were delivered to both the TG and CG members at the same time. In addition, a hair sample was taken to obtain information about cortisol concentrations. Those assigned to the TG were informed of the starting date and time of their therapy. Participants of the CG were told to follow their standard routine care, which consists of three medical visits during the entire pregnancy with their midwives. At the end of the therapy, the assessment tools described above were re-administered to participants in both groups. During this second extraction of hair, only the two centimetres closest to the root were used to avoid overlap between pre- and post-treatment samples.

Once the therapy sessions had ended, all the participants were contacted back during the first week after giving birth, following at that moment the established protocol (Sauvé et al., 2007). A lock of hair was taken from the newborns and kept in an aluminium foil envelope for later analysis. In those cases when newborns had not enough hair to collect, more hair is cut from the nape of the neck to obtain at least 2.5 mg. As demonstrated by other authors, HHC in newborn infants could be a good indicator of chronic stress (Hoffmann et al., 2017; Yamada et al., 2007)

To finish, 6 months after each baby's birth, the babies were evaluated using the Bayley-III test (Bayley, 2006). The evaluations were conducted at the Mind, Brain and Behaviour Research Centre at the University of Granada. They were all performed in the

same room and with the same researcher. During this appointment, a hair sample was collected again from the baby.

Data analysis

First, a comparative analysis of the sample was carried out using Student's *t* tests (continuous variables) and Chi-square (categorical variables). The objective was to check any differences between the two groups of pregnant women (CG vs TG) based on the main sociodemographic variables, obstetric history, variables related to childbirth, as well as maternal Intelligence Quotient (IQ).

Firstly, to test whether the results found for cognitive-behavioral therapy in the first part of the study with the full sample are also found in the sample used for follow-up, the mothers of the infants who participated in the follow-up study were included in a linear mixed repeated measures model. Group (CG and TG) and time (pre and post) were specified as main effects, and a group \times time interaction was defined. Moreover, participant was entered as a random effect to account for repeated measures of the data. The dependent variables were scores in PSS, PDQ, CD-RISC-10, the SCL-90-R subscales and HHC. F-statistics and *p*-values were reported. Then, dependent *t*-tests analyses were performed on the variables presenting group*time interaction to study the differences between pre and post intervention. In addition, to check the therapy's size effect, Cohen's *d* was calculated: $d = 0.20$ low effect size, $d = 0.50$ medium size and $d = 0.80$ large effect size (Cohen, 1988).

Subsequently, non-parametric Mann Whitney *U* tests were performed to study any hair cortisol concentration differences between the babies born to women in the TG versus the CG group. Finally, in order to check whether there were differences between both groups (TG vs. CG) regarding the neurodevelopment of the infants at 6 months, different Mann

Whitney *U* tests were performed in the different scales of the Bayley-III test (Bayley, 2006). Hedges' *g* was used to calculate the effect size of the differences between neurodevelopment and cortisol of infants in the two groups. In contrast to Cohen's *d*, Hedges' *g* has the inclusion of a correction factor for small sample sizes. The values used to interpret the effect size were 0.20 (small), 0.50 (moderate) and 0.80 (large) (Durlak, 2009).

Regarding the statistical analysis of cortisol in hair, a logarithmic transformation (natural logarithm; ln base e) was carried out to adjust to a normal distribution. The *t*-test, Mann Whitney test and Chi-square analyses were performed with the Statistical Package for the Social Sciences 26.0 (SPSS), while the linear mixed models were carried out using with R 4.1.3 software (R Core Team, 2022) using the *lme4* package (Douglas, 2015).

Results

Description of participants

After performing the intervention and follow-up these women, their babies were evaluated, 24 of them belonging to the CG, with a mean age of 32.61 years (SD = 3.78) and the remaining 24 to the TG ($M = 32.71$ years; $SD = 4.83$).

The participant sample was found to be even with respect to the main sociodemographic variables, obstetric history, IQ and somatometric variables of the newborns (Table 2).

Table 2.

Comparison of the main sociodemographic variables, obstetric history and delivery variables, between women who attended therapy and women in the control group.

		Control (n = 24) X(SD)/n(%)	Therapy (n=24) X(SD)/n(%)	Contrast test*	<i>p</i>
Sociodemographic variables and IQ					
Age		32.61(3.78)	32,71(4.83)	-.079	.938
Civil status	Married/Cohabiting	24(100)	24(100)		
Nationality	Spain	21(87.5)	21(87.5)	.003	.955
	Immigrant	3(12.5)	3(12.5)		
Level of studies	Secondary	4(17.4)	7(29.2)	.908	.341
	University	19(82.6)	17(70.8)		
Employment situation	Unemployed	5(21.7)	7(29.2)	.341	.559
	Working	18(78.3)	17(70.8)		
Weekly hours of sport		2.67(0.72)	2.44(0.70)	.217	.829
Smoke	Yes	2(8.7)	-	2.180	.140
	No	21(91.3)	24(100)		
Maternal IQ	Verbal	109.60(7.96)	109.65(8.87)	-.012	.990
	Non-verbal	108.60(8.53)	107.52(9.82)	.227	.822
	Composite	107.60(9.15)	106.48(11.8)	.199	.844
Obstetric variables					
Weeks of gestation	T ₀	24.30(3.58)	26.08(3.91)	-1.564	.125
	T ₁	33.27(2.58)	34.08(3.93)	-.832	.410
Primigravida	Yes	9(39.1)	12(50)	.561	.454
	No	14(60.9)	12(50)		
Planned pregnancy	No	2(8.7)	4(16.7)	.670	.413
	Yes	21(91.3)	20(83.3)		
Type of pregnancy	Spontaneous	21(91.3)	21(87.5)	.179	.672
	Assisted reproduction	2(8.7)	3(12.5)		
Baby gender	Boy	13(54.2)	14(60.9)	.216	.642
	Girl	11(45.8)	9(39.1)		
Delivery variables					
Gestational age		39.68(0.82)	39.35(1.33)	.984	.332
Birth weight (g)		3188.00(459.17)	3302.75(479.39)	-.773	.444

Note: *The statistics reflect *t*-test for quantitative variables and Chi-square for categorical variables. IQ = Intelligence Quotient; T₀ = Pre-intervention; T₁ = Post intervention.

Efficacy of CBT in controlling stress during pregnancy: HHC, pregnancy-specific stress, perceived stress, resilience and psychopathological symptoms.

Results of analyses of participants who attended the intervention during pregnancy and completed follow-up of the infants ($n = 24$ for CG; $n = 24$ for TG), the linear mixed models results showed a statistically significant group*time interaction in: hair cortisol concentrations [$F(1,40) = 5.40$; $p = .025$]; PDQ scores [$F(1,44) = 9.14$; $p = .004$], PSS scores [$F(1,44) = 5.22$; $p = .027$], IVE scores [$F(1,42) = 5.33$; $p = .026$], obsession-compulsion dimension of the SCL-90-R [$F(1,44) = 4.99$; $p = .030$], hostility dimension of the SCL-90-R [$F(1,44) = 7.21$; $p = .010$] and the general scales of the SCL-90-R, GSI [$F(1,43) = 5.10$; $p = .029$] and PSDI [$F(1,44) = 7.00$; $p = .011$].

The average scores of the variables showing group*time interaction in both groups in the pre and post are shown in Table 3. Subsequent between-group analyses revealed differences between CG and TG after stress therapy.

Table 3.*Differences in post intervention scores between TG and CG.*

Outcomes	Group	T ₀	T ₁	<i>t</i>	<i>p</i>	<i>d</i>
HHC	TG	5.04(1.12)	4.65(1.37)	1.514	.144	.30
	CG	5.40(0.77)	5.72(0.79)	-2.170	.044*	.40
PDQ	TG	17.30(5.17)	12.91(4.50)	3.561	.002**	.91
	CG	12.09(4.90)	12.09(3.98)	.001	.999	.00
PSS	TG	24.39(7.35)	20.65(6.90)	2.189	.040*	.52
	CG	26.38(1.32)	26.62(1.40)	-.849	.411	.17
IVE	TG	6.62(3.85)	4.71(3.22)	2.024	.050*	.54
	CG	4.05(4.89)	4.86(4.59)	-1.030	.315	.17
OBS (SCL-90-R)	TG	78.74(17.50)	66.96(26.83)	2.362	.027*	.52
	CG	51.59(31.41)	56.45(33.32)	-.859	.400	.15
HOS (SCL-90-R)	TG	56.52(26.69)	40.00(32.05)	2.133	.044*	.56
	CG	36.14(27.03)	44.32(29.33)	-1.474	.155	.29
GSI (SCL-90-R)	TG	67.83(24.71)	53.70(29.00)	2.202	.040*	.52
	CG	39.86(29.76)	43.18(29.18)	-.861	.399	.11
PSDI (SCL-90-R)	TG	49.13(23.91)	34.13(24.10)	2.562	.018**	.62
	CG	40.68(28.21)	46.23(23.43)	-.946	.355	.21

Note: *Significant at the $p \leq .05$ level; **significant at the $p \leq .02$ level; HCC = Hair Cortisol Concentrations; PDQ = Pregnancy Distress Questionnaire; PSS = Perceived Stress Scale; IVE = Stress Vulnerability Inventory; OBS = Obsession-compulsion; HOS = Hostility; GSI = Global Severity Index; PSDI = Positive Symptom Distress Index; CG = Control Group; TG = Therapy Group; T₀ = Pre-intervention; T₁ = Post intervention.

Pre and post-intervention changes in TG and CG

Dependent *t*-tests were performed to detect changes in pre and post intervention. There were statistically pre-post intervention changes in CG in HHC, the mean score of the CG in this variable was higher after the intervention. Regarding TG, no significant statistically changes were found in the HHC, remaining stable. However, significant changes were found and the secondary outcomes: PDQ scores, PSS scores, IVE scores, obsession-compulsion dimensions of the SCL-90-R, hostility dimensions of the SCL-90-R, and on the overall scales of the GSI SCL-90-R and PSDI. The mean scores of the TG

in these variables being higher before the therapy than after. No significant changes were found in the secondary outcomes in CG.

The means of the variables, the standard deviations and the analysis of differences of the GT and CG before and after the intervention are shown in Table 3.

Neurodevelopment and baby cortisol concentration differences between the mothers in the stress management therapy group and the non-therapy group.

First, Mann Whitney *U* test analyses showed statistically significant differences between TG and CG group women regarding babies' cortisol concentrations at birth ($U = 63$; $p = .002$; Hedges' $g = 1.13$) (Table 4).

Regarding infant neurodevelopment at 6 months of age, the results showed that there were statistically significant differences between babies born to women in the TG and babies born to women in the CG. Specifically, these differences were found for scores referring to the cognitive scale: total score, scalar, composite and percentile. In addition, with respect to the motor scale, differences were found in the total and scalar fine motor score, and in the scalar score and total gross motor skills. Moreover, differences were found in scalar, composite and percentile scores on the general motor skills scale. Among all the differences found in the variables mentioned above, 6-month-old babies born to mothers belonging to the TG obtained higher scores.

On the other hand, there were no statistically significant differences between groups in the language scale scores. The variable medians, range and the analysis of differences between both groups are shown in Table 4. In addition, the mean percentile scores for the three general scales are shown in Figure 2.

Table 4.

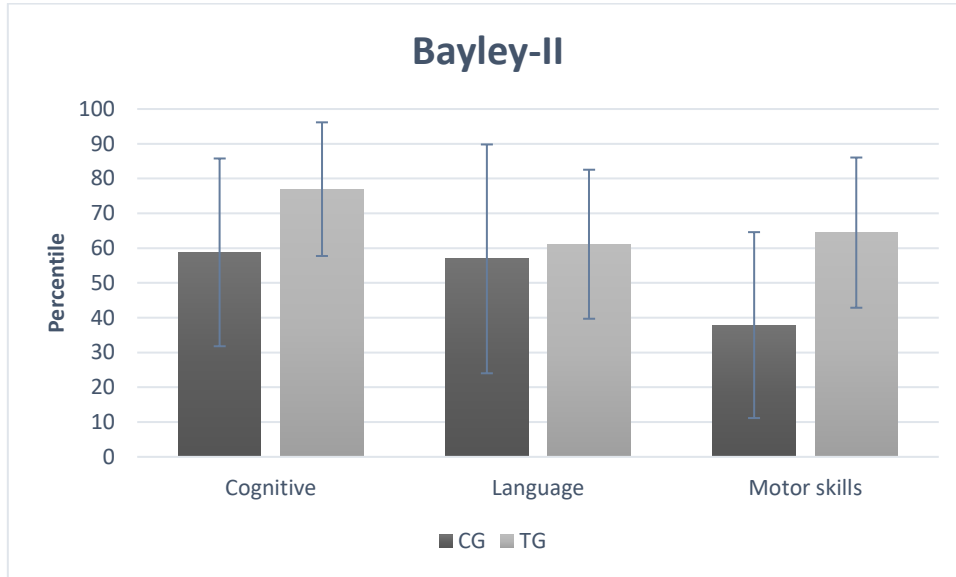
Difference between neurodevelopment and cortisol levels in hair between babies of mothers who attend therapy versus mothers of the control group.

			Control Median (Range)	Therapy Median (Range)	Mann Whitney	<i>p</i>	Hedges' <i>g</i>
Cortisol	Birth (In)		7.93(3.23)	6.50(2.17)	63	.002**	1.13
	6 months (In)		6.28(3.98)	6.37(2.71)	116	.722	0.34
Cognitive	Total		30(14)	32(10)	186	.034*	0.53
	Scalar		11(15)	13(7)	155	.006**	0.64
	Composite		105(55)	115(35)	162.50	.009**	0.61
Language	Percentile		63(90)	84(70)	162.50	.009**	0.77
	Responsive communication	Total	11(8)	10(4)	219	.139	0.28
		Scalar		11(11)	11(7)	274.50	.775
	Expressive Communication	Total	9(13)	9(8)	279	.851	0.10
		Scalar		11(13)	11(10)	282	.901
	Scalar		20.50(19)	21(14)	272.50	.748	0.04
	Composite		101.50(56)	103(41)	265.50	.642	0.09
	Percentile		54(94)	58(71)	265.50	.642	0.15
Motor skills	Fine motor	Total	20(9)	22(78)	172.50	.016**	0.40
		Scalar		9.50(9)	12(9)	145	.003**
	Gross motor	Total	24(10)	25(11)	190.50	.043*	0.64
		Scalar		8(10)	10(9)	152.50	.005**
	Scalar		18(17)	22(15)	137.50	.002**	0.92
	Composite		92.50(51)	107(87)	136.50	.002*	0.63
	Percentile		30.50(91)	68(68)	121	.001**	1.09

Note: *Significant at the $p \leq .05$ level; **significant at the $p \leq .02$ level

Figure 2.

Percentile score on the general cognitive, language and motor scales of babies born to women belonging to the CG and TG.



Note: Bayley-III = Bayley Scales of Infant Development-III; TG = Therapy Group; CG = Control Group.

Discussion

The aim of this study was to test whether CBT followed during pregnancy to manage stress, has implications on hair cortisol at birth and subsequent neurodevelopment and on the capillary cortisol concentrations of the mothers' infants at 6 months of age. For this purpose, in the first part of this study related to a previous publication, we found a reduction in hair cortisol concentrations, perceived and pregnancy-specific stress, psychopathological symptoms and an increase in resilience in pregnant women through CBT (Romero-Gonzalez et al., 2020). In the current follow-up study, we first checked whether the results found previously in the full sample were maintained in the subsample that participated in the follow-up. We then analysed the cortisol levels of the participants' infants at birth and at six months, as well as their neurodevelopment at 6 months.

Firstly, in relation to the results of CBT for stress management, the results for the subsample used in this study show similar reductions in psychopathological symptoms, perceived and pregnancy-specific stress and an increase in cortisol levels in the control group but not in the intervention group. Although cortisol levels vary across trimesters of pregnancy (Garcia-Leon et al., 2018), the weeks of pregnancy of the two groups were equal at both the beginning and end of the intervention. Therefore, variations in cortisol levels during pregnancy should affect both groups equally if there were no influence of therapy. However, the increase in cortisol at the post-intervention assessment was only found in the CG. Finally, we did not find an increase in resilience levels as in the previous results with the full sample (Romero-Gonzalez et al., 2020).

Secondly, with respect to cortisol levels and the neurodevelopment of babies, the results showed that the TG's babies had a lower concentration of cortisol at birth, as well as a higher level of cognitive and motor development at six months. However, no significant differences were found between the two groups in relation to cortisol levels at 6 months and language neurodevelopment.

Regarding the baby's cortisol concentrations, it should be noted that the babies whose mothers had attended the TG had lower cortisol concentrations at birth than the babies belonging to the CG. We hypothesise that lower infant cortisol concentrations at birth could be caused, at least partially, by the combined reduction and control of the three parameters of the mothers in the third trimester (hair cortisol, perceived stress and pregnancy-specific stress) (Kapoor et al., 2016; Romero-Gonzalez et al., 2018). On the other hand, no differences were found between the groups in cortisol levels at 6 months of age, so that the effects of CBT on mothers could have an implication on children's cortisol levels only in the short term. However, the precise mechanism by which these effects on cortisol levels are equalized between both groups of children at 6 months of

age remains unknown. One hypothesis is that, from birth, children are exposed to different environments and factors (the socio-economic status of the family, the pattern of upbringing and education, the type of attachment, the child's temperament, etc.), as well as to different breastfeeding and sleeping patterns, that may affect their cortisol levels differently (Flom, et al., 2017).

On the other hand, with respect to neurodevelopment, it is worth noting that the babies of mothers who had followed the therapy showed higher cognitive and motor neurodevelopment scores. Furthermore, very noticeably with medium and large effect sizes. The results of this research are compatible with that of other studies, which found that high maternal cortisol concentrations were related to poorer cognitive and motor neurodevelopment in babies at 6 months of age (Buitelaar et al., 2003; Caparros-Gonzalez et al., 2019a). In our study, controlling the increase in cortisol concentrations during pregnancy increased infant neurological development in these two main cognitive and motor spheres.

This finding highlights the relationship between maternal cortisol and infant neurodevelopment. According to the Developmental Programming of Health and Disease Hypothesis (Arabin et al., 2021; Barker, 1998; Langley-Evans, 2006; Seckl & Holmes, 2007), changes experienced by mothers during their pregnancy condition their baby's health and subsequent development (Barker et al., 1993). In this sense, both groups of mothers (CG and TG) developed different processes during pregnancy, resulting in an improvement in stress control in TG women. This stress reduction, whose physiological correlate is defined by the mother's cortisol secretion, could have an impact on the formation of the foetal brain. Specifically, some experts indicate the importance of the HPA axis in newborn brain maturation, particularly in the development of the hypothalamus and the limbic system, which could be affected in the last moments of

gestation (Rakers et al., 2017). The third trimester of gestation presents particular susceptibility to these changes. In this third trimester, the left amygdala increases its connectivity with frontal and temporal lobe regions in the foetus, this rapid development being sensitive to signals of maternal stress, as well as alterations in the maternal HPA axis; it might cause long-term neurodevelopment delays, and even different psychopathologies (Davis et al., 2018). In this way, a possible control of the increase in cortisol secretion resulting from therapy during pregnancy could mitigate future effects on brain and the neurodevelopment of newborns, at least in the short term (Arabin et al., 2021). Furthermore, the fact that the levels of psychological stress were reduced through therapy could also explain the better neurological development of the babies of these women (Glover, 2015). It is important to treat these two factors separately, as some authors found an association between cortisol levels and psychological stress, e.g., Kalra et al. (2007), but others did not (Arco-Garcia et al., 2020; Romero-Gonzalez et al., 2018). Therefore, both could be independent predictors of infants' neurodevelopment (Sandman et al., 2016).

On the other hand, another factor that could benefit infant neurological development was that mothers who received CBT managed their stressful situations better than mothers in the CG after childbirth and the postnatal period, resulting in better mental health, parenting behaviour and relationship with their babies. Thus, training in deactivation techniques, as well as training in the detection and transformation of cognitive distortions, together with training in social skills such as "saying no" without feeling guilty, could have provided the mother with key tools for coping with the psychological stress related to having a child. Finally, it is well known that CBT, through the acquisition of these skills, prevents emotional disturbances in the postpartum period

such as postpartum depression, which could have implications for the baby (Sockol, 2015). However, further studies are needed to test these hypotheses.

However, no relationship was found with the neurodevelopment of language in any of the studies mentioned. One explanation could be the way in which language develops, i.e., in a more gradual manner, with language acquisition becoming more intense at around 2 years of age (Ylinen et al., 2017). For this reason, the variability among babies regarding the language aspect was minimal and almost negligible at 6 months of age. To better examine the relationship between the mother's stress and the neurodevelopment of language, it would be necessary to evaluate language closer to the 2-year stage. It would indeed be possible to study at this latter evolutionary moment in time whether or not a relationship exists between stress reduction and language development.

This study has important implications: it is one of the first to show that a reduction in prenatal stress, as well as control of cortisol levels through CBT during pregnancy, may be associated with better neurodevelopment in offspring. Considering that the effect of prenatal stress on infant development and the regulation of neonatal stress is explained by the foetal programming of the HHA (Beijers et al., 2014; Davis et al., 2011), it is important to continue to explore desirable levels of neonatal cortisol. This could contribute to preventing subsequent diseases, and to building knowledge about neurodevelopment changes, since it has been strongly related to different disorders such as the autism spectrum or ADHD (Bhutta et al., 2002; Perou et al., 2013). In the same way, it would be interesting to follow up these babies throughout childhood to examine how foetal programming can influence later ages and detect possible changes in the neurodevelopment of language.

This investigation, however, presents some limitations. Firstly, it is important to consider that the groups had differences on some psychological variables at baseline. Still, the evident change on the remaining studied variables cannot be discredited, since its reduction due to the intervention was significant. Even though there were baseline differences between groups, the efficacy of therapy reflected in the effect sizes, demonstrate the great impact therapy can have on pregnant women. On the other hand, the sample size was reduced due to the loss of participants during the procedure. It would thus be of interest to replicate the study with larger samples and even include other variables that have not been taken into account, such as parenting patterns. In addition, although there were no statistical differences between groups with respect to socio-demographic, obstetric and delivery variables, some variations in these variables could have some influence on child comparisons due to the sample size.

To conclude, the findings of this study are novel and have a number of repercussions. On the one hand, the effectiveness of CBT has been proven once again in the field of research. In addition, the shows that CBT could be used as a measure that promotes health when applied during pregnancy, with potential benefits not only for the pregnant woman but also for her offspring.

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6.3 Artículo 3

Puertas-Gonzalez, J. A., Mariño-Narvaez, C., Peralta-Ramirez, M. I., & Romero-Gonzalez, B. (2021). The psychological impact of the COVID-19 pandemic on pregnant women. *Psychiatry Research*, 301, 113978.

<https://doi.org/10.1016/j.psychres.2021.113978>

The psychological impact of the COVID-19 pandemic on pregnant women

Abstract

The aim was to examine the psychological effects caused by the COVID-19 pandemic on pregnant women, as well as the factors influencing these effects. The study design was cross-sectional and the participants were 200 pregnant women. The first group called the Pandemic Group (PG) included 100 women who were evaluated with psychological assessment instruments during the COVID-19 pandemic. The second group titled Pre-Pandemic Group (PPG) consisted of 100 women who were evaluated prior to the pandemic. Perceived stress, prenatal concerns and psychopathological symptoms were evaluated and compared. Pandemic Group scored significantly higher than Pre-Pandemic Group in the depression dimension of the SCL-90, in the phobic anxiety dimension, and in the Perceived Stress Scale. In addition, insomnia, along with having recently suffered the loss of a loved one explained 25% of the score variance in the depression dimension of the SCL-90. Insomnia also explained 13% of the variance of the results found in the Perceived Stress Scale. The fear of contagion by COVID-19 increased the scores obtained in the phobic anxiety dimension, explaining 11% of the variance. Thus, the COVID-19 pandemic could produce an increase in psychopathological symptomatology and stress, which can lead to negatively affecting pregnant women's mental health.

Keywords: *COVID-19, pregnancy, anxiety, depression, prenatal stress.*

Introduction

In December 2019 an outbreak of the new coronavirus pneumonia disease (COVID-19), of unknown aetiology, appeared in Wuhan, the capital of Hubei Province in China (Chen et al., 2020). Thus, in March 2020, a few months after the onset of COVID-19, the World Health Organization (WHO) declared a pandemic caused by the new disease (World Health Organization, 2020). Due to the impact of the outbreak in Spain, the Spanish Government declared a national state of alarm and health alert on 14 March 2020. In addition to numerous deaths, the pandemic caused by COVID-19 has generated stress, agitation and anxiety among the population, for fear of contagion and its adverse consequences (Wang et al., 2020). Previous studies developed in China describe among other consequences of living in lockdown, increases in levels of stress, anxiety, depression and general emotional dysphoria in persons highly predisposed to these conditions (Wang et al., 2020). In this line, different studies conducted during the initial phases of expansion of the previous 2003 pandemic caused by Severe Acute Respiratory Syndrome (SARS) showed an increase in psychiatric disorders. These disorders included: anxiety, depression, panic attacks, psychotic symptoms and even cases of suicide (Liu et al., 2003; Maunder et al., 2003).

One particularly vulnerable group could be pregnant women due to their condition. In fact, it is well known that during pregnancy the likelihood of experiencing mental disorders increases. For example, 22% of pregnant women have anxiety, and 12% experience depression (Palladino et al., 2012; Woody et al., 2017). Moreover, several studies conducted in different countries (United States, China, Canada, Italy, Turkey and Greece) suggest that the prevalence of anxiety and depression symptoms may have increased in pregnant women during the pandemic (Hessami, 2020; Liu, 2020; Wu et al., 2020).

A study carried out in Spain by Romero-Gonzalez et al. 2020, has shown that perceived stress, specific pregnancy stress, as well as insomnia are predictive variables in most anxiety and depressive symptoms related to COVID-19 in pregnant women. However, this study did not have a control group to compare the psychopathology of pregnant women prior to the pandemic and after the pandemic. We hypothesize an increase in the rate of mental health symptoms from before to during the pandemic, among women in Spain. Thus, the objective of this study was to analyse this psychological impact on pregnant women and the factors that may influence these effects. Specifically, the objective was to study the psychological health of pregnant women during the pandemic by evaluating psychopathological symptomatology and stress. In addition, we sought to understand how the different variables relating to the COVID-19 pandemic and the lockdown could affect the psychological state of pregnant women.

Methods

Participants

The sample was made up of a total of 200 pregnant women, aged on average 33.1 years ($SD = 4.6$), in their second or third trimesters of pregnancy ($X = 26.9$ weeks of pregnancy; $SD = 8.9$).

All study participants were informed about the procedure and objectives of the study and participated voluntarily. The inclusion criteria were as follow: being aged over 18 years; being pregnant; and knowing how to read and write in Spanish. The exclusion criteria consisted of being actively treated with psychopharmaceuticals.

Thus, the sample was made up of a total of 200 pregnant women divided into two groups: Pandemic Group (PG), consisting of 100 (50%) pregnant women evaluated with psychological assessment instruments during the COVID-19 pandemic; and Pre-

Pandemic Group (PPG), consisting of 100 (50%) pregnant women who were evaluated prior to the pandemic.

Ethical approval for the study was granted by the Human Ethics Research Committee of the University of Granada, Spain (reference 1518/CEIH/2020).

Procedure

All questionnaires were created using Google Forms. Both groups of participants were recruited at San Cecilio University Hospital, Góngora and Mirasierra health centers in Granada. When the potential participants attended their pregnancy follow-up appointment with their midwife, they were given information about the study and were offered the possibility of participating. Later, the contact details of the women who consented to take part in the study were noted and the online questionnaires were subsequently sent to them. At this moment, they were also asked to put us in contact with potential participants to include them in the study.

Pre-Pandemic Group (PPG) participants were recruited and evaluated between March and June 2019. The PPG participants were part of a previous study called Gestastress. In addition to recruitment through their medical professionals, the participants in Pandemic Group (PG) were also recruited through various social network groups of pregnant women (through WhatsApp, Facebook and internet forums) and evaluated between March and June 2020, during the COVID-19 state of health emergency in Spain. The use of two groups in different years has already been used to study the effects of the pandemic on psychological health in the perinatal period (Zanardo, 2020).

Instruments

Sociodemographic, obstetric, and confinement related variables were collected using a questionnaire designed with the previously mentioned target for the present investigation. This questionnaire evaluated different dimensions related to the COVID-

19 pandemic and the confinement, through dichotomous and Likert-type responses. The dimensions covered were: losses, leisure, fear of contagion and social support ("Have you recently suffered the loss of a loved one? "; "Have you taken advantage of the lockdown to spend time on hobbies, pending tasks, tidying, etc.?" ; "From 0 to 10, how afraid are you of going out for fear of contagion?"; "Have you spoken to family or friends by phone or audio-visual media during the lockdown?"). In addition, the following psychological assessment tools were used:

- The Symptom Checklist-90-Revised (SCL-90-R) (Derogatis, 1994; Caparrós-Caparrós et al., 2007): this is a 90-item scale scored using a 5-point Likert scale from 0 (never) to 4 (extremely). This instrument is used to assess 9 dimensions: Somatization, Obsession-compulsion, Interpersonal sensitivity, Depression, Anxiety, Hostility, Phobic anxiety, Paranoid ideation, and Psychoticism. The scale also has 7 extra items distributed among 3 global indexes of distress: the GSI, which measures overall psychological distress; the PSDI, which is used to measure the intensity of symptoms; and Positive Symptom Total, used to measure the number of self-reported symptoms. Using the author's instructions, the scores are transformed to percentiles (0 100). Percentiles ≥ 75 represent clinical symptoms in any of the subscale of this instrument. The nine dimensions show an acceptable reliability, with a Cronbach's alpha for internal consistency between 0.69 and 0.97 in its Spanish version (Caparrós-Caparrós et al., 2007).

- Perceived Stress Scale (PSS) (Cohen et al, 1983; Remor, 2006): the PSS provides information on the perception of general stress during the preceding month. It consists of 14 items scores on a 5-point Likert scale (0 = never, 1 = almost never, 2 = once in a while, 3 = often, 4 = very often). Scores range from 0 to 56 (higher scores

represent higher levels of stress). Spanish reliability alpha's Cronbach coefficient is 0.81 (Remor, 2006).

- Prenatal Distress Questionnaire (PDQ) (Yali and Lobel, 1999; Caparros-Gonzalez et al., 2019): this is a 12-item scale that measures pregnancy-specific stress related to maternal concerns about pregnancy, such as medical problems, labour and delivery, physical symptoms, bodily changes and the baby's health. Responses are given using a 5-point Likert-type scale where 0 = not at all and 4 = very much. The Cronbach's alpha reliability coefficient is 0.71 in its Spanish version (Caparros-Gonzalez et al., 2019).

-Athens Insomnia Scale (AIS) (Soldatos et al., 2000; Portocarrero and Jiménez-Genchi, 2005): this scale has a self-administrated format and allows to evaluate the subjective presence of insomnia, based on the diagnostic criteria of the Classification of Mental Disorders and of Behavior (ICD-10) (World Health Organization, 1992). It is composed of a total of 8 items, the first 5 measure the difficulty of sleep induction, early awakening, nocturnal awakenings, total duration of sleep and overall sleep quality. The other three assess the daytime consequences of insomnia: daytime drowsiness, functioning and problems concerning the feeling of wellbeing. Cronbach's alpha reliability coefficient is 0.90 in its Spanish version (Portocarrero and Jiménez-Genchi, 2005).

Data analysis

The analyses were performed using the *Statistical Program for Social Sciences* (SPSS) version 25.0 package for Windows (SPSS, Armonk, New York). First, a series of comparisons were conducted between the groups to check whether the two groups were evenly homogenous regarding the main sociodemographic and obstetric variables. To do this, we used Student's t-test for continuous variables and the Chi-square test (χ^2) for the categorical variables.

Secondly, in order to verify whether there were differences between pregnant women during the COVID-19 pandemic versus pregnant women who had not experienced the pandemic, various Student's t-tests were performed on the major psychological variables. Prior to that, the normality of psychological variables was verified using the Kolmogorov-Smirnov test and homoscedasticity, using Levene's test. The assumptions of normality were met. In variables where significant differences were found, the size of the effect was subsequently calculated using *Cohen's d*, and interpreted based on the following values: small effect size > 0.20 , median effect size > 0.50 and large effect size > 0.80 (Cohen, 1988).

Finally, in order to verify which pandemic variables were related to the psychopathological symptoms presented, linear regressions were performed. The dependent variables were the psychological variables for which significant differences were found between the groups; and the predictor variables were the variables related to the participants' lockdown.

Results

Sample description

A total of 200 pregnant women participated in the study. Pandemic Group (PG) ($n = 100$) formed by women who were pregnant during the COVID-19 pandemic and Pre-Pandemic Group (PPG) ($n = 100$), formed by women who were pregnant prior to the COVID-19 pandemic. The main sociodemographic and obstetric variables of the two groups were compared. No significant differences between them were found so they were homogenous. These results are shown in Table 1.

Table 1. Sociodemographic and obstetric variables compared to Student and Chi-square t-tests.

		Pregnant women during the pandemic (n = 100) M(SD)	Pregnant women prior to the pandemic (n = 100) M(SD)	<i>t</i>	<i>p</i>
Age		33.20(4.71)	33.04(4.45)	.247	.805
Weeks of pregnancy		26.47(9.12)	27.26(8.70)	-.628	.531
		Pregnant women during the pandemic (n = 100) n(%)	Pregnant women prior to the pandemic (n = 100) n(%)	χ^2	<i>p</i>
<i>Sociodemographic variables</i>					
Current couple	Yes	97(97%)	95(95%)	.521	.470
	No	3(3%)	5(5%)		
Nationality	Spanish	93(93%)	88(88%)	1.454	.228
	Inmigrant	7(7%)	12(12%)		
Education level	Primary school	2(2%)	1(1%)	.352	.839
	Secondary school	26(26%)	27(27%)		
	University	72(72%)	72(72%)		
<i>Obstetric information</i>					
Primiparous	No	38(38%)	46(46%)	1.314	.252
	Yes	62(62%)	54(54%)		
Pregnancy method	Spontaneous	89(89%)	88(88%)	.049	.825
	Fertility treatment	11(11%)	12(12%)		
Previous miscarriages	0	71(71%)	68(68%)	.214	.898
	1	21(21%)	23(23%)		
	≥ 2	8(8%)	9(9%)		
Previous children	0	67(67%)	61(61%)	1.247	.536
	1	29(29%)	32(32%)		
	≥ 2	4(4%)	7(7%)		
Risk pregnancy	No	84(84%)	78(78%)	1.170	.279
	Yes	16(16%)	22(22%)		

Differences in psychological symptomatology and stress between groups

Regarding differences in psychological symptoms between women who were pregnant during the COVID-19 pandemic (PG) versus women who were pregnant prior to the COVID-19 pandemic (PPG), the difference of Student's t-test means showed that

significant differences existed in the depression dimensions of the SCL-90 [t x 3.493; p .001; (d) .50]; SCL-90 phobic [t x 2.185; p .030; (d) .31]; and in the PSS [t x 2.260; p .025; (d) .33]. PG obtained higher scores than PPG with an average effect size in the depression dimension of the SCL-90, and with a small effect size in the phobic anxiety dimension of the SCL-90 and in the PSS. No statistically significant differences were found between the groups in the other 7 dimensions of the SCL-90 or in the PDQ. The results are broken down in Table 2.

Table 2. Comparison of means through student t-test of psychological variables.

	Pregnant women during the pandemic (n = 100) M(SD)	Pregnant women prior to the pandemic (n = 100) M(SD)	<i>t</i>	<i>p</i>	Cohen's <i>d</i>
SCL-90 Somatization	66.34(22.97)	61.22(24.08)	1.538	.126	0.22
SCL-90 Obsession- compulsion	71.65(23.36)	69.14(25.47)	.726	.469	0.10
SCL-90 Interpersonal sensitivity	54.66(31.40)	54.91(29.58)	-.058	.954	0.01
SCL-90 Depression	65.17(28.45)	51.56(26.61)	3.493	.001**	0.50
SCL-90 Anxiety	64.56(25.02)	63.26(26.60)	.356	.722	0.05
SCL-90 Hostility	50.65(32.07)	50.66(29.66)	-.002	.998	0.01
SCL-90 Phobic anxiety	66.59(30.55)	56.45(34.93)	2.185	.030*	0.31
SCL-90 Paranoid ideation	38.28(33.60)	46.15(35.19)	- 1.617	.107	0.23
SCL-90 Psychoticism	54.28(35.50)	60.80(33.87)	- 1.349	.179	0.19
SSP	25.76(4.56)	24.14(5.18)	2.260	.025*	0.33
PDQ	16.34(6.68)	15.33(5.72)	1.150	.252	0.16

Note. * = $p < 0.05$; ** = $p < 0.02$; SCL-90 = The Symptom Checklist-90- Revised; PSS = Perceived Stress Scale; PDQ = Prenatal Distress Questionnaire.

Lockdown variables as predictors of the psychological state

Finally, to verify that pandemic variables were predictors of psychological states in pregnant women, simple linear regressions were performed using the enter method including only PG. To do this, the scores of the three variables that presented differences between groups were used as result variables: the two dimensions of SCL-90 (depression and phobic anxiety) and PSS scores. The objective was to know which pandemic variables and lockdown-related variables could be influencing the results obtained. The predictor variables in the three models were: insomnia scores obtained on the AIS; the answers to the question "Have you recently suffered the loss of a loved one? "; the answers to the question "Have you taken advantage of the lockdown to spend time on hobbies, pending tasks, tidying, etc.?" ; the answers to the question "From 0 to 10, how afraid are you of going out for fear of contagion?"; answers to the question "Have you spoken to family or friends by phone or audio-visual media during the lockdown?".

Thus, based on the first analysis, it was found that insomnia, together with having recently lost a loved one, increased the scores obtained in the depression dimension of the SCL-90, explaining 25% of the variance [$R^2 = .254$ ($F = 6.335$; $p = .001$)]. Regarding phobic anxiety of the SCL-90, it was found that the fear of contagion increased the scores obtained in this dimension, explaining 11% of the variance [$R^2 = .111$ ($F = 2.331$; $p = .048$)]. Finally, regarding the predictive variables of the PSS scores, it was found that insomnia increased perceived stress, this variable explaining 13% of the variance [$R^2 = .131$ ($F = 2.568$; $p = .033$)]. The results are shown in Table 3.

Table 3. Linear regressions with the variables of the pandemic and lockdown from the pregnant women of Pandemic Group as predictors.

	β	R-squared	F	<i>t</i>	<i>p</i>
IV: SCL-90 Depression		.254	6.335		.001**
Insomnia	2.745			4.889	.001**
Have you recently suffered the loss of a loved one?	21.237			2.596	.011**
Have you taken advantage of the lockdown to spend time on hobbies, pending tasks, tidying, etc.?	-.416			-.147	.883
From 0 to 10, how afraid are you of going out for fear of contagion?	1.422			1.310	.193
Have you spoken to family or friends by phone or audiovisual media during the lockdown?	-3.831			-1.381	.171
IV: SCL-90 Phobic anxiety		.111	2.331		.048*
Insomnia	.875			1.299	.197
Have you recently suffered the loss of a loved one?	5.956			.607	.545
Have you taken advantage of the lockdown to spend time on hobbies, pending tasks, tidying, etc.?	-2.947			-.869	.387
From 0 to 10, how afraid are you of going out for fear of contagion?	3.618			2.780	.007**
Have you spoken to family or friends by phone or audiovisual media during the lockdown?	-3.554			-1.068	.288
IV: PSS		.131	2.568		.033*
Insomnia	.325			3.124	.002**
Have you recently suffered the loss of a loved one?	-.308			-.195	.846
Have you taken advantage of the lockdown to spend time on hobbies, pending tasks, tidying, etc.?	-.038			-.073	.942
From 0 to 10, how afraid are you of going out for fear of contagion?	-.185			-.932	.354
Have you spoken to family or friends by phone or audiovisual media during the lockdown?	-.320			-.620	.537

Note. * = $p < 0.05$; ** = $p < 0.02$; IV = independent variable; SCL-90- Revised = The Symptom Checklist-90; PSS = Perceived Stress Scale.

Discussion

The present study focused on the psychological health of pregnant women during the COVID-19 pandemic in Spain. The psychopathological symptoms and stress of a group of women who were pregnant prior to the COVID-19 pandemic were compared with that of a group of women who were pregnant during the COVID-19 pandemic. Finally, the factors that could potentially influence the differences found between both groups were studied.

First, the group of women who were pregnant during the COVID-19 pandemic (PG) were found to present more psychopathological symptoms than the group of women who did experience the COVID-19 pandemic during their pregnancy (PPG). Specifically, PG showed higher levels of depression and phobic anxiety. These results support the data obtained in another similar situation: that of the previous 2003 pandemic caused by SARS, during which an increase in anxiety and depression morbidity was found (Liu et al., 2003; Maunder et al., 2003). Furthermore, the results obtained are compatible with studies carried out in other countries, in which an increase in anxiety and depression levels was found, as well as an increase in the severity of symptoms in this population. (Hessami, 2020; Liu, 2020; Wu et al., 2020).

Moreover, the group of women who were pregnant during the pandemic also showed higher levels of perceived stress than the group of women who were pregnant before the pandemic. Uncertainty, high contagion rate, high mortality rate and, consequently, fear of contracting the disease, jointly affecting the mother and foetus, may be stressors underlying these increases in levels in pregnant women during the pandemic, compared to those who were not pregnant in the pandemic (Craske and Stein, 2016). Thus, the radical change of life caused by lockdown could increase these stress levels in especially vulnerable populations such as that of pregnant women (Smith, 2020; Wang et

al., 2020). Furthermore, it is worth noting that increases in these types of symptoms during pregnancy could lead to: an increased risk of postpartum depression, preeclampsia and hypertension, low foetal weight, premature delivery, and a greater risk of spontaneous abortion (Woods et al., 2010; Christian, 2012; Caparros-Gonzalez, 2017; Kaboli, 2017).

Regarding the variables related to this increase in psychopathology and stress, insomnia was found to increase depressive symptoms and stress. This relationship is well established scientifically, since insomnia is considered a precedent for depression (Fang et al., 2019). Reduced physical activity and decreased exposure to sunlight, as well as increased use of electronic devices (mobile phones, television, computers, etc.) could affect circadian rhythms (Voitsidis et al., 2020). Thus, several studies have found that levels of insomnia rose in the general population during the COVID-19 pandemic (Huang and Zhao, 2020; Kokou-Kpolou et al., 2020; Rossi, 2020; Voitsidis et al., 2020). However, it is important to mention that the relationship between insomnia and stress can be bidirectional, so insomnia could increase stress levels, and stress could increase insomnia levels (Garefelt, 2020). On the other hand, having recently lost a loved one was also found to influence depressive symptom increases. This latter fact is highly coherent, as the emotions of sadness and depression are understood to be strongly associated with grief. Lastly, the fear of contagion by COVID-19 was found to increase phobic anxiety levels in this population. These results reflect that the steady increase in the number of deaths and infections caused by COVID-19, its serious threat to life and the uncertainty of the future due to lack of knowledge of the new disease and its evolution may have provoked fear among this population, thus increasing levels of specific phobia in response. Possibly as a method of self-protection (Wang et al., 2020).

Finally, the results of the study may have various explanatory factors. A number of previous studies have in fact demonstrated increases in psychological dysphoria,

anxiety and depression during pandemics (Taha et al., 2014; Wheaton et al., 2012). A possible explanation may be the population having to personally confront the situation in order to adapt to an unconventional context and its uncertain evolution. Thus, this sudden and abrupt change may have had direct consequences on the lifestyle of the Spanish and international population, radically restricting people's liberty to leave their homes and move freely (Cornwell and Laumann, 2015; Santini et al., 2020). For pregnant women, this may be an even greater source of anxiety and stress, since awareness of a direct biological connection to the foetus could lead to a higher state of alertness and self-protection (Wu, 2020). Moreover, concerns linked to the economic crisis deriving from the COVID-19 health crisis may affect pregnant women's future prospects of quality of life and the upbringing of their children, an uncertainty that could increase these depressive symptoms. In addition, the media's constant streaming (press, radio, television, etc.) of the severity and lethality of the virus may also play a key role in increasing symptoms of anxiety, depression and psychological dysphoria (Smith, 2020).

Regarding the study's limitations, it is worth mentioning that the psychological evaluation instruments used were limited to the psychological state experienced in the last month. It was not possible to follow-up on the participants' psychological health throughout the COVID-19 pandemic. This would have been of interest, as it would have allowed examining the psychological variances according to the different weeks of the pandemic. Besides, it would be interesting to study in which trimesters of pregnancy women are more vulnerable to stress and psychopathology for future interventions. In addition, in the future, it would be important to also evaluate the fathers' psychological states, to understand how the pandemic and lockdown may affect their psychological health. On the other hand, the fact that the two group of women were recruited through different means (the first through a provider, and the other through a provider and social

networks), and the use of some single-item variables used in the regression models are methodological limitation of this research. Therefore, the results should be interpreted with caution. Finally, it is important to note that the evaluation of Pandemic Group was carried out during the lockdown due to the COVID-19 pandemic in Spain. Therefore, it is possible that apart from the COVID-19 pandemic, the lockdown may have influenced the increase in the psychopathological symptoms and stress in the participants.

Conclusions

Pregnant women are particularly vulnerable to anxious and depressive symptomatology (Palladino et al., 2012; Woody et al., 2017) which, based on the results of this study, could increase in situations of pandemic and lockdown.

These results are compatible with studies that showed that pandemics were a precursor of an increase in psychopathological symptomatology and could affect pregnant women's mental health. In addition, the factors of insomnia, the recent loss of a loved one, and the fear of contagion by COVID-19 medium were found to predict an increase or decrease in this symptomatology. However, this is the only study in Spain that shows that pregnant women during the pandemic suffer more stress and psychopathology than pregnant women in the previous year, prior to the pandemic, highlighting which psychopathological symptoms are most affected, which gives us key information for the intervention.

To finish, the finding, in this study, that pregnant women's psychological health worsened during the COVID-19 pandemic reveals the need to encourage the use of psychological tools that have proven to be effective in reducing both stress and psychological discomfort in this population (Romero-Gonzalez et al., 2020). One such tool would be cognitive behavioural therapy.

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6.4 Artículo 4

Puertas-Gonzalez, J. A., Mariño-Narvaez, C., Romero-Gonzalez, B., & Peralta-Ramirez, M. I. (2021). Giving birth during a pandemic: From elation to psychopathology. *International Journal of Gynecology & Obstetrics*, *155*(3), 466-474. <https://doi.org/10.1002/ijgo.13803>

Giving birth during a pandemic: from elation to psychopathology

Abstract

Objective: Postpartum is a complicated period in a woman's life. Many psychological adaptations take place and women may be subject to psychological alterations during this period. In addition, women who gave birth during the COVID-19 crisis may show greater psychological vulnerability, due to the specific situation experienced during the pandemic. Therefore, the objective of this study was to compare the postpartum psychopathological symptoms of women who gave birth before the pandemic with those of women who had their baby during the pandemic.

Methods: A total of 212 women participated in the study, of which 96 gave birth before the pandemic and 116 during the pandemic. Psychopathological symptoms, postpartum depression, perceived stress and resilience were evaluated.

Results: Women who gave birth during the pandemic had higher scores on somatisations, obsessions and compulsions, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety and psychoticism. In addition, perceived stress was the common predictor of an increase in these symptoms.

Conclusion: The COVID-19 pandemic may have played a role in the increase in psychopathological symptoms after childbirth. Detecting possible symptoms postpartum plays a crucial role, because it allows intervening and preventing the development of psychopathologies. In addition, intervening to reduce perceived stress during pregnancy and postpartum could prevent the development of psychopathological symptoms.

Keywords: *COVID-19; postpartum; psychopathology; anxiety; depression, stress.*

Introduction

Postpartum brings about many transformations in a woman's life: changes in hormones and in the brain, as well as social and psychological modifications. One major change takes place in the brain: to ensure the newborn's survival and care, the brain increases its functional and structural plasticity [1]. In this line, it has been found that parts of women's brains related to threat detection, as well as emotional recognition, are more active in the postpartum period [2].

These adjustments in the brain are associated with emotional transformations, which make postpartum women more susceptible to psychological alterations. Postpartum is thus a critical period for the detection of such changes and for the prevention of psychopathological disorders [3].

In addition, it has also been found that before delivery, pregnant women show more symptoms of somatisations, phobic anxiety or paranoid ideation than non-pregnant women [4]. These results suggest that mothers possibly undergo some form of "psychological vulnerability" both during pregnancy and postpartum [1].

In a similar line, other studies have shown that events experienced during pregnancy and postpartum may be the precursors of more serious diseases [5].

Traumatic or unusual experiences, such as the current COVID-19 worldwide pandemic, may encourage the development of psychological disorders. In the light of this historical event, the psychological impact of the crisis on the population has been an object of study. It has been observed that, due to fear of contagion, the anxiety symptoms and stress levels have considerably risen among the population [6].

In the case of pregnant women, higher levels of stress, anxiety and depression have been found due to being exposed to the stressful life event of living through a

pandemic [7-8]. In the same way, various studies have explored postpartum depressive symptoms in women who gave birth during the pandemic and higher levels of postpartum depression were found [9]. However, these studies did not perform an in-depth examination of the wide range of psychopathological symptoms that women may present after childbirth.

Given the psychological repercussions of both giving birth and experiencing the pandemic, it has become all the more essential to study women's psychological health. Therefore, the objective of this study was to verify the psychological and emotional state of women who had their baby during the pandemic with respect to women who had given birth before it. The psychopathological symptoms of women who had their baby before the pandemic were compared with those who gave birth during their quarantine. Possible variables related to these symptoms were also verified.

Materials and Methods

Participants

A total of 240 women were recruited and consented to take part in the study. Of those, 212 women finally participated in this study ($n = 13$ did not fill any questionnaire out; $n = 10$ filled the questionnaires out after one month of delivery; $n = 5$ women had been diagnosed of one physical or psychological disease in the previous year). Their average age was 33.46 years ($SD = 4.35$). The inclusion criteria were: to be of legal age; to have given birth at some point before or after the State of Alert was decreed in Spain; to complete questionnaires within the first month after delivery; to read and write in Spanish; and to have an internet connection. The exclusion criteria were to suffer from physical or mental illness at the moment of having been diagnosed of any of them in the previous year.

All participants gave their informed consent before being included in the study. Their participation was voluntary, and the study was conducted in accordance with the Helsinki Declaration (World Medical Association, 2013) and the European Union Good Clinical Practice Directive (Directive 2005/28/EC). The protocol was approved by the Ethics Committee for Human Research of the University of Granada (reference code 1580/CEIH/2020 and reference number 881).

Instruments

First, sociodemographic variables were collected from the participants, as well as variables related to childbirth and the newborn. In addition, a psychological evaluation was conducted using the two evaluation instruments described next.

- The Symptom Checklist-90-Revised (SCL-90-R) [10]: It is a 90-item self-report inventory and items are scored using a 5-point Likert-type scale (1 = never and 5 = very often). It measures psychopathological symptomatology in nine dimensions (somatisation, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism) and three global indices of psychological distress. The Cronbach's alpha reliability coefficients of the Spanish version ranged between $.67 < \alpha < .94$ [10].

- Perceived Stress Scale (PSS) [11] is a self-report questionnaire which evaluates the perceived stress level in the previous month. Besides, it assesses the degree in which people find their lives unpredictable, uncontrollable or overcharged. It consists of 14 items scoring in a Likert-scale with four response alternatives. The Spanish version of the PSS (14 items) showed a high internal consistency = 0.81.

- Connor-Davidson Resilience Scale (CDRISC) [12]. It reflects the capacity to tolerate experiences such as change, personal problems, illness, pressure, failure, and

feelings of pain. The CD-RISC-10 consists of 10 items Likert scale with 5 response options. The CD-RISC-10 has a The Cronbach's alpha reliability coefficient of 0.85

- Edinburgh Postnatal Depression Scale (EPDS) [13]. This scale consists of 10 Likert items with 4 response options and is used to assess the risk of postpartum depression. Its reliability, in terms of internal consistency, is acceptable ($\alpha = 0.79$).

In addition, in the group of women who gave birth during pandemic, the following assessment tool was used, *Birth Satisfaction Scale-Revised (S-BSS-R)* [14]. The instrument consisted of 10 items with 5 Likert-type response options. Three subscales measured overall satisfaction with childbirth: stress during childbirth, personal attributes and quality of care. The instrument presented adequate internal reliability ($\alpha = 0.77$).

Procedure

First, prior to the pandemic, and coinciding with the Gestastress research protocol, women who had just given birth in Spanish hospitals were recruited. These women, who gave birth between March 2019 and February 2020, constituted the group of women who gave birth before the pandemic. The procedure for recruiting these women was as follows: they were informed of the study after giving birth, and those who agreed to participate filled in the informed consent form. At this point, the questionnaires were sent to them online, using Google forms (sociodemographic variables, SCL-90R, PSS, EDPS and CD-RISC), and they were given a maximum of one month to fill them in, according to the inclusion criteria.

Secondly, after the sudden onset of the pandemic, and following the declaration of a State of Alarm by the Spanish Government, participants continued to be recruited. However, those women who agreed to participate (through the procedure explained

above) were included in the group of women who gave birth during the pandemic (from 1 April 2020 to 1 July 2020).

This left two groups (women who gave birth before the pandemic vs. those who gave birth during the pandemic), in order to analyse the data obtained and the differences between the two.

Data analysis

A descriptive analysis (mean and standard deviation) was performed of the sample's main continuous variables, of a sociodemographic and obstetric nature. A frequency analysis was carried out for the remaining categorical variables.

In order to verify whether there were any significant differences in psychopathological symptoms between women who gave birth before and during the pandemic, a Student's t-test was performed: the dependent variables were the scores of the nine main dimensions of the SCL-90- R and postpartum depression score; and the independent variable was the moment of delivery (before or during the pandemic). Whether the woman was primiparous or not was included as a covariate.

Finally, to verify which psychological variables could predict psychopathological symptoms in women who gave birth during the pandemic, various hierarchical linear regression analyses were conducted, the dependent variables being the scores on the SCL-90-R subscales. The variables related to delivery were included in step 1 (gestational age at birth, being primiparous or not, vaginal or instrumental delivery and satisfaction with delivery), and in step 2, the predictive variables were the perceived stress and resilience (PSS, CD-RISC) scores. A collinearity diagnosis was performed to examine variable associations. Tolerance greater than 0.3 and a variance inflation factor below 10 indicate the absence of multicollinearity.

The analyses were carried out using the statistical package Statistical Program for Social Sciences (SPSS) version 26.0 for Windows (SPSS, Armonk, New York).

Results

Sample description

The total participant sample was divided into two groups: the first group consisted of 96 women (M = 32.96 years; SD = 3.97) who gave birth in the prepandemic period. The second group consisted of 116 women (M = 33.86 years; SD = 4.60) who gave birth during the pandemic.

Both groups were found to be even in relation to the main sociodemographic and obstetric history variables. Statistically significant differences were found between both groups, however, regarding whether they were primiparous or multiparous ($\chi^2 = 5.62$; $p = .018$) (Table 1).

Table 1. Description and comparison of the two groups in sociodemographic variables and obstetric history, in women who gave birth before and during the pandemic.

		Before pandemic (n = 96) M(SD)/n(%)	During pandemic (n = 116) M(SD)/n(%)	t/χ^2	p
Sociodemographic variables					
Age		32.96(3.97)	33.86(4.60)	.46	.13
Nationality	Spanish	77(83.7%)	86(74.1%)	2.76	.09
	Inmigrant	15(16.3%)	30(25.9%)		
Marital status	Married/cohabiting	91(98.9%)	109(94%)	3.39	.06
	Single/widow	1(1.1%)	7(6%)		
Level of education	No studies	1(1.1%)	-	1.49	.68
	Primary school	1(1.1%)	2(1.7%)		
	Secondary school	17(18.7%)	20(17.2%)		
	University	72(79.1%)	94(81%)		
Obstetric information					
Nulliparous	Yes	46(50%)	75(66.4%)	5.62	.018*
	No	46(50%)	38(33.6%)		
Delivery	Vaginal	63(64.3%)	77(66.4%)	.103	.748
	Instrumental	35(35.7%)	39(33.6%)		
Sex of baby	Male	43(44.8%)	59(50.9%)	.77	.37
	Female	53(55.2%)	57(49.1%)		
Gestational age		39.48(1.34)	39.06(1.79)	2.77	.06
Birthweight		3283.39(462.76)	3228.19(484.31)	.44	.39

Note: In some variables there are missing values, so N may not correspond to the corresponding one for each group. *Significance at $p < .05$

Differences in psychopathological symptoms and postpartum depression between women who gave birth before and during the pandemic

Mean comparison analyses showed statistically significant differences between the prepandemic group of women and the group of women who gave birth during the

pandemic in most SCL-90-R subscales, specifically for: somatisations, obsessions and compulsions, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety and psychoticism. In addition, all scores were higher in the group of women who gave birth during the pandemic, notably regarding obsessions and compulsions, presenting clinical scores over 70. The results are shown in Table 2.

Table 2. Mean differences in psychopathological symptoms among women who gave birth before and during the pandemic

	Before pandemic (n = 96)	During pandemic (n = 116)	F	p
SCL-90-R				
Somatisations	46.54(27.19)	59.86(26.84)	11.24	.001*
Obsessions and compulsions	46.71(32.43)	72.39(28.06)	33.52	.000*
Interpersonal sensitivity	40.18(34.87)	62.82(32.37)	21.92	.000*
Depression	41.47(30.06)	66.12(30.36)	32.31	.000*
Anxiety	39.74(30.42)	62.20(29.68)	26.52	.000*
Hostility	42.48(33.04)	55.79(32.84)	7.79	.006*
Phobic anxiety	40.97(36.01)	60.14(36.76)	12.05	.001*
Paranoid ideation	40.49(36.31)	48.65(36.64)	2.53	.113
Psychoticism	45.33(37.37)	57.74(37.14)	5.24	.023**
EPDS	7.78(4.75)	7.70(5.42)	.000	.983

Note: *Significance at $p \leq .01$ and ** $p \leq .05$

No differences were found for postpartum depression, with 26% (n = 25) displaying depressive symptomatology (score above 10 in EPDS) in the prepandemic group, compared to 28.4% (n = 33) in the case of the group who gave birth during the pandemic.

Predictive psychological variables of psychopathological symptoms in women who gave birth during the pandemic

Psychological variables were analysed as predictors of psychopathological symptoms, using hierarchical linear regression analysis. All models were significant after controlling for variables related to delivery (gestational age at birth, type of delivery, primiparous or not, and satisfaction with delivery). Furthermore, perceived stress was the only predictor variable for the following psychopathological symptoms: somatisations, obsession and compulsion, interpersonal sensitivity, anxiety, phobic anxiety, and psychoticism. In the case of depression, resilience was found as a predictor, along with perceived stress. Regarding hostility, the two predictors were perceived stress and being primiparous. These data can be consulted in Table 3.

Table 3. Hierarchical linear regression analyses for psychological variables as predictors of psychopathological symptoms.

				β	p	R-square	Increased R-square	F
Model 1 Dependent variable: Somatisations	Block 1	<i>Gestational age</i>	.100	.281	.080	.080	2.345	
		<i>Delivery</i>	.036	.712				
		<i>Primiparous</i>	-.012	.906				
		<i>S-BSS-R</i>	-.259	.010				
	Block 2	<i>Gestational age</i>	.127	.127	.254	.174	6.022*	
		<i>Delivery</i>	.031	.732				
		<i>Primiparous</i>	.026	.774				
		<i>S-BSS-R</i>	-.062	.533				
		<i>Perceived stress</i>	.453	.000				
		<i>Resilience</i>	-.070	.413				
Model 2 Dependent variable: Obsessions and compulsions	Block 1	<i>Gestational age</i>	-.026	.780	.079	.079	2.314	
		<i>Delivery</i>	-.038	.698				
		<i>Primiparous</i>	-.087	.374				
		<i>S-BSS-R</i>	-.295	.003				
	Block 2	<i>Gestational age</i>	.010	.907	.285	.206	7.045*	
		<i>Delivery</i>	-.039	.661				
		<i>Primiparous</i>	-.054	.543				
		<i>S-BSS-R</i>	-.074	.443				
		<i>Perceived stress</i>	.503	.000				
		<i>Resilience</i>	-.015	.859				
Model 3 Dependent variable: Interpersonal sensitivity	Block 1	<i>Gestational age</i>	.018	.846	.106	.106	3.194**	
		<i>Delivery</i>	.135	.226				
		<i>Primiparous</i>	-.117	.165				
		<i>S-BSS-R</i>	-.279	.005				
	Block 2	<i>Gestational age</i>	.059	.463	.306	.238	9.235*	
		<i>Delivery</i>	.137	.106				
		<i>Primiparous</i>	-.084	.320				
		<i>S-BSS-R</i>	-.041	.659				
		<i>Perceived stress</i>	.542	.000				
		<i>Resilience</i>	.010	.902				
Model 4 Dependent variable: Depression	Block 1	<i>Gestational age</i>	.031	.741	.091	.091	2.695**	
		<i>Delivery</i>	.100	.306				
		<i>Primiparous</i>	-.109	.266				
		<i>S-BSS-R</i>	-.272	.006				
	Block 2	<i>Gestational age</i>	.066	.363	.464	.374	15.321*	
		<i>Delivery</i>	.089	.245				
		<i>Primiparous</i>	-.050	.512				
		<i>S-BSS-R</i>	.011	.894				
		<i>Perceived stress</i>	.653	.000				
		<i>Resilience</i>	-.141	.049				
Model 5 Dependent variable: Anxiety	Block 1	<i>Gestational age</i>	-.043	.643	.087	.087	2.566**	
		<i>Delivery</i>	.029	.521				
		<i>Primiparous</i>	-.063	.764				
		<i>S-BSS-R</i>	-.292	.003				
	Block 2	<i>Gestational age</i>	-.009	.909	.334	.247	8.861*	

			<i>Delivery</i>	.024	.815			
			<i>Primiparous</i>	-.020	.775			
			<i>S-BSS-R</i>	-.055	.554			
			<i>Perceived stress</i>	.543	.000			
			<i>Resilience</i>	-.068	.397			
Model Dependent Hostility	6	Block 1	<i>Gestational age</i>	-.075	.417	.100	.100	3.004*
			<i>Delivery</i>	.051	.597			
			<i>Primiparous</i>	-.218	.026			
			<i>S-BSS-R</i>	-.273	.006			
		Block 2	<i>Gestational age</i>	-.051	.547	.278	.177	6.786*
	<i>Delivery</i>		.043	.624				
	<i>Primiparous</i>		-.177	.047				
	<i>S-BSS-R</i>		-.078	.424				
	<i>Perceived stress</i>		.450	.000				
	<i>Resilience</i>		-.097	.249				
Model Dependent Phobic anxiety	7	Block 1	<i>Gestational age</i>	-.093	.329	.042	.042	1.179
			<i>Delivery</i>	.041	.686			
			<i>Primiparous</i>	-.027	.789			
			<i>S-BSS-R</i>	-.170	.092			
		Block 2	<i>Gestational age</i>	-.063	.480	.173	.131	3.695*
	<i>Delivery</i>		.041	.663				
	<i>Primiparous</i>		-.001	.991				
	<i>S-BSS-R</i>		.006	.951				
	<i>Perceived stress</i>		.402	.000				
	<i>Resilience</i>		-.002	.985				
Model Dependent Psychoticism	8	Block 1	<i>Gestational age</i>	-.065	.482	.091	.091	2.703**
			<i>Delivery</i>	.078	.407			
			<i>Primiparous</i>	-.081	.424			
			<i>S-BSS-R</i>	-.276	.005			
		Block 2	<i>Gestational age</i>	-.028	.734	.312	.221	7.999*
	<i>Delivery</i>		.078	.366				
	<i>Primiparous</i>		-.046	.592				
	<i>S-BSS-R</i>		-.048	.614				
	<i>Perceived stress</i>		.521	.000				
	<i>Resilience</i>		-.012	.883				

Note: Delivery (vaginal or instrumental); S-BSS-R = Birth Satisfaction Scale Revised; *Significance at $p < .01$ and ** $p < .05$

Discussion

The objective of this study was to verify the psychological and emotional status of women who have given birth during a pandemic. To do this, we first verified whether

any differences could be found in a range of psychopathological symptoms between women who had given birth before and during the pandemic. We subsequently checked that birth and psychological variables were related to, or acted as, predictors of such psychopathological symptoms.

Our results indicate that women who had given birth during the pandemic presented more psychopathological symptoms than those who had given birth during the prepandemic period, specifically: somatisations, obsessions and compulsions, interpersonal sensitivity, anxiety, depression, hostility, phobic anxiety and psychoticism.

Some authors have shown that, during this pandemic, women consider postpartum as a period that involves even more challenges than before; this perception can lead to psychological stress and make women more vulnerable to emotional disturbances. It can also reduce their psychological well-being [15]. In addition, various studies have shown that levels of stress and depression increased during pregnancy as a result of the pandemic [8,16]. Moreover, a woman's concerns about the pandemic and everything around her, such as fear of contagion, being alone during childbirth, or possible vertical transmission to the foetus, simply contribute to the development of these anxiety symptoms [17].

Other psychopathological symptoms such as obsessions, compulsions and phobic anxiety are equally more widespread in the current situation, characterised by excessive hygiene and fear of contagion [18]. The latter, coupled with the fact that during postpartum, the likelihood of suffering obsessions and compulsions increases twofold, could explain the differences found and the growth in symptomatology [19]. However, it should be noted that the scores found in this study exceeded, on average, the 70th percentile. This latter psychopathological dimension thus presented clinical scores, with all its therapeutic implications.

As far as somatisations are concerned, they increased during pregnancy, due to the complex emotional and physiological processes proper to gestation [4]. Although the role of postpartum somatisations is currently unknown, they have been found to increase in different population samples. Therefore, it would be unsurprising if they were found to increase after childbirth as a result of the pandemic [20].

Finally, symptoms such as interpersonal sensitivity, hostility and psychoticism can be explained by the social restrictions imposed on the population [9]. The pandemic's side effects include rise in individualism and loneliness derived from a halt to social relations. These latter side effects may lead to accentuating this type of symptomatology [21]. In addition, the pregnancy's own evolutionary perspective means that the mother is capable of detecting threats in the environment to protect her baby, and reject anyone outside her "group", which may exacerbate the symptoms described at the same time [4,22].

As far as postpartum depression is concerned, no difference was found between the two groups in our study. One possible explanation is that this problem presents a high incidence during postpartum anyway, making it unlikely to detect differences in symptomatology [23]. Some authors have reported a rise in these depressive symptoms [24]. However, the fact of failing to find any differences shows us that women are vulnerable to postpartum depression no matter the moment during which it is experienced, and the first signs of the disease must be addressed.

Most of these psychopathological symptoms, which were more widespread in women who gave birth during the pandemic, shared a common predictor variable: that of perceived stress. Stress is one of the psychological problems that has increased the most during this pandemic. And unsurprisingly, because the unpredictability of the situation added to a sense of low personal control over it are factors that increase stress levels [25].

In addition, other authors have found that during pregnancy, perceived stress is also a predictor of psychopathology [4]. Resilience, a very important pregnancy variable, equally seems to be a possible predictor and could dampen the severity of psychopathological symptoms [26]. This is a very significant finding because it allows us to focus on the levels of perceived stress when preparing interventions directed towards pregnant woman's psychological health and the postpartum stage.

A limitation of this study is the fact that the sample was exclusively composed of Spanish women. This restricts the possibility of generalising the results, as they can only be attributed to women who experienced the pandemic in Spain. Nevertheless, given the pandemic's global nature, similar results are likely to be found in other countries.

To conclude, the results of this study highlight the delicate period women endure around childbirth, and such conditions have been aggravated by a pandemic. The COVID-19 pandemic has affected the whole world, and these women, who have to live through the extremely important life process of childbirth, have increased psychopathological symptoms. In this way, it has become essential to work on psychopathological symptoms during pregnancy, to alleviate the effects and their exacerbation after childbirth. Especially now, when we live in a world that generates uncertainty and fear. In addition, assessing the perceived stress that women experience constitutes an essential step. Indeed, early detection leads to timely intervention and provides women the support and tools they need to help them cope.

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6.5 Artículo 5

Puertas-Gonzalez, J. A., Mariño-Narvaez, C., Romero-Gonzalez, B., Vilar-López, R., & Peralta-Ramirez, M. I. (2022). Resilience, stress and anxiety in pregnancy before and throughout the pandemic: a structural equation modelling approach. *Current Psychology*, 1-11. <https://doi.org/10.1007/s12144-022-03305-6>

Resilience, stress and anxiety in pregnancy before and throughout the pandemic: a structural equation modelling approach

Abstract

The present study explored and compared the link between resilience and pregnancy-related stress, perceived stress, and anxiety, employing two structural equation models. One model focused on pregnant women before the outbreak of the pandemic, and the other on pregnancies throughout the pandemic. For this purpose, a total sample of 690 women during their pregnancy were collected: the Pre-Pandemic Group (P-PG) was composed of 341 pregnant women evaluated prior to the pandemic; and 349 pregnant women assessed at the time of the pandemic constituted the Pandemic Group (PG). The resilience, pregnancy-related stress, perceived stress, and anxiety symptomatology of the women were assessed. For both samples, resilience was found to lower levels of pregnancy-specific stress, as well as general perceived stress, and anxiety symptomatology. Furthermore, pregnancy-specific stress and perceived stress showed a covariance relationship and, that these, in turn, increased the anxiety. Moreover, the PG showed greater levels of pregnancy-specific stress, anxiety, somatisations, and obsessions-compulsions, while the P-PG presented higher perceived stress levels.

Keywords: *SEM; pandemic; COVID-19; pregnancy; resilience; stress; anxiety.*

Introduction

Due to COVID-19, a worldwide pandemic was announced to start in the month of March 2020 (WHO, 2020). Because of the health threat, economic ramifications, and disruption of everyday routines, the COVID-19 has had an enormous impact on individuals and can be considered a worldwide stressor. In addition to the death toll, the pandemic has caused widespread agitation and concern among the general population, due to fears of contagion and its consequences, bringing about a rise in various psychopathological symptoms such as anxiety (Wang, et al., 2020).

A particularly vulnerable population group is pregnant women. Indeed, their levels of pregnancy-specific stress, as well as general stress and anxiety were found to have increased (Boekhorst et al., 2021; Lebel et al., 2020; Medina-Jimenes et al., 2020; Romero-Gonzalez et al., 2021). Pregnancy-related stress with general stress has a strong comorbidity during pregnancy (Alderdice et al., 2021; Romero-Gonzalez, et al., 2020a), and were also shown to be predictors of psychopathological symptomatology, including anxiety, at various times during pregnancy, before and at the time of the pandemic (Moyer et al., 2020; Peñacoba-Puente et al., 2016; Romero-Gonzalez, et al., 2020a). This symptomatology, when suffered persistently throughout pregnancy, raises the probability of developing postpartum depression, as well as the risk of preeclampsia and hypertension, miscarriages, the need for instrumented deliveries, preterm births, low birth weight and low scores on the Apgar test (Accortt et al., 2015; Bayrampour et al., 2016; Caparros-Gonzalez et al., 2017; Coussons-Read, 2013; Grigoriadis et al., 2018; Qu et al., 2017; Rondo et al., 2003; Romero-Gonzalez et al., 2019; Stein et al., 2014). Moreover, those symptoms could impact on the mother's state of mind and on the development of the foetus because they can lead to alterations regarding physical activity, nutrition and sleep (Coussons-Read, 2013). Furthermore, Offspring of women that experience large

amounts of stress at the time of their pregnancy have a greater likelihood of developing both cognitive and behavioural deficits, and an increased likelihood of suffering from mental health problems further on in life (Glover, 2014; MacKinnon et al., 2018; Van den Bergh et al., 2017; Van den Bergh, Dahnke & Mennes, 2018).

Given such negative consequences, resilience acts as an important buffer against psychological distress both in the population in general (Oken et al., 2015), and in women during their pregnancy (García-León et al., 2019). Resilience indeed represents an individual's set of personal resources allowing them to optimally face stressors and difficulties (Fletcher & Sarkar, 2013; Newman, 2005). Thus, several investigations have discovered a negative association between resilience and anxiety during pregnancy (Lubian Lopez, et al., 2021), and between resilience towards stress and anxiety in other populations at the time of the pandemic (Braun-Lewensohnet al., 2021; Satici et al., 2020; Wang et al., 2021). Additionally, previous researches carried out before the pandemic have proven the protective role of resilience regarding these variables in the perinatal stage (Armans et al., 2020; García-León et al., 2019).

Nevertheless, to date no study has analysed and compared resilience's position as a buffer for psychological stress and anxiety in pregnant women at two different moments in time: before society faced a devastating event such as the COVID-19 pandemic, and when it erupted. Hence, the purpose of this investigation was to explore and compare the link of resilience to general perceived stress, pregnancy-specific stress and anxiety, and to study the relationships of these variables, using two structural equation models. The first model focused on pregnant women before the pandemic, and the second on women that were pregnant at the time of the COVID-19.

The first hypothesis of the structural equation models is that resilience negatively influences pregnancy-related stress, and also perceived stress and anxiety symptomatology.

A second hypothesis is that pregnancy-related stress and perceived stress present a correlation and these, in turn, positively influence anxiety symptomatology.

Finally, if the hypothesised models present a good fit, the variables included in the samples will be compared to check whether any differences exist, or whether, on the contrary, these variables are similar.

Methods

Participants

The sample was composed of 690 pregnant women, which were split into two different subgroups: Pre-Pandemic Group (P-PG), formed by 341 (49.4%) pregnant women evaluated before the COVID-19 pandemic (mean age = 33.35, SD = 4.53), and Pandemic Group (PG), made up of 349 (49.6%) pregnant women assessed throughout the pandemic (mean age = 33.9, SD = 4.15).

All participants of the research were briefed on the procedure and objectives and participated on a voluntary basis. The following were the conditions for participating in the study: knowing how to write and read properly in Spanish; being at least 18 years old; and being pregnant. On the other hand, the exclusion criterion was active treatment with psychopharmaceuticals.

The present research was approved by the ethics board committee of the University of Granada (reference 881; and reference 1518/CEIH/2020).

Instruments

Obstetric and socio-demographic variables were gathered and, in parallel, the subsequent psychological assessment tools were applied:

- The Connor-Davidson Resilience Scale (CD-RISC) (Connor & Davidson, 2003) in the Spanish abbreviated form (Notario-Pacheco et al., 2014): it was employed to estimate this variable. It measures the ability to deal with different life circumstances such as diseases, changes, stress, failures, personal difficulties and feelings of grief. It is responded on a Likert scale with five alternatives from 0 = "almost never" to 4 = "almost always", and is composed as a set of 10 items. The Cronbach's alpha was 0.88 in this research.

- The Perceived Stress Scale (PSS) (Cohen et al., 1983; Spanish validation by Remor, 2006): this instrument reports on perceived general stress in the past month. PSS provides scores between 0 and 56 (greater ratings indicate greater perceived stress) and it is made up of fourteen items scored on a five-point Likert scale ("very often", "often", "once in a while", "almost never", "never"). Its Cronbach's alpha was 0.73 in this research.

- The Prenatal Distress Questionnaire (PDQ) (Yali & Lobel, 1999; Spanish validation by Caparros-Gonzalez et al., 2019): the PDQ consists of a scale of 12 items for evaluating pregnancy-related stress (g., worries regarding health problems, childbirth, body symptoms, corporal alterations and/or the baby's general health). The answers of this instrument are provided through a Likert-type scale from 0 = "not at all" to 4 = "very much". Its Cronbach's alpha was 0.77 in this study.

- The Symptom Checklist-90-Revised (SCL-90-R) (Derogatis, 1994; Spanish validation by Caparros-Caparros et al., 2007): were applied to measure the level of anxiety symptoms. Specifically, the scales in this instrument assessing anxiety disorders

are the obsessions and compulsions dimension, the anxiety dimension and the phobic anxiety dimension. These use a Likert scale with five answer alternatives from 0 = “never” to 4=” extremely”. In addition, we added the somatisation scale because of their link with anxiety and the other measures included in the models. Thus, some studies have shown that COVID-19 has enhanced somatisations along anxiety in the population as a whole (Wang et al., 2020), while other pre-pandemic research focusing on pregnant women found correlations between resilience and stress with somatisations and anxiety (García-León et al., 2019; Scharlau et al., 2018). The four dimensions had an acceptable reliability, the Cronbach’s alpha ranging from 0.75 to 0.84 for all four dimensions in this study.

Procedure

The two groups of participants in this research were enlisted at the San Cecilio University Hospital and at the Góngora and Mirasierra health centres in Granada, Spain. When potential participants went to their appointment with the midwife for their pregnancy follow-up, they were provided with study information and were offered the possibility to participate in the research. Subsequently, the contact information of the women that agreed their participation in the research were collected and the survey questionnaires were submitted to them online. The questionnaires were all with Google Forms. At that time, they were also asked to inform us of any potential persons interested in participating to include them in the study.

The P-PG participants were recruited and evaluated between late 2017 and early 2020, as they formed part of an earlier research study entitled Gestastress. In addition to the recruitment via their medical practitioners, PG members were also captured through several social media networks of pregnant women (via internet forums, WhatsApp and Facebook) and assessed between March 2020 and March 2021 at the time of the

pandemic. Other studies have used two groups from different years to evaluate the worldwide pandemic disease's impact on prenatal mental health (Puertas-Gonzalez, et al., 2021; Sanardo et al., 2020).

Data analysis

First, the two groups were compared to examine if they were evenly homogeneous in relation to primary sociodemographic and obstetrical characteristics. For continuous variables, t-test was applied while the Chi-square test was performed in order to analyse qualitative variables.

Subsequently, with the aim of checking whether the latent variable presented an adequate goodness-of-fit for constituent factors (anxiety, phobic anxiety, somatisation and obsessive-compulsive) in both groups, a preliminary confirmatory factor analysis (CFA) has been carried out. The factor load for each factor was set to at least 0.50, in order to ensure a good fit (Hair et al., 1998). Additionally, before carrying out the Structural Equation Modelling (SEM), zero-order correlations were also calculated between all variables in the model were also calculated.

Then, the SEM was performed with the Maximum Likelihood Estimator (ML), considering the appropriate statistical requirements to be fulfilled to guarantee a good model fit. Thus, for both models, cut-off points for the comparative fit index (CFI) and the Tucker-Lewis index (TLI) were set at > 0.95 . While for the standardised root mean square residual (SRMR) was set at < 0.08 and for the root mean square error of approximation (RMSEA) was also set at < 0.08 (Hu & Bentler, 1999).

Finally, both groups were compared in relation to the psychological variables measured. In addition, for continuous variables in which statically significant discrepancies were identified, the effect size was calculated on the basis of Cohen's *d*,

and then interpreted according to values proposed by Cohen (1988): large effect size (≥ 0.80); medium (≥ 0.50); and, finally, small (≥ 0.20).

For the CFA and SEM analysis, the software R 4.0.1 (R Core Team, 2020) was used, implementing the “lavaan” package (Rosseel, 2012).

Results

Sample description

Of the 341 participants who formed the P-PG, 20 (5.9%) were in their first trimester of pregnancy (weeks 1-12), 175 (51.3%) in their second trimester (weeks 13-26), and 146 (42.8%) in their third trimester (weeks 27-40). In turn, of the 349 participants in the PG group, 32 (9.3%) were in the 1st trimester of gestation, 167 (47.9%) in the 2nd, and 150 (43%) in the 3rd. No significant differences were found regarding the P-PG and PG for the primary socio-demographic and obstetric variables. These results are set out in Table 1.

Table 1. Analysis of obstetric and socio-demographic variables.

		P-PG (n = 341) M(SD)	PG (n = 349) M(SD)	<i>t</i>	<i>p</i>
Age of participants		33.35 (4.53)	33.96 (4.15)	1.836	.067
		P-PG (n = 341) n(%)	PG (n = 349) n(%)	χ^2	<i>p</i>
<i>Socio-demographic characteristic</i>					
Current partner	No	8 (2.3%)	14 (4%)	1.550	.213
	Yes	333 (97.7%)	335 (96%)		
Nationality	Spanish	293 (85.9%)	305 (87.4%)	1.364	.505
	Inmigrant	48 (14.1%)	44 (12.6%)		
Education level	Primary school	5 (1.5%)	2 (0.6%)	3.892	.143
	Secondary school	95 (27.9%)	80 (22.9%)		
	University	240 (70.6%)	267 (76.5%)		
<i>Obstetric information</i>					
Trimester of pregnancy	1°	20 (5.9%)	32 (9.2%)	2.918	.232
	2°	175 (51.3%)	167 (47.9%)		
	3°	146 (42.8%)	150 (43%)		
Pregnancy method	Spontaneous	298 (87.4%)	309 (88.5%)	.215	.643
	Fertility treatment	43 (12.6%)	40 (11.5%)		
Previous miscarriages	0	202 (59.6%)	228 (65.3%)	8.921	.063
	1	76 (22.3%)	84 (24.1%)		
	2	40 (11.7%)	25 (7.2%)		
	3	13 (3.8%)	6 (1.7%)		
	≥4	10 (2.9%)	6 (1.7%)		
Previous children	0	192 (56.3%)	207 (59.3%)	5.521	.063
	1	118 (34.6%)	126 (36.1%)		
	≥2	31 (9.1%)	16 (4.6%)		
Primiparous	No	179 (52.5%)	160 (45.8%)	3.049	.081
	Yes	162 (47.5%)	189 (54.2%)		
Risk pregnancy	No	274 (80.4%)	274 (84.2%)	1.792	.181
	Yes	67 (19.6%)	55 (15.8%)		

Note: P-PG = Pre-Pandemic Group; PG = Pandemic Group.

Confirmatory factor analysis results

For each group, a CFA analysis was conducted to check whether the latent variable of anxious symptomatology showed adequate goodness of adjustment in terms of the all factors that comprise it (anxiety, phobic anxiety, somatisation and obsessive-compulsive). In relation to P-PG, the CFA showed an acceptable fit for anxiety symptomatology: $\chi^2 = 6.032$ with 2 degrees of freedom ($p = .049$); CFI = 0.99; TLI = 0.96; RMSEA = 0.07 (90% CI: 0.04, 0.15; $p = .195$); SRMR = 0.02. With regard to PG a good fit was also obtained: $\chi^2 = 1.215$ with 2 degrees of freedom ($p = .545$); CFI = 1.00; TLI = 1.01; RMSEA = 0.01 (90% CI: 0.01, 0.09; $p = .763$); SRMR = 0.01. In both groups with standardized factor loadings for the four variables > 0.50 . Therefore, the latent variable of anxiety symptomatology met the criteria for inclusion in the models for both groups. Moreover, all observable variables were also subjected to zero-order correlations (Figure 1).

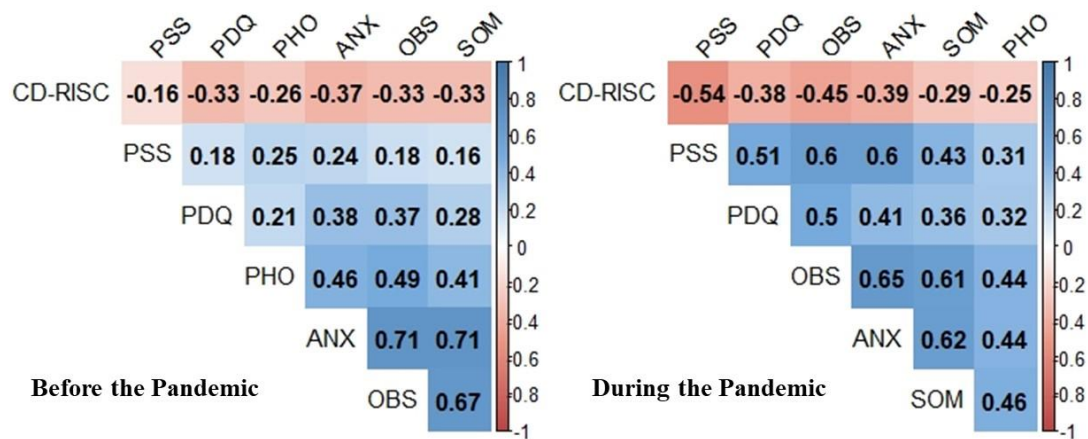


Figure 1. Zero-ordered correlations for all observable variables in the models of both groups.

Note: Significant correlations at $p < .05$ are highlighted in red (negative) or blue (positive); CD-RISC = Connor Davidson Resilience Scale; PSS = Perceived Stress Scale; PDQ = Pregnancy Distress Questionnaire.; ANX = SCL-90-R Anxiety Dimension; OBS = SCL-90-R Obsession-Compulsion Dimension; SOM = SCL-90-R Somatization Dimension; PHO = SCL-90-R Phobic Anxiety Dimension.

Structural equation modelling results

In relation to the P-PG, the SEM model proposed presented a good adjustment: $\chi^2 = 20.020$ with 11 degrees of freedom ($p = .045$); CFI = 0.99; TLI = 0.98; RMSEA = 0.05 (90% CI: 0.01, 0.08); SRMR = 0.03. Resilience variable was shown to be negatively associated with anxiety symptoms ($\beta = -0.29$; SE = 0.07; $p = .001$). Furthermore, anxiety symptoms were positively influenced by perceived stress ($\beta = 0.15$; SE = 0.06; $p = .003$) and pregnancy-specific stress ($\beta = 0.29$; SE = 0.07; $p = .001$). In turn, resilience negatively influenced perceived stress ($\beta = -0.16$; SE = 0.06; $p = .004$) and pregnancy-specific stress in the SEM ($\beta = -0.33$; SE = 0.05; $p = .001$). Moreover, the perceived stress and the pregnancy-specific stress presented a significant correlation ($\phi = 0.13$; SE = 0.05; $p = .017$). Finally, resilience indirectly negatively influenced anxiety symptomatology through perceived stress ($\beta = -0.05$; SE = 0.02; $p = .012$), as well as through pregnancy-specific stress ($\beta = -0.10$; SE = 0.03; $p = .001$). Thus, this model explained 28% of the variance, through R^2 , of anxious symptomatology in pregnancy prior the COVID-19 (Figure 2 and Table 2).

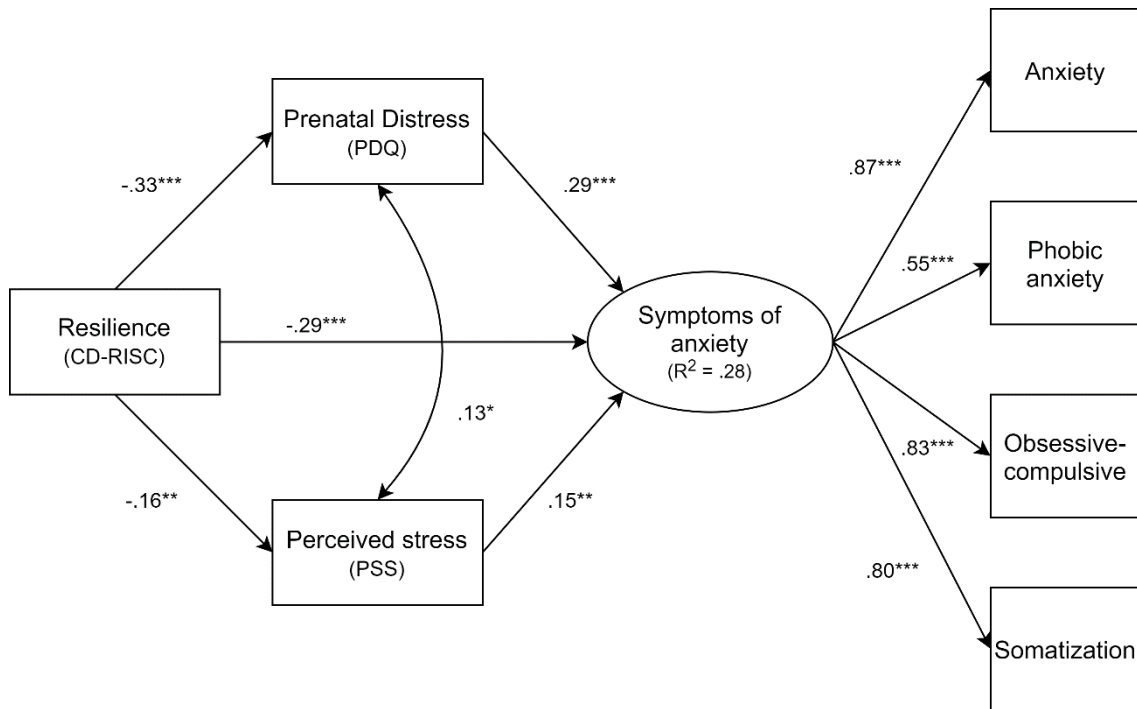


Figure 2. Structural equation model with standardized path coefficients predicting anxiety symptomatology in the Pre-Pandemic Group. The statistical values of the latent variable anxiety symptomatology correspond to the standardized factor loadings of the indicators.

Note: *** $p < .001$; ** $p < .01$; * $p < .05$

Table 2. Results of structural equation modelling.

Model	β/φ	SE	<i>p</i>	χ^2	df	CFI	TLI	RMSEA	SRMR	R ²
<i>Model 1: Pre-Pandemic Group</i>										
CD-RISC → PDQ	-0.33	0.05	.001**	20.020	11	0.99	0.98	0.05	0.03	0.28
CD-RISC → PSS	-0.16	0.06	.004**							
CD-RISC → Anxiety	-0.29	0.07	.001**							
PDQ ↔ PSS	0.13	0.05	.017*							
PDQ → Anxiety	0.29	0.07	.001**							
PSS → Anxiety	0.15	0.06	.003**							
CD-RISC → PDQ → Anxiety	-0.10	0.03	.001**							
CD-RISC → PSS → Anxiety	-0.05	0.02	.012*							
<i>Model 2: Pandemic Group</i>										
CD-RISC → PDQ	-0.38	0.05	.001**	31.574	11	0.98	0.96	0.07	0.03	0.54
CD-RISC → PSS	-0.55	0.04	.001**							
CD-RISC → Anxiety	-0.18	0.08	.023*							
PDQ ↔ PSS	0.38	0.04	.001**							
PDQ → Anxiety	0.24	0.08	.001**							
PSS → Anxiety	0.51	0.09	.001**							
CD-RISC → PDQ → Anxiety	-0.05	0.03	.030*							
CD-RISC → PSS → Anxiety	-0.06	0.04	.026*							

Notes: * = $\leq .05$; ** = $p \leq .01$; SE = standard error; CD-RISC = The Connor-Davidson Resilience Scale; PDQ = The Pregnancy Distress Questionnaire; PSS = The Perceived Stress Scale.

With respect to the PG, the SEM model also presented a good fit: $\chi^2 = 31.574$ with 11 degrees of freedom ($p = .001$); CFI = 0.98; TLI = 0.96; RMSEA = 0.07 (90% CI: 0.05, 0.10; $p = .093$); SRMR = 0.03. Anxiety symptoms were negatively influenced by resilience ($\beta = -0.18$; SE = 0.08; $p = .023$) and positively by perceived stress ($\beta = 0.51$; SE = 0.09; $p = .001$) and pregnancy-specific stress ($\beta = 0.24$; SE = 0.08; $p = .001$). Moreover, resilience presented a negative influence on the perceived stress variable ($\beta = -0.55$; SE = 0.04; $p = .001$) and pregnancy-specific stress ($\beta = -0.38$; SE = 0.05; $p = .001$). The latter in turn showed a significant correlation ($\phi = 0.38$; SE = 0.04; $p = .001$). Finally, resilience negatively influenced anxiety symptomatology indirectly for perceived stress ($\beta = -0.06$; SE = 0.04; $p = .026$) and pregnancy-specific stress ($\beta = -0.05$; SE = 0.03; $p = .030$). Overall, this model explained 54% of the variance, through R^2 , of the anxious symptoms in pregnancy at the time of the pandemic (Table 2 and Figure 3).

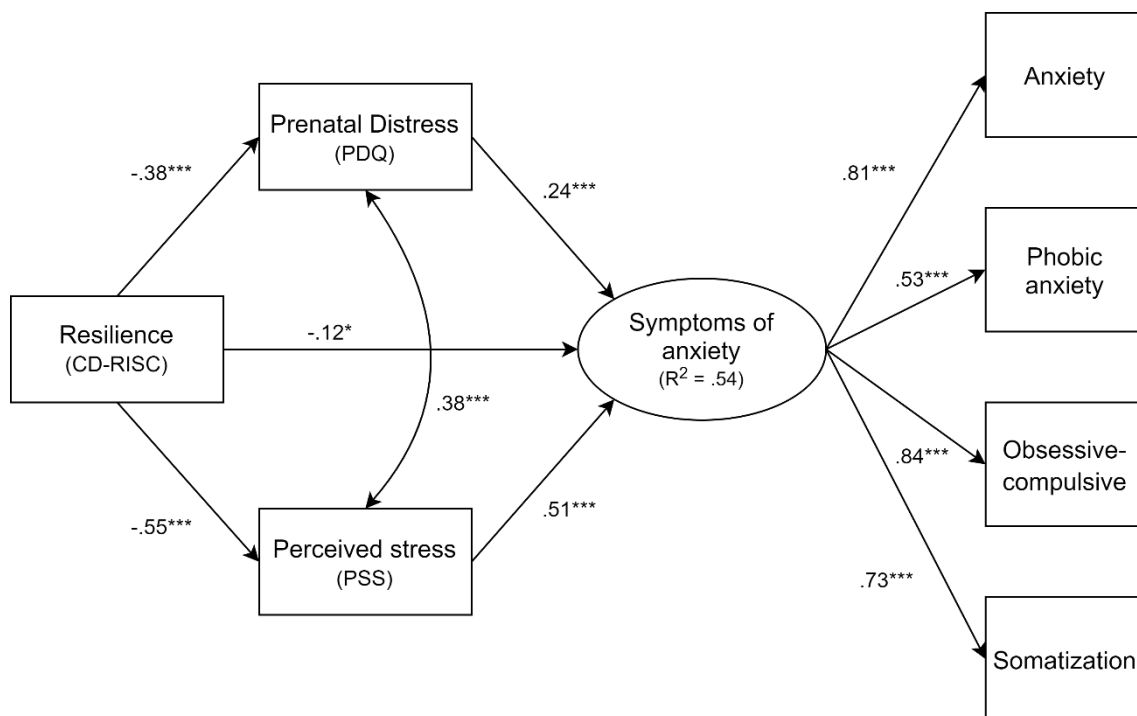


Figure 3. Structural equation model with standardized path coefficients predicting anxiety symptomatology in the Pandemic Group. The statistical values of the latent variable anxiety symptomatology correspond to the standardized factor loadings of the indicators. *Note:* *** $p < .001$; ** $p < .01$; * $p < .05$

Differences in resilience, anxiety symptomatology and stress between groups

The comparative analysis between groups using *Student's t* showed statistically significant differences regarding the SCL-90-R dimensions: obsession-compulsion [$t(688) = 2,589; p = .010; d = 0.20$], anxiety [$t(679) = 3.059; p = .002; d = 0.23$] and somatisations [$t(688) = 2.676; p = .008; d = 0.20$]. In addition, statistically significant differences were found for pregnancy-specific stress [$t(681) = 5,323; p = 0.001; d = 0.41$] and perceived stress [$t(504) = -4.808; p = 0.001; d = 0.36$]. PG scored higher in all the above variables except for perceived stress, where it scored lower than the P-PG. However, there were no significant differences regarding P-PG and PG on either the resilience variable or the phobic anxiety. These results are set out in Table 3.

Table 3. Comparison of means of psychological variables by Student's t-test.

	P-PG (n = 341) M(SD)	PG (n = 349) M(SD)	<i>t</i>	<i>p</i>	Cohen's d
CD-RISC	28.14 (5.87)	27.58 (6.55)	-1.194	.233	0.09
PSS	26.45 (4.40)	23.83 (9.16)	-4.808	.001**	0.36
PDQ	14.54 (6.18)	17.22 (6.99)	5.323	.001**	0.41
SCL-90-R Anxiety	62.79 (29.28)	69.32 (26.71)	3.059	.002**	0.23
SCL-90-R Phobic anxiety	57.10 (35.99)	60.51 (34.74)	1.267	.206	0.10
SCL-90-R Obsession- compulsion	68.06 (26.90)	73.23 (25.55)	2.589	.010**	0.20
SCL-90-R Somatisation	61.44 (25.05)	66.52 (24.88)	2.676	.008*	0.20

Note: * = $\leq .05$; ** = $p \leq .01$; P-PG = Pre-Pandemic Group; PG = Pandemic Group; CD-RISC = The Connor-Davidson Resilience Scale; PDQ = The Pregnancy Distress Questionnaire; PSS = The Perceived Stress Scale.

Discussion

The objective was to examine and compare the association between pregnancy-related stress, anxiety and resilience in pregnant women. For this aim, two structural equation models were carried out, one with participants prior to the pandemic and the other with women whose pregnancies occurred during the pandemic. Two hypotheses were raised. According to the first, resilience would negatively influence perceived stress and pregnancy-related stress as well as anxiety symptomatology in both groups. The second hypothesis was that, in turn, perceived stress and pregnancy-specific stress would show a positive relationship with anxiety symptomatology, and the latter would present a covariance relationship. This hypothesis was fulfilled, since all the relationships

proposed at the beginning were found in both groups, based on the two structural equations models.

In relation to the information provided by the structural equations model during the pandemic, resilience was found to present a negative relationship with anxiety during pregnancy. These findings support those presented by Lubian Lopez et al. (2021), in which they found the same negative relationship in pregnant women. In addition, it is worth mentioning that our results are in line with those of other authors who used structural equations models during the pandemic in other populations. Thus, they are consistent with the results of Wang et al., 2021, which found a direct negative relationship of resilience to stress and anxiety in a sample of medical personnel in a hospital in Wuhan, Hubei Province's provincial capital (China)—the location of the first outbreak of COVID-19. They also support the results of Rodríguez-Hidalgo et al. (2020), who showed a direct relationship between stress and anxious symptoms in university students throughout the COVID-19, again through a structural equation model. Therefore, the results demonstrate how resilience plays a protective role in pregnant women in times of crisis in the face of stress, pregnancy worries and anxiety symptomatology during the pandemic. This may be because resilience is defined as the psychological resources that allow a person to cope optimally with changes and adversities (Fletcher & Sarkar, 2013; Newman, 2005), and resilient people would present more adaptive coping. In turn, a deficit in personal resources for coping with adversity would lead to greater levels of psychological distress, leading to a sub-optimal adaptation to changes arising from the pandemic, such as lockdowns or mobility restrictions. These results imply that resilience can prevent the long-term negative effects of psychological stress and long-term anxiety, such as postpartum depression or the baby's low birth weight (Caparros-Gonzalez et al., 2017; Coussons-Read, 2013; Rondo et al., 2003)

With respect to the results provided by the model before the pandemic, our findings also globally support previous studies showing how resilience can diminish stress as well as anxiety in the perinatal stage (García-León et al., 2019). Thus, our findings are in line with those provided by structural equation models in other studies. For example, they support those found by Armans et al. (2020), who showed that resilience negatively influenced pregnancy-specific stress, or those found by Peñacoba-Puente et al. (2016), which demonstrated how pregnancy worries had an impact on anxiety symptoms before the pandemic. The results provided by this model showed that resilience also acts as buffering factor in relation to stress, pregnancy worries and anxious symptoms in women during their pregnancy before the COVID-19, and not only in times of crisis or great adversity. Therefore, resilience is also a protector against daily stress during pregnancy, e.g., attending follow-up medical appointments, psychosocial changes such as sick leave, delegating responsibilities regarding household tasks, etc. Nevertheless, this is the first study conducted with pregnant women before and at the time of the pandemic, and the first to investigate the connection between these factors using two structural equation models.

The results that showed an increased symptomatology of anxiety and pregnancy-related stress during the COVID-19 are in agreement with the studies that found such an increase in pregnancy throughout the pandemic (Boekhorst, et al., 2021; Hessami, et al., 2020; Lebel et al., 2020; Wu et al., 2020). The increase in anxiety, as well as the increase in prenatal worries, may be due to different factors arising from the pandemic, such as: fear of the disease's spread and possible negative effects on health and foetus; fear of losing loved ones; financial worries and the loss of direct social contacts due to the restrictions aimed at controlling contagion (Wang et al., 2020).

Nevertheless, in our study, we found that pregnant women before the pandemic reported greater levels of perceived stress compared to pregnant women during the pandemic. These results are contrary to those of Medina-Jimenes et al. (2020), who had previously found increased stress in women who were pregnant throughout the pandemic in Mexico. It is worth noting, however, that the present study has substantial differences with this latter one: the earlier investigation did not involve a control group before the pandemic and the present work was conducted in Spain, where the restrictions and lockdowns to stop the contagion are different. In addition, in the current investigation, the sample was recruited over a longer period during the pandemic. The causes for the lower levels of perceived stress in pregnancies throughout the pandemic may be multifactorial. One reason for this decrease in stress may be the increase in time stayed at home during periods of lockdown and the reduction of daily stressors such as: visits to the supermarket and other stores during the week; activities and/or presential courses; presential work; events and/or social commitments, etc. On the other hand, the promotion of teleworking and the flexible hours that often result from it may also have contributed to reducing the stress levels perceived by women pregnant during the pandemic.

In general terms, resilience, pregnancy-specific stress, and general stress better predicted the anxiety symptomatology appearing in the wake of the pandemic. These results may be due to differences with respect to these variables between groups, as pregnant women at the time of the pandemic showed greater levels of pregnancy-specific stress, anxiety, somatisation, obsessions-compulsions and similar levels of resilience. Before the pandemic, however, the pregnant women showed greater levels of perceived stress. These differences resulted not only in a stronger relationship in the pandemic group between resilience and perceived stress, but also between perceived stress and anxiety symptoms. This could indicate that in the pre-pandemic group, there could be other

factors influencing perceived stress levels that would not be influencing the pandemic group, e.g. work stress, less time with a partner, less free time, etc. On the other hand, the raised levels of anxiety in the pandemic group could be a reflection of the increased pregnancy-specific stress found; as it has a stronger relationship with it compared to the pre-pandemic group, and could be due to pandemic-related concerns, such as fear of contagion and disruption of the gestational process. Thus, while exhibiting the same levels of resilience, variations in perceived stress and pregnancy-related stress show that they are influenced by different contextual factors in the two groups, reflecting different relationships with resilience itself, as well as with anxious symptoms.

A first conclusion is that resilience, stress and pregnancy worries better explained anxiety symptoms during the pandemic than before the pandemic. In addition, resilience played an important buffer role against general stress, pregnancy-related worries and anxiety symptomatology at both moments in time. Second, the pandemic may have increased pregnant women's levels of anxiety and pregnancy-specific stress because of infection fear and the possible negative implications for them and their babies, in addition to uncertainties regarding the future. On the other hand, throughout the pandemic, women in the gestational period had lower levels of perceived stress, possibly due to reduced daily stress resulting from lockdowns and restrictions and increased hours at home. Based on all the above, this study has significant clinical implications: it is necessary to promote tools that have been shown to be effective at increasing resilience and reducing stress in pregnant women, thus preventing increases in anxiety symptoms in crisis situations (Puertas-Gonzalez, et al., 2021; Romero-Gonzalez, et al., 2020b).

Strengths

A notable strength of this work was the inclusion of two samples from two different temporal and contextual moments (before and at the time of the pandemic).

Limitations

Despite the findings, there are some limitations to this research. Firstly, as the instruments used for the assessment were sent online to the participants and therefore there was no control by a researcher at the time of completion, we cannot ensure that all questionnaires have been completed by pregnant women. However, as participants were not paid or rewarded for completing the questionnaire, and as it was a long questionnaire with a duration of 30-40 minutes, it was assumed that the people who completed the questionnaire were pregnant women. Secondly, no participant follow up was conducted to verify whether the results persisted over other periods, for example, during the postpartum period, so we propose this for future research.

Finally, given that we have demonstrated relationships between resilience and stress and anxiety in pregnancy, both in crisis situations and in normal life contexts, it would be highly interesting for future studies to test whether these relationships are the same for each trimester of pregnancy, as this would have implications for planning a specific psychological intervention for this population.

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6.6 Artículo 6

Puertas-Gonzalez, J. A., Mariño-Narvaez, C., Romero-Gonzalez, B., & Peralta-Ramirez, M. I. (2021). Stress and Psychopathology Reduction in Pregnant Women through Online Cognitive Behavioural Therapy during COVID-19: A Feasibility Study. *Behavioral Sciences, 11*(7), 100. <https://doi.org/10.3390/bs11070100>

Stress and Psychopathology Reduction in Pregnant Women through Online Cognitive Behavioural Therapy during COVID-19: A Feasibility Study

Abstract

Background: The global pandemic has affected the psychological health of the population, including pregnant women. Due to the difficulty of offering conventional therapies to reduce stress in this population, studies are needed to show the effect of online therapies. Therefore, the objective was to test the effect of online cognitive behavioural therapy in pregnant women during the pandemic on the main variables of stress and psychopathology. Methods: The sample consisted of 16 pregnant women who participated in a weekly cognitive behavioural intervention for 8 weeks. Prenatal concerns, general stress, stress vulnerability, resilience and psychopathology were assessed. Results: The results show a reduction in prenatal concerns, perceived stress, stress vulnerability and psychopathology, as well as an increase in resilience. Conclusions: Online cognitive behavioural intervention may be effective in pregnant women, so it is important to conduct a randomised controlled trial to certify these findings.

Keywords: *cognitive behavioural therapy; pregnancy; resilience; stress; online therapy.*

Introduction

The appearance of an outbreak of a new pneumonia disease caused by coronavirus (COVID-19) in December 2019 has led to drastic changes in the population's way of life, carrying new challenges to be faced, as well as changes in social relations and personal liberties [1].

In this way, a population that has been particularly affected are pregnant women, who have presented an increase in their stress levels, depression and/or anxiety during pregnancy [2,3]. This increase can have serious consequences on maternal and infant health, as years of studies have demonstrated the close relationship between stress and the development of depression in pregnancy and postpartum depression, increased risk of preeclampsia and hypertension, increased risk of miscarriage, need for instrumental deliveries, low foetal weight and premature birth [4–6]. In addition to these negative consequences, it was recently shown that women who have gave birth during the pandemic also experienced a low satisfaction with their delivery, higher levels of stress during childbirth and increased symptoms of postpartum depression [7]. For that reason, different psychological interventions have emerged with the aim of reducing the levels of stress in pregnant women, such as mindfulness-based programs (MBPs) [8,9], relaxation techniques such as progressive muscle relaxation and guided imagery [10] and even sport based interventions such as yoga [11,12]. However, evidence-based medicine highlights cognitive behavioural therapy (CBT) as a treatment to reduce a wide range of psychopathology and stress [13]. CBT aims to modify distorted cognitive thoughts and interpretations of reality that lead to disturbing emotions and feelings [14,15]. CBT for stress coping has shown great results in reducing stress in pregnant women [16], or in reducing anxiety or depression levels [17]. Thus, promoting such interventions during pregnancy can help reduce the negative effects of stress and improve maternal and infant

health. Thus, promoting such interventions during pregnancy can help reduce the negative effects of stress and improve maternal and infant health.

The pandemic has been a major barrier to psychological treatments, as they must now be carried out online in many cases. However, some studies highlight the applicability of this type of treatment, since video calls also allow for face-to-face interaction [18]. In addition, the patient's self-efficacy may increase, as success is less likely to be attributed solely to the work of the therapist [19].

Therefore, it is necessary to test the feasibility of CBT for stress management in times of pandemic, conducted telematically, in order to verify whether a subsequent randomised controlled trial is appropriate. Thus, the aim of this study was to test the effect of online cognitive behavioural stress management therapy (o-CBT) in pregnant women, applied during the COVID-19 pandemic, on the main variables of psychological stress and psychopathology.

Materials and Methods

Participants

This study included a total of 16 pregnant women. The inclusion criteria were: pregnant women with a good command of spoken and written Spanish and with an internet connection to follow the sessions. Exclusion criteria included having suffered from a psychological illness in the past year or at present, or suffering from a current medical illness. Given that some research recommends 12 participants as a minimum for pilot studies [20], and taking into account our study objectives, design and intervention, research suggests that a sample size of 16 participants is reasonable [21,22].

All women who agreed to participate read an information sheet and gave their consent through an online questionnaire platform. The protocol of this study was

reviewed and approved by the Biomedical Ethics Research Committee of the Junta de Andalucía (internal code 0401-M1-17). Moreover, this study followed the guidelines of the Helsinki Declaration (AMM, 2008) and the Good Clinical Practice Directive (Directive 2005/28/EC) of the European Union.

Instruments

First of all, participants were asked to answer some questions regarding sociodemographic and obstetric information. After that, the following instruments were used for the psychological evaluation of the participants:

- The Symptom Checklist-90-Revised (SCL-90-R) [23,24]. This is a 90-item scale with 5 points, ranging from 0 (never) to 4 (extremely). This instrument is used to evaluate nine different measurements: somatization, obsession–compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. There are also seven additional items on the scale distributed among 3 global indexes of distress: the GSI, which measures overall psychological distress; the PSDI, which is used to calculate the intensity of symptoms; and Positive Symptom Total, used to measure the number of self-reported symptoms. The scores are converted to percentiles (0–100) according to the author’s instructions. Percentiles ≥ 75 represent clinical symptoms in any of the subscales of this instrument. The nine dimensions show a reasonable reliability, with a Cronbach’s alpha for internal consistency of 0.81.

- Pregnancy Distress Questionnaire (PDQ) [25,26]. This is a 12-item scale that measures pregnancy-specific stress related to maternal concerns about pregnancy, such as medical problems, labour and delivery, physical signs and symptoms, bodily changes and the baby’s health. A 5-point Likert-type scale is used to collect responses where 4 = very much and 0 = not at all. The Cronbach’s alpha reliability coefficient is 0.71.

- Perceived Stress Scale (PSS) [27,28]. The PSS collects data on people's perceptions of general stress over the previous month. It is made up of 14 elements that are rated on a 5-point Likert scale. (0 = never, 1 = almost never, 2 = once in a while, 3 = often, 4 = very often). Scores range from 0 to 56 (higher scores represent higher levels of stress). The Spanish Cronbach's reliability alpha coefficient is 0.81.

- Stress Vulnerability Inventory (IVE) [29]. It consists of 22 items that assess a person's proclivity to be affected by perceived stress. It has a Yes/No answer format. Items receiving an affirmative answer add 1 point. The range of scores on the scale is 0 to 22, with higher scores corresponding to greater vulnerability to stress. The scale is highly reliable, with a Cronbach's alpha of 0.87.

- Connor Davidson Resilience Scale (CD-RISC) [30,31]. It reflects the ability to cope with stressful situations such as changes, personal problems, illness, pressure, failure and feelings of pain. The CD-RISC-10 consists of 10 items, and a Likert scale with 5 response options ranging from 0 ("almost never") to 4 ("almost always"). It has a Cronbach's alpha reliability coefficient of 0.86.

Procedure

The participants were recruited through the dissemination in social networks of news published in different newspapers and media for two weeks. These news items included the contact information of a researcher from the team, so that interested pregnant women could get in touch. All women who wished to participate read the study information sheet and gave their consent through an online questionnaire platform. The objective was to carry out two groups of 8–10 people each. Finally, 25 participants were interested in participating, of which 6 did not meet the inclusion criteria. The remaining

19 took part in two pilot groups to test the efficacy and feasibility of the online version of the treatment, of which 16 completed the intervention.

Participants attended 8 consecutive weekly o-CBT sessions of 1.5 to 2 h duration with two trained psychologists with a master's degree of 900 h of training in psychological treatment. o-CBT was performed through Google Meet. In addition, the psychologists had conducted the same intervention on several occasions in face-to-face format prior to the pandemic. A Google Forms link was administered, through which participants completed the pre-treatment assessment, composed of the previously described assessment instruments.

The intervention was adapted from a previous treatment program [32], whose efficacy has been demonstrated in pregnant women [16]. The program consists of 8 sessions with the following content: (1) psychoeducation: what stress is, its characteristics, how to identify stressors, how to react to them and what are its effects; (2) deactivation strategies (thematic imagination and diaphragmatic breathing); (3) cognitive restructuring: cognitive distortions; (4) cognitive restructuring: irrational beliefs; (5) alternative ways to control your thoughts: self-instructional training and time management; (6) training in social skills: assertiveness, fundamental assertive rights, saying no and requesting a change of behaviour; (7) relationship between anger and stress: emotional self-control; and (8) optimism and sense of humour summary.

Each intervention followed the same structure and the same guidelines to assume the standardisation of the contents. At the beginning of the session, participants received an email with the link to connect to the virtual session, the documents needed to work during the session, the behavioural self-report and the tasks to work on at home that week related to the topic of the session. In order to maximize the benefits of the online intervention, it was recommended at the beginning of each session to activate the camera

and to use headphones and microphone. In addition, all participants were encouraged to participate in the sessions with different actions, such as: talking about their experiences, expressing difficulties about the tasks between sessions, role-playing, etc.

At the conclusion of treatment, the evaluation instruments described above were administered again.

Data Analysis

First, a descriptive and frequency analysis was carried out to check the distribution of the sample in the main sociodemographic and obstetric history variables.

Secondly, the Shapiro–Wilk test was used to test the normality of the data. In the case of the SCL-90-R scores, since they did not present a normal distribution, the Wilcoxon W test was performed for two related samples (pre and post). The rest of the scores (EEP, PDQ, IVE, CDRISC) met the assumption of normality and therefore a Student's t test was performed for two related samples (pre and post).

Finally, to calculate the effect size of the statistically significant changes of the parametric variables that were analysed with the Student's t test, Cohen's d was used (small effect size > 0.20, medium effect size > 0.50 and large effect size > 0.80). The calculation is based on Borenstein's formulas [33] for calculating the effect size in a *t*-analysis for dependent samples. In the case of non-parametric variables, the formula proposed by Cohen [34] ($r = Z/\sqrt{N}$) was used, where [Z] is the absolute value of the Z score and [N] is the total number of observations. This effect size comprises values from 0 to 1, for which Cohen (1988) recommended the following interpretations: $r > 0.10$ small effect size, $r > 0.30$ medium effect size and $r > 0.50$ large effect size.

Analyses were performed using the Statistical Package for the Social Sciences 26.0 for Windows (SPSS, Armonk, NY, USA).

Results

Sample Description

A total of 16 pregnant women took part in the pilot study, with a mean age of 36.63 years ($SD = 3.36$) and who were between 6 and 31 weeks of pregnancy ($M = 20.50$ weeks gestation; $SD = 7.81$). All of them were Spanish and were married or cohabiting with their partner ($n = 16$; 100%). In addition, 87.5% ($n = 14$) had a university degree. The rest of the variables can be consulted in Table 1.

Table 1. Sociodemographic variables and obstetric information of the sample.

		Therapy Group (<i>n</i> = 16)
		M(SD)/%
<i>Sociodemographic variables</i>		
Age		36.63 (3.36)
Weeks of gestation	T ₀	20.50 (7.81)
	T ₁	28.50 (7.81)
Married/cohabiting	Yes	16 (100%)
Nationality	Spanish	16 (100%)
Education level	High school	2 (12.5%)
	University	14 (87.5%)
Employment situation	Employed	2 (12.5%)
	Part-time employment	1 (6.3%)
	Full-time employment	13 (81.3%)
<i>Obstetric information</i>		
Primiparous	Yes	7 (43.8%)
	No	9 (56.3%)
Pregnancy method	Spontaneous	14 (87.5%)
	Fertility treatment	2 (12.5%)
Wanted pregnancy	Yes	14 (87.5%)
	No	2 (12.5%)
Previous miscarriages	0	9 (56.3%)
	1	6 (37.5%)
	≥2	1 (6.3%)

Note: T₀ = pre-intervention; T₁ = post-intervention.

Changes in Psychological Variables at the End of Therapy in Pregnant Women

First, Student's *t*-analyses for dependent samples showed statistically significant differences in: pregnancy-specific stress ($t = 4.446$; $p \leq 0.001$) with a medium effect size ($d = 0.671$); perceived stress ($t = 3.243$; $p \leq 0.005$) with a high effect size ($d = 0.909$);

stress vulnerability ($t = 3.982$; $p \leq 0.001$) with a low effect size ($d = 0.348$); and resilience ($t = -2.643$; $p \leq 0.01$) with a medium effect size ($d = 0.608$). As can be seen in Table 2, after finalizing the treatment women showed decreased scores in these variables.

Table 2. Differences in psychological measures before and after therapy.

	Measures	T ₀	T ₁	t/Z	p	d/r
	PDQ	19.88(7.15)	15.25(6.49)	4.446	0.001**	0.671
	PSS	28.75(5.62)	22.69(7.43)	3.243	0.005**	0.909
	IVE	9.69(5.49)	7.50(5.98)	3.982	0.001**	0.348
	CD-RISC	21.19(5.35)	24.63(5.89)	-2.643	0.018*	0.608
	SOM	61.19(29.02)	53.69(32.48)	-1.616	0.106	0.403
	OBS	86.88(13.20)	78.88(16.50)	-2.556	0.011*	0.638
	SEN	67.75(30.13)	59.81(30.12)	-1.207	0.227	0.301
	DEP	76.31(22.52)	68.56(27.56)	-1.310	0.190	0.327
	ANS	78.75(18.36)	68.81(22.90)	-3.201	0.001**	0.801
SCL-90-R	HOS	62.63(28.32)	58.69(32.74)	-0.772	0.440	0.192
	FOB	67.56(31.09)	52.88(36.54)	-2.003	0.045*	0.501
	PAR	55.00(41.50)	48.94(41.99)	-0.840	0.401	0.209
	PSI	79.94(20.47)	67.75(26.98)	-2.202	0.028*	0.550
	IGS	79.94(19.23)	68.88(28.13)	-2.030	0.042*	0.507
	SP	81.56(19.00)	73.19(24.59)	-2.207	0.027*	0.551
	PSDI	63.69(20.33)	50.00(27.14)	-2.336	0.019*	0.584

Note: T0 = pre-intervention; T1 = post-intervention; * = p value ≤ 0.05 ; ** = p value ≤ 0.01 ; PDQ = Pregnancy Distress Questionnaire; PSS = Perceived Stress Scale; IVE = Stress Vulnerability Inventory; CD-RISC = Connor Davidson Resilience Scale; SCL-90-R = The Symptom Checklist-90-Revised; SOM = somatizations; OBS = obsession and compulsion; SEN = interpersonal sensitivity; DEP = depression; ANS = anxiety; HOS = hostility; FOB = phobic anxiety; PAR = paranoid ideation; PSI = psychoticism; IGS = global severity index; SP = positive symptoms; PSDI = positive symptoms distress index.

Regarding the non-parametric analyses performed for the scores in the different dimensions of the SCL-90-R, statistically significant differences were found in obsessions and compulsions ($Z = -2.556$; $p \leq 0.01$) with a high effect size ($r = 0.638$); anxiety ($Z = -3.201$; $p \leq 0.01$) with a high effect size ($r = 0.80$); phobic anxiety ($Z =$

-2.003; $p \leq 0.05$) with a medium effect size ($r = 0.501$); psychoticism ($Z = -2.202$; $p \leq 0.05$) with a medium effect size ($r = 0.550$); and in the general scales of global severity index ($Z = -2.030$; $p \leq 0.05$), positive symptoms ($Z = -2.207$; $p \leq 0.05$) and positive distress index ($Z = -2.336$; $p \leq 0.05$). In addition, it should be noted that the study population showed clinical scores (greater than 70) on the SCL-90-R subscales of obsessions and compulsions, depression, anxiety and psychoticism prior to treatment. These data and the means for each measure can be found in Table 2. As can be seen, after treatment, not only was there a decrease in the psychopathological symptom scores in these women, but also in depression, anxiety and psychoticism, in which they went from clinical scores to normal scores.

Discussion

The aim of this study was to verify the effect of o-CBT on stress management in pregnant women. In order to achieve it, a 2 month online intervention (eight sessions) was implemented with a total of 16 women.

Firstly, it was proven that women who completed the intervention had a significant reduction in their stress levels, both in perceived stress and pregnancy-specific stress. The main component of o-CBT is stress management; thus, the online version of the therapy supports the results found by previous authors in a randomised controlled trial [16]. Additionally, this reduction could have direct repercussions on maternal and foetal health, since pregnancy-specific stress has been considered as a powerful predictor of negative outcomes [35].

Additionally, there was a reduction in the vulnerability to stress and an increase in resilience scores. These results are highly relevant, taking into account that not only the problematic factors, such as stress levels, reduce, but it goes one step forward,

increasing resilience, which could also carry improvements in coping mechanisms, self-esteem and general wellbeing [36,37].

In addition, there was found to be a decrease in various psychopathological symptoms in the women who participated in the therapy. On one hand, obsession and compulsion levels and phobic anxiety decreased; these are characteristic symptoms related to the actual pandemic situation. The need to maintain extreme hygiene to avoid contagion, or the fear of vertical transmission of the virus to the foetus, could underlie the presence of this symptomatology [38,39]. Reducing these levels is a matter of extreme importance, since obsessions and phobias, maintained during pregnancy, can shunt into intense fears that disable the pregnant woman, occasionally resulting in a phobia towards childbirth, which in addition generates low satisfaction towards it, a higher chance of suffering a traumatic childbirth and even the need to require an instrumentalised procedure [6,40,41].

Furthermore, anxiety is highly related to the stress suffered and the phobic anxiety previously described. Around 8% of pregnant women report suffering symptoms of anxiety [42], which are related to the development of severe psychopathological disorders after childbirth, such as postpartum depression, a higher chance of a preterm birth and internalizing problems on the offspring [4,43].

Finally, psychoticism symptoms also reduced after therapy. Other authors have stated that this symptomatology increases in pregnant women, probably due to an evolutionary aspect of pregnancy, where the mother considers external agents as a threat [44]. During pandemics such as the one we are enduring, this symptomatology can increase, because in order to avoid contagion there is an aversion to meet new people or maintain a social life [45]. o-CBT offers the possibility of increasing social support without having to be in direct contact with their peers, which could be related to the

diminishment of this symptom. Additionally, on average, the participants started the therapy in the second trimester and finished in the first weeks of the third trimester, where the psychological state of pregnant women typically worsens [4]. As it has been verified, o-CBT palliated this psychological worsening in the sample, helping to improve the psychological health during the third trimester of pregnancy.

Despite the promising findings reported, this study presents a limitation; since this is an applicability study, and does not have a control group, the changes found cannot be related exclusively to the therapy's efficacy. Moreover, despite following previous research recommendations for sample size [20-22], the sample size is quite small, which could affect statistical power. Apart from that, it would be interesting to include working-class women in the future study, to see how stress is reduced in this sample. Therefore, it is of great relevance to continue research of the efficacy of o-CBT, implementing at least one control group. It would also be interesting to include an additional control group centred on social support, in order to guarantee that the changes found are due to the abilities acquired through the therapy and not just the supportive environment where pregnant woman share experiences with their peers.

Preliminary results show an unquestionable improvement in the psychological health of women who participated in the therapy, which is in accordance with the results of a face-to-face version [16]. It is important to raise the fact that as the pregnant women had no psychological illnesses in our sample, this may be a step towards implementing this therapy as a health-promoting measure. Nowadays, these interventions are especially necessary during pregnancy as a means to promote health, in order to avoid the loneliness and abandonment that is produced by a situation such as the pandemic we are living in and to provide the pregnant women with strategies that help them palliate the negative psychological effects caused by the pandemic.

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6.7 Artículo 7

Puertas-Gonzalez, J. A., Marino-Narvaez, C., Romero-Gonzalez, B., Sanchez-Perez, G. M., & Peralta-Ramirez, M. I. (2022). Online cognitive behavioural therapy as a psychological vaccine against stress during the COVID-19 pandemic in pregnant women: A randomised controlled trial. *Journal of Psychiatric Research*, *152*, 397-405. <https://doi.org/10.1016/j.jpsychires.2022.07.016>

Online cognitive behavioural therapy as a psychological vaccine against stress during the COVID-19 pandemic in pregnant women: A randomised controlled trial.

Abstract

The COVID-19 pandemic has affected the population's levels of stress and anxiety due to its contagious nature and the uncertainties generated by its novelty. One population that is especially vulnerable to these psychological consequences are pregnant women. This is why the objective of this study was to test the efficacy of an online stress management programme of a cognitive behavioural nature on pregnant women during the COVID-19 pandemic, in Spain. The trial was controlled and randomised, with a total of 207 pregnant women divided into three groups: the Online Cognitive Behavioural Therapy group (o-CBT) (N=70); the Online Psychological Support group (o-PS) (N=69); and the Usual Care group (UC) (N=68). To test the therapy's efficacy, the women's resilience, perceived stress, pregnancy-specific stress and psychopathological symptoms were assessed before and after the intervention. The o-CBT and o-PS consisted of a programme of 8 group sessions (one per week). The results showed that pregnant women who participated in the o-CBT group presented lower rates of pregnancy-specific stress and perceived stress, as well as greater resilience and lower anxiety, depression and obsessions-compulsions symptoms. These data show the efficacy of the treatment programme and thus confirm the importance of implementing these types of interventions during a woman's pregnancy, especially over periods of major stress, such as during a pandemic.

Keywords: COVID-19; *Cognitive behavior therapy; pregnancy; stress; resilience; psychopathology.*

Introduction

In March 2020, the World Health Organisation declared the outbreak of a new pandemic triggered by the international spread of a coronavirus disease (COVID-19) (World Health Organization, 2020). Its highly contagious nature and the resulting lockdown measures led to an increase in anxiety and depressive symptomatology (Wang et al., 2020).

A particularly vulnerable group within the population are pregnant women, as they are more likely to suffer, due to their very pregnancy, from psychological stress, anxiety and depression, symptoms which have been aggravated by the pandemic and concerns about their personal health and foetal health (Woody et al., 2017; Wu et al., 2020). In fact, different studies have shown that women who were pregnant during the COVID-19 pandemic presented higher levels of stress, depression, anxiety, phobic symptomatology and thoughts of self-harm, than women who were pregnant before the pandemic (Liu et al., 2021; Mariño-Narváez et al. 2021; Puertas-Gonzalez, et al., 2021a; Wu et al., 2020). These results reflect a possibly negative pandemic impact on maternal mental health, which in turn has a significant effect on their babies (Liu et al., 2021; Puertas-Gonzalez, et al., 2021a; Wu et al., 2020).

In order to reduce the negative consequences of stress during pregnancy, various intervention techniques have been developed and brought to light by Cognitive Behavioural Therapy (CBT). Such a therapy is based on scientific evidence and treatment efficacy with respect to various psychopathologies, as well as stress reduction (Butler et al., 2006). Specifically, a recent study showed a reduction in the level of pregnancy-specific stress, perceived stress, cortisol in hair, together with lower general psychopathological symptomatology in women who followed stress-management CBT during their pregnancy (Romero-Gonzalez et al., 2020).

As the pandemic has unfolded, there has been a boom in telemedicine, providing evidence that online CBT is a viable method for the symptomatic reduction of certain mental disorders, such as somatic disorders, major depressive disorder, panic disorder or post-traumatic stress disorder (Carlbring et al., 2018; Chipps et al., 2020). Particularly during the pandemic, Wahlund, et al. (2021) studied whether a brief self-guided online cognitive behavioural intervention could reduce the degree of dysfunctional worry related to the COVID-19, in a sample of the general adult population in Sweden. They found that the sample group that received the intervention showed a significant reduction in COVID-19-related worry. In Germany, Heckendorf et al. (2022) also investigated the benefits of an Internet-based, unguided cognitive behavioural self-help intervention in the general population. They reported that the intervention group showed significantly less worrying after the interventions than controls. Finally, Bryant et al. (2022) found that a brief group psychological intervention delivered via videoconferencing to adults in Australia distressed by the pandemic reduced symptoms of depression and anxiety and fears related to COVID-19. The programme used included strategies on management of pandemic-related concerns, compensation for limited access to positive activities, and access to social supports during closure (Bryant et al., 2022).

As for the online health modality during the perinatal period, it has generated promising results for the reduction of maternal mental health problems (Ashford et al., 2016). Nevertheless, not all the studies developed meet the requirements of randomised and controlled trials (RCTs), since most lack a control group or have not been randomised (González-Blanch et al., 2018). Furthermore, to our knowledge, no study has been conducted during the pandemic to evaluate the efficacy of an online psychological intervention aimed at reducing stress in pregnant women in Spain.

Given the importance of a psychological approach to pregnant women during a pandemic and the need to adapt the psychological intervention to an online format (because of

the characteristics of the pandemic itself), the objective of this study was to test the efficacy of online cognitive behavioural therapy in pregnant women in managing stress during the COVID-19 pandemic through a randomised controlled study. Three groups of participants were included: pregnant women who received online cognitive-behavioural therapy; pregnant women who received online psychological support; and pregnant women who received the usual care.

Methods

Participants

The study was constituted by 207 pregnant women. Information sheets and posters were produced with the information, objective and contact (phone number and email) to participate in the study and different means of recruitment were used, such as: dissemination in hospitals and health centres, city councils, radio programmes and, finally, through different social networks by sending the study information to pregnant women's groups on WhatsApp and Facebook. Women interested in participating contacted a study researcher, through the contact provided on the information sheets, who checked that they met the criteria for participation in the study and enrolled them. Once enrolled, they were sent a study informed consent form to sign and return to the researchers. Recruitment was conducted from September 2020 to June 2021, during the COVID-19 state of alert. Participants were randomly divided into three groups: the online cognitive behavioural therapy group (o-CBT) (N=70); the psychological support group (o-PS) (N = 69); and the usual care group (UC) (N = 68).

The inclusion criteria were as follow: pregnant women; between the twelfth and twenty-eighth week of gestation; with a good command of the Spanish language (oral and written comprehension); and having an internet connection. The weeks selected as inclusion criterion were chosen considering that from the twelfth week, the probability of having a spontaneous

abortion decreases (Regan & Rai, 2000). The twenty-eighth week was also selected to ensure that the participants could finish the treatment.

The exclusion criteria were as follow: having a medical condition; suffering from a diagnosed psychiatric disorder; using of psychiatric medication; and receiving psychotherapy.

All participants, after reading the study information sheet, signed the informed consent document, in which they undertook to participate in the study voluntarily. They were assigned a code to guarantee their anonymity.

The study's protocol was reviewed and approved by the Biomedical Ethics Research Committee of the Junta de Andalucía (internal code 0401- M1-17). In addition, the present work followed the guidelines of the Declaration of Helsinki (WMA, 2008) and the Directive on Good Clinical Practice (Directive 2005/28/EC) of the European Union. The study was registered as a single-blind randomised controlled trial with the code: NCT03404141. The trial is reported according to CONSORT guidelines.

Instruments

First, the pregnant women completed the entire evaluation using *Google-Form*, which asked questions about sociodemographic variables (age, weeks of pregnancy, nationality, level of education, marital status, among others) and obstetric information (whether they were primiparous or not, method of gestation, whether it was a planned pregnancy or a high-risk pregnancy). For the psychological evaluation, the participants completed the several instruments, divided into primary outcomes and secondary outcomes. The primary outcomes were those that were focus of the intervention: stress (perceived stress, pregnancy-specific stress and vulnerability to stress) and resilience, which is define as the ability to cope with stressful situations. In addition to being the main target of the therapy, stress and resilience have been showed to be highly associated before and throughout the pandemic in pregnancy

(Puertas-Gonzalez et al., 2022). On the other hand, the secondary outcomes were psychopathological symptoms, which were not a direct target of therapy but they could be reduced by increasing resilience and reducing stress levels (Lupien et al., 2022; Puertas-Gonzalez et al., 2022).

Primary outcome: stress and resilience

- Perceived Stress Scale (PSS-14) (Cohen et al., 1983; Remor,2006). The PSS-14 provides information on the perception of general stress during the preceding month. It consists of 14 items scores on a 5-point Likert scale (0 = never, 1 = almost never, 2 = once in a while, 3 = often, 4 = very often). Scores range from 0 to 56 (higher scores represent higher levels of stress). Cronbach's alpha was 0.90 in this study.

- Prenatal Distress Questionnaire (PDQ) (Yali and Lobel, 1999; Caparros-González, et al., 2019a). This is a 12-item scale that measures pregnancy-specific stress related to maternal concerns about pregnancy, such as medical problems, labor and delivery, physical symptoms, bodily changes and the baby's health. Responses are given using a 5-point Likert-type scale where 0 = not at all and 4 = very much. Cronbach's alpha was 0.75 in this study.

- Stress Vulnerability Inventory (IVE) (Beech et al., 1986; Robles-Ortega et al., 2006). It consists of 22 items that evaluate the person's predisposition to feel affected by perceived stress. It has a Yes/No answer format. Items receiving an affirmative answer add 1 point. The range of scores on the scale is 0 to 22, higher scores corresponding to greater vulnerability to stress. Cronbach's alpha was 0.87 in this study.

- Connor Davidson Resilience Scale (CD-RISC) (Connor and Davidson, 2003; García-León et al., 2019) in its abridged Spanish version (Notario-Pacheco et al., 2014). This instrument assesses resilience, understood as the ability to cope with stressful situations such as changes, personal problems, illness, pressure, failure and feelings of pain. The CD-RISC-10

consists of 10 items, and a Likert scale with 5 response options ranging from 0 (“almost never”) to 4 (“almost always”), which had a single dimension. Some of the items it presents are: " I think of myself as a strong person when dealing with life’s challenges and difficulties, " or " I am able to adapt when changes occur ". The scale provides a total score ranging from 0 to 40, and higher scores indicate a higher level of resilience. Moreover, the instrument has high construct, divergent and convergent validity, and the Cronbach’s alpha was 0.87 in this study.

Secondary outcome: psychopathological symptoms

- The Symptom Checklist-90-Revised (SCL-90-R) (Derogatis, 1983; Caparrós et al., 2007). As psychopathological symptoms were not the main focus of the intervention, this scale was used to assess secondary treatment outcomes. The nine main dimensions of this instrument have been used in this research: somatization, obsession–compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. This instrument is a 90-item scale with 5 points, ranging from 0 (never) to 4 (extremely). The scores are converted to percentiles (0–100) according to the author’s instructions. Percentiles 75 represent clinical symptoms in any of the subscales of this instrument. Cronbach's alpha ranged between 0.68 and 0.87 for the nine dimensions in this study.

Procedure

The participants were captured online following the method described above. They were informed that an online group therapy (delivered by synchronous videoconferencing in groups of 8-10 participants) was being conducted based on the Gestastress-Childstress projects, to control stress in pregnant women during the pandemic.

Furthermore, they were explained that the programme included 8 weekly sessions lasting approximately 1.5 to 2 hours each, in both the o-CBT and the o-PS groups. An email address was provided for further information and to enrol in the programme.

Participants were randomly divided into three groups: o-CBT, o-PS and UC. Randomisation was applied using the Statistical Package for Social Sciences (SPSS) version 25.0 for Windows (SPSS, Armonk, New York), via a computer-generated random number sequence in which participants were randomly assigned (1:1:1) to the o-CBT, o-PS or UC. The data management system automatically assigned numbers from the list of random numbers to the study participants. Randomisation sequences, participant registration, and treatment assignments were performed by a research assistant who was unaware of the participants' data.

Before starting the programme, an email was sent to the participants with a link to the session during which they would be assessed using the questionnaires described in the instruments section. A psychologist answered the questions raised during the evaluation session and checked that all the instruments were completed.

The participants assigned to the therapy group attended 8 consecutive weekly sessions of online cognitive behavioural therapy, lasting 1.5 to 2 hours each, imparted by two professionals with extensive training and experience in psychological therapy. These psychologists were licensed psychotherapists and they had conducted the programme in face-to-face settings before the pandemic. The structure of each session was as follows: after an initial welcome, the participants told how the week had gone for them and they were given feedback regarding what they had recorded in the behavioural self-records; they were then taught a new skill which they subsequently practiced through role-play; questions were answered, and to finish, they were given homework. They were given a behavioural self-record by email each week with the aim of writing down the day and time of the week when they put into practice the technique they had worked on that week in the therapy session, the thoughts they had and the difficulties they had found in putting them into practice. The same steps were followed for the online psychological support group, but therapy was replaced with psychoeducation and had no homework because they had not worked on coping skills to

practice them. The treatment was based on the adaptation of a programme backed by extensive scientific evidence: the Program for Stress Management (Robles-Ortega and Peralta-Ramirez, 2010), with demonstrated effectiveness in pregnant women (Romero-Gonzalez, et al., 2020). It was given online. The programme consists of 8 sessions that cover the following contents:

- 1) psychoeducation: what is stress, its characteristics, identification of stressors, responses and consequences;
- 2) deactivation techniques (diaphragmatic breathing and thematic imagination);
- 3) cognitive restructuring: cognitive distortions;
- 4) cognitive restructuring: irrational beliefs;
- 5) other complementary strategies: self-instructional training and time organisation;
- 6) training in social skills: assertiveness, basic assertive rights, saying no and how to request a change of behaviour;
- 7) relationship between anger and stress and emotional self-regulation;
- 8) good mood and optimism: summary.

The summary of the modules and themes of the sessions can be found in Table 1. During the first session, the definition and consequences of pregnancy-specific stress were explained, as well as examples and main characteristics and differences between stress and pregnancy-specific stress were shown. In addition, all the stress management techniques presented in the programme were aimed at being applied to both stress and pregnancy-specific stress. Finally, the psychologists in charge of implementing the intervention programme, at the beginning of each session allowed the participants to talk about their fears regarding the pandemic that week (e.g., fear of contagion, concerns about facing medical appointment without relatives or partners, loss of social contact, etc.). Moreover, all the concepts and techniques learned during the sessions were related through examples to the fears that pregnant women showed during the previous months in Spain associated with the COVID-19 pandemic (Chaves et al., 2021; Puertas-Gonzalez, et al., 2021a; Romero-Gonzalez et al., 2021), with the objective of being implemented in order to deal with them.

Table 1. Summary of the content of the sessions of the cognitive behavioural therapy group and the psychological support group.

Cognitive Behavioural Therapy Group			Psychological Support Group	
Sesion number	Module	Session topic	Module	Session topic
1	Psycho-education	Psychoeducation: what is stress, its characteristics, identification of stressors, responses and consequences	Psycho-education	What stress is and types of stressors
2	Relaxation	Diaphragmatic breathing and thematic imagination	Psycho-education	Physiological stress response
3	Cognitive restructuring	Cognitive distortions	Psycho-education	Stress in pregnancy
4	Cognitive restructuring	Irrational beliefs	Psycho-education	Anxiety and depression as consequences of stress
5	Alternative thought control techniques	Self-instructional training and time organisation	Psycho-education	Physical consequences of stress
6	Training in social skills	Assertiveness, basic assertive rights, saying no and how to request a change of behaviour;	Psycho-education	Stress, sleep and memory
7	Emotional self-regulation	Relationship between anger and stress	Psycho-education	Types of attachment and their importance
8	Good mood and optimism	Humour's benefits and summary	Psycho-education	Optimism and summary

Participants assigned to the online psychological support group received psychoeducation in stress and pregnancy-specific stress. This group was taught online and the aim was to offer a credible therapeutic alternative. In this way, non-specific therapeutic factors

could be controlled for, so that the possible psychological improvements of o-CBT could be attributed to its therapeutic components beyond the benefits of emotional support provided by group therapy with people in the same life situation. The session contents were mainly linked to: the use of empathy and active listening as emotional drainage strategies; psychoeducation, both in stress and pregnancy-specific stress; psychoeducation based on the information obtained from the book “Un villano llamado estrés” (Peralta-Ramírez, 2019). The topics addressed in the 8 sessions were: 1) What stress is and types of stressors; 2) Physiological stress response; 3) Stress in pregnancy; 4) Anxiety and depression as consequences of stress; 5) Physical consequences of stress; 6) Stress, sleep and memory; 7) Type of attachment; 8) Optimism and summary. The summary of topics covered in the psychological support group sessions can be found in Table 1. The psychologists who conducted the psychological support groups were the same psychologists who ran the therapy groups.

A total of 8 groups per arm (o-CBT, o-PS and UC) with 8-10 participants each were constituted at different times. The online sessions for o-CBT and o-PS were conducted in synchronous videoconferences between the therapists and the group participants using a camera and microphone via the Google Meet platform; before the sessions started, participants received an email with a link to connect to the Google Meet room.

In parallel, participants in the usual care group followed their standard routine care, which consisted of regular medical visits to their midwives throughout their pregnancy.

At the end of the sessions, all the participants were summoned to a new session and the questionnaires described in the instruments section were administered once more.

Statistical analysis

First, a factorial ANOVA (continuous variables) and Chi-square (categorical variables) analysis were performed to verify whether the groups (o-CBT, o-PS and UC) were even regarding the main sociodemographic and obstetric variables.

In addition, to check the efficacy of online cognitive behavioural therapy against online psychological support and the usual care group, a linear mixed model for repeated-measures data was performed, with group (o-CBT, o-PS and UC) and time (pre-intervention and post-intervention) as main effects, and a group x time interaction. The dependent variables were the scores obtained in the primary and secondary outcomes: PDQ, PSS-14, IVE, CD-RISC and SCL-90-R. In addition, we specified participant as a random effect to account for the repeated-measures nature of the data. Deviation tables were performed and reported with F statistics and p-values. Subsequently, a multiple-comparison post hoc analysis was performed for the variables in which the interaction was found, using Tukey post hoc test in order to check whether any differences existed between the pre- and post- scores in the three groups.

Finally, the partial eta squared (η^2_p) was calculated for the models to know the effect size, taking as a criterion 0.01 as a small effect size, 0.05 as a moderate effect size, and 0.08 as a large effect size (Cohen, 1969). Moreover, to check the size of the effect of the therapy, Cohen's d was calculated: $d \leq 0.20$ low effect size, $d \leq 0.50$ medium size and $d \leq 0.80$ large effect size (Cohen, 1988).

According to the intention-to-treat analysis and following the recommendations made by other researchers (García-Silva et al., 2018; Montori and Guyatt, 2001), the transfer method of the last observation was used to impute the missing values, i.e., loss of subjects throughout the study. All the results presented were based on the intention-to-treat imputed data. The linear mixed models were undertaken using the R 4.1.3 software (R Core Team, 2022) using the *lme4* package (Douglas, 2015)

Sample size

The G*Power software (version 3.1.9.7, Universität Düsseldorf, Düsseldorf, Germany, 2007) was used to estimate the sample size. This programme was used to ensure that the number of participants was suitable to guarantee 95% power and $\alpha \leq 0.05$ for all analyses; the need to compare data at two different moments in time was taken into account, considering the existence of three groups (o-CBT, o-PS and UC), G*Power determined that the total number of required participants was 189 (effect size $f = 0.25$ -mean).

Results

Sample description and adherence to treatment

A total of 219 women were interested in participating in the study. Of these, 207 met the inclusion criteria. The remaining 12 were therefore excluded from the study. Of the 207 women who participated in the study, 70 belonged to o-CBT with a mean age of 35.11 years (SD=3.60) (M=19.04 weeks of gestation), 69 belonged to the o-PS with a mean age of 35.59 years (SD=4.41) (M=21.28 weeks gestation), and, finally, 68 belonged to the UC with a mean age of 34.31 (SD= 4.85) (M= 20.56 weeks of gestation). In relation to treatment adherence, the average attendance of the o-CBT participants for the 8 sessions was 6.93 (SD=.95) and that of the o-PS participants was 6.60 (SD=1.23). In addition, 82.86% and 85.29% of o-CBT and o-PS participants completed treatment, respectively. Finally, 57.97% of UC participants completed the post-evaluation. The flow of participants across the various moments of the study, as well as the motives for exclusion from the total sample can be consulted in the CONSORT flowchart in Figure 1.

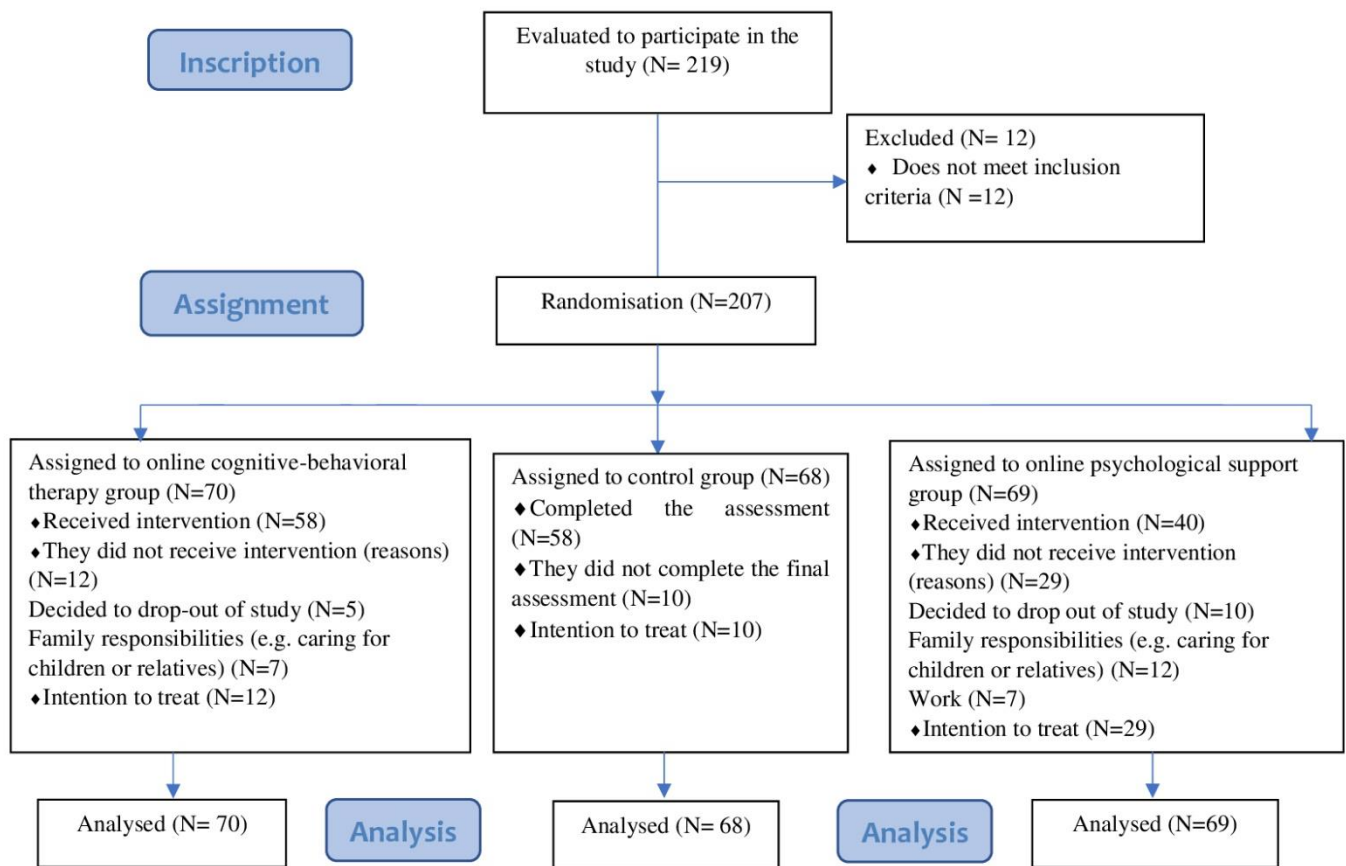


Figure 1. CONSORT flow chart

The groups were even regarding the main sociodemographic, habits and obstetric history variables, as shown in Table 2.

Table 2. Differences in sociodemographic, habit and obstetric variables between the online therapy group, the online psychological support group and the usual care group.

Variables		Online therapy group (n=70) M(SD) / %	Online psychological support group (n=69) M(SD) / %	Usual care group (n=68) M(SD) / %	F// χ^2	p
<i>Sociodemographic variables</i>						
Age		35.11(3.60)	35.59(4.41)	34.31(4.85)	1.554	.214
Married/cohabiting	Yes	69(98.6%)	63(91.3%)	62(91.2%)	4.231	.121
	No	1(1.4%)	6(8.7%)	6(8.8%)		
Nationality	Spanish	67(95.7%)	61(88.4%)	61(89.7%)	2.664	.264
	Other	3(4.3%)	8(11.6%)	7(10.30%)		
Level of Education	High school	7(10%)	10(14.5%)	15(22.1%)	6.128	.190
	University	63(90%)	59(85.5%)	52(76.5%)		
Employment situation	Unemployed	8(12.5%)	7(10.9%)	11(17.5%)	4.143	.387
	Part-time employment	4(6.3%)	9(14.1%)	4(6.3%)		
	Full-time employment	52(81.3%)	48(75%)	48(76.2%)		
Smoking	Yes	1(1.4%)	4(5.8%)	2(2.9%)	2.090	.352
	No	69(98.6%)	65(94.2%)	66(97.1%)		
Alcohol	Yes	2(2.9%)	1(1.4%)	2(2.9%)	.308	.857
	No	68(97.1%)	68(9.6%)	66(97.1%)		
<i>Obstetric variables</i>						
Gestational age (weeks)	T ₀	19.04(7.40)	21.28(7.19)	20.56(7.43)	1.679	.189
	T ₁	27.26(7.45)	29.61(7.30)	29.13(7.12)		
Primiparous	Yes	30(42.9%)	35(50.7%)	29(42.6%)	1.180	.554

	No	40(57.1%)	34(49.3%)	39(57.4%)		
Type of pregnancy	Spontaneous	63(90%)	52(75.4%)	57(83.8%)	4.612	.100
	Fertility treatment	7(10%)	17(24.6%)	11(16.2%)		
High-risk pregnancy	Yes	13(18.6%)	12(17.4%)	11(16.2%)	.138	.933
	No	57(81.4%)	57(82.6%)	57(83.8%)		
Wanted pregnancy	Yes	60(85.7%)	64(92.8%)	61(89.7%)	1.825	.402
	No	10(14.3%)	5(7.2%)	7(10.3%)		

Note: (*) = statistically significant difference; T₀ = pre-intervention; T₁ = post-intervention.

Efficacy of online stress management CBT during the COVID-19 pandemic in reducing stress and increasing resilience

The linear mixed models showed interaction in pregnancy-specific stress scores (PDQ) ($F(2, 197.48) = 6.27; p \leq .002; \eta^2 = .06$) and perceived stress scores (PSS-14) ($F(2, 192.78) = 5.02; p \leq .007; \eta^2 = .05$) between the pre- and post-treatment. With respect to the PDQ, the three groups reduced their scores in the post-treatment, the o-CBT notably presenting a median effect size ($d = 0.62$), while the remaining two showed a small effect size. As for the PSS-14, the o-CBT presented a medium, almost large change effect size ($d = 0.76$) in stress reduction, while the o-PS and UC showed a small effect size. No interaction was found for the vulnerability to stress variable. These results can be found in Table 3.

Table 3. Linear mixed models and mean differences after intervention in the three groups on the main measures of stress, resilience and psychopathology.

Group	Linear Mixed Models			Tukey post hoc test			
	T ₀ M(SD)	T ₁ M(SD)	F(df)	p	η^2	p	d
PDQ			6.27(2, 197)	.002**	.06		
o-CBT	19.81(6.23)	15.70(6.95)				.001**	0.62
o-PS	18.78(6.80)	16.79(6.48)				.001**	0.15
UC	17.93(6.17)	16.59(6.86)				.022*	0.20
PSS-14			5.02(2, 197)	.007**	.05		
o-CBT	27.7(7.67)	21.54(8.65)				.001**	0.76
o-PS	25.25(9.06)	22.59(8.47)				.003**	0.15
UC	26.31(9.09)	23.57(9.55)				.002**	0.29
CD-RISC			7.08(2, 192)	.001**	.07		
o-CBT	23.87(5.96)	26.90(6.24)				.001**	0.24
o-PS	26.52(6.26)	27.65(6.62)				.050	0.09
UC	27.97(7.04)	28.07(6.78)				.852	0.01
SCL-90-R OBS			8.13(2, 197)	.001**	.08		
o-CBT	84.93(17.3)	73.81(25.2)				.001**	0.51
o-PS	78.12(23.5)	75.40(26.4)				.483	0.05
UC	74.34(26.7)	75.54(24.8)				.597	0.02
DEP			6.23(2, 197)	.002**	.06		
o-CBT	75.23(23.4)	59.00(29.5)				.001**	0.61
o-PS	70.03(28.4)	65.06(29.9)				.036*	0.17
UC	71.54(26.6)	66.53(28.2)				.049*	0.19
ANX			7.05(2, 197)	.001**	.07		
o-CBT	77.43(18.9)	66.06(23.1)				.001**	0.54
o-PS	75.93(22.5)	71.40(26.2)				.039*	0.18
UC	71.81(28.2)	71.47(26.2)				.873	0.01

Note: *p < .05; **p < .01; T₀ = pre-intervention; T₁ = post-intervention; PDQ = Pregnancy Distress Questionnaire; PSS-14 = Perceived Stress Scale-14; CD-RISC = Connor Davidson Resilience Scale; SCL-90-R = The Symptom Checklist-90-Revised; OBS = obsession-compulsion; DEP = depression; ANX = anxiety; o-CBT = online cognitive-behavioral therapy group; o-PS = online psychological support group; UC = usual care group.

Figure 2 below shows the main differences between pre- and post-stress intervention.

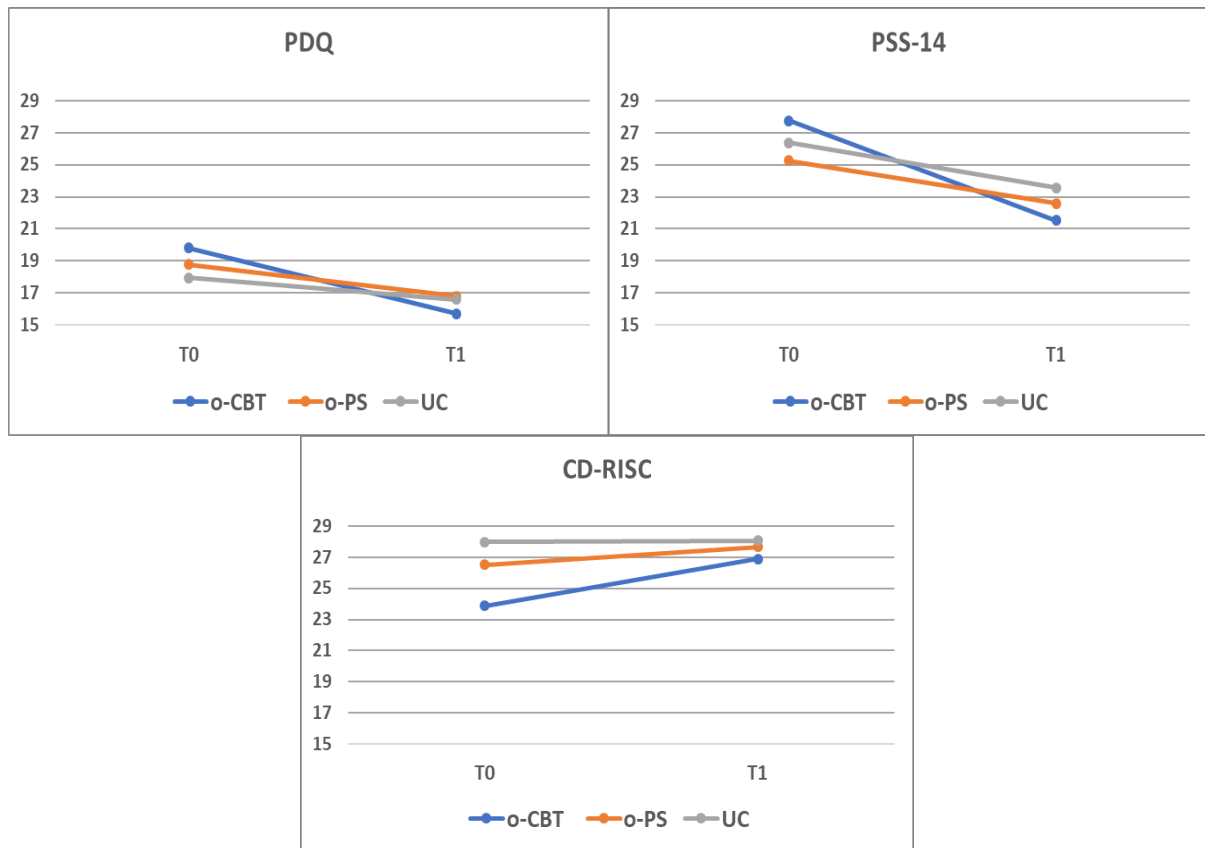


Figure 2. Perceived stress, pregnancy-specific stress and resilience scores before and after the intervention of the three groups.

Note: T₀ = pre-intervention; T₁ = post-intervention; o-CBT = online cognitive-behavioral therapy group; o-PS= online psychological support group; UC= usual care group; PDQ= Pregnancy Distress Questionnaire; PSS-14= Perceived Stress Scale-14; CD-RISC= Connor Davidson Resilience Scale.

In addition, a linear mixed model presented interaction in the resilience variable (CD-RISC) ($F(2, 192.78) = 7.08, p \leq .001; \eta^2 = .07$). In this way, the o-CBT increased its post-treatment scores. The o-PS and HC showed no improvement in relation to their scores between the first and second evaluation. These results can be found in Table 3 and Figure 2.

Efficacy of online stress management CBT during the COVID-19 pandemic in reducing psychopathological symptoms

As far as the psychopathological symptoms are concerned, interaction was found via the linear mixed models in the symptom scores of obsession-compulsions (OBS), depressives (DEP) and anxious (ANX) between pre- and post-treatment. As observable in Table 3, the scores decreased after treatment for the variables: anxiety, depression and obsession-compulsion, all variables presenting a medium effect size. For its part, o-PS presented a drop in depressive symptomatology and anxiety, with an effect size that does not reach the cut-off point to be considered a small effect size (<0.20) (see Table 3). To finish, Figure 3 shows the main pre- and post-intervention differences in obsession-compulsion, depression and anxiety symptomatology.

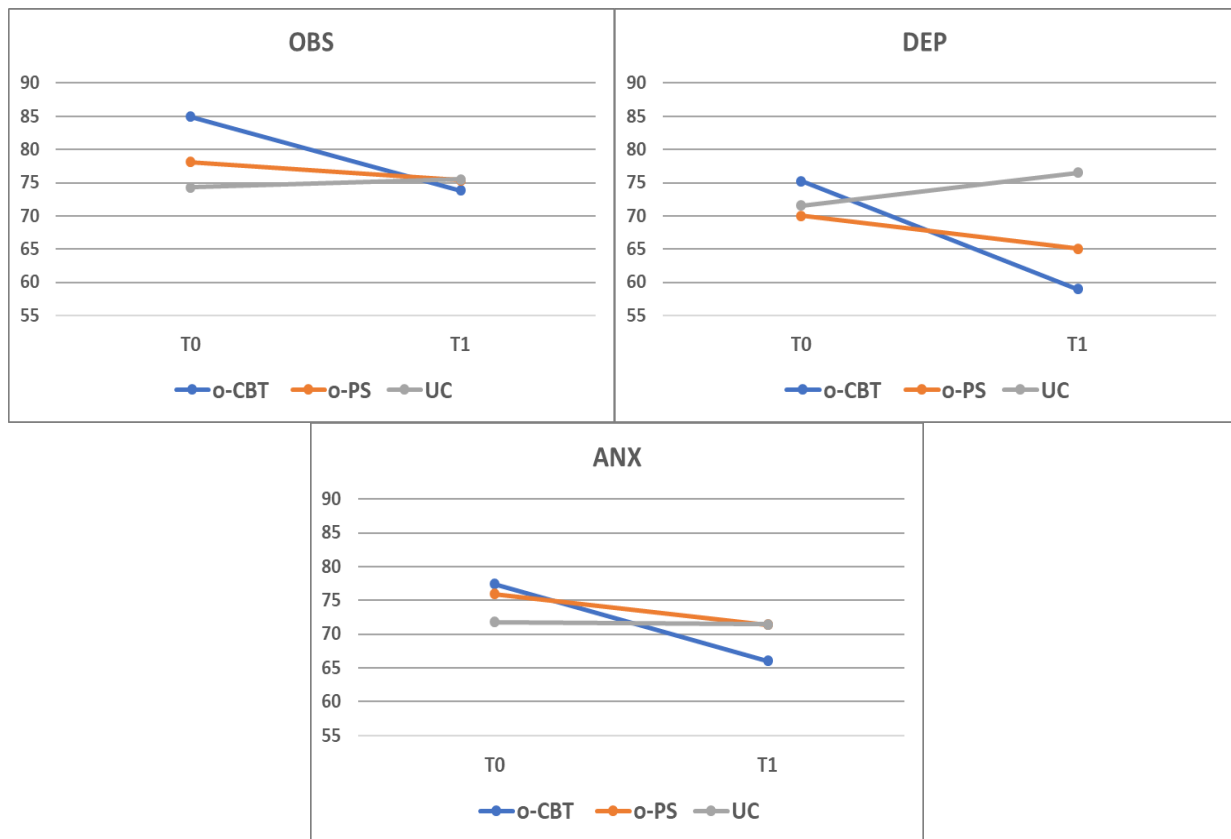


Figure 3. Obsession-compulsion, depression and anxiety scores before and after the intervention of the three groups.

Note: T₀ = pre-intervention; T₁ = post-intervention; o-CBT = online cognitive-behavioral therapy group; o-PS= online psychological support group; UC= usual care group; OBS= obsession-compulsion; DEP= depression; ANX= anxiety.

Discussion

The objective of this study was to test the efficacy of an online cognitive behavioural stress management therapy in pregnant women during the COVID-19 pandemic in Spain. In order to achieve this goal, three groups of pregnant women were compared, one group that attended online stress management therapy, another group of online psychological support and another that received standard medical care.

The results showed that pregnancy-specific stress levels and perceived stress levels significantly decreased after treatment to a greater extent in the o-CBT group than in the other groups. There was no evidence of improvement in any of the groups regarding vulnerability to stress, understood as a person's predisposition to be influenced by perceived stress. These results are in line with that of previous studies that examined the efficacy of this therapy in a presential modality before the pandemic (Romero-Gonzalez, et al., 2020), and which found a reduction in both pregnancy-specific stress and perceived stress in the therapy group. These data also support that of other authors who found a decrease in perceived stress in pregnant women who had gestational diabetes (Zaheri, et al., 2017).

Improvements in coping with stress are critical for this population, as they are vulnerable to stress due to their pregnancy (Romero-Gonzalez, et al., 2020). It is also particularly relevant due to the current pandemic situation where the symptomatology associated with stress is aggravated (Puertas-Gonzalez, et al., 2021a). Thus, training in deactivation techniques (diaphragmatic breathing and thematic imagination), as well as training in detecting and transforming distortions and irrational thoughts, together with training in social skills and time management, have probably provided participants with key tools to cope with the psychological stress related to the COVID-19 pandemic. In this way, participants had a wider range of ways of coping with direct (e.g. fear of infection) and indirect (e.g. confinement, lack of social contact, etc.) fears and concerns caused by the pandemic. These

results have major clinical implications, since prenatal stress can negatively affect a baby's cognitive and motor neurodevelopment (Caparros-González, et al., 2019b). Improving maternal mental health would therefore be a protective factor regarding potential neurodevelopmental problems in babies.

On the other hand, it is worth noting that the participants who attended online therapy considerably improved their resilience, while no change was observed with respect to this variable in the psychological support group or in the usual care group. These results support the findings of Puertas-González, et al., which also reflected the improved resilience of pregnant women who attended therapy (Puertas-González, et al., 2021b). Resilience is an ability to cope with adverse situations (Connor and Davidson, 2003), which is why, in the current situation of pandemic and the vulnerability entailed by gestation, an increase in resilience represents a key buffer against negative psychological effects during this critical period of life (Puertas-González, et al., 2021b). The increase in resilience in the treatment group may be due to the stress coping techniques taught during the sessions. Indeed, women are trained in cognitive distortions and irrational beliefs, which strengthens their resilience. This increase was not found in the psychological support group who were only trained in psychoeducation and active listening. In this sense, stress management learning techniques can increase the ability to cope with adverse situations.

With respect to psychopathology, the o-CBT group showed a significant reduction in anxiety, depression and obsessions after treatment. These data are in line with those found by several studies that showed a decrease in psychopathology symptomatology after conducting a presentational intervention for stress reduction in different fields (Bradbury et al., 2008; Linares-Ortiz et al., 2014; Romero-Gonzalez, et al., 2020; Santos-Ruiz et al., 2017). In this way, reducing psychological stress and increasing resilience is expected to lead to a reduction in anxiety, depression and obsessions, thus improving the psychological state of pregnant women

in a highly threatening situation such as living through a global pandemic, both for women and for their babies. In addition, these data are also consistent with a study conducted before the pandemic, which found that internet-based cognitive behavioural therapy for prenatal depression reduced levels of depression in pregnant women (Forsell et al., 2017).

Added to the above, it is worth noting that many changes in the body during pregnancy can bring about poor psychological adaptation (Nayak et al., 2015). Therapy could thus be a protective factor by reducing symptoms, considering that greater participation in healthy practices affects women's general well-being (Alhusen et al., 2016); in this line, psychological support produces an improvement in psychopathological symptoms, although not as significantly as therapy, active listening and the use of empathy being notably relevant factors to consider in interventions. There is clear evidence, however, of the importance of learning specific stress control techniques during therapy and the reduction of associated psychopathological symptomatology that comes with it.

Despite the findings, this study presented various limitations. A major limitation was the fact that the variables were measured at two different moments in time without any follow-up. A long-term follow-up of participants could provide us with data on the progression of changes found in the participants. In addition, the trimester in which the participants found themselves at the time of joining the study is significant, because depending on the pregnancy trimester, the woman's stress levels, their origin and biological manifestation may differ (Nayak et al., 2015). It is important to take this data into account when recruiting participants in future works. On the other hand, although the intervention groups were led by two different psychologists with extensive experience, there was not fidelity monitoring to assess deviation from the protocol. Another limitation is that although the instrument used in order to assess pregnancy-specific stress (Prenatal Distress Questionnaire; PDQ) is robust and widely used, there is a new version of this questionnaire (Prenatal Distress Questionnaire Revised; NuPDQ).

This new version seems to have conceptual and methodological advantages (Ibrahim & Lobel, 2020), but when we designed the study, the Spanish validation had not yet been published. For this reason, we encourage the use of the new version in future similar research.

To conclude, clear evidence was obtained that online cognitive-behavioural intervention during the COVID-19 pandemic brings about positive results for pregnant women: improvements took place regarding pregnancy-specific stress and perceived stress, psychopathological symptomatology was reduced, and resilience increased. These factors are of vital importance in coping with crises. Therefore, cognitive behavioural therapy for stress management in pregnant women could prevent increased stress and psychopathological symptoms resulting from a pandemic, acting as a "psychological vaccine" or buffer, in a metaphorical sense.

Lastly, it is important to understand the psychological impact of pregnancy on the well-being of both the mother and child, pregnancy often being considered as the golden stage of a woman's life. Yet pregnancy entails a series of physical and mental challenges that often go unnoticed, added to the knowledge that the gestation period can affect the child's mental and physical health in the long term. Despite awareness of these data, psychological aspects are often overlooked during pregnancy and the vast majority of women are not conscious of the consequences that mental health problems can have during the period of gestation, childbirth, lactation and even the baby's neurodevelopment (Caparros-González et al., 2017; Caparros-González, et al., 2019b, 2019c; Kumar-Nayak et al., 2015).

These data thus highlight the importance of implementing intervention programmes during pregnancy, not only to facilitate adequate maternal mental health during the gestation period, but also as a long-term protective factor of good public health.

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DISCUSIÓN GENERAL

7. DISCUSIÓN GENERAL

El objetivo general de la presente Tesis Doctoral fue evaluar la eficacia de la Terapia Cognitivo-Conductual (TCC) para el manejo del estrés en mujeres gestantes, aplicada en modalidad presencial y telemática. Para ello, esta tesis compendia siete estudios publicados en revistas indexadas en el *Journal Citation Report* (JCR), divididos en dos bloques de objetivos

El primer bloque titulado “Eficacia de la TCC en mujeres embarazadas y efectos en la descendencia” se centra en dos objetivos específicos. El primer objetivo específico de este bloque fue investigar si los niveles de cortisol en pelo y/o el estrés psicológico durante el momento de la concepción y las primeras semanas de embarazo presentan una relación con el sexo fetal. Para la consecución de este, se ha presentado el estudio 1, que contó con un diseño de cohorte retrospectivo e investigó la relación entre los niveles de cortisol en cabello de la madre y el sexo fetal durante el tiempo de concepción y las primeras semanas de embarazo. Los resultados indicaron una asociación entre niveles más elevados de concentración de cortisol en cabello durante dicho periodo y una mayor probabilidad de tener un feto femenino. Sin embargo, no se halló una relación entre el estrés psicológico de la madre y el sexo fetal.

Por consiguiente, los resultados de la investigación parecen respaldar las teorías explicativas que sugieren que esta hormona tiene un papel crucial en la determinación del sexo del feto, durante el momento de la concepción y primera etapa del embarazo. Estos hallazgos se encuentran en sintonía con los informados por Chason y cols. (2012), quienes mostraron que las mujeres que presentaban niveles más altos de cortisol en la saliva antes de la concepción tenían menos probabilidades de tener un feto masculino. Por otro lado, Enlow y cols. (2019) encontraron concentraciones de cortisol en el cabello materno más altas durante los tres trimestres de embarazo para las madres cuyo feto era masculino, de forma contraria Vrijkotte

y cols. (2023) hallaron niveles de cortisol más elevados, en mujeres que estaban embarazadas de fetos femeninos, entre las semanas 12 y 20 de embarazo, pero no hallaron diferencias antes de la semana 12 durante el embarazo temprano. De este modo, aunque nuestro estudio y el de Chason y cols. (2012) muestran resultados que van en la misma línea, encontramos contradicciones entre los resultados de Enlow y cols. (2019) y Vrijkotte y cols. (2023), lo que refleja la necesidad de continuar estudiando las influencias del cortisol materno y el sexo fetal a lo largo de embarazo temprano y tardío.

Como conclusión, el estudio 1 apoya la hipótesis de que la activación del eje Hipotálamo-Hipófisis-Adrenal (HHA) tiene implicaciones en la determinación de sexos durante el momento de la concepción, en la misma línea que el estudio de Chason y cols. (2012). Una posible explicación es que la activación del eje HHA y la liberación de cortisol modifica las concentraciones de hormonas sexuales en el momento de la concepción (James y Grech, 2017). Por ejemplo, los niveles de cortisol podrían modular en distintos periodos reproductivos los niveles de testosterona maternal y estos podrían influir en la concepción (Grant, 2007). Además, las variaciones en la viscosidad del moco cervical podrían dar ventaja a los espermatozoides portadores del cromosoma X en determinados contextos, por lo que cuando se producen cambios hormonales estos podrían atravesar el moco cervical en mayor proporción que los portadores del cromosoma Y (Navara, 2018). Sin embargo, los mecanismos subyacentes a las interacciones anteriores se desconocen actualmente y la relación entre el estrés, la viscosidad del moco cervical y la selección de espermatozoides aún no está claramente establecida, y se requieren más estudios para confirmar o refutar las hipótesis comentadas.

El siguiente trabajo de la presente Tesis Doctoral, el estudio 2, responde al segundo objetivo específico del primer bloque, el cual fue comprobar la eficacia en la reducción del estrés de la TCC en las mujeres embarazadas, tanto a nivel psicológico como a nivel hormonal,

y cómo se relaciona dicha eficacia con el posterior neurodesarrollo y cortisol del bebé. Dicho estudio fue un seguimiento de un ensayo controlado aleatorio, el cual contó con dos grupos de mujeres embarazadas, uno que recibió TCC para el control de estrés durante el embarazo y un grupo control. Posteriormente, se evaluaron los niveles de cortisol de los bebés de las participantes tras el nacimiento y a los 6 meses de vida, así como, su neurodesarrollo también a los 6 meses. Por un lado, en relación con la TCC para el manejo del estrés, los resultados de la submuestra utilizada en este estudio muestran reducciones similares en Grupo de Terapia (GT) a las del estudio previo con respecto a los síntomas psicopatológicos, el estrés percibido y específico del embarazo y, un aumento de los niveles de cortisol en el Grupo Control (GC). De este modo, las diferencias halladas entre los bebés de ambos grupos pueden ser parcialmente atribuibles a los efectos de la terapia.

Así, con respecto a los niveles de cortisol, los bebés del TG presentaron menor concentración de cortisol al nacer, sin embargo, no se encontraron diferencias significativas entre los dos grupos en relación con los niveles de cortisol a los 6 meses. La reducción de la concentración de cortisol en el cabello de los bebés en el momento del nacimiento puede ser debida a la disminución de tres parámetros en la madre al final del embarazo: niveles de cortisol en pelo, estrés percibido y estrés específico del embarazo (Kapoor y cols., 2006). Por otro lado, a los 6 meses no se halló esta diferencia entre los grupos, lo que indica que los efectos de la TCC en la madre durante el embarazo tuvieron implicaciones únicamente en los niveles de cortisol de los bebés a corto plazo. Estos resultados nos hacen hipotetizar que tras el nacimiento del bebé existen numerosos factores que pueden estar influyendo como son el patrón de crianza y apego, estatus socioeconómico de la familia, temperamento del niño, etc., e incluso diferentes patrones de lactancia y/o sueño, que pudieron influir de modos distintos en los niveles de cortisol de los participantes (Flom, y cols., 2017).

Con respecto al neurodesarrollo, los resultados mostraron que los bebés de los TG presentaban un mayor neurodesarrollo cognitivo y motor a los 6 meses, pero no en relación con el neurodesarrollo del lenguaje. Estos hallazgos son compatibles con los de otros estudios que encontraron que las concentraciones elevadas de cortisol materno se relacionaban con un peor neurodesarrollo cognitivo y motor en los bebés a los 6 meses (Buitelaar y cols., 2003; Caparros-González y cols., 2019). En consonancia con la hipótesis de los orígenes evolutivos de la salud y la enfermedad (Arabin y cols., 2021; Barker, 1998; Langley-Evans, 2006; Seckl y Holmes, 2007), que afirma que los cambios experimentados por las madres durante el embarazo pueden influir en la salud del bebé y por consiguiente en su posterior neurodesarrollo (Barker y cols., 1993). En este caso, la TCC podría haber otorgado, a las madres de dicho grupo, herramientas eficaces de afrontamiento para abordar los cambios vitales y situaciones estresantes, desembocado en beneficios psicológicos y fisiológicos para las mismas, que a su vez pudieron influir positivamente en el ambiente uterino y en los primeros meses de vida de sus bebés.

A modo de conclusión del primer bloque, los estudios 1 y 2 revelan que existe una relación entre la concentración de cortisol de la madre durante el momento de la concepción y los primeros meses de embarazo y el sexo fetal. Además, la TCC para el afrontamiento del estrés aplicada durante el embarazo, es eficaz en la reducción de síntomas psicopatológicos, estrés percibido y específico del embarazo estrés, así como en la amortiguación del incremento de los niveles de cortisol al final del embarazo. Finalmente, la disminución y control de estos parámetros en la madre durante el embarazo, podría tener implicaciones en las concentraciones de cortisol de los bebés a corto plazo y en el neurodesarrollo motor y cognitivo a medio y largo plazo. Así, de acuerdo con la hipótesis de los orígenes evolutivos de la salud y la enfermedad, del mismo modo que un ambiente desfavorable durante el periodo fetal puede tener consecuencias negativas futuras, un ambiente favorable durante el periodo fetal puede ser clave

para prevenir enfermedades y promover un marco favorable de desarrollo durante períodos críticos (Behnam y cols., 2022; McDonald y cols., 2022).

El segundo bloque de objetivos se titula “Eficacia de la TCC implementada de manera telemática durante una crisis sanitaria” y cuenta con tres objetivos específicos. El primero de ellos consistió en estudiar la salud psicológica perinatal durante la pandemia en el transcurso del embarazo y tras dar a luz. Para la consecución de este objetivo se llevaron a cabo dos trabajos: el estudio 3 y el estudio 4.

En el estudio 3 se comparó la sintomatología psicopatológica, el estrés percibido y el estrés específico del embarazo de dos cohortes de mujeres durante su embarazo: el primer grupo evaluado antes de la pandemia por la COVID-19; y el segundo grupo evaluado durante dicha crisis sanitaria. Los resultados mostraron que el grupo de mujeres gestantes durante la crisis sanitaria presentaban mayores niveles de sintomatología depresiva y de ansiedad fóbica, así como, mayores niveles de estrés percibido. Además, los niveles de insomnio, junto con haber sufrido recientemente la pérdida de un ser querido, explicaron el 25% de la varianza de los niveles de depresión, mientras que, el miedo al contagio por COVID-19 predecía el incremento en los niveles de ansiedad fóbica, explicando el 11% de la varianza. Finalmente, el insomnio también explicó el 13% de la varianza de los síntomas de estrés percibido. Así, la pandemia causada por la COVID-19 produjo un aumento de sintomatología psicopatológica y el estrés, que pudo afectar negativamente la salud mental de las gestantes.

Por otro lado, el estudio 4, el cual corresponde al segundo estudio destinado a cubrir el tercer objetivo específico, consistió en comparar los síntomas psicopatológicos, depresión posparto, estrés percibido y resiliencia de dos cohortes: un grupo de mujeres que dieron a luz antes de la crisis sanitaria derivada por la COVID-19; y, un segundo grupo de mujeres que dieron a luz durante la misma. Las participantes de ambos grupos fueron evaluadas durante el

mes inmediatamente posterior al parto. Los resultados arrojaron que las mujeres que dieron a luz durante la pandemia presentaban niveles más altos de depresión, ansiedad, hostilidad, ansiedad fóbica, somatización, obsesiones y compulsiones, sensibilidad interpersonal y psicoticismo. Asimismo, se halló que el estrés percibido fue el predictor común de dichos síntomas psicopatológicos, presentando una relación lineal positiva con los mismos.

Por lo tanto, los estudios 3 y 4 nos revelan que la salud mental de las mujeres en España durante el embarazo se vio afectada por la crisis sanitaria derivada por la pandemia por la COVID-19. Los resultados hallados se encuentran en consonancia con otros estudios que han investigado la salud mental durante otras crisis sanitarias, como, por ejemplo, los trabajos que mostraron un incremento de los niveles de depresión y ansiedad durante la pandemia provocada por el SARS en 2003 (Liu y cols., 2003; Maunder y cols., 2003). Asimismo, también se encuentran en línea con los resultados encontrados por otros autores realizados en diferentes países y que han encontrado un aumento de sintomatología psicopatológica y estrés en mujeres embarazadas durante la pandemia por la COVID-19 (Hessami y cols., 2020; Liu y cols., 2021; Wu y cols., 2020).

El incremento de sintomatología psicopatológica y estrés en las mujeres durante el embarazo pudo atender a diferentes razones. Por un lado, durante dicho periodo, la población tuvo que afrontar situación repentina, novedosa y marcada por la incertidumbre, lo que provocó que la población española e internacional tuvieran que adaptarse a un contexto no convencional y de evolución incierta. Así, este repentino y abrupto cambio derivó en consecuencias directas en el estilo de vida, ya que, con el objetivo de reducir la expansión del virus, se restringió radicalmente la libertad de las personas para salir de sus hogares y circular libremente, así como el contacto social entre la población. Además, el miedo a la infección (Nanjundaswamy y cols., 2020) y la transmisión constante por parte de los medios de comunicación de la gravedad y letalidad del virus, también pudo jugar un papel clave en el aumento de los síntomas de

ansiedad, depresión y disforia psicológica (Smith y cols., 2020). Concretamente, para las mujeres embarazadas, esto pudo ser una fuente aún mayor de ansiedad y estrés, puesto que la conciencia de una conexión biológica directa con el feto podría conducir a un mayor estado de alerta y autoprotección (Wu y cols., 2020). Finalmente, las preocupaciones vinculadas al futuro, relacionadas con una posible crisis económica derivada de la pandemia, pudo afectar a las perspectivas futuras de la calidad de vida de las mujeres embarazadas y de sus hijos, factores que pudieron influir negativamente sobre la sintomatología ansiosa y depresiva.

El segundo objetivo específico del segundo bloque, consistió en investigar la interacción de la resiliencia, estrés y ansiedad en mujeres embarazadas en dos situaciones de estrés distintas: antes y durante la pandemia por la COVID-19. Para abordar este objetivo se llevó a cabo el estudio 5, en el cual se estudió la relación entre la resiliencia psicológica, estrés percibido, estrés específico del embarazo y ansiedad, del mismo modo que en los dos estudios previos, a través de dos cohortes de mujeres gestantes: el primero evaluado antes de la pandemia; y, el segundo evaluado durante la misma. Para estudiar la relación de dichas variables se aplicó en ambos grupos un modelo de ecuaciones estructurales. Asimismo, se compararon los niveles de cada variable entre las dos muestras.

En ambos grupos, los modelos presentaron un buen ajuste y se observó que la resiliencia disminuía los niveles de estrés específico del embarazo y el estrés general percibido, así como la sintomatología de ansiosa. Por otro lado, el estrés específico del embarazo y el estrés percibido presentaron correlación entre ambos y, éstos a su vez, predecían el aumento de los síntomas de ansiedad. Estos hallazgos están en consonancia con estudios previos que evaluaron la resiliencia y sus relaciones con la salud perinatal (García-León y cols., 2019; Lubián-López y cols., 2021).

Asimismo, aunque ambos modelos presentaron un buen ajuste, el modelo aplicado al grupo evaluado durante la pandemia explicó una mayor varianza de la sintomatología de ansiosa. Las diferencias entre la variabilidad explicada de los síntomas de ansiedad entre ambos modelos, podría deberse, al menos parcialmente, a las diferencias entre los niveles de cada una de las variables psicológicas estudiadas entre las participantes de ambas muestras, las cuales estaban viviendo en contextos distintos debido a la pandemia. Concretamente, la cohorte evaluada durante la crisis sanitaria mostró mayores niveles de estrés específico del embarazo, ansiedad, somatizaciones y obsesiones-compulsiones, mientras que el grupo evaluado antes de la pandemia presentó mayores niveles de estrés percibido.

Es conveniente destacar, en contraste con el artículo 3, que las mujeres del grupo evaluado en pandemia presentaron menores niveles de estrés percibido que el grupo evaluado previa a la misma. Esta discrepancia puede atender al hecho de que en el estudio 3 se contó con un marco temporal más reducido, puesto que el grupo de la pandemia fue evaluado entre marzo y junio de 2020, mientras que, en el presente estudio, el grupo correspondiente al periodo de pandemia fue evaluado entre marzo de 2020 y marzo de 2021. De este modo, el estudio 3 aportó información a corto plazo de la salud perinatal de la pandemia y el estudio 5 reveló información a largo plazo. Así, se puede deducir que al inicio de la pandemia las mujeres embarazadas presentaron un incremento de sus niveles de estrés percibido y, posteriormente, estos se fueron reduciendo.

Una de las posibles explicaciones para la reducción de los niveles de estrés a largo plazo durante la pandemia, puede ser, que al inicio la situación novedosa y repentina propiciara que la pandemia actuase como disparador del estrés en esta población, sin embargo, una vez que las personas se habituaron y se adaptaron a la situación esos síntomas disminuyesen. Asimismo, que esos síntomas disminuyesen incluso hasta el punto de presentar menores niveles de estrés que la misma población en una situación pre-pandemia, pudo ser debido al aumento del tiempo

en casa y a la eliminación y/o reducción de estresores cotidianos, tales como: visitas al supermercado y otras tiendas durante la semana; trabajo presencial; eventos y/o compromisos sociales, etc. Además, la promoción del teletrabajo y la flexibilidad horaria que se derivó de la crisis sanitaria también pudo contribuir a reducir los niveles de estrés percibido.

Finalmente, con respecto al objetivo que cubre el estudio 5, se puede concluir que la resiliencia actúa como un factor protector frente a los síntomas de estrés percibido, estrés específico del embarazo y ansiedad en las mujeres en periodo de gestación, tanto en situaciones vitales ordinarias, como en situaciones envueltas en crisis sanitarias.

El tercer y último objetivo específico del segundo bloque, fue estudiar la viabilidad y eficacia de la TCC para el control del estrés en mujeres embarazadas, aplicada telemáticamente durante la pandemia. Para la consecución de dicho objetivo se llevaron a cabo los estudios 6 y 7.

En el estudio 6 se investigó la viabilidad de la TCC para la gestión del estrés en mujeres embarazadas, aplicada de manera telemática durante la pandemia, sobre las principales variables de estrés psicológico y psicopatología. Así, se aplicó de manera telemática un programa de 8 semanas basado en la TCC para el manejo del estrés (programa investigado en modalidad presencial en el estudio 2) a un grupo reducido de mujeres embarazadas, durante la pandemia de COVID-19. Los resultados mostraron que las participantes presentaban al finalizar la intervención, un aumento significativo de la resiliencia psicológica, reducción significativa en los niveles de estrés percibido y estrés específico del embarazo, así como, una reducción en diferentes síntomas psicopatológicos: obsesiones-compulsiones, ansiedad, psicoticismo y ansiedad fóbica.

Por lo tanto, el programa mostró indicios de ser viable para promover la salud psicológica durante el embarazo, aplicado de manera telemática en un contexto de crisis

sanitaria. Asimismo, se hizo necesaria la aplicación de un ensayo controlado aleatorizado, con el fin de comprobar la eficacia del programa en una muestra representativa de la población estudiada, lo que da paso al siguiente estudio.

Finalmente, el estudio 7, consistió en estudiar la eficacia de la TCC para el control del estrés en mujeres embarazadas, aplicada telemáticamente durante la pandemia, a través de un ensayo controlado aleatorizado. Para ello, en este estudio se contó con un grupo de mujeres embarazadas que a su vez se dividió aleatoriamente en tres grupos: un primer grupo al que se aplicó el programa de intervención para el manejo del estrés de manera telemática; un segundo grupo que recibió apoyo emocional, también de manera telemática; y, un tercer grupo que únicamente recibió los cuidados habituales del embarazo.

Mediante este estudio se comprobó que el grupo que recibió el programa para el control del estrés, presentó una reducción mayor en los niveles de estrés percibido y estrés específico del embarazo que los otros grupos, así como también, una reducción mayor de sintomatología depresiva y ansiosa. Además, el grupo que recibió el programa fue el único grupo que presentó un aumento de la resiliencia psicológica y una reducción estadísticamente significativa en obsesiones-compulsiones. Por lo tanto, el programa resultó eficaz, no únicamente para reducir los niveles de estrés y aumentar la resiliencia, sino que también consiguió reducir la sintomatología psicopatológica de ansiedad, depresión y obsesiones-compulsiones. Asimismo, estos resultados concuerdan con los de estudios anteriores que examinaron la eficacia de esta terapia en una modalidad presencial antes de la pandemia (Romero-Gonzalez y cols., 2020).

Por consiguiente, el entrenamiento en técnicas de desactivación, como la respiración diafragmática y la imaginación temática, junto con el entrenamiento en la identificación y transformación de distorsiones y pensamientos irracionales, así como en habilidades sociales y gestión del tiempo, proporcionaron a las participantes herramientas esenciales para enfrentar

el estrés psicológico asociado a la pandemia de COVID-19. De esta manera, las participantes contaban con un conjunto amplio de estrategias para abordar temores y preocupaciones directas (por ejemplo, miedo a la infección) e indirectas (por ejemplo, confinamiento, falta de contacto social, etc.) derivadas de la pandemia.

A modo de conclusión del bloque 2, las situaciones de crisis sanitarias como las pandemias, en las que se adoptan medidas restrictivas sobre la libre circulación de las personas y el contacto social, desembocan en un aumento del estrés y los síntomas psicopatológicos en el periodo perinatal. Sin embargo, la resiliencia psicológica puede actuar como un factor protector del aumento del estrés y los síntomas ansiosos, tanto en situaciones de crisis como en contextos ordinarios. Por último, un programa de intervención psicológica basado en la TCC para el manejo del estrés, aplicado de manera telemática, puede aumentar los niveles de resiliencia psicológica y reducir los niveles de estrés y los síntomas psicopatológicos en mujeres gestantes, en la misma medida que lo hace un programa de intervención presencial.

En relación a las limitaciones de la presente Tesis Doctoral, hubiera sido interesante durante la aplicación de las intervenciones llevar a cabo evaluaciones del progreso, de esta forma se podrían haber obtenido conclusiones sobre la eficacia de cada módulo de manera independiente. Por tanto, comprobar la eficacia de cada módulo del programa se plantea como perspectiva futura. Por otro lado, también hubiese sido de interés realizar un seguimiento de estas mujeres durante todo el embarazo, incluso durante y después del parto.

**CONCLUSIONES, PERSPECTIVAS FUTURAS E
IMPLICACIONES METODOLÓGICAS Y
CLÍNICAS**

8. CONCLUSIONES, PERSPECTIVAS FUTURAS E IMPLICACIONES METODOLÓGICAS Y CLÍNICAS

8.1 Conclusiones

Como resultado de los estudios que han sido incluidos en esta Tesis Doctoral, se pueden obtener las siguientes conclusiones:

- La activación del eje Hipotálamo-Hipófisis-Suprarrenal (HHA), en el momento de la concepción y las primeras semanas de embarazo, puede tener implicaciones en la determinación del sexo fetal. Concretamente, mayores concentraciones de cortisol en el cabello de la madre durante este periodo se asocian con el sexo fetal femenino.

- La TCC para el afrontamiento del estrés, aplicada durante el embarazo en modalidad presencial, puede utilizarse para la promoción de la salud psicológica, con beneficios potenciales, no únicamente para la mujer gestante, sino también para su descendencia.

- Las crisis sanitarias, como las pandemias, derivan en un aumento de síntomas psicopatológicos y estrés en las mujeres durante el embarazo y el postparto.

- La resiliencia actúa como factor protector frente a los niveles de estrés específico del embarazo, estrés percibido y ansiedad, tanto en situaciones vitales ordinarias, como en el marco de crisis sanitarias como son las pandemias.

- La TCC para el manejo del estrés, aplicada en situaciones de crisis en modalidad telemática, puede aumentar los niveles de resiliencia psicológica y reducir los niveles de estrés y los síntomas psicopatológicos en mujeres gestantes.

8.2 Perspectivas futuras

Como perspectivas futuras y cuestiones objeto de estudio para el futuro, se plantean las siguientes:

- Realizar un seguimiento, a largo plazo, de los niveles de cortisol y del neurodesarrollo de la descendencia de mujeres que han recibido el programa de intervención para el manejo del estrés durante su embarazo.

- Evaluar los síntomas psicopatológicos y el temperamento de la descendencia de las participantes del programa, para comprobar beneficios potenciales en dichas áreas.

- Investigar si el programa de control de estrés basado en la TCC aplicado telemáticamente durante el embarazo, también presenta implicaciones en la descendencia.

- Comprobar la eficacia de cada módulo del programa de manera independiente, llevando a cabo evaluaciones del progreso de la intervención al final cada módulo.

- Estudiar la eficacia a corto y a largo plazo de los programas de control de estrés basados en la TCC aplicados en el postparto.

8.3 Implicaciones metodológicas y clínicas

8.3.1 Implicaciones metodológicas

Los estudios de la presente Tesis Doctoral aportan las siguientes implicaciones metodológicas:

- Puesto que el desarrollo tecnológico presenta un crecimiento exponencial y, con el fin de aumentar la accesibilidad, se hace necesario contar con una versión telemática de las terapias psicológicas que se han venido aplicando a mujeres gestantes de manera presencial. De este modo, cada mujer podría acceder a la modalidad que mejor se adapte y encaje con sus

necesidades y rutinas diarias, puesto que ambas modalidades pueden aportar beneficios en la salud perinatal.

- La combinación de diferentes métodos de evaluación como los biomarcadores y los autoinformes para abordar un constructo, puede ayudar a profundizar en la comprensión del mismo, dando una visión más completa con especial atención a la conexión mente y cuerpo.

8.3.2 *Implicaciones clínicas*

De las investigaciones incluidas en presente Tesis Doctoral se derivan las siguientes implicaciones clínicas:

- Se recomienda como método de promoción de la salud ofrecer la posibilidad de recibir la terapia psicológica de carácter cognitivo-conductual para el manejo del estrés, a toda mujer gestantes que lo requiera, ya que se han encontrado beneficios potenciales, tanto para la futura madre, como para su descendencia.

- En situaciones de crisis sanitarias se debe poner especial atención en la salud mental perinatal, evaluando en las revisiones médicas del embarazo y postparto los niveles de estrés y síntomas psicopatológicos, con el objetivo de detectar tempranamente incrementos significativos de los mismos.

- Es recomendable la sensibilización de los profesionales de la sanidad de la importancia de la resiliencia psicológica en las mujeres gestantes, ya que detectar niveles bajos de la misma podría ser indicativo de mujeres en mayor riesgo de presentar niveles altos de estrés percibido, estrés específico del embarazo y ansiedad.

- Incluir en los tratamientos psicológicos destinados a mujeres gestantes, módulos de intervención específicos destinados a incrementar la resiliencia psicológica, ya que se ha comprobado que ésta puede reducir los niveles de estrés y ansiedad.

- Se recomienda ofrecer recursos y la formación necesaria relacionada con el uso de nuevas tecnologías, a las mujeres gestantes que quieran acceder a la modalidad virtual de una intervención psicológica que le sea ofrecida, facilitando la inclusión y el acceso a dicha intervención.

INTERNATIONAL PhD

9. INTERNATIONAL PhD

9.1 Conclusions

As a result of the studies that have been included in this Doctoral Thesis, the following conclusions can be drawn:

- Activation of the Hypothalamic-Pituitary-Adrenal (HPA) axis at conception and in the first weeks of pregnancy may have implications for fetal sex determination. Specifically, higher levels of cortisol in maternal hair during this period are associated with female fetal sex.

- CBT for stress coping, applied during pregnancy in a face-to-face modality, can be used for the promotion of psychological health, with potential benefits, not only for the pregnant woman, but also for her offspring.

- Health crises, such as pandemics, result in increased psychopathological symptoms and stress in women during pregnancy and postpartum.

- Resilience acts as a protective factor against pregnancy-specific stress levels, perceived stress and anxiety, both in ordinary life situations and in the context of health crises such as pandemics.

- CBT for stress management, applied in crises in telematic modality, can increase levels of psychological resilience and reduce stress levels and psychopathological symptoms in pregnant women.

9.2 Future perspectives

In regards to perspectives and issues to be studied in the future, the following research area are proposed:

- Conduct long-term follow-up of cortisol levels and neurodevelopment in the offspring of women who have received the stress management intervention program during pregnancies.
- Assess the psychopathological symptoms and temperament of the offspring of program participants, to test for potential benefits in these areas.
- Investigate whether the CBT-based stress management program applied telematically during pregnancy also has implications for offspring.
- Test the effectiveness of each module of the program independently, conducting evaluations of the progress of the intervention at the end of each module.
- Study the short-term and long-term efficacy of CBT-based stress management programs applied in the postpartum period.

9.3 Methodological and clinical implications

9.3.1 Methodological implications

The studies in this Doctoral Thesis provide the following methodological implications:

- Given the exponential growth of technological development, it is necessary to have a telematic version of the psychological therapies that have been applied to pregnant women in person. In this way, accessibility is increased allowing each woman to access the modality that best suits her needs and daily routines, since both modalities can provide benefits for perinatal health.
- Combining different assessment methods such as biomarkers and self-reports to address a construct can help to deepen the understanding of the construct, giving a more complete picture with special attention to the mind-body connection.

9.3.2 *Clinical implications*

The following clinical implications are derived from the research included in this Doctoral Thesis:

- It is recommended as a health promotion method to offer the possibility of receiving cognitive-behavioral psychological therapy for stress management to all pregnant women who require it, since potential benefits have been found, both for the expectant mother and for her offspring.

- In health crises, special attention should be paid to perinatal mental health, evaluating stress levels and psychopathological symptoms during pregnancy and postpartum medical check-ups, with the aim of detecting significant increases in these levels early on.

- It is advisable to raise awareness among healthcare professionals of the importance of psychological resilience in pregnant women, since detecting low levels of psychological resilience could be indicative of women at high risk of presenting increased levels of perceived stress, pregnancy-specific stress and anxiety.

- Include specific intervention modules aimed at increasing psychological resilience in psychological treatments for pregnant women, since it has been proven that this can reduce stress and anxiety levels.

- It is recommended to offer resources and the necessary training related to the use of new technologies to pregnant women who wish to access the virtual modality of a psychological intervention offered to them, facilitating inclusion and access to such intervention.

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