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Title: Resilience as a Protective Factor in Pregnancy and Puerperium: Its Relationship with the Psychological State, and with Hair Cortisol Concentrations.

Article Type: Original Research

Keywords: resilience; stress; psychopathological symptoms; postpartum depression; Hair Cortisol Concentrations

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Abstract: Purpose: Stress is considered an important risk factor for the physical and psychological health of pregnant women. Hence, it is very important to study those protective factors that attenuate the negative effects of stress, such as resilience. The objective of this study was to verify the role of resilience as a stress-reducing factor during pregnancy.

Methods: A total of 151 pregnant women were assessed in this study: high resilience (n = 55) and low resilience (n = 96). Assessment consisted on perceived stress, pregnancy-specific stress, psychopathological symptoms, psychological wellbeing and Hair Cortisol Concentrations (HCC) during the third trimester of pregnancy and the puerperium, as well as postpartum depression.

Results: The results show that there were statistically significant differences between women with high and low resilience in: perceived stress [F (1,150) = 8.40; p = .005)], HCC [F (1,150) = 9.70; p = .002], pregnancy-specific stress [F (1,150) = 9.62; p = .002], and various subscales of psychopathological symptoms. Specifically, women with high resilience had lower levels of perceived stress, pregnancy-specific stress, psychopathological symptoms, psychological wellbeing, and Hair Cortisol Concentrations during the third trimester. During the puerperium, women in the high resilience group showed higher psychological wellbeing, lower psychopathological symptoms, and lower postpartum depression scores.

Conclusions: These results highlight the protective role of resilience when pregnant women are confronted by the negative effects of stress, and therefore the potential utility of resilience to improve the health of pregnant women and their neonates.

REVIEWERS' COMMENTS

Reviewer #1:

The authors have improved the manuscript in response to the reviewers' critiques. However, I still have two concerns. First, although the authors added correlational analyses as requested and presented the results of the correlations in the tables, they omit

(1) mentioning what is being correlated in the table captions,

The information about what is being correlated has been added to the table caption as follow:

"(Note.) Correlation: indicates the correlation between resilience assessed by CD-RISC and the corresponding variable."

(2) describing the results of the correlational analyses in the Results, and

The description about the results of the correlation analyses has been included in the Results section for each subsection, as follow:

(Resilience, stress and HCC in pregnant women in the third trimester and in puerperium)

"The additional correlation analyses performed show statistically significant correlation between resilience and perceived stress, pregnancy specific stress and hair cortisol concentration in both periods, third trimester and puerperium, except for hair cortisol concentration during puerperium. However, the Pearson coefficient correlation (r), between .18 and .37, indicates a weak relationship."

(Resilience and psychopathological symptoms in the third trimester of pregnancy, and in the puerperium)

"Finally, the additional correlation analyses performed show statistically significant correlation between resilience and all the SCL-90-R subscales and postpartum depression in both periods, third trimester and puerperium, except for somatization (SOM) and positive symptom distress Index (PSDI) during puerperium. The Pearson coefficient correlation (r), between .21 and .43, indicates a weak/moderate relationship."

(Resilience and psychological wellbeing)

"All these variables also show statistically significant correlation with resilience, with a Pearson coefficient correlation (r) between .22 and .49, which indicates a weak/moderate relationship."

(3) adding discussion of the correlational results to the Discussion section. All of those additions should be made.

Information about correlational results have been included in the Discussion section:

"Additional correlation analyses have shown a relationship between resilience and the same variables that show statistically significant differences between groups. Although the strength of the relation varies among weak to moderate, these results reinforce the conclusions about differences between pregnant woman with low and high resilience."

Second, the authors seem to dismiss my significant concern about the extremely high hair cortisol values they report. They cite two EARLY studies reporting relatively high values, but (1) the present values are even HIGHER than those early values, and (2) the hair cortisol field has to a large extent come to recognize that the early high values obtained by some labs using immunoassays are no longer considered accurate. The authors should at least reply as to whether they rechecked the method of calculating pg cortisol per mg hair weight from the assay output.

First of all, as you indicate, we have reviewed the calculations and they are correct. As described in recent bibliography, ELISA methods result in higher absolute values compared to LC-MS/MS likely due to the latter being more specific. To advance the field, different studies have been carried out and the results obtained by four of the commonly used commercially available ELISA kits were found to have a strong correlation with the more specific LC-MS/MS method (r2 ranges from 0.88 to 0.97). Work by Slominski et al. reported a correlation of rs=0.972 (p < .0001) between LC-MS/MS and ELISA with pooled samples. It is important to note that the ELISA kit used by our group to analyze samples was the Alpco ELISA (Alpco,Salem, NH), the same one used by Russell et al. (2015) in a study carried out by 4 leading laboratories in hair testing (Western University, ON, Canada, Dresden University of Technology, Germany, University of Colorado, Denver-Anschutz Medical Campus, and Erasmus Medical Center, the Netherlands). In this study, four immunoassay methods and 2 liquid chromatograph-mass spectrometry (LC-MS/MS) methods were compared by analyzing the same hair samples representing the low, intermediate, and high ranges of hair cortisol concentrations (HCC). The results of this study showed that HCC determined by the 4 immunoassay methods were highly and positively intercorrelated (r2 between 0.92 and 0.97; all P <0,0.0001) in all comparisons of individual laboratories. Additionally, each laboratory's immunoassay HCC had significant positive correlations (r2 between 0.88 and 0.97; all P <0,0.0001) with each of the 2 LC–MS/MS methods, which produced practically identical

results. Also, in this study, the results obtained by Western laboratory with ALPCO ELISA for hair cortisol values expressed in ng/g show values within a similar range to that obtained in our study. Rusell's study concludes that when all laboratories analyze a common batch of hair, HCC determined by each laboratory are highly correlated with each other and with the benchmark LC–MS/MS methods. This can allow each laboratory using its immunoassay to use a correction factor that will convert their results into standard LC–MS/MS equivalents, and it is in this way, on which they will focus their next studies.

- E. Russell, C. Kirschbaum, M.L. Laudenslager, T. Stalder, et al., Toward standardization of hair cortisol measurement: results of the first international interlaboratory round robin, Ther. Drug Monit. 37 (2015) 71–75.
- 2. R. Slominski, C.R. Rovnaghi, K.J.S. Anand, Methodological considerations for hair cortisol measurements in children, Ther Drug Monit. 37 (2015) 812–820.

At minimum, the authors need to acknowledge in the Discussion the high values obtained in their study, citing not only OLDER publications such as those mentioned in the response to reviewers but also studies published within the past few years.

We have included this information in the Discussion section as follow:

"Furthermore, it should be pointed out that hair cortisol concentrations in our sample are notably high. According to Russel et al. (2015), hair cortisol values obtained with ALPCO ELISA varies in a range similar to that obtained in our study. And what is more, they have shown that results from different laboratories and hair cortisol values determined by different immunoassay methods and liquid chromatograph-mass spectrometry are highly and positive intercorrelated."

In addition, upon re-reading the Methods, I noticed that the authors make no mention of washing the hair strands prior to grinding. Please indicate whether or not this was done, since washing reduces the measured cortisol content due to removal of external cortisol derived from sweat and sebum. Current procedures almost always include a wash step for the reason just mentioned. If a wash step was not included, then that omission could be offered as at least one reason for the high reported cortisol concentrations. If washing WAS performed, please add that step to the Methods section. In that case, I know of no methodological issues that could account for the data.

The information about washing the hair strand has been included in the Method section, as indicated this information was missing in the previous version of the manuscript:

"The samples were first washed twice in isopropanol, to remove any cortisol from the outside of the hair shaft that had been deposited from sweat or sebum. After drying, the samples were weighed..."

Reviewer #2:

This revised manuscript has addressed many of the concerns of the reviewers and as a result is stronger. The primary concern is the measurement of 3cm of hair postpartum. The authors were responsive to the reviewer's request for more details regarding the timing of the hair collection.

The mean timing of the prenatal sample was 33.5 weeks and the PPD sample was 15.79 days (2.25 weeks). Understanding that 3cm of hair samples is approximately 12.85 weeks and assuming the babies were born full term at approx. 40 weeks, there is a clear overlap of about 4 weeks (1 month) in the prenatal and PPD hair samples. Perhaps that is why some of the comparisons between groups were not maintained in the puerperium. Perhaps controlling for the prenatal HCC result could help??

The desing of our study follows the same protocol that previous studies (Romero-Gonzalez et al., 2018; Caparros-Gonzalez et al., 2017). Notwithstanding, this overlap of time for hair cortisol measures from the two periods may entail a limitation. However, comparing the timing for the hair samples collection between both groups (low and high resilience) there is no statistically significant differences between groups for both periods of time (third trimester and puerperium). Furthermore, the fact that HCC is higher in both groups during the puerperium and there is not statistically significant differences between groups in this period is supported by the well known effect of hormones during delivery on maternal cortisol (Glynn et al., 2013). On the other hand, HCC during the third trimester has an effect on postpartum depression (Caparros-Gonzalez et al. 2017) and our results show statistically significant differences between groups during this period of time.

We have included the differences in the time collection between groups in Table 1 and the previous information as a limitation in the manuscript as follow:

"In relation to hair cortisol sample collection, the time overlap of about four weeks in the prenatal and postnatal assessment may entail a limitation. However, comparisons between groups show no statistically significant differences in the timing of collection. Furthermore, the facts that HCC is higher in both groups during the puerperium and that there is not statistically significant differences between groups in this period, is supported by the well known effect of hormones during delivery on maternal cortisol (ref.). Notwithstanding, it would be necessary to control the collection timing for future research."

Other minor concerns are as follows:

1. Please define HCC prior to the first use of the acronym in the abstract/text

We have included the definition of HCC in the abstract, in the first use. The definition is also included in the last paragraph of the Introduction section.

2. The last sentence of the second paragraph of the introduction is a bit awkward and seems to suggest that PPD can occur in women who have not been pregnant.

The sentence has been modified as follow for a better understanding:

"At this level, it is noteworthy that postpartum depression is the psychological disorder with the highest incidence in pregnant women after delivery, with an incidence ranging from 10 to 15%, and postpartum depression also is a risk factor for the health and wellbeing of the mother and the development of the baby."

3. In the background, the statement regarding HCC as a measure of chronic stress of the preceding 3 months needs clarification. Either remove the specifics of 3 months or clarify that 1cm=1month history of stress

We have clarified the information in the introducion section as follow:

"Alternatively, testing via hair cortisol levels is an innovative technique that offers a retrospectively chronic stress measure of the preceding 3 months by collecting a 3cm segment of hair (assuming an average growth rate of 1 cm per month), is not invasive, is not affected by the time of the day, and is easy to transport and preserve"

And in the discussion section as follow:

"Cortisol is a primary biomarker of stress since it reflects the activity of the HPA axis and when analyzed in hair, it would represent the chronic stress experienced in the three months prior to the collection of the sample by collecting a 3 cm segment of hair."

4. Under the sociodemographic and obstetric variables, avoid using "etc" or refer to a larger list.

We have complete the information related to the variables avoiding the use of etc:

"Information was collected on sociodemographic and pregnancy variables: marital status, educational level, occupation, number of children, life habits, pregnancy method, previous miscarriages, fetal sex, if the mother was primiparous or it was a wanted pregnancy."

5. Under the measurement section for HCC, there is reference to the HPA axis and in other places the authors refer to HCC as a measure of chronic stress. Please be consistent.

In the measurement section we refer to a chronic activation of the HPA axis, considering the period of time (3 months) that embrace this measure. We have clarify it in the Method section: "For the purpose of assessing the chronic activation of the hypothalamic-pituitary-adrenal axis..."

6. In the first paragraph of the results, are the authors referring to 41.8% of women with low resilience?

This percentage is referred to low resilience pregnant woman, we have included this information as follow:

"41.8% of the women in the low resilience group having experienced one or more miscarriages compared to 19.8% in the high resilience group of pregnant women."

7. It might be interesting to add something in the discussion about the higher rate of miscarriages among women with low resilience. Can the authors comment on this association considering the impact it had on the results?

Considering there are no previous works studying the relation between resilience and miscarriages, we have provided a possible explanation to these results in the Discussion section:

"Both groups were equivalents in all the sociodemographic and obstetric variables except for the number of previous miscarriages, which were higher in low resilience pregnant woman. There are no previous studies analyzing this relationship. Considering resilience as a protective factor against negative effects of stress and the risk of miscarriage one of these adverse consequences of stress (Dunkel, Schetter & Tanner, 2015), resilience might have a buffer effect protecting from negative consequences as miscarriages in high resilient pregnant women."

8. A number of sentences are awkward and could be edited for clarity.

Reviewing the manuscript we have find several mistakes and corrected them, for example:

"..there are no studies that investigate the relationships between the mother's resilience as a protective factor of her mental health status before and after giving birth."

"Another important psychological process that is experienced by a pregnant is stress."

"As aforementioned in the introduction to this paper, studies on the role of resilience in pregnancy are sparse."

Additionally, the manuscript has been revised by an English speaker who has performed improvements and corrections.

7. In the discussion, be careful with the use of the term "increase" when the authors may mean "higher".

We have changed the wrong term "increase" by the correct term "higher" considering the context in the next phrase from the Discussion section:

"Specifically, in terms of the higher punctuations in psychopathological symptoms"

April, 2019Holly P Kennedy, PhD, CNMAssociate Editor, MidwiferyManuscript Ref. No.: YMIDW-D-18-00419Title: Resilience as a Protective Factor in Pregnancy and Puerperium: Its Relationship with thePsychological State, and with Hair Cortisol Concentrations.

Dear Dr. Holly P Kennedy,

Thank you for your letter dated 03 March 2019. We were pleased to know that our manuscript continue being rated as potentially acceptable for publication in Midwifery, subject to adequate revision and response to the comments raised by the reviewers.

Sincerest thanks for your response and reviewers comments on our manuscript "Resilience as a Protective Factor in Pregnancy and Puerperium: Its Relationship with the Psychological State, and with Hair Cortisol Concentrations". We hope that a revised version of the manuscript will still be considered by Midwifery.

We have modified the paper in response to the extensive and insightful reviewer comments. Appended to this letter is our point-by-point response to the comments raised by the reviewers and the manuscript with the all the suggested changes and improvements. As you may notice, we agreed with all the reviewers comments.

We would like to take this opportunity to express our sincere thanks to the reviewers who identified areas of our manuscript that still needed corrections or modifications.

We would also like to thank you for allowing us to resubmit a new revised version of our manuscript.

Yours sincerely,

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Resilience as a Protective Factor in Pregnancy and Puerperium: Its Relationship with the Psychological State, and with Hair Cortisol Concentrations.

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Conflict of interest: None declared.

Ethical approval: The University of Granada ethics committee approved the study, number 881.

Highlights

- 1. Higher levels of resilience are associated with lower psychopathological symptoms during pregnancy and puerperium.
- 2. Higher levels of resilience are associated with lower levels of pregnancy stress and lower levels of hair cortisol.
- 3. Higher levels of resilience are associated with higher levels of psychological wellbeing during pregnancy and puerperium.
- 4. Resilience buffers stress effects during pregnancy, it has a potential role in preventive actions.

Resilience as a Protective Factor in Pregnancy and Puerperium: Its Relationship with the Psychological State, and with Hair Cortisol Concentrations.

ABSTRACT

Purpose: Stress is considered an important risk factor for the physical and psychological health of pregnant women. Hence, it is very important to study those protective factors that attenuate the negative effects of stress, such as resilience. The objective of this study was to verify the role of resilience as a stress-reducing factor during pregnancy.

Methods: A total of 151 pregnant women were assessed in this study: high resilience (n = 55) and low resilience (n = 96). Assessment consisted on perceived stress, pregnancy-specific stress, psychopathological symptoms, psychological wellbeing and Hair Cortisol Concentrations (HCC) during the third trimester of pregnancy and the puerperium, as well as postpartum depression.

Results: The results show that there were statistically significant differences between women with high and low resilience in: perceived stress [F(1,150) = 8.40; p = .005)], HCC [F(1,150) = 9.70; p = .002], pregnancy-specific stress [F(1,150) = 9.62; p = .002], and various subscales of psychopathological symptoms. Specifically, women with high resilience had lower levels of perceived stress, pregnancy-specific stress, psychopathological symptoms, psychological wellbeing, and Hair Cortisol Concentrations during the third trimester. During the puerperium, women in the high resilience group showed higher psychological wellbeing, lower psychopathological symptoms, and lower postpartum depression scores.

Conclusions: These results highlight the protective role of resilience when pregnant women are confronted by the negative effects of stress, and therefore the potential utility of resilience to improve the health of pregnant women and their neonates.

Keywords: resilience; stress; psychopathological symptoms; postpartum depression; Hair Cortisol Concentrations.

Introduction

Pregnancy is a sensitive period in which exposure to risk factors can have negative consequences for both the physical and psychological health of the mother and the baby, and their subsequent development. Several systematic reviews show that high levels of stress during pregnancy, as a consequence of exposure to life events (e.g., natural catastrophe, death of a relative, etc.), or even chronic stress or financial stress, are related to maternal and neonatal adverse outcomes, such as a higher risk of preterm delivery, an increased risk of miscarriage, low birth weight, or intrauterine growth restriction (IUGR) (Beydoun and Saftlas, 2008; Schetter and Tanner, 2012; Shapiro et al., 2013; Staneva et al., 2015). In addition, pregnancy-specific stress, a distinctive syndrome characterized by concerns about the health and wellbeing of the neonate, medical symptoms, birth and delivery, and the maternal role, are predictors of adverse maternal and infant outcomes (Caparros-Gonzalez et al., 2017; Schetter and Tanner, 2012).

Post-traumatic stress disorder (PTSD) during the puerperium, depression or anxiety appear as the main adverse consequences related to maternal mental health derived from stress during pregnancy. In fact, the main psychopathological symptoms that have been studied during pregnancy are depression and anxiety, which have been shown to have a great influence on the neonate neurodevelopment. Results also show a relation between anxiety, depression and psychopathological symptoms during pregnancy are associated with low-birth-weight (LBW), preterm birth (Schetter and Tanner, 2012) and a higher incidence of postpartum depression (Caparros-Gonzalez et al., 2017; Field et al., 2010; Flynn et al., 2006). At this level, it is noteworthy that postpartum depression is the psychological disorder with the highest incidence in pregnant women after delivery, with an incidence ranging from 10 to 15%, and postpartum depression also is a risk factor for the health and wellbeing of the mother and the development of the neonate (Yim et al., 2015).

The hypothalamic-pituitary-adrenal (HPA) axis, which is involved in the stress response, is altered during pregnancy by the presence of the placenta, a major endocrine organ of fetal origin. The HPA axis produces the release of cortisol from the adrenal glands through the increase of corticotropin-releasing hormone (CRH) from the placenta (Glynn et al., 2013). Besides, mood disorders during pregnancy can modify the activation of the maternal HPA axis, which can subsequently affect the functioning of the neonatal HPA axis (Charil et al., 2010; Glover, 2014; Lara-Cinisomo et al., 2017; Romero-González et al., 2018) and the psychological wellbeing of the mother (Schetter and Tanner, 2015). Cortisol levels during the first and third trimester of pregnancy are related to postpartum depression (PPD) (Caparros-Gonzalez et al., 2017). These findings support the fact that maternal subjective experience of stress and the HPA axis are associated with maternal and neonatal health.

Cortisol levels, as a measure of the stress response, have been generally assessed from urine, saliva, blood, or amniotic fluid samples in pregnant women (Bergman et al. 2010; De Rezende et al. 2010). Those samples offer information about the stress levels the women were experiencing at the time the sample was taken, these assessment methods require a relatively invasive technique and can be affected by situational variables or circadian rhythms (Stalder & Kirschbaum, 2012). Alternatively, testing via hair cortisol levels is an innovative technique that offers a retrospectively chronic stress measure of the preceding 3 months by collecting a 3 cm segment of hair (assuming an average growth rate of 1 cm per month), is not invasive, is not affected by the time of the day, and is easy to transport and preserve (Wikenius et al. 2016; Wosu et al. 2013).

Resilience represents a set of personal resources that protect the individual from the negative effects of stressors (Fletcher and Sarkar, 2013). Resilience is a very important factor that acts as a protector against stress in the general population (Oken et al., 2015). However, to our knowledge, studies regarding resilience and pregnant women have only focus on the protective role of resilience against psychopathology in pregnant women who have experienced highly traumatic events, such as hurricanes (Harville et al., 2010), violence (Gagnon and Stewart, 2014), or child abuse (Sexton et al., 2015). Only one study evaluating resilience levels, and its association with stress levels and sleep quality of pregnant women found women with high levels of resilience resulted to have low stress levels during pregnancy (Li et al., 2016). According this, maternal resilience may have a protective role against maternal stress during pregnancy and its negative consequences.

Despite the existing association between maternal stress and maternal mental health during pregnancy, to our knowledge, there are no studies investigating the role of resilience as a protective factor against maternal stress during pregnancy and the puerperium. The aim of this study was to determine whether there were differences between pregnant women with high and low resilience in their levels of perceived stress, pregnancy-specific stress, psychopathological symptoms, psychological wellbeing and Hair Cortisol Concentrations (HCC) before and after delivery. Postpartum depression was also compared between both groups (high and low resilience levels).

Material and Methods

Participants

A total of 151 pregnant women in the third trimester of pregnancy (M = 34.94 weeks of gestation, SD = 3.34) participated in this study. The inclusion criteria were a low risk pregnancy, over 18 years of age, and proficiency of the Spanish language. The exclusion criterion was the presence of clinical psychopathology before or during pregnancy. In order to minimize the confounding effects of risk variables, additional exclusion criteria were pregnant women with Cushing disease, asthma, steroid use, diabetes, and other conditions that may affect cortisol levels.

This study was approved by the Human Ethics Research Committee of the University of XXXX (reference XXX), the Biomedical Ethics Research Committee and the Ethics Research Committee of the Health Centers, and the hospital where this study was implemented. 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. Participation was voluntary and an informed written consent document was read and signed by every participant.

Instruments

Sociodemographic and obstetric variables

Information was collected on sociodemographic and pregnancy variables: marital status, educational level, occupation, number of children, life habits, pregnancy method, previous miscarriages, fetal sex, primiparity and planned pregnancy. For this purpose, the official pregnant woman's health document from the Government of XXXX was used. Additionally, information on hair characteristics that could affect HCC, such as the use of dyes, was collected.

Psychological variables

Resilience: The Connor-Davidson Resilience Scale (CD-RISC; Connor and Davidson, 2003) in its abridged Spanish version (CD-RISC-10; Notario-Pacheco et al., 2014) was used to calculate this variable. The CD-RISC-10 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 ranging from 0 ("almost never") to 4 ("almost always"). The CD-RISC-10 has a The Cronbach's alpha reliability coefficient of .85 (Notario-Pacheco et al., 2014).

Perceived stress: Psychological stress was assessed by means of the 14-item Perceived Stress Scale in its Spanish version (PSS; Cohen et al., 1983; Remor, 2006) to evaluate the perception of general stress during the preceding month. Each of the 14 items scores on a 5-point Likert scale (0 = never, 1 = almost never, 2 = once in a while, 3 = often, 4 = very often). The Cronbach's alpha reliability coefficient of the Spanish version is $\alpha = .81$ (Remor, 2006).

Psychopathological symptoms: In this respect, the Spanish version of the Symptoms Check List-90-Revised (SCL-90-R; Derogatis, 1975; Caparrós-Caparrós et al. 2007) was used to assess psychopathological symptoms. This 90-item scale is scored using a 5-point Likert scale from 0 (never) to 4 (extremely). This instrument was 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 was used to measure the intensity of symptoms; and Positive Symptom Total, used to measure the number of self-reported symptoms. The Cronbach's alpha reliability coefficients of the Spanish version range are between $.67<\alpha<.94$ (Caparrós-Caparrós et al. 2007).

Pregnancy-specific stress. For this purpose, the Spanish version of the Prenatal Distress Questionnaire (PDQ; Yali and Lobel, 1999; Caparros-Gonzalez et al., 2019) was used to assess pregnancy-specific stress. It is a 12-item instrument scored on a 5-point Likert scale from 0 (none at all) to 4 (extremely) to assess specific worries and concerns pregnant women experience regarding medical problems, physical symptoms, body changes, labor, childbirth, relationships, and the neonate's health. The Cronbach's

alpha reliability coefficient of the Spanish version is $\alpha = .74$ (Caparros-Gonzalez et al., 2019).

Measurement of postpartum depression. The Spanish version of the Edinburgh Postnatal Depression Scale (EPDS; Cox et al., 1987; Maroto-Navarro et al., 2005) was used to assess the risk of postpartum depression. This 10-item instrument is scored on a 4-point Likert scale ranging from 0 (as always) to 3 (absolutely not). The Cronbach's alpha reliability coefficient of the Spanish version is $\alpha = .79$ (Maroto-Navarro et al., 2005).

Psychological wellbeing: Ryff's Psychological WellBeing Scale (PWBS, Ryff, 1989, Spanish version by Díaz et al., 2006) was used to assess this variable. The PWBS consists of six dimensions: self-acceptance, positive relationships with other people, autonomy, control of the environment, purpose in life, and personal growth. The instrument consists of 29 items with Likert-type response scale with 6 response options ranging from 1 ("totally disagree") to 6 ("totally agree"). The PWBS presents good reliability in its Spanish version with a Cronbach's alpha reliability coefficient of $\alpha = .68$ (Díaz et al., 2006).

Hair Cortisol Concentrations

For the purpose of assessing the chronic activation of the hypothalamicpituitary-adrenal axis, HCC were measured through hair samples proximal to the scalp with a length of 3 cm (assuming an average growth rate of 1 cm/month, a 3 cm segment contains cortisol that has been deposited over approximately the last 3 months). Samples consisting of approximately 150 strands of hair were collected from the posterior vertex of the head (Sauvé et al. 2007). The hair samples were wrapped in a piece of aluminum foil to protect them from light and humidity and were stored in an envelope at room temperature. Afterwards the hair samples were first washed twice in isopropanol, to remove any cortisol from the outside of the hair shaft that had been deposited from sweat or sebum. After drying, the samples were weighed and ground to a fine powder to break up the hair's protein matrix and increase the surface area for extraction using a ball mill. Cortisol from the interior of the hair shaft was extracted into HPLC-grade methanol by incubation of the sample for 72 hours at room temperature in the dark with constant inversion using a rotator. After incubation, the supernatant was evaporated until completely dry using a vacuum evaporator and the extract was reconstituted in 150 ul of phosphate buffered saline at a pH of 8.0. The reconstituted sample was immediately frozen at -20°C for later analysis (Chen et al. 2013; Meyer et al. 2014; Russell et al. 2015). The cortisol in the hair sample was measured using the Cortisol Salivary ELISA© kit (Alpco Diagnostics) with the reagent provided following the manufacturer's directions.

Using a salivary ELISA cortisol kit is a validated method to assess HCC and is highly positive correlated with liquid chromatograph±mass spectrometry (LC±MS/MS) (Russell et al. 2015). The sensitivity of the cortisol ELISA kit is 1.0 ng/ml as reported by the manufacturer and the cross reactivity is as follows: Prednisolone 13.6%, Corticosterone 7.6%, Deoxycosticosterone 7.2%, Progesterone 7.2%, Cortisone 6.2%, Deoxycortisol 5.6%, Pednisone 5.6% and Dexamethasone 1.6%. No cross-reaction was detected with DHEAS and Tetrahydrocortisone. The intra- and inter-assay variations were analyzed on internal quality controls used for routine salivary cortisol measurement, measured in duplicate on eight consecutive assays. The intra-assay coefficients of variance (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%, respectively.

Procedure

Pregnant women attending antenatal appointments at 3 public health centers in XXXX and XXXX, and a general hospital in XXXX, completed a battery of self-report questionnaires during the third trimester of pregnancy, and during the puerperium. Participants received informative leaflets and stated their intention to participate at the next prenatal appointment. In our context, pregnant women attend an appointment with a General Practitioner (GP) before visiting a midwife. Following the written consent, a specifically trained midwife, according to suitable guidelines, obtained hair samples and participants completed the psychological questionnaires (CD-RISC-10, SCL-90-R, PDQ, PSS and PWBS) at home during the third trimester (M = 33.5 weeks of gestation; SD = 2.84). After delivery, participants attending a postnatal appointment (M = 15.79 days after birth; SD = 9.78) with a midwife at a public health center were assessed; a hair sample was obtained and the following scales completed: SCL-90-R, PSS, EBP and PWBS.

Analysis

First, all data were explored and HCC outliers of more than three standard deviations (Field, 2012) were excluded. Then, participants were divided into two groups according to their score on the CD-RISC-10, using 27 as a cut-off criteria between low and high resilience, following the guidelines suggested by Notario-Pacheco et al. (2014). The low resilience group consisted of 55 pregnant women and the high resilience group consisted of 96 pregnant women.

The Kolmogorov-Smirnov (K-S) test showed that the data on HCC did not have a normal distribution, and hence a logarithmic transformation was performed to reduce the statistical asymmetry. To perform the statistical analyses, the transformed values were used. Tables 1 to 2 show the means and standard deviations values in the original unit of measure (pg/mg).

To verify an absent of differences between the two groups in terms of the main sociodemographic data, obstetric data and in terms of hair characteristics of all participants, the Student's T-test was used for quantitative variables and the Chi-Square test was used for qualitative variables.

Finally, in order to verify whether there were significant differences between pregnant women with high and low resilience in the different variables of stress, psychopathology, and HCC, different analysis of variance (ANOVA) tests were performed with two levels between independent groups (high and low resilience). The dependent variables were the scores on perceived stress, psychopathological symptoms, pregnancy-specific stress, postpartum depression, psychological well-being and HCC. Similarly, an analysis of covariance (ANCOVA) was performed for all the variables, Due to significant differences between groups was found regarding the number of miscarriages, this variable was included in the model as a covariate. The analysis of differences in means was carried out in both the third trimester and in the puerperium. Additionally Pearson correlations between resilience and the rest of variables were calculated.

Results

Description of the sample: Main sociodemographic and obstetric variables

A total of 151 pregnant women with an age ranging from 22 to 44 years (M = 33.01, SD = 4.42) participated in the study. Table 1 shows through the Student's T-test

and Chi-square analyses that both groups (women with high resilience vs. women with low resilience) are equivalent in the main sociodemographic, obstetric and hair characteristics variables except in the number of previous miscarriages (t = 8.44, p =.005), with a higher number of miscarriages in the low resilience group of pregnant women; 41.8% of the women in the low resilience group having experienced one or more miscarriages compared to 19.8% in the high resilience group of pregnant women.

Resilience, stress and HCC in pregnant women in the third trimester and in puerperium

The results regarding the relationship of resilience and perceived stress, as measured using the PSS, show that there are statistically significant differences in perceived stress levels among the high and low resilience groups of pregnant women in the study in the third quarter [F(1,150) = 5.73; p = .018] and in the puerperium [F(1,150) = 8.40; p = .005]. The results present higher levels of perceived stress in the low resilience group of pregnant women. When introducing the number of miscarriages as a covariate, the differences remain significant in the puerperium.

Regarding pregnancy-specific stress, as measured using the PDQ in the third trimester, statistically significant differences were found in the low resilience group of pregnant women presenting a higher level of pregnancy-specific stress [F (1,150) = 11.22; p = .001].

Finally, in terms of HCC, statistically significant differences were found between the high and low resilience groups of women in the third trimester of pregnancy [F(1,150) = 6.57; p = .01]. Specifically, the low resilience group of pregnant women had higher HCC. No statistically significant differences were found in the HCC in the hair samples that were collected during the puerperium. The additional correlation analyses performed show statistically significant correlation between resilience and perceived stress, pregnancy specific stress and hair cortisol concentration in both periods, third trimester and puerperium, except for hair cortisol concentration during puerperium. However, the Pearson coefficient correlation (r), between .18 and .37, indicates a weak relationship.

All of the means, standard deviations, and results of the ANOVA, ANCOVA and correlation analyses are presented in Table 2.

Resilience and psychopathological symptoms in the third trimester of pregnancy, and in the puerperium

Regarding the psychopathological symptoms during the third trimester, and their relationship with resilience, statistically significant differences were found between the high and low resilience groups of pregnant women in the following subscales: Interpersonal Sensitivity (INT) [F(1150) = 1.43; p = .007], Depression Severity (DEP) [F(1,150) = 8.90; p = .003], Anxiety (ANX) [F(1,150) = 7.46; p = .007], Hostility (HOST) [F(1,150) = 11.20; p = .001], Paranoid Ideation (PAR) [F(1,150) = 4.70; p = .032], Psychoticism (PSYC) [F(1,150) = 3.97; p = .048], and in the Global Severity Index (GSI) [F(1,150) = 6.86; p = .010]. Although there were significant differences between groups in the Positive Symptom Distress Index (PSDI) [F(1,150) = 3.93; p = .049], they were not maintained when introducing the number of miscarriages as a covariate. In general, the group of pregnant women who showed low scores in resilience had higher scores than the high resilience group in all of the described subscales, thus they show greater psychopathology.

In the puerperium, statistically significant differences were found between the high and low resilience groups in the following subscales of the SCL-90-R: Obsessive Compulsive Disorder (OCD) [F(1,150) = 5.68; p = .020], Anxiety (ANX) [F(1,150) = 6.80; p = .010], Hostility (HOST) [F(1,150) = 5.37; p = .020], Phobic Anxiety (PHOB) [F(1,150) = 11.01; p = .001], Paranoid Ideation (PAR) [F(1,150) = 5.71; p = .020] and in the Global Severity Index (GSI) [F(1,150) = 3.02; p = .080] and Positive Symptom Distress Index (PSDI) [F(1,150) = 4.79; p = .030]. In these variables, significant differences were maintained by including the number of previous miscarriages as a covariate. Similarly, the low resilience group of pregnant women had higher scores than the high resilience group in all the described subscales. Results are shown in Table 3.

With regard to postpartum depression, as measured using the EPDS, statistically significant differences were found between the high and low resilience groups of pregnant women [F(1,150) = 7.60; p = .007]. The low resilience group presented higher depression symptoms (M = 9.92; SD = 5.23) compared to the high resilience group (M = 6.79; SD = 4.21).

Finally, the additional correlation analyses performed show statistically significant correlation between resilience and all the SCL-90-R subscales and

postpartum depression during the third trimester and the puerperium, except for somatization (SOM) and positive symptom distress Index (PSDI) during the puerperium. The Pearson coefficient correlation (r), between .21 and .43, indicates a weak/moderate relationship.

Resilience and psychological wellbeing

Finally, in order to check whether resilience was also related to psychological wellbeing, different inter-group comparisons were carried out. Regarding the levels of psychological wellbeing during the third trimester and the puerperium, as measured using the PWBS, statistically significant differences were found between the high and low resilience groups in the following subscales: Self-acceptance [third quarter: F(1,150) = 20.33; p = .001; Puerperium: F(1,150) = 5.49; p = .020]; Personal Growth [third quarter: F(1,150) = 7.35; p = .008; puerperium: F(1,150) = 4.48; p = .030], Purpose in Life [third quarter: F(1,150) = 34.18; p = .001; Puerperium: F(1,150) =16.63; p = .001]; and Autonomy [third quarter: F(1,150) = 4.38; p = .030; Puerperium: F(1,150) = 5.98; p = .010]. In all of the subscales, the high resilience group presented higher scores, both in the third trimester and the puerperium. All these variables also showed statistically significant correlation with resilience, with a Pearson coefficient correlation (r) between .22 and .49, which indicates a weak/moderate relationship. When introducing the number of miscarriages as a covariate, the results showed significant differences during the third trimester in Self-acceptance, Personal Growth and Purpose in Life; and during the puerperium in Purpose in Life and Autonomy (see Table 4).

Discussion

In accounting for the importance of the impact of stress and related variables to pregnant woman and nenoates, the aim of this study was to verify whether maternal resilience during pregancy is a protective factor related to psychopathological symptoms, psychological stress, pregnancy-specific stress, psychological well-being, and HCC before and after childbirth. To achieve this, we divided the sample of pregnant women into two groups, a high resilience group and a low resilience group. Both groups were equivalents in all the sociodemographic and obstetric variables except for the number of previous miscarriages, which were higher in low resilience pregnant woman. There are no previous studies analyzing this relationship. Considering resilience as a protective factor against negative effects of stress and the risk of miscarriage on these adverse consequences of stress (Dunkel, Schetter & Tanner, 2015), resilience might have a buffer effect protecting from negative consequences, such as miscarriages, in high resilient pregnant women. Among the most remarkable findings, was that women with lower resilience had higher scores in psychopathology, stress and HCC than women with high resilience. These differences between groups were maintained in the puerperium in most variables except HCC. Additional correlation analyses have shown a relationship between resilience and the same variables that show statistically significant differences between groups. Although the strength of the relation varies among weak to moderate, these results reinforce the conclusions about differences between pregnant woman with low and high resilience.

Specifically, in terms of the higher punctuations in psychopathological symptoms during the third trimester of pregnancy in the low resilience group of pregnant women compared to the high resilience group of pregnant women, we found significant differences in interpersonal sensitivity, depression, anxiety, hostility, paranoid ideation, and psychoticism. Similarly, for puerperium results we found statistically significant differences in obsession, compulsion, anxiety, hostility, phobic anxiety, and paranoid ideation. As aforementioned in the introduction, studies on the role of resilience in pregnancy are sparse. The results of the present research are in line with the study carried out by Sexton et al. (2015) that shows how resilience buffers the incidence of psychopathology, whereby in that particular study the resilience in pregnant women was derived from experiencing child maltreatment, with the finding of less post-traumatic stress symptomatology in the high resilience group of pregnant women. Taking this into account, and including the results of other studies in the literature that highlight the protective role of resilience in psychopathology within the general population (Aburn et al., 2015), the results of the present study indicate the necessary placement of a special emphasis on the protective role of resilience in periods of greater stress and vulnerability, such as during pregnancy.

Postpartum depression is highly associated with psychopathology. The results of the present study show that high levels of resilience are associated with lower symptoms of postpartum depression in the women who were evaluated. Although postpartum depression has been a widely studied disorder, to our knowledge, its relationship with resilience has not been studied. It is noteworthy, that our research findings relate low resilience with greater risk of postpartum depression. However, this relationship has not been found in relation to depression scores on the SCL-90-R subscale. This could be due to the fact that both scales measure constructs that might appear similar but contain different nuances. Thus, the Edinburgh Postnatal Depression Scale (EPDS) may have a greater sensitivity than the depression subscale of the SCL-90-R in detecting this particular type of depressive symptomatology. Therefore, it is essential to overemphasize the importance of using pregnancy and puerperium specific assessment instruments for disorders associated with specific situations or characteristics.

Another important psychological process that is experienced by pregnant women is stress. The level of perceived stress has been widely studied, since it is a risk factor for both the mother and the neonate. With respect to the variable of stress, our results show that women with low resilience show higher levels of stress after childbirth. Similarly, we find identical results in relation to levels of pregnancy-specific stress experienced during pregnancy, which further relates to higher levels of resilience when there is less stress experienced. This latter relationship is particularly relevant, since it has been shown that the most relevant stress measure related to negative consequences for both pregnant women and childbirth is pregnancy-specific stress (Schetter and Tanner, 2012). Our results are in accordance with the only previous study on resilience and stress in pregnant women by Li et al. (2016), in which high levels of resilience are related to lower levels of perceived stress during pregnancy. In addition, in our study we found no differences in perceived stress in the third trimester when we introduced the variable 'number of previous miscarriages' as a covariate. However, significant differences in pregnancy-specific stress may indicate that the number of previous miscarriages has a greater weight on the perceived stress during the previous months before pregnancy. Nevertheless, an absence of statistically significant differences in pregnancy-specific stress would be more determined by the levels of resilience.

Cortisol is a primary biomarker of stress since it reflects the activity of the HPA axis and when analyzed in hair, it would represent the chronic stress experienced during the three months prior to the collection of the sample by collecting a 3 cm segment of hair. With regard to cortisol, our results indicate that women with high levels of resilience had lower hair cortisol levels in the third trimester of pregnancy. Although, to our knowledge, there are no previous studies analyzing the relationship between resilience and HCC among pregnant women, a previous study assessed this relationship in salivary or urine cortisol levels in the general population. In the review by Walker et al. (2017), the role of resilience is highlighted as a shock absorber of HPA axis activation in the face of stressful events. This could translate into a lower level of longterm cortisol in resilient people who are exposed to high levels of stress. In this way, the findings in the present research are consistent with a buffering/protective effect that resilience would exert against external stressors, resulting in less activation of the HPA axis compared to pregnant women with low resilience. This effect, however, is not maintained after childbirth. Considering a previous study by Caparros-Gonzalez et al. (2017) reporting that cortisol levels during the preconception period and the second trimester of pregnancy could predict the levels of postpartum depression, it could be assumed that the period under study is supposed to be a critical period, with greater stress and uncertainty, in which maternal resilience could exert a greater buffering effect than in the puerperium. Furthermore, it should be pointed out that hair cortisol concentrations in our sample are notably high. According to Russel et al. (2015), hair cortisol values obtained with ALPCO ELISA varies in a range similar to that obtained in our study. And what is more, they have shown that results from different laboratories and hair cortisol values determined by different immunoassay methods and liquid chromatograph-mass spectrometry are highly and positive intercorrelated.

Finally, it is noteworthy to mention that we also found an important relationship between the psychological wellbeing and resilience of pregnant women during the third trimester of pregnancy and after childbirth. Specifically, women with high resilience have greater psychological wellbeing, with higher scores in the PWBS subscales of selfacceptance, personal growth and purpose in life during the third quarter of pregnancy. Likewise, higher scores for women with high resilience were obtained in the scales of purpose in life and autonomy after childbirth, than for women with low resilience. This is in accordance with previous studies performed on the general population, reporting higher scores of psychological well-being and resilience (Brooks et al., 2015; Cofini et al., 2014; Connor and Davidson, 2003). However, this relationship had not been studied in pregnant women. The present study is the first to establish the relationship between wellbeing and resilience in a sample of pregnant women.

Despite this being the first study to demonstrate the relationship between the psychological state of the mother and her resilience, this research has some limitations. From our point of view, the main limitation is the failure to evaluate stressful life

events, as these could be influencing previous levels of perceived stress and psychopathological symptoms. Likewise, previous stressful life events endured by the woman could modulate levels of resilience and even increase the risk of postpartum depression (PPD). Therefore, after pursuing this first approach in future studies, it would be very important to implement these measures before pregnancy or immediately at the onset of pregnancy.

In addition, future studies should monitor the measures used in the study throughout pregnancy, including resilience. Longitudinally assessing stress and hair cortisol levels during the first, second, and third trimester would offer information on fluctuation and association during the whole process of pregnancy. In relation to hair cortisol sample collection, the time overlap of about four weeks in the prenatal and postnatal assessment may entail a limitation. However, comparisons between groups show no statistically significant differences in the timing of collection. Furthermore, the facts that HCC is higher in both groups during the puerperium and that there is not statistically significant differences between groups in this period, is supported by the well known effect of hormones during delivery on maternal cortisol (Glynn et al., 2013). Notwithstanding, it would be necessary to control the collection timing for future research. Despite the limitations of the present research, it is noteworthy that the present study addressed stress from a double-tracked perspective, using self-report measures related to psychological variables, and hair cortisol, which is a biological measure of HPA axis activation. In addition, we undertook measures at two key stages of pregnancy, namely, the third trimester and the puerperium.

The present study is the first to analyze the relationship between maternal resilience during pregnancy with respect to their psychological wellbeing, psychopathology and stress with self-reporting measures, and using hair cortisol to biomonitorize levels of stress. The importance of including resilience in future research in pregnant women has highlighted by analyzing the information on the protective role of resilience in the physical and psychological health of the mother and in the results of her pregnancy, and the subsequent development of the neonate. At the clinical level, we consider it pertinent to study, and to propose training in, skills and tools that increase resilience levels in intervention programs that are aimed at improving the psychological health of pregnant women. This would be a key element for a good approach to the vital changes that occur while having a baby.

References

- Aburn, G., Gott, M., Hoare, K., 2016. What is resilience? An Integrative Review of the empirical literature. *Journal of Advanced Nursing* 72, 980–1000. http://doi.org/10.1111/jan.12888
- Bergman, K., Sarkar, P., Glover, V., & O'Connor, T. G. (2010). Maternal prenatal cortisol and infant cognitive development: Moderation by infant–mother attachment. *Biological psychiatry*, 67(11), 1026-1032.
- Beydoun, H., Saftlas, A.F., 2008. Physical and mental health outcomes of prenatal maternal stress in human and animal studies: a review of recent evidence. *Paediatric Perinatal Epidemiology 290*, 595-596. https://doi.org/10.1111/j.1365-3016.2008.00951.x
- Brooks, S. K., Dunn, R., Sage, C. A. M., Amlôt, R., Greenberg, N., Rubin, G. J., 2015. Risk and resilience factors affecting the psychological wellbeing of individuals deployed in humanitarian relief roles after a disaster. *Journal of Mental Health 24*, 385–413. http://doi.org/10.3109/09638237.2015.1057334
- Caparros-Caparros, B., Villar-Hoz, E., Juan-Ferrer J., Viñas-Poch F., 2007. Symptom Check- List-90-R: Fiabilidad, datos normativos y estructura factorial en estudiantes universitarios. *International Journal of Clinical and Health Psychology* 7, 781-794. http://hdl.handle.net/10256/8599
- Caparros-Gonzalez, R. A., Romero-Gonzalez, B., Strivens-Vilchez, H., Gonzalez-Perez, R., Martinez-Augustin, O., Peralta-Ramirez, M. I., 2017. Hair cortisol levels, psychological stress and psychopathological symptoms as predictors of postpartum depression. *PLoS ONE 12*, 1–17. https://doi.org/10.1371/journal.pone.0182817
- Caparros-Gonzalez, R. A., Perra, O., Alderdice, F., Lynn, F., Lobel, M., García-García, I., & Peralta-Ramírez, M. I. (2019). Psychometric validation of the Prenatal Distress Questionnaire (PDQ) in pregnant women in Spain. *Women & health*, 1-16. https://doi.org/10.1080/03630242.2019.1584143
- Charil, A., Laplante, D. P., Vaillancourt, C., King, S., 2010. Prenatal stress and brain development. *Brain Research Reviews* 65, 56–79. https://doi.org/10.1016/j.brainresrev.2010.06.002

- Chen, Z., Li, J., Zhang, J., Xing, X., Gao, W., Lu, Z., Deng, H., 2013. Simultaneous determination of hair cortisol, cortisone and DHEAS with liquid chromatographyelectrospray ionization-tandem mass spectrometry in negative mode. *Journal of Chromatography* 929, 187-194. https://doi.org/10.1016/j.jchromb.2013.04.026
- Cofini, V., Carbonelli, A., Cecilia, M. R., Di Orio, F., 2014. Quality of life, psychological wellbeing and resilience: a survey on the Italian population living in a new lodging after the earthquake of April 2009. *Ann Ig 26*, 46–51. http://doi.org/10.7416/ai.2014.1957
- Cohen, S., Kamarck, T., Mermelstein, R., 1983. A global measure of perceived stress. Journal of health and social behavior 24, 385-396. https://doi.org/10.2307/2136404
- Connor, K. M., Davidson, J. R. T., 2003. Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). *Depression and Anxiety 18*, 76–82. http://doi.org/10.1002/da.10113
- Cox J. L., Holden J. M., Sagovsky R., 1987. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *The British Journal of Psychiatry 150*, 782–786. <u>https://doi.org/10.1192/bjp.150.6.782</u>
- De Rezende, M. G., Garcia-Leal, C., de Figueiredo, F. P., de Carvalho Cavalli, R., Spanghero, M. S., Barbieri, M. A., ... & Del-Ben, C. M. (2016). Altered functioning of the HPA axis in depressed postpartum women. *Journal of affective disorders*, 193, 249-256.
- Derogatis L. R., 1975. *SCL-90-R: Administration, scoring, and procedures manual.* Baltimore: Clinical Psychometrics Research Unit.
- Díaz, D., Rodríguez-Carvajal, R., Blanco, A., et al., 2006. Adaptación española de las escalas de bienestar psicológico de Ryff. *Psicothema 18*, 572-577.
- Dunkel Schetter, C., & Tanner, L. (2015). Anxiety, depression and stress in pregnancy: implications for mothers, children, research, and practice. *Current Opinion in Psychiatry*, 25(2), 141–148. http://doi.org/10.1097/YCO.0b013e3283503680.Anxiety

Field, A. (2012). Discovering Statistics Using SPSS. London: Sage Publications.

- Field, T., Diego, M., Hernandez-Reif, M., et al., 2010. Comorbid depression and anxiety effects on pregnancy and neonatal outcome. *Infant Behavior and Development 33*, 23–29. http://doi.org/10.1016/J.INFBEH.2009.10.004
- Fletcher, D., Sarkar, M., 2013. Psychological Resilience. *European Psychologist 18*, 12–23. http://doi.org/10.1027/1016-9040/a000124
- Flynn, H. A., O'mahen, H. A., Massey, L., Marcus, S., 2006. The Impact of a Brief Obstetrics Clinic-Based Intervention on Treatment Use for Perinatal Depression. *Journal of Women's Health 15*, 1195–1204. http://doi.org/10.1089/jwh.2006.15.1195
- Gagnon, A. J., Stewart, D. E., 2014. Resilience in international migrant women following violence associated with pregnancy. *Archives of Women's Mental Health* 17, 303–310. http://doi.org/10.1007/s00737-013-0392-5
- Glover, V., 2014. Maternal depression, anxiety and stress during pregnancy and child outcome; what needs to be done. *Best Practice and Research: Clinical Obstetrics* and Gynecology 28, 25–35. http://doi.org/10.1016/j.bpobgyn.2013.08.017
- Glynn, L. M., Davis, E. P., Sandman, C. A., 2013. New insights into the role of perinatal HPA-axis dysregulation in postpartum depression. *Neuropeptides* 47, 363–70. http://doi.org/10.1016/j.npep.2013.10.007
- Harville, E. W., Xiong, X., Buekens, P., et al., 2010. Resilience after hurricane Katrina among pregnant and postpartum women. *Women's Health Issues : Official Publication of the Jacobs Institute of Women's Health 20*, 20–7. http://doi.org/10.1016/j.whi.2009.10.002
- Lara-Cinisomo, S., Grewen, K. M., Girdler, S. S., Wood, J., Meltzer-Brody, S., 2017. Perinatal depression, adverse life events, and hypothalamic–adrenal–pituitary axis response to cold Pressor stress in Latinas: an exploratory study. *Women's Health Issues 27*, 673-682. https://doi.org/10.1016/j.whi.2017.06.004
- Li, G., Kong, L., Zhou, H., Kang, X., Fang, Y., Li, P., 2016. Relationship between prenatal maternal stress and sleep quality in Chinese pregnant women : the mediation effect of resilience. *Sleep Medicine* 25, 8–12. http://doi.org/10.1016/j.sleep.2016.02.015

- Maroto-Navarro G., Garcia-Calvente M. M., Fernandez-Parra A., 2005. Evaluation of mood in the postpartum period with the Edinburgh Postnatal Depression Scale. *International Journal of Clinical and Health Psychology 5*, 305–318. http://doi.org/10.1016/j.jad.2010.01.069
- Meyer, J., Novak, M., Hamel, A., Rosenberg, K., 2014. Extraction and analysis of cortisol from human and monkey hair. *Journal of visualized experiments* 83, 50882. http://doi.org/10.3791/50882
- Notario-Pacheco, B., Martínez-Vizcaíno, V., Trillo-Calvo, E., Pérez-Yus, M. C., Serrano-Parra, D., García-Campayo, J., 2014. Validity and reliability of the Spanish version of the 10-item CD-RISC in patients with fibromyalgia. *Health and quality* of life outcomes 12, 14. https://doi.org/10.1186/1477-7525-12-14
- Oken, B. S., Chamine, I., Wakeland, W., 2015. A systems approach to stress, stressors and resilience in humans. *Behavioural Brain Research* 282, 144–154. http://doi.org/10.1016/j.bbr.2014.12.047
- Remor E., 2006. Psychometric Properties of a European Spanish Version of the Perceived Stress Scale. *Spanish Journal of Psychology*, 9, 86-93. doi:10.1017/s1138741600006004
- Romero-Gonzalez B, Caparros-Gonzalez RA, Gonzalez-Perez R, Delgado-Puertas P, Peralta-Ramirez MI, 2018. Newborn infants' hair cortisol levels reflect chronic maternal stress during pregnancy. PLoS ONE, 13: e0200279. https://doi.org/10.1371/journal.pone.0200279
- Russell, E., Kirschbaum, C., Laudenslager, M. L., et al., 2015. Toward standardization of hair cortisol measurement: results of the first international interlaboratory round robin. *Therapeutic drug monitoring 37*, 71-75. https://doi.org/10.1097/FTD.00000000000148
- Ryff, C., 1989. Happiness is everything, or is it? Explorations on the meaning of psychological well-being. *Journal of Personality and Social Psychology* 57, 1069-1081.

- Sauvé, B., Koren, G., Walsh, G., Tokmakejian, S., Van Uum, S. H., 2007. Measurement of cortisol in human hair as a biomarker of systemic exposure. *Clinical and Investigative Medicine 30*, 183-191. doi:10.25011/cim.v30i5.2894
- Schetter, C., Tanner, L., 2012. Anxiety, depression and stress in pregnancy: implications for mothers, children, research, and practice. *Current Opinion in Psychiatry* 25, 141–148. http://doi.org/10.1097/YCO.0b013e3283503680.Anxiety
- Sexton, M. B., Hamilton, L., McGinnis, E. W., Rosenblum, K. L., Muzik, M., 2015. The roles of resilience and childhood trauma history: main and moderating effects on postpartum maternal mental health and functioning. *Journal of Affective Disorders 174*, 562–8. http://doi.org/10.1016/j.jad.2014.12.036
- Shapiro, G. D., Fraser, W. D., Frasch, M. G., Séguin, J. R., 2013. Psychosocial stress in pregnancy and preterm birth: associations and mechanisms. *Journal of perinatal medicine 41*, 631-645. <u>https://doi.org/10.1515/jpm-2012-0295</u>
- Stalder, T., & Kirschbaum, C. (2012). Analysis of cortisol in hair–state of the art and future directions. *Brain, behavior, and immunity*, 26(7), 1019-1029.
- Staneva, A., Bogossian, F., Pritchard, M., Wittkowski, A., 2015. The effects of maternal depression, anxiety, and perceived stress during pregnancy on preterm birth: a systematic review. *Women and Birth* 28, 179-193. https://doi.org/10.1016/j.wombi.2015.02.003
- Walker, F. R., Pfingst, K., Carnevali, L., Sgoifo, A., Nalivaiko, E., 2017. In the search for integrative biomarker of resilience to psychological stress. *Neuroscience and Biobehavioral Reviews* 74, 310–320. http://doi.org/10.1016/j.neubiorev.2016.05.003
- Wikenius, E., Moe, V., Kjellevold, M., Smith, L., Lyle, R., Waagbø, R., ... & Myhre, A.
 M. (2016). The association between hair cortisol and self-reported symptoms of depression in pregnant women. *PloS one*, *11*(9), e0161804.
- Wosu, A. C., Valdimarsdóttir, U., Shields, A. E., Williams, D. R., & Williams, M. A. (2013). Correlates of cortisol in human hair: implications for epidemiologic studies on health effects of chronic stress. *Annals of epidemiology*, 23(12), 797-811.

- Yali, A. M., Lobel, M., 1999. Coping and distress in pregnancy: An investigation of medically high risk women. *Journal of Psychosomatic Obstetric and Gynecology*, 20, 39-52. http://doi.org/10.3109/01674829909075575
- Yim, I. S., Stapleton, L. R. T., Guardino, C. M., Hahn-Holbrook, J., Schetter, C. D., 2015. Biological and psychosocial predictors of postpartum depression: systematic review and call for integration. *Annual Review of Clinical Psychology* 11, 99–137. http://doi.org/10.1146/annurev-clinpsy-101414-020426

Table 1. Differences in sociodemographic, obstetrics and hair characteristics between

pregnant women with low and high resilience levels.

		Low Resilience	High Resilience	Test a	р
		(n=55)	(n=97)		
		M(SD) %	M(SD) %		
Sociodemographic	variables				
Age		33.04(4.10)	33(4.62)	1.49	.96
Civil status	Single/divorced	1.80	0	1.75	.36
	Married/cohabitant	98.20	100		
Employment status	Employed	67.30	79.20	2.67	.12
	Unemployed	32.70	20.80		
Education level	Secondary school	36.40	24	2.64	.13
	University	63.60	76		
Sport	Yes	49.10	58.30	1.20	.31
	No	50.90	41.70		
Smoking	Yes	7.30	7.30	.23	1
	No	92.70	92.70		
Alcohol	Yes	1.80	3.10	.23	1
consumption	No	98.20	96.90		
Hair aspect	Natural	41.80	45.80	.22	.73
	Dyed	58.20	54.20		
Hair sample time collection	Third trimester (weeks)	32.69 (2.86)	33.79 (2.39)	1.12	.26
	Puerperium (days)	15.81 (9.2)	15.88 (7.4)	.05	.95
Obstetric informat	ion				
Primiparous	Yes	58.20	62.50	.27	.60
	No	41.80	37.50		

Wanted pregnancy	Yes	94.50	97.90	1.24	.35
	No	5.50	2.10		
Pregnancy method	Spontaneous	80	88.50	2.05	.16
	Fertility treatment	20	11.50		
Sex of the fetus	Male	63.60	50	.90	.34
	Female	36.40	50		
Previous	No	58.20	80.20	8.44	.005*
miscarriages	Yes	41.80	19.80		

Note. **Significant at the $p \le .02$ level. a. T-test of student used to quantitative variables and Chi-square test to categorical variables.

Table 2. Differences in perceived stress, pregnancy-specific stress and hair cortisol

concentration between pregnant women with low and high resilience levels.

			ANOVA		ANCOVA+		Correlation	
	Low Resilience M(SD)	High Resilience M(SD)	F	р	F		r	р
Third Trimester								
PSS	27.23 (1.38)	26.51 (1.91)	5.73	.018*	2.60	.10	184	.023*
PDQ	15.90 (5.07)	12.80 (5.47)	11.22	.001**	9.62	.002**	374	.001**
Hair Cortisol (pg.mg)	482.69 (565.11)	293.9 (285.97)	6.57	.01*	9.70	.002**	195	.035*
Puerperium								
PSS	27.35 (1.71)	26.21 (1.53)	8.40	.005*	8.28	.005*	356	.002**
Hair cortisol (pg.mg)	622.89 (627.81)	868.25 (1534.1)	.91	.13	.07	.79	.009	.949

Note. *Significant at the $p \le .05$ level; **Significant at the $p \le .02$ level. + The variable previous miscarriages was introduced as covariate. Correlation: indicates the correlation between resilience assessed by CD-RISC and the corresponding variable. PSS = Perceived Stress

Scale; PDQ = Prenatal Distress Questionnaire.

				ANOVA		ANCOVA+		Correlation	
		Baja Resiliencia X(DT)	Alta Resiliencia X(DT)	F	р	F	р	r	р
Third trim	ester								
SCL-90-R	SOMS	62.04 (29.11)	54.03 (25,98)	2.89	.09	2.65	.10	280	.001*
	OBS	67.94 (31.16)	60.05 (29,76)	2.27	.13	2.29	.13	292	.001*
	SEN	59.28 (31.19)	45.17 (29,13)	7.43	.007*	7.21	.008*	326	.001*
	DEP	58.96 (29.98)	44.36 (27,22)	8.90	.003*	6.96	.009*	363	.001*
	ANX	66.50 (28.74)	52.76 (29,28)	7.46	.007*	6.24	.014*	313	.001*
	HOS	57.91 (28.77)	41.25 (28,80)	11.20	.001**	8.35	.004*	319	.001*
	PHOB	60.39 (35.36)	54.78 (36,57)	.80	.37	1.04	.30	214	.008*
	PAR	63.04 (33.36)	50.44 (33,36)	4.70	.032*	4.33	.039*	298	.001*
	PSIC	65.11 (34.96)	53.35 (33,62)	3.97	.048*	4.51	.035*	264	.001*
	GSI	65.83 (31.09)	51.77 (31)	6.86	.010*	6.01	.015*	356	.001*
	SP	63.76 (28.98)	53.19 (31,85)	3.93	.049*	3.54	.06	265	.001*
	PSDI	51.21 (26.58)	43.56 (32,13)	3.20	.07	1.53	.21	253	.004*
Puerperiur	n								
SCL-90-R	SOMS	57.57 (28.31)	43.37 (23,31)	2.46	.12	3.07	.08	183	.132
	OBS	57.00 (33.85)	38.70 (27,31)	5.68	.02*	8.09	.006*	348	.003*
	SEN	40.17 (35.57)	29.00 (30,74)	1.77	.18	2.19	.14	262	.029*
	DEP	45.83 (29.86)	33.60 (27,28)	2.81	.09	3.64	.06	271	.024*
	ANX	48.00 (34.33)	28.84 (24,78)	6.80	.01*	8.27	.005*	362	.002*
	HOS	50.61 (35.30)	31.51 (29,93)	5.37	.02*	7.25	.009*	271	.024*
	PHOB	60.26 (33.73)	32.21 (32,17)	11.01	.001**	14.08	.001**	406	.001*
	PAR	50.91 (35.58)	30.70 (31,12)	5.71	.02*	7.08	.01*	363	.002*
	PSIC	54.30 (38.40)	38.53 (33,20)	3.02	.08	3.74	.057	238	.049*
	GSI	49.48 (34.73)	31.16 (28,86)	5.22	.02*	6.87	.01*	337	.005*
	SP	47.04 (34.07)	29.93 (28,06)	4.79	.03*	5.88	.01*	29	.016*
	PSDI	42.96 (24.93)	35.74 (23,07)	1.38	.24	1.64	.20	147	.229
	EPDS	9.92 (5.23)	6.79 (4.21)	7.60	.007*	5,95	.01*	431	.001*

Table 3. Differences in psychopathologyca	al symptoms between	pregnant wome	n with low
and high resilience levels.			

Note. Significant at the $p \le .05$ level; **Significant at the $p \le .02$ level. + The variable

previous miscarriages was introduced as covariate. Correlation: indicates the correlation

between resilience assesed by CD-RISC and the corresponding variable. (SOMS= Somatization;

OBS= Obsessive-compulsive; SEN = Interpersonal sensitivity; DEP = Depression; ANX =

Anxiety; HOS= Hostility; PHOB= Phobic anxiety; PAR = Paranoid ideation; PSI =

Psychoticism; GSI = Global severity index; PST = Positive symptoms total; PSDI = Positive

symptoms distress index).

Table 4. Differences in psychological well being between pregnant women with low and

high resilience levels.

				ANOVA		ANCO	ANCOVA+		ion
		Low	High	F	р	F	р	r	р
		Resilience	Resilience						
		M(SD)	M(SD)						
Third trim	ester								
PWBS	SELF-A	16.62 (3.61)	19.11 (2.89)	20.33	.001**	17.86	.001**	.466	.001**
	CONTR	19.12 (1.77)	19.63 (1.98)	2.42	.12	3.02	.08	.06	.459
	GROW	16.33 (2.33)	17.38 (2.16)	7.35	.008*	9.43	.002**	.317	.001**
	RELA	17.19 (2.92)	16.43 (2.86)	2.27	.13	1.85	.17	131	.106
	PURP	20.38 (3.05)	22.91 (2.08)	34.18	.001**	28.84	.001**	.496	.001**
	AUTON	19.92 (3.94)	18.58 (3.36)	4.38	.03*	3.39	.06	227	.005*
Puerperiur	n								
PWBS	SELF-A	16.65 (3.77)	18.78 (3.66)	5.49	.02*	5.79	.019	.370	.001**
	CONTR	19.35 (1.38)	19.45 (1.87)	0.05	.81	.02	.96	04	.73
	GROW	15.96 (2.37)	17.36 (2.87)	4.48	.03*	3.82	.054	.286	.012*
	RELA	15.88 (1.92)	16.53 (3.16)	0.89	.34	1.41	.23	.174	.13
	PURP	20.31 (2.65)	22.57 (2.04)	16.63	.001**	12.97	.001**	.363	.001**
	AUTON	20.12 (3.46)	17.91 (3.79)	5.98	.01*	5.10	.02*	263	.021*

Note. Significant at the $p \le .05$ level; **Significant at the $p \le .02$ level. + The variable previous miscarriages was introduced as covariate. Correlation: indicates the correlation between resilience assessed by CD-RISC and the corresponding variable. PWBS = Psychological Well-being Scale (SELF-A= self-aceptance, CONTR = Control of the environment, GROW = personal growth, RELA = positive relationships, PURP = purpose in life, AUTON = autonomy). Not Applicable

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