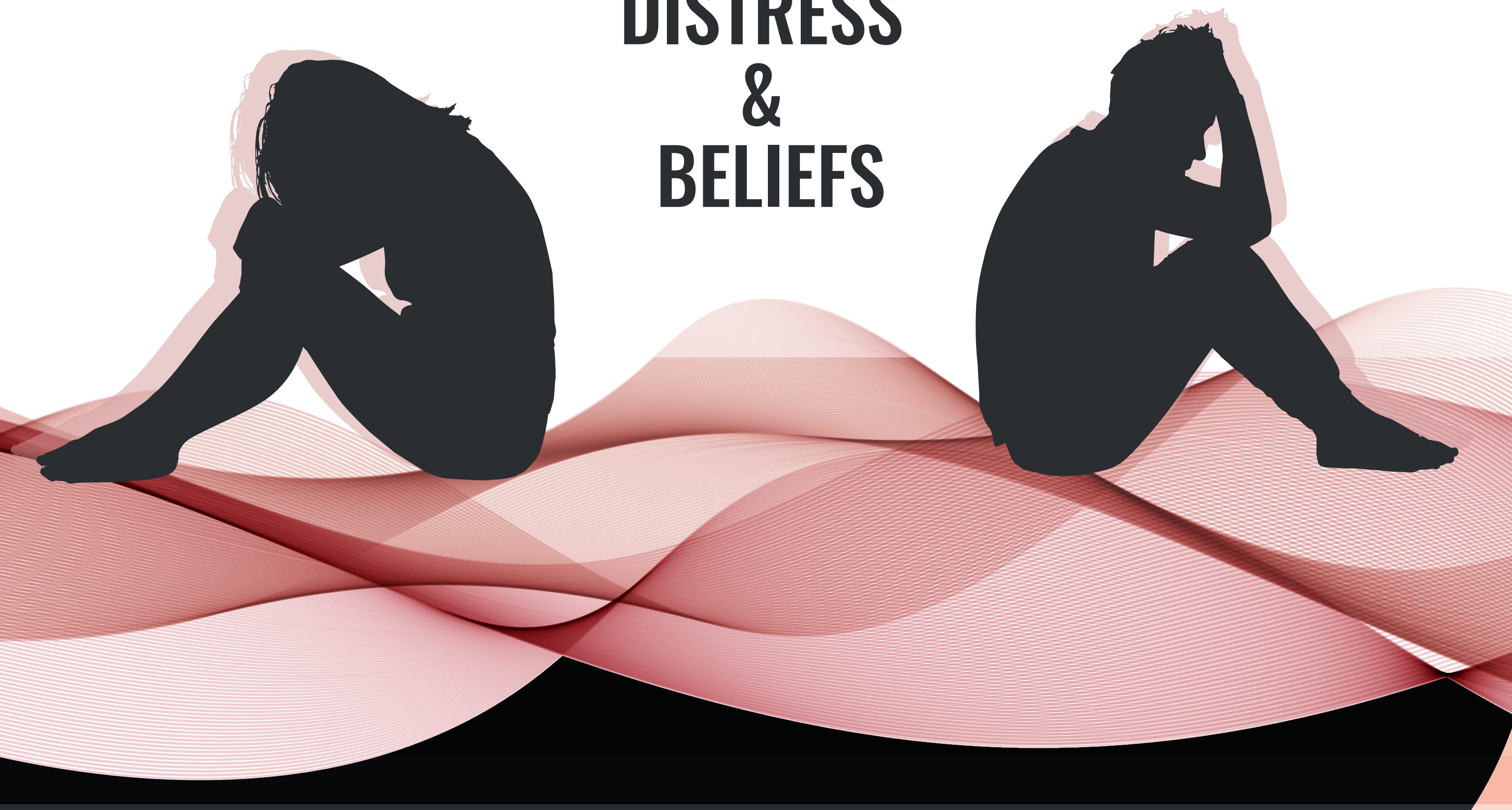
SEXUALITY IN HIDRADENITIS SUPPURATIVA:

DYSFUNCTION, DISTRESS & BELIEFS



TESIS DOCTORAL
MEDICINA CLÍNICA Y SALUD PÚBLICA
CARLOS CUENCA BARRALES

UNIVERSIDAD
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SEXUALITY IN HIDRADENITIS SUPPURATIVA: DYSFUNCTION, DISTRESS & BELIEFS

Tesis Doctoral que presenta Carlos Cuenca Barrales para aspirar al Título de Doctor con Mención Internacional.

Granada, 15 de marzo de 2021

Director de la Tesis Doctoral

Dr. Alejandro Molina Leyva

Facultativo Especialista de Área de Dermatología y Venereología

A mis padres

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2. Cuenca-Barrales C; Molina-Leyva A. Risk factors of sexual dysfunction in patients with hidradenitis suppurativa: a cross-sectional study. Dermatology. 2020; 236(1):37-45. doi: 10.1159/000501905. **Factor de Impacto: 3.695. Dermatology - SCIE Q1 (10/68).**

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COMUNICACIONES ORALES Y PÓSTERES PRESENTADOS

1. Sexualidad en pacientes con hidrosadenitis supurativa. Cuenca-Barrales C; Vega-Castillo JJ; Aguayo-Carreras P; Ródenas-Herranz T; Linares-González L; Espadafor-López B; Ruiz-Villaverde R; Molina-Leyva A. XIII Reunión Nacional de Residentes de la AEDV. Marbella, octubre de 2018.

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6. Hidradenitis suppurativa and sexuality: a systematic review. Cuenca-Barrales C; Montero-Vílchez T; Szepietowski J; Matusiak L; Molina-Leyva A. 29th EADV Congress. Congreso virtual online debido a la pandemia por COVID-19, octubre de 2020.

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ABSTRACT

BACKGROUND

Hidradenitis suppurativa (HS) is a chronic autoinflammatory skin disease with an estimated prevalence ranging from 0.5% to 4% worldwide and 0.7% to 1.2% in Western countries, being about 3 times more frequent in women, although progression to more severe disease is more common in men. It usually presents after puberty with acute inflammatory lesions (nodules and abscesses) in the apocrine gland-bearing areas of the body, such as the axilla, breast, groin, genitals and buttocks. In the absence of disease control, it can cause tissue damage with the appearance of fistulae or scars. HS manifests with bothersome symptoms, such as pain, itching, suppuration and unpleasant odour. Treatment is usually challenging, requiring the combination of several drugs to control the inflammatory load and surgical procedures to solve the structural damage.

The impairment to quality of life in patients with HS is one of the highest among dermatological patients, and comparable to that of other diseases such as diabetes mellitus, cardiovascular disease, chronic obstructive pulmonary disease and cancer. Disease symptoms, such as pain or pruritus, may have an impact on quality of life in these patients. HS is associated with different psychological and social problems including depression, anxiety, low self-esteem, loneliness, stigmatization, suicide risk and impact on working life. Other comorbidities related to HS are diabetes mellitus, obesity, hypertension, dyslipidaemia, metabolic syndrome and cardiovascular disease, among others, and there is a high prevalence of smoking.

Despite the evidence of this cumulative physical and psychological burden, sexuality, a basic human need and a central aspect of health and quality of life that can be affected by all these factors and comorbidities, has been poorly researched in patients with HS. The dermatologist is the key specialist in the care of these patients. In many cases, it is difficult to achieve complete control of the disease. However, it may be possible to improve several aspects of patients' quality of life such as sexual functioning. To this end, it is necessary to measure the real burden of the problem, to detect patients with a high-risk profile for sexual impairment and to identify the sexual beliefs and needs of patients with HS. Thus, we asked ourselves the following questions: How often do women with HS present sexual dysfunction? How often do men with HS present erectile dysfunction? What are the factors associated with such dysfunction? What degree of sexual distress do these patients experience and what are the associated factors? Do these patients have difficulties and needs in their sexual relationships? What is the available scientific evidence about sexuality in patients with HS?

PATIENTS AND METHODS

Our research was divided into two stages: 1) a crowdsourced online questionnaire and 2) a systematic review of the available scientific literature.

1) To estimate the prevalence of sexual and erectile dysfunction, levels of sexual distress and the beliefs and needs of patients with HS, and to identify the risk profile of patients with sexual impairment, we conducted a cross-sectional study by means of an online crowdsourced questionnaire. Participants were recruited from 1 March to 1 April 2018. The Spanish hidradenitis suppurativa patients' association (ASENDHI) hosted the questionnaire and invited people with HS to participate in the study. The selection criterion was self-referred diagnosis of HS.

Socio-demographic data, biometric parameters, use of medication for other comorbidities and several characteristics of the disease such as age of onset, time under medical attention and affected areas were collected. Disease severity was assessed by patients' self-reported Hurley stage, since patients with HS can self-assess their Hurley stage with a good correlation with physician assessment. Disease activity was assessed by Patients' Global Assessment (PtGA), including five categories (inactive, very low, low, mild and severe), and the intensity of symptoms by Numeric Rating Scales (NRS), where 0 is the minimum intensity of the symptom and 10 the maximum.

Sexual dysfunction in women was assessed by means of the Female Sexual Function Index-6 (FSFI-6), a validated questionnaire that explores the six domains of female sexual function (desire, arousal, lubrication, orgasm, overall satisfaction and pain), each with a single question. A score of 19 or less indicates sexual dysfunction with 96.1% sensitivity and 90.9% specificity.

Erectile dysfunction in men was assessed by means of the International Index of Erectile Function-5 (IIEF-5), a validated questionnaire with 5 questions about erectile function. A score of 21 or less indicates erectile dysfunction with 98% sensitivity and 88% specificity.

Sexual distress was evaluated with a NRS for the impact of HS on sex life, where participants were asked to measure how much the disease affected their sex life on a scale of 0 to 10. Its concordance with the FSFI-6 and the IIEF-5 was also assessed.

Finally, due to the lack of validated tools, several questions were created by both the researchers and a group of patients from ASENDHI based on the scientific evidence available through clinical guidelines on sexual function assessment to find out the beliefs, behaviours and needs of patients with HS. Questions about difficulties in their sex life due to HS, which healthcare professional they would trust to share their sexual problems with, perceived attractiveness and sexual orientation were included. In the case of patients in a stable relationship, there were also questions about the role of their partners and how HS affects their relationships. In the case of single patients, there were also questions about their feelings when they meet new people and how HS affects their opportunities to meet people/establish a relationship. Since these questions were new and not validated, a control group of healthy acquaintances was also recruited by ASENDHI and a survey with all the questions not directly related to HS was distributed among them.

2) To evaluate our results in light of current evidence and to define future lines of research, we decided to conduct a systematic review of the available scientific literature. A literature search of major clinical databases including Medline and Embase was conducted in February 2020 using the following search term: ("Hidradenitis suppurativa" OR "acne inversa") AND ("sex" OR "sexual" OR "sexuality" OR "erectile"). All types of epidemiological studies regarding sexuality and sexual function in patients with HS were included and analyzed. Reviews, guidelines, protocols, conference abstracts and case reports were excluded. Two researchers independently reviewed the titles and abstracts of the articles obtained in the first search to assess relevant studies. The full texts of all articles meeting the inclusion criteria were reviewed, and their bibliographic references were checked for additional sources. The articles considered relevant by both researchers were included in the analysis; in the event of disagreement, a third researcher analyzed the article. The variables assessed were study design, level of scientific evidence according to the Centre for Evidence-Based Medicine, sample size, tools used to assess sexuality or sexual function, statistical analysis and results.

RESULTS

1) We observed a high prevalence of sexual dysfunction in women (51%, 95% CI 45%-57%) and erectile dysfunction in men (60%, 95% CI 49%-70%). Factors associated with sexual dysfunction in women were a high education level, disease activity, the intensity of pain and unpleasant odour and the absence of a stable relationship. Factors associated with erectile dysfunction were ageing, the presence of lesions in genitals and the total number of areas affected by active lesions.

Patients also suffered from high levels of sexual distress, with women more affected than men, 7.27 (2.77) vs 6.39 (3.44) on the NRS for the impact of HS on sex life. Other risk factors for sexual distress apart from female sex were the presence of active lesions in the groin and genitals, the intensity of pain and unpleasant odour and the absence of a stable relationship. Sexual distress correlated both with sexual and erectile dysfunction.

Most patients felt fear of rejection or of the reaction of their sexual partners during sexual relations, with a higher prevalence than in the healthy control group. Younger age, the absence of a stable relationship and the number of areas affected by scars were factors related to this feeling. Patients found that symptoms, especially pain in women and suppuration in men, and some treatments interfered with their sexual relations. The sexual orientation of most patients was heterosexual, as observed in the control group. Around 40% of the patients considered themselves to be less attractive than average, a higher percentage than the healthy controls, with the absence of a stable relationship and the intensity of unpleasant odour and suppuration being factors associated with this consideration. Among patients in a stable relationship, women reported more support and help with overcoming the fear of rejection than men, whereas help with lesion dressing in intimate areas was higher in men. Around 70% of patients stated that HS negatively affected their relationships, with disease activity being a risk factor for this perception. Among single patients, women experienced greater fear of rejection when they met someone they could have a relationship or sexual relations with, and the percentage of women who did not want to meet people because of HS was also higher. Less than a quarter of participants felt excited when they met new people. These percentages were significantly worse than those of the control group. Almost 95% of women and more than 80% of men stated that HS had a negative influence on their chances of having a relationship or sexual relations. Almost 40% of patients would not share their sexual problems with any healthcare staff, in contrast with the healthy control group, where more than 95% would share them. Among patients who would like to talk about their sexual problems, women preferred a psychologist/sexologist, while men felt most comfortable with their dermatologist.

2) In our systematic review, 11 epidemiological studies representing 42,729 patients with HS were considered relevant and analysed. Most studies had a cross-sectional design with or without comparison group(s), were conducted in an outpatient setting or through surveys and included patients with mild to moderate HS. Apart from the results of our research, the review also showed that patients with HS had a higher incidence of sexual dysfunction than the healthy population. The presence of sexual and erectile dysfunction had a large impact on quality of life.

The incidence of sexual dysfunction was higher in patients with HS suffering from depression and anxiety, although the role of these mood disturbances was not clear. Only one study evaluated the effect of surgery on sexual function, showing an inconsistent improvement. The effect of other treatments on sexual function has not been evaluated.

DISCUSSION

In our research we found a profound impairment of sexuality in patients with HS. The prevalence of sexual dysfunction in women and erectile dysfunction in men was high, 51% and 60% respectively. These percentages are higher than those reported in other investigations using the same questionnaires, either in the general population, in a population attending a screening programme for prostate cancer or in patients suffering from other dermatological diseases such as psoriasis. Patients also suffered from high levels of sexual distress. They experience greater feelings of rejection and lower perceived attractiveness than healthy people. In addition, there is a noticeable impact on stable relationships, and a high percentage of single participants thought that the disease decreased their possibilities of having a sexual/sentimental partner, reflecting their lack of confidence.

Our investigation also helps to detect patients at higher risk of sexual impairment. Women seem to be more affected than men. Disease activity, the presence of active lesions in certain locations such as the groin and genitals and symptoms such as pain and unpleasant odour represent important risk factors. Body image alteration may also play a role. On the other hand, the presence of a stable partner is a prominent protective factor, probably because the trust built in a relationship can relieve symptoms of shame, shyness and rejection.

Identifying the real burden of a problem and the patients most vulnerable to suffering from it is an initial and primary action in order to undertake strategic health actions. Information and communication technologies are changing both medical assistance and research. Our approach to the issue through an online crowdsourced questionnaire helped us to achieve our goals. The privacy and anonymity offered by the Internet was an important advantage for patients to feel comfortable expressing themselves freely, as approaching a topic such as sexuality through a clinical interview can be complex and embarrassing for both the patient and the clinician. In addition, crowdsourcing made it possible to reach a large number of people around the world and to recruit a large sample size (the largest to date in research on sexual dysfunction in HS using validated questionnaires), which is advantageous in an exploratory study such as ours and may have been decisive in finding risk factors not identified in previous studies.

The systematic review showed that much remains to be done in research on sexuality in patients with HS. Most of the studies had a level of scientific evidence 4 according to the Centre for Evidence-Based Medicine and could have been affected by selection biases. Some of them did not use validated tools and/or validated cut-off points to assess sexual function. Although risk factors associated with sexual dysfunction, erectile dysfunction and sexual distress have been identified, as well as the impact of sexual impairment on quality of life, the mechanisms by which this impairment occurs in patients with HS have not been fully explained. The human sexual cycle response is complex and can be affected by both psychological and organic/physical factors. In HS, the role of psychological factors and mood disturbances like anxiety or depression, as well as the importance of comorbidities associated with sexual dysfunction such as hypertension, diabetes mellitus or metabolic syndrome, needs to be determined. The effect of systemic immunomodulatory drugs should be assessed, in light of what has been observed in other diseases such as psoriasis, where significant improvement can be achieved. Research on changes in sexual function after surgical procedures assessed this 3 and 6 months after surgery, but surgical treatment may take longer to improve complex life activities such as sexual function. In addition, it would be interesting to investigate the impairment of sexuality in the partners of patients with HS, due to the importance they seem to have for patients.

Dermatologists must be primarily responsible for the care of HS patients, so attention should be paid to sexual problems in order to manage the disease with a holistic approach, since it is currently still not possible to achieve a cure or a complete control of HS in most patients. The dermatologist should facilitate patients to express themselves, initiate treatment according to the origin of the problem and refer patients to the appropriate specialists when required.

CONCLUSIONS

Sexuality is an unmet need in patients with HS. The presence of profound impairment to sexual function and high levels of distress in relation to various clinical-epidemiological features is frequent. The disease limits personal relationships, both in patients with a partner and in single patients. Patients often feel the need to share their sexual problems with healthcare professionals. Dermatologists are the key staff to address this problem, as they are the main specialists in the care of these patients.

1. INTRODUCCIÓN

1.1 DEFINICIÓN DE HIDRADENITIS SUPURATIVA

La hidradenitis supurativa (HS) es una enfermedad inflamatoria cutánea crónica de origen multifactorial. Fue descrita por primera vez en 1854 por el cirujano francés Aristide Auguste Stanislas Verneuil, denominándola así por su predominio en áreas con abundantes glándulas sudoríparas apocrinas(1). Sin embargo, a pesar de su nombre, el origen no se encuentra en dichas glándulas, sino en el folículo piloso asociado a las mismas(2).

A nivel clínico se caracteriza por la aparición de nódulos inflamatorios y abscesos predominantemente en áreas intertriginosas, como axilas, ingles, glúteos, genitales, periné o región submamaria(3). Estas lesiones inflamatorias agudas producen síntomas como dolor, supuración, mal olor o prurito(4). El curso de la enfermedad es crónico, con aparición de brotes recurrentes. A medio-largo plazo, si no se consigue un control adecuado de la carga inflamatoria de la enfermedad, se produce un daño estructural en forma de fístulas, que actúan como reservorios perpetuando la inflamación por factores endógenos y formación de *biofilms* bacterianos, cronificando la enfermedad(5).

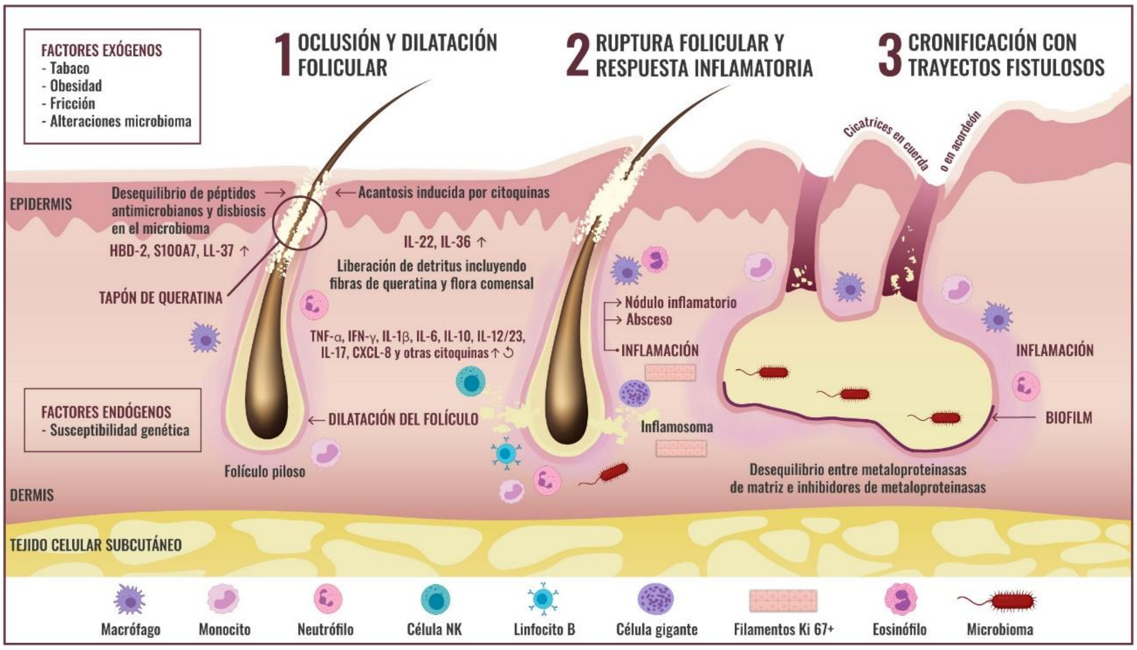
1.2 EPIDEMIOLOGÍA

Aunque ha sido una entidad considerada como enfermedad rara hasta hace unos años, probablemente debido a un infradiagnóstico(6), su prevalencia en la población general se ha estimado entre el 0,5% y el 4% según diversos estudios(6-10), si bien muchos de ellos podrían contener sesgos de selección(11). Más recientemente, se ha estimado que la prevalencia en nuestro medio se sitúa entre el 0,7% y el 1,2%(12). La edad media de inicio de la enfermedad está en torno a los 20 años, siendo raro que comience antes de la adolescencia, etapa en la que las glándulas sudoríparas apocrinas comienzan a ser funcionales(13). La HS es unas 3 veces más frecuente en las mujeres, aunque en los hombres es más común la evolución a formas más graves(9, 13). Los datos sobre su distribución racial son escasos y variados, con algunos estudios apuntando a una mayor prevalencia en raza negra(14) y otros en raza blanca(8, 10). La prevalencia de tabaquismo entre los pacientes con HS es elevada, oscilando entre el 42% y el 90% dependiendo del estudio(8, 9, 11). La media de retraso diagnóstico es de 7 años(15), aunque se ha llegado a estimar hasta en 14 años(6). Este dato es importante, ya que en ausencia de tratamiento la enfermedad tiene un curso destructivo, dando lugar a disfunción física y psíquica que se acumula en el tiempo(16). Es importante un diagnóstico precoz y tratamiento temprano de la enfermedad, pues el retraso diagnóstico puede conducir a un tratamiento inapropiado, cronificación del dolor y estrés emocional y psicológico.

1.3 ETIOPATOGENIA

La HS es una enfermedad de origen multifactorial, habiéndose implicado en su desarrollo factores genéticos, ambientales, infecciosos, hormonales e inmunológicos(17). El fenómeno etiopatogénico primario consiste en la obstrucción de los folículos pilosos asociados a glándulas sudoríparas apocrinas, debido a la hiperqueratosis infundibular de la porción terminal del folículo piloso, con su consiguiente dilatación por acúmulo de detritus celulares, ruptura y liberación de queratina y bacterias a la dermis circundante, lo cual genera una importante respuesta inflamatoria mediada por neutrófilos, linfocitos y macrófagos(18, 19). Como se ha comentado previamente, estos episodios inflamatorios repetidos en el tiempo acaban produciendo alteraciones estructurales en forma de trayectos fistulosos(2). Figura 1.

Figura 1. Esquema de la secuencia de eventos que subyacen a la etiopatogenia de la HS



Modificado de Vossen A *et al.* 2018(2)

Factores genéticos

Alrededor de un tercio de los pacientes tienen historia familiar de HS, con un patrón de herencia autosómico dominante(20). Se han detectado mutaciones con pérdida de función en genes del complejo de las γ-secretasas, fundamentalmente en el gen de la nicastrina (NCSTN)(2); estas mutaciones producen alteraciones en la vía de señalización notch, implicada en el desarrollo normal de los folículos pilosos(21) y en la modulación negativa de las respuestas inmunes adquiridas mediadas por linfocitos T(22). También se han encontrado mutaciones en el gen PSTPIP1 (*Proline-serine-threonine phosphatase interacting protein* 1), una proteína alterada en múltiples dermatosis neutrofílicas y síndromes autoinflamatorios y que tiene acción inmunomoduladora al inhibir a los linfocitos CD2, regular la actividad de la tirosín quinasa c-Abl e interactuar con otras proteínas como la pirina o la proteína WASp (*Wiskott-Aldrich syndrome protein*)(2). Recientemente, se ha determinado una mayor frecuencia del alelo *DQB1**03:01 del HLA en 106 pacientes con HS que en controles sanos en población cántabra(23).

Factores ambientales

Los factores más conocidos son el tabaco, la obesidad y la fricción. El tabaco produce una activación de los queratinocitos y de los fibroblastos, favoreciendo el taponamiento folicular(24). Asimismo, promueve un estado proinflamatorio con activación de neutrófilos y linfocitos Th17(17), aumenta la virulencia de *Staphylococcus aureus*(17), favorece la formación de *biofilm* bacteriano(25), disminuye la formación de péptidos antimicrobianos(26) y altera la vía de señalización notch(27). La obesidad también supone un estado proinflamatorio crónico, así como una mayor fricción en las zonas de pliegues y por consiguiente mayor estrés mecánico, que empeora los procesos de oclusión y ruptura folicular(28). Tanto el tabaco como la obesidad se relacionan con la actividad de la HS(29), y la corrección de estos factores puede mejorar el curso de la enfermedad(30, 31). Por otro lado, la aparición de lesiones de HS en áreas de fricción, áreas ajustadas por la ropa o zonas de traumatismos ha planteado la posibilidad de que se produzca el fenómeno de Koebner en la enfermedad(32).

Factores infecciosos

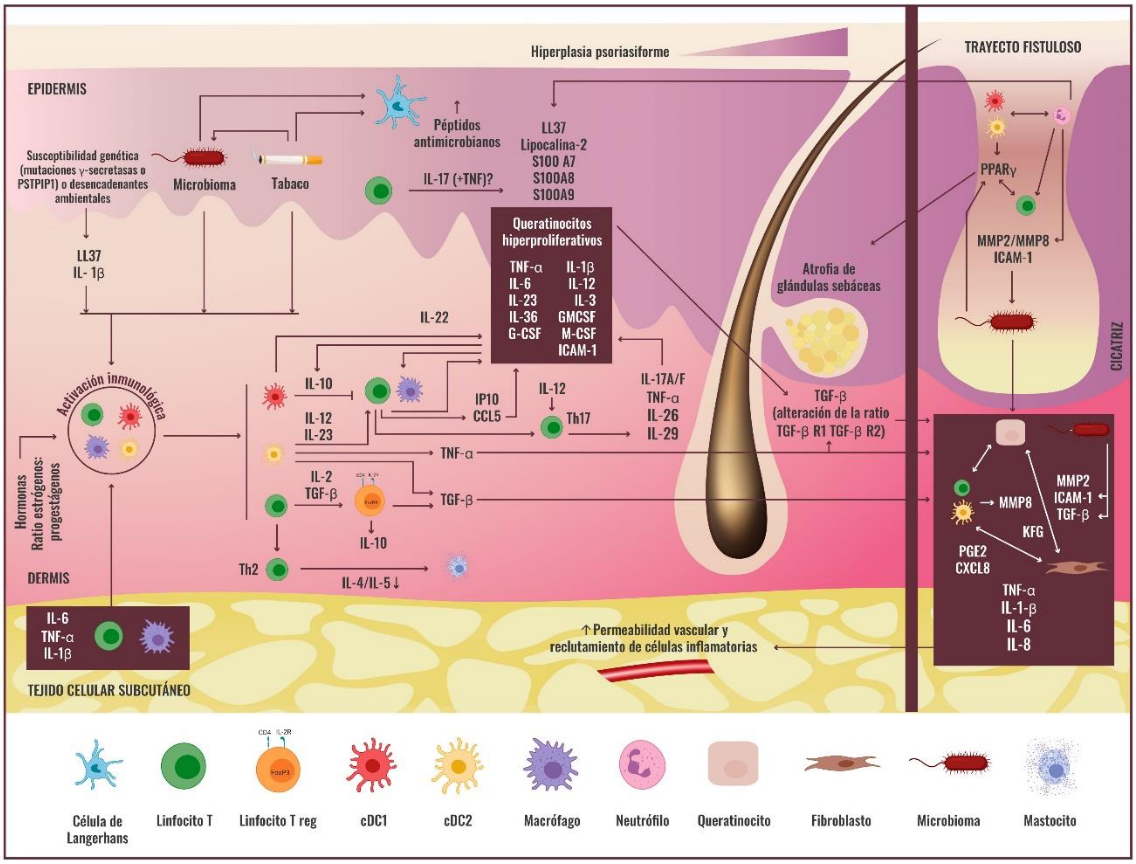
El papel de las infecciones en la HS es controvertido. Actualmente, no se considera que la enfermedad esté causada primariamente por infecciones, pero determinados microorganismos pueden colonizar secundariamente las lesiones de HS, especialmente aquellas que suponen un daño estructural como las fístulas, y cronificar de este modo la inflamación(2). Se han encontrado diferencias entre el microbioma de la piel lesional y perilesional de los pacientes y la piel de sujetos sanos, con mayor formación de *biofilms* bacterianos(5). Asimismo, diversos estudios han determinado un predominio de ciertos microorganimos como anaerobios (actinomicetos, *Prevotella* o *Porphyromonas*), *Streptococcus milleri* o estafilococos coagulasa-negativos como el *Staphylococcus lugdunensis*(33-35). Las bacterias del género *Porphyromonas* se han asociado con enfermedades inflamatorias sistémicas y con el desarrollo de arteriosclerosis a través de una señalización aberrante de los receptores *Toll-like* 4. Además, la presencia de bacterias de los géneros *Fusobacterium* y *Parvimonas* se ha asociado a la gravedad de la HS(33).

Factores inmunológicos

Al igual que en la enfermedad de Crohn o en la psoriasis, en la HS existe una sobreexpresión de linfocitos Th1 y Th17. Determinados estímulos, como pueden ser los factores ambientales o los infecciosos, así como la liberación tras la ruptura de los folículos de filamentos de queratina, PAMPs (*pathogen-associated molecular patterns*) o DAMPs (*damage-associated molecular patterns*), activan una respuesta inmunológica en personas genéticamente predispuestas. Como consecuencia de esta respuesta, las células dendríticas y los linfocitos T producen una hiperplasia psoriasiforme de queratinocitos a través de la vía de la IL-12/IL-23, con predominancia de la respuesta Th17, y con participación también de la inmunidad innata (activación de inflamosomas y de receptores *Toll-like*, especialmente los TLR2)(2, 36). Asimismo, existe una alteración de los péptidos antimicrobianos en la epidermis. La interacción entre la dermis inflamada y la epidermis hiperplásica perpetúa la respuesta inflamatoria mediante la IL-36, IL-1β y el TNF-α(36). La sobreexpresión de metaloproteinasas, sobre todo MMP2, ICAM-1 y TGF-β 1, 2 y 3 debido a la activación continua del sistema inmune acaba produciendo las alteraciones estructurales con formación de fístulas(2, 36). En este punto, la acción del TNF-α, de la PGE2 y del CXCL2 pueden perpetuar la respuesta inflamatoria. Figura 2.

Las citoquinas y proteínas inflamatorias que se han hallado elevadas en piel lesional de los pacientes con HS son IL-1β, IL-6R, IL-10, IL-17A, IL-36α, IL-36β, IL-36γ, IL-36RA, TNF-α, sTNFR2, hBD1, hBD2, hBD3, s100A7, LL37/catelicidina, CCL3, CCL5, CCL27 y BLC; en la piel perilesional IL-1β, IL-17, IL-36β, IL-36RA, IL-37, IL-38 y TNF-α; en el exudado de lesiones activas TNF-β e IFN-γ; y en el suero IL-1β, IL-6, IL-8, IL-10, IL-12p70, IL-17, TNF-α, sTNFR1, PCR, VSG, LC2 y MMP2. Muchas de las citoquinas que se encuentran elevadas, sobre todo en piel lesional, son producidas por los queratinocitos activados, mientras que otras son producidas por los linfocitos T, las células dendríticas, los monocitos o los neutrófilos, que son atraídos por los factores quimiotácticos liberados en la respuesta inflamatoria(36). También es destacable un incremento de los mastocitos en piel lesional y perilesional con producción de IL-4 e IL-5, lo que podría explicar en algunos casos el prurito que sufren los pacientes(37).

Figura 2. Representación esquemática de las vías inflamatorias en la HS



Modificado de Frew *et al.* 2018(36)

Factores hormonales

Aunque en algunos estudios no se ha determinado una diferencia en el perfil hormonal ni en la actividad de receptores androgénicos ni estrogénicos en piel lesional de pacientes con HS(38), un 43% de las mujeres desarrollan brotes en relación con las menstruaciones(39), así como cambios durante el embarazo y mejoría a partir de la menopausia. En dos estudios europeos realizados mediante cuestionarios, se encontró que entre el 30-71% de las mujeres embarazadas presentaban mejoría de la HS durante el embarazo, entre el 20-53% no presentaban cambios y entre el 9-17% empeoraban(30, 39). Esto contrasta con un estudio estadounidense en el que solo el 8% mejoraban, el 30% se mantenían sin cambios y el 62% empeoraban; este estudio se realizó revisando las historias de las pacientes, y en el 44% de los casos no había datos disponibles, lo que puede suponer un importante sesgo de selección (podrían ser mujeres sin cambios o con mejoría de la enfermedad y que por tanto no quedaron recogidas en los registros)(40). El incremento de peso, con aumento de la oclusión y fricción en los pliegues, y el aumento del tejido adiposo, con mayor secreción de mediadores inflamatorios como el TNF-α, pueden explicar el empeoramiento de algunas mujeres durante el embarazo, mientras que la elevación de los niveles de progesterona (que durante el embarazo son 5-10 veces mayores que los de estrógenos) explican la mejoría de otras pacientes, ya que la progesterona, al contrario que los estrógenos, inhibe la proliferación de linfocitos CD4+ y la diferenciación a linfocitos Th17(41). Además, en el grupo de pacientes estadounidense se observó un empeoramiento de la enfermedad durante el periodo de postparto en el 66% de las mujeres(40). Los descensos de los niveles de progesterona y el incremento relativo de los niveles de estrógenos que se producen tras el parto son probablemente los responsables de estos rebrotes.

1.4 FENOTIPOS

Se han propuesto varias clasificaciones de la HS en distintos fenotipos en función fundamentalmente de características clínicas como la distribución o el tipo de lesiones, aunque la utilidad de estas clasificaciones es limitada y en general no existe una buena correlación genotipo-fenotipo(42). Ejemplos de clasificaciones en fenotipos son la de Canoui-Poitrine *et al.*(43), que definieron los fenotipos LC1 (*latent class* 1) o axilar-mamario, LC2 o folicular y LC3 o glúteo, la de van der Zee *et al.*(44), que dividieron la enfermedad en 6 fenotipos (regular, forúnculos friccionales, foliculitis cicatricial, conglobata, sindrómica y ectópica), o la de Thorlacius *et al.*(45) que definieron los subtipos "alto" (lesiones predominantemente en axilas y mamas) y "bajo" (lesiones predominantemente en ingles, genitales, región perianal y glúteos). Recientemente se ha propuesto otra clasificación basada en el patrón de lesiones elementales y su capacidad para producir lesiones coalescentes complejas (figura 3)(46):

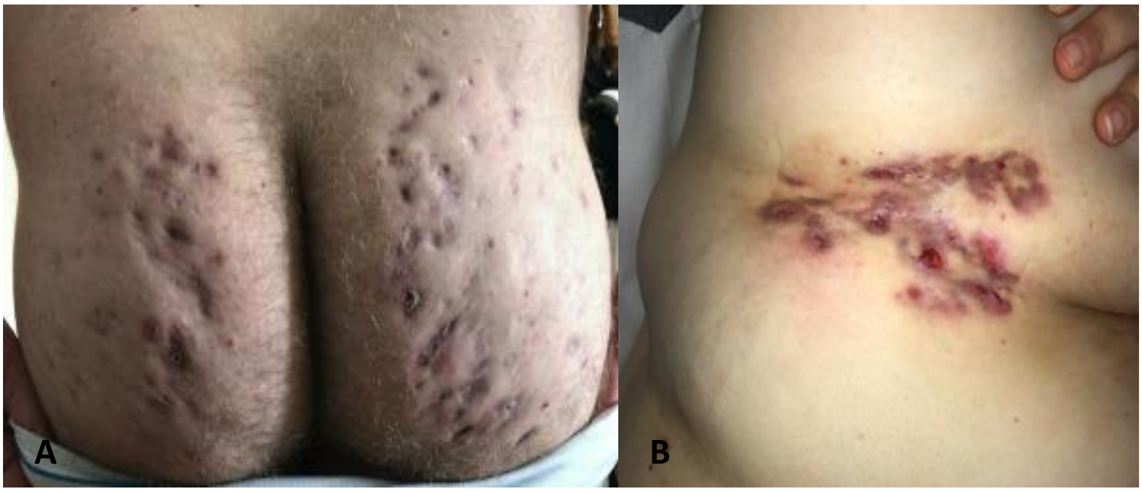
Fenotipo folicular

El fenotipo folicular se caracteriza por la presencia de lesiones tipo foliculitis y comedones, tanto abiertos como cerrados. La principal lesión inflamatoria activa son los nódulos, tanto superficiales como profundos. Los abscesos son poco frecuentes en este subtipo, mientras que las fístulas son excepcionales y, en caso de producirse, son finas y no coalescentes. La edad media de comienzo de la enfermedad en este grupo se situaría en torno a los 17,6 años, con una media de retraso diagnóstico cercana a los 14 años. Son más frecuentes los antecedentes familiares de HS que en el fenotipo inflamatorio, así como de acné papuloso y nodular.

Fenotipo inflamatorio

El fenotipo inflamatorio se caracteriza por la ausencia de lesiones foliculares y comedones, con presencia de abscesos y de trayectos fistulosos gruesos como lesiones fundamentales, que tienden a confluir en placas inflamatorias y cicatriciales pobremente definidas. Se pueden detectar fístulas penetrantes subcutáneas o interfasciales. Los nódulos son excepcionales. Este fenotipo sería más frecuente en hombres, con una edad media de comienzo de 26,7 años, una media de retraso diagnóstico de casi 9 años y un IMC (índice de masa corporal) 2 puntos mayor (30,4 vs 28,7) que el del fenotipo folicular. La localización en ingles, genitales y periné es más frecuente en este grupo. La enfermedad en el fenotipo inflamatorio se manifiesta de forma más grave, con mayor frecuencia de estadios de Hurley avanzados (52,8% en estadio II y 45,3% en estadio III), mayor carga inflamatoria y mayor frecuencia de brotes. Exceptuando el prurito, el resto de los síntomas son referidos por los pacientes con mayor intensidad que en el fenotipo folicular. Los antecedentes familiares de acné conglobata y acné fulminans son más frecuentes. Los pacientes con fenotipo inflamatorio tienen mayores niveles de PCR y mayor riesgo cardiovascular que aquellos con fenotipo folicular, y son más propensos a recibir tratamiento con corticoides sistémicos y adalimumab(47).

Figura 3. Fenotipos folicular (A) e inflamatorio (B) de HS



Imágenes de la Unidad de Hidradenitis Supurativa del Hospital Universitario Virgen de las Nieves

1.5 DIAGNÓSTICO Y ESTADIAJE

El diagnóstico de la HS es clínico. De acuerdo con la definición modificada de Dessau(48), deben cumplirse tres criterios: presencia de lesiones típicas (nódulos inflamatorios, abscesos, fístulas, cicatrices "en acordeón" o comedones múltiples), afectación de localizaciones típicas (axilas, región submamaria, ingles, periné, genitales, región perianal o glúteos) y cronicidad (aparición de 2 o más brotes separados al menos 6 meses). Estos tres criterios, por sí solos, tienen una alta sensibilidad y especificidad para el diagnóstico de HS(49).

En cuanto al estadiaje de la enfermedad, existen varios sistemas:

Estadios de Hurley

El sistema de estadificación de Hurley(50) fue el primero en aparecer, y actualmente sigue siendo uno de los más conocidos y utilizados por su sencillez. Según este sistema, la enfermedad se divide en 3 estadios (figura 4):

- Estadio I: abscesos aislados solitarios o múltiples, sin formación de cicatrices ni trayectos fistulosos.
- Estadio II: abscesos recurrentes, lesiones solitarias o múltiples separadas, con formación de trayectos fistulosos.
- Estadio III: afectación difusa o extensa, con múltiples trayectos fistulosos interconectados y abscesos.

Figura 4. Estadios I, II y III de Hurley en región axilar

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De este modo, es un sistema cualitativo y estático, ya que no cuantifica el número de lesiones ni la carga inflamatoria y se basa en la presencia de lesiones estructurales poco modificables con el tratamiento médico, siendo por tanto de escasa utilidad para valorar la respuesta terapéutica. En diversos estudios se ha estimado que entre el 7 y el 68% de los pacientes se encuentran en estadio I, entre el 28 y el 83% en estadio II y entre el 4 y el 22% en estadio III(51).

International Hidradenitis Suppurativa Severity Score System (IHS4)

El *International Hidradenitis Suppurativa Severity Score System* o IHS4 es un sistema de estadificación dinámico basado en el contaje de lesiones inflamatorias. Por tanto, permite cuantificar la carga inflamatoria de la enfermedad y monitorizar la respuesta a los tratamientos médicos. Consiste en una fórmula que se calcula de la siguiente manera: nº de nódulos inflamatorios + nº de abscesos multiplicado por 2 + nº de fístulas inflamatorias/drenantes multiplicado por 4. De esta manera, se obtiene un número que nos indica la carga inflamatoria de la enfermedad: si es < 4, la carga es baja; si está entre 4-10, la carga es moderada; y si es > 10, la carga es alta(52).

Hidradenitis Suppurativa Clinical Response (HiSCR)

El *Hidradenitis Suppurativa Clinical Response* o HiSCR es un parámetro muy usado como variable de resultado en ensayos clínicos y estudios farmacológicos en HS. Se define como una reducción ≥ 50% en el contaje de lesiones inflamatorias (nódulos inflamatorios + abscesos) sin que aumenten el nº de abscesos ni el nº de fístulas inflamatorias(53). Es, por tanto, una variable dicotómica.

Otros sistemas de estadiaje

Otros sistemas que también se han desarrollado para el estadiaje de la HS son el *Sartorius score*(54), modificado posteriormente por Revuz(55), el *Hidradenitis Suppurativa Physician's Global Assessment*(56), el *Hidradenitis Suppurativa Severity Index*(57), el *Acne Inversa Severity Index*(58) o el *Severity Assessment of Hidradenitis Suppurativa score*(59). En líneas generales, tienen en cuenta parámetros como el número y tipo de lesiones, el número de áreas afectadas, la distancia entre las lesiones, la superficie corporal afecta o BSA (por sus siglas en inglés), el número de lesiones en el último mes o la intensidad de los síntomas.

1.6 TRATAMIENTO

El tratamiento de la HS incluye diversas terapias médicas y procedimientos quirúrgicos, pudiendo resultar en ocasiones complejo. Ninguno de estos tratamientos es definitivo ni completamente efectivo, y el objetivo principal es el control de la inflamación en etapas tempranas, para prevenir la evolución de la enfermedad a estadios avanzados. En el caso de aparición de daño estructural, es necesario recurrir a técnicas quirúrgicas para su resolución. Aunque existen múltiples fármacos en estudio y desarrollo, el arsenal terapéutico disponible para el tratamiento de la HS es más limitado que para otras patologías dermatológicas como la psoriasis. Los principales tratamientos son(60-62):

Clindamicina +/- rifampicina

La clindamicina es uno de los fármacos más empleados como primera línea en la HS, tanto de forma tópica (en solución, emulsión o gel) como oral(60-62). Inhibe la síntesis proteica de las bacterias al unirse a la subunidad 50s de los ribosomas(63), y además tiene efecto antiinflamatorio al inhibir a los neutrófilos(64). Las reacciones adversas más frecuentes son las gastrointestinales, sobre todo diarrea, náuseas, vómitos o dolor abdominal. En raras ocasiones, puede producirse una colitis pseudomembranosa por *Clostridium difficile*. La posología suele ser 300 mg cada 12 horas durante 10-12 semanas, pudiendo realizarse nuevos ciclos en caso de brotes(60-62). Clásicamente, la clindamicina se ha usado en combinación con rifampicina en el tratamiento de la HS, con la misma posología. Sin embargo, los estudios en los que se basaba esta combinación de antibióticos son series de casos sin grupo control(65-70). La mayor proporción de reacciones adversas con la combinación, sobre todo gastrointestinales, la gran cantidad de interacciones medicamentosas de la rifampicina al ser un inductor del citocromo p450 3A4(71), incluyendo con la propia clindamicina reduciendo sus niveles plasmáticos, y la importancia de la rifampicina en el tratamiento de la tuberculosis, de infecciones protésicas y de otros microorganismos multirresistentes han llevado a que en los últimos tiempos se tienda a abandonar la combinación en favor del uso de la clindamicina en monoterapia(72-74).

Doxiciclina

La doxiciclina es una tetraciclina semisintética de segunda generación con efecto bacteriostático al inhibir la síntesis proteica debido a su unión a la subunidad 30s de los ribosomas(75). También posee efecto antiinflamatorio, debido entre otros a su efecto sobre la quimiotaxis de los neutrófilos, sobre diversas metaloproteinasas y sobre citoquinas inflamatorias como TNF-α, IL-1β, IL-6 o IL-8(76), factores todos ellos implicados en la etiopatogenia de la HS. La posología suele ser de 200 mg al día durante 12 semanas. Recientemente, en un estudio de cohortes multicéntrico a nivel europeo se ha determinado una eficacia similar de la doxiciclina en monoterapia y la combinación de clindamicina y rifampicina, si bien existían diferencias basales significativas en los grupos de comparación, al tener una enfermedad más grave y con mayor carga inflamatoria los pacientes que recibían el tratamiento combinado(77). Las reacciones adversas más comunes son nuevamente las gastrointestinales (pirosis, erosión esofágica, diarrea, náuseas y vómitos)(78).

Corticoides

Los corticoides producen una rápida disminución del dolor y otros síntomas relacionados en un plazo de 48-72 horas en pacientes con HS(60). Por ello, pueden ser muy útiles como tratamiento concomitante para el abordaje de lesiones agudas(79). Se usan tanto por vía oral, como la prednisona o la dexametasona en pulsos, como inyectados intralesionalmente, como el acetónido de triamcinolona(60-62). Tienen efecto antiinflamatorio, al inhibir la producción de prostaglandinas, leucotrienos y citoquinas inflamatorias como el TNF-α o el IFN-γ, inmunosupresor, antiproliferativo y vasoconstrictor(60). Las reacciones adversas aparecen sobre todo con tratamientos prolongados y/o a dosis elevadas, lo cual limita su uso a los periodos de mayor actividad o como terapia puente a otros tratamientos de mantenimiento(62). Los más frecuentes son osteoporosis, úlceras gástricas/duodenales, diabetes, obesidad central (cara y tronco), insuficiencia corticosuprarrenal secundaria, alteraciones cutáneas como acné, hirsutismo o estrías, glaucoma, cataratas, alteraciones del estado de ánimo o disfunción sexual(60, 62). Estos efectos se minimizan con la administración intralesional.

Retinoides orales

Los retinoides orales son análogos de la vitamina A. Actúan regulando la queratinización del folículo piloso, así como inhibiendo la quimiotaxis de los neutrófilos y la liberación de mediadores proinflamatorios por parte de éstos(80). El retinoide más empleado en HS es el acitretino(81-83), aunque también se han usado la isotretinoína(84, 85) y la alitretinoína(86). Los efectos adversos más comunes son la sequedad de piel y mucosas, sobre todo labial, nasal y conjuntival. Otras reacciones adversas frecuentes son el aumento de los triglicéridos, dolores musculares, sobre todo en relación con el ejercicio, y las reacciones de fotosensibilidad. Su uso durante el embarazo está totalmente contraindicado por el riesgo de malformaciones fetales graves, debiendo usarse un método anticonceptivo efectivo durante el tratamiento y al menos hasta 1 mes después de finalizado en el caso de la isotretinoína y de la alitretinoína y 3 años en el caso del acitretino(62).

Tratamientos hormonales

En ocasiones se emplean fármacos como anticonceptivos con perfil antiandrogénico, acetato de ciproterona o espironolactona(87-90), aunque la evidencia disponible para su uso es limitada(91). Estos fármacos pueden ser especialmente útiles en mujeres con empeoramientos perimenstruales, signos de hiperandrogenismo clínico y/o bioquímico o síndrome de ovario poliquístico, bien como monoterapia en casos leves-moderados o en combinación con otros tratamientos en casos graves(62). También para este perfil de pacientes se han propuesto los tratamientos con metformina(92) y con finasterida(93).

Adalimumab

Adalimumab es el único fármaco biológico aprobado hasta la fecha para su uso en HS. Es un anticuerpo monoclonal humano que se une con gran afinidad y especificidad al TNF-α. Se usa en los casos más graves de la enfermedad y con mayor carga inflamatoria, administrado por vía subcutánea y, a diferencia de en la psoriasis, la posología de mantenimiento es de 40 mg semanales(94). Los efectos adversos más frecuentes son reacciones locales en el punto de inyección, gastrointestinales, hipertensión arterial, dolor de cabeza, dolores musculares, alteraciones del estado de ánimo, asma, reacciones cutáneas, conjuntivitis, vértigo, dislipemia y aumento del riesgo de infecciones(60).

Otros tratamientos médicos

En ocasiones, se recurre a otros tratamientos antiinflamatorios/inmunomoduladores, como la ciclosporina, la colchicina o el apremilast, o a otros antibióticos como el moxifloxacino, el metronidazol, el ertapenem, la dapsona, el trimetoprima-sulfametoxazol o el linezolid, con evidencia para su uso limitada a pequeñas series de casos en la mayoría de ellos(60-62). Asimismo, también se emplean ocasionalmente otros fármacos dirigidos frente al TNF-α como el Infliximab (con la ventaja de que puede ajustarse la dosis en función del peso del paciente), Etanercept, Golimumab o Certolizumab pegol(60-62). Anakinra, un antagonista del receptor humano de la IL-1, puede considerarse en caso de fallo a fármacos anti-TNF-α(61, 62). Además, se está estudiando la utilidad en la HS de otros fármacos biológicos empleados para la psoriasis y dirigidos contra la IL-17 o la IL-23, como por ejemplo Secukinumab, Risankizumab, Ustekinumab, Guselkumab o Bimekizumab(95-97), y existen diversos fármacos biológicos en desarrollo que podrían ayudar a mejorar el control de la enfermedad.

Tratamientos quirúrgicos

Cuando se ha producido daño estructural debido a la cicatrización, es necesaria la cirugía de la zona afectada. Hay diversos procedimientos quirúrgicos, siendo la extirpación amplia en bloque de la zona lesionada con curación por segunda intención la técnica asociada a menores recurrencias(98). El uso de ecografía cutánea para la delimitación prequirúrgica de las lesiones puede disminuir el riesgo de recidivas(99). En el caso de pacientes que estén recibiendo tratamiento biológico, no es necesario suspenderlo en el momento de la cirugía, siendo además las recurrencias más leves en el caso de que se produzcan que en los pacientes que no reciben tratamiento biológico(100).

En ocasiones, también se puede optar por la cobertura de la zona afectada con colgajos o con injertos, a veces mallados. Otras opciones son la extirpación simple con cierre directo para defectos pequeños o el *deroofing*, que consiste en eliminar el techo de la fístula y dejar que cicatrice por segunda intención(60, 61).

En general, se trata de procedimientos quirúrgicos agresivos, que comportan un importante estrés físico y psíquico, con periodos de recuperación postoperatorios prolongados, y con elevados costes directos e indirectos, especialmente cuando se producen recurrencias(101, 102). Estas cirugías podrían evitarse o simplificarse con el uso intralesional de células mesenquimales inyectadas en las fístulas(103).

También se han propuesto el tratamiento con láser de CO_2, la eliminación de los folículos pilosos con láser Nd:YAG o IPL o la terapia fotodinámica con ácido 5-aminolevulínico, con evidencia limitada(60, 61).

1.7 COMORBILIDADES

Cada día se tiende a considerar más a la HS como una enfermedad inflamatoria con repercusión sistémica. En este sentido, se ha observado una asociación de la HS con diversas patologías:

Enfermedad inflamatoria intestinal

La HS se ha asociado a enfermedad inflamatoria intestinal, sobre todo a enfermedad de Crohn, con la que comparte vías patogénicas y características clínicas(104). La prevalencia de enfermedad de Crohn en pacientes con HS se ha estimado entre el 0,2% y el 2%, siendo la odds de padecer enfermedad de Crohn entre 1,2 y 3,1 veces superior en pacientes con HS que en población general(105-109). Por su parte, la prevalencia de colitis ulcerosa en pacientes con HS se ha estimado entre el 0,3% y el 1,3%, siendo la odds de padecer colitis ulcerosa entre 1,3 y 1,8 veces superior en pacientes con HS que en población general(105-107).

Diabetes mellitus

En múltiples estudios se ha observado una mayor frecuencia de diabetes mellitus en pacientes con HS que en población general, con prevalencias de entre 7,1% y 24,8%(110); dos metaanálisis han determinado una odds de padecer diabetes mellitus en pacientes con HS de 2,17 [1,9-2,6](111) y de 2,8 [1,8-4,3](112) veces la de los controles sanos.

Dislipemia

Diversas investigaciones han estimado una mayor frecuencia de dislipemia en pacientes con HS que en controles sanos, con prevalencias entre 3,3% y 45,3%(110); en un metaanálisis, la odds de hipertrigliceridemia fue de 1,7 [1,1-2,5] y la de HDL disminuida de 2,5 [1,5-4,2](113) veces la de los controles sanos.

Obesidad

La obesidad ha sido ampliamente relacionada con la HS, con prevalencias de obesidad en pacientes con HS de entre 5,9% y 73,1%(110); en un metaanálisis se estimó una odds de obesidad de 3,5 [2,2-5,4] veces la de los controles sanos(113).

Síndrome metabólico

Se ha estimado una prevalencia de síndrome metabólico en pacientes con HS de entre 10,4% y 50,6%(110), siendo la odds de padecerlo entre 1,8 y 2,2 veces la de los controles sanos(111, 113, 114). Se ha sugerido que podría existir un origen común de la HS y la resistencia a la insulina a través de alteraciones en la proteína mTOR (*mammalian target of rapamicyn*)(115).

Enfermedad cardiovascular

El tabaquismo y la obesidad son factores relacionados tanto con la HS como con el desarrollo de hipertensión arterial. En 6 de 8 estudios llevados a cabo sobre la materia se ha encontrado mayor riesgo de hipertensión arterial en pacientes con HS que en controles sanos, con odds ratios entre 1,2 y 2,1 veces las de los controles sanos y una prevalencia de hipertensión de entre 7,8% y 56,3%(110).

Como se ha visto, además de a hipertensión arterial, la HS se asocia a otros factores de riesgo de eventos cardiovasculares mayores (infarto de miocardio y accidente cerebrovascular) como son la diabetes mellitus, la dislipemia, la obesidad o el síndrome metabólico, y muchas de las citoquinas que se encuentran elevadas en los pacientes con HS están implicadas en la formación de las placas de ateroma, disfunción endotelial y arteriosclerosis, como por ejemplo el TNF-α, la IL-6 o la IL-17(116). En una investigación de base poblacional en Dinamarca, la HS se asoció con mayor riesgo de infarto de miocardio, accidente cerebrovascular isquémico, eventos cardiovasculares mayores, mortalidad cardiovascular y mortalidad por todas las causas que la población general, y con mayor riesgo de mortalidad cardiovascular que los pacientes con psoriasis grave(117). Asimismo, se ha observado que el grosor íntima-medio carotídeo, un parámetro asociado a disfunción endotelial y riesgo cardiovascular, es mayor en pacientes con HS que en controles sanos(118, 119).

Síndrome de ovario poliquístico

En diversos estudios se ha estimado una prevalencia de síndrome de ovario poliquístico en mujeres con HS de entre el 0,4% y el 9%, siendo la odds de padecer la enfermedad entre 1,2 y 13,4 veces la de los controles(110).

Espondiloartropatías

Las espondiloartropatías y la HS comparten algunas vías etiopatogénicas y marcadores inflamatorios, como el TNF-α, la IL-1 o la IL-17. En 2 investigaciones se ha determinado una prevalencia de espondiloartropatía en pacientes con HS de 3,7% y 28,2%(120, 121), precediendo la HS a los síntomas articulares en un 90% de los casos una media de 3,6 años(121). Asimismo, se ha observado una prevalencia de HS del 9,1% entre los pacientes con espondiloartropatías(122).

Pioderma gangrenoso

El pioderma gangrenoso y la HS tienen similitudes en algunas características clínicas, como la presencia de supuración, infiltrados ricos en neutrófilos en la histopatología y respuesta a fármacos que inhiben la quimiotaxis de los neutrófilos o dirigidos frente a TNF-α; además, ambos pueden formar parte de síndromes autoinflamatorios más complejos asociados a otras enfermedades. Se ha estimado una prevalencia de pioderma gangrenoso de entre 0,2% y 0,4% en pacientes con HS, siendo del 3,7% en pacientes con HS y enfermedad de Crohn concomitante(105, 123). La odds de padecer pioderma gangrenoso es 20 veces mayor en pacientes con HS que en controles sanos(123).

Síndromes autoinflamatorios

Los síndromes autoinflamatorios son un grupo heterogéneo de enfermedades poligénicas caracterizadas por una activación aberrante del sistema inmune innato, con especial activación de la vía de la IL-1 y relacionados con el espectro de las dermatosis neutrofílicas(20). En ocasiones, la HS forma parte de estos cuadros, como en los casos de los síndromes PASH (pioderma gangrenoso-PG-, acné y HS), PAPASH (artritis piógena, PG, acné y HS), PsAPASH (artritis psoriásica, PG, acné y HS), PASS (PG, acné conglobata, HS y espondiloartropatía axial) o SAPHO (sinovitis, acné, pustulosis, hiperostosis y osteítis)(124).

Tétrada de oclusión folicular

El acné conglobata, el sinus pilonidal, la celulitis disecante del cuero cabelludo y la HS conforman la denominada tétrada de oclusión folicular, al ser enfermedades en las que el fenómeno etiopatogénico central consiste en el taponamiento folicular. En diversas investigaciones se ha observado una asociación de la HS con estas entidades(9, 105, 125).

Síndrome de Down

En el síndrome de Down la expresión de la proteína precursora de amiloide (APP por sus siglas en inglés) está incrementada. Esta proteína produce en la epidermis una estimulación de la migración, proliferación y adhesión de los queratinocitos, lo que puede conllevar que estos pacientes sean más susceptibles a la hiperqueratosis y taponamiento folicular. Se ha determinado un mayor riesgo de desarrollar HS en los pacientes con síndrome de Down y a edades más tempranas que la población general(126).

1.8 CALIDAD DE VIDA E HIDRADENITIS SUPURATIVA

La Organización Mundial de la Salud (OMS) define la calidad de vida como “la percepción que un individuo tiene de su posición en la vida, dentro del contexto cultural y del sistema de valores en los que vive y en relación con sus objetivos, expectativas, normas e inquietudes”. Se trata de un concepto amplio que está influido de forma compleja por la salud física del sujeto, su estado psicológico, sus creencias personales, sus relaciones sociales y su relación con los elementos principales del entorno(127). La calidad de vida es un aspecto fundamental de la salud y objeto de múltiples intervenciones en salud, por lo que es de gran importancia su determinación como indicador de gravedad de enfermedades. Esto es especialmente relevante en enfermedades crónicas que no tienen curación, en las que el éxito en la atención sanitaria es difícilmente valorable en términos absolutos, debiendo emplearse variables de resultado más genéricas y globales como la calidad de vida relacionada con la salud. La presencia de enfermedades crónicas puede disminuir la calidad de vida(128).

Un aspecto fundamental de la calidad de vida es la salud sexual. Múltiples investigaciones han puesto de manifiesto una relación directa entre la función sexual y la calidad de vida(129-131). De acuerdo con la OMS, “la salud sexual es un estado de bienestar físico, mental y social en relación con la sexualidad. Requiere un enfoque positivo y respetuoso de la sexualidad y de las relaciones sexuales, así como la posibilidad de tener experiencias sexuales placenteras y seguras, libres de toda coacción, discriminación y violencia”. Para que la salud sexual sea alcanzada y mantenida, los derechos sexuales de todas las personas deben ser respetados, protegidos y cumplidos(132). La sexualidad es una necesidad básica del ser humano y un elemento que no puede ser separado de otros aspectos de la vida, siendo muy importante para mantener una buena salud mental(133). Las enfermedades crónicas pueden disminuir la funcionalidad sexual, debido a factores relacionados con la propia enfermedad, con su tratamiento o con alteraciones de la imagen corporal(134).

Debido al curso crónico de la HS, con recurrencias espontáneas de aparición imprevisible, y a las características de la enfermedad, con lesiones que pueden ser desfigurantes y disfuncionales, aparte de los síntomas clásicos de dolor, mal olor y supuración, resulta esperable que la HS afecte a la calidad de vida de los pacientes(4).

La herramienta más empleada para medir la afectación de la calidad de vida en la HS ha sido el *Dermatology Life Quality Index* (DLQI). Las puntuaciones medias obtenidas en este cuestionario oscilan entre 8,3 y 12,7 según la investigación(29, 135-141). Estas puntuaciones indican que la HS es la patología dermatológica con mayor afectación de la calidad de vida, por encima de otras como psoriasis, acné, atopia, tumores cutáneos(140), alopecia, urticaria crónica, enfermedad de Darier o enfermedad de Hailey-Hailey(139). Las peores puntuaciones se obtienen en las preguntas acerca de los síntomas y de la vergüenza(142). El principal predictor de disminución en la calidad de vida es la gravedad clínica, medida en muchos estudios mediante el sistema de estadificación de Hurley; otros factores asociados son el número de brotes, de áreas afectadas o la localización anogenital de las lesiones(142).

Otras investigaciones han empleado como herramienta el *EuroQol-5 Dimensions questionnaire* (EQ-5D). Sus resultados se correlacionan con los del DLQI(143-145). Las puntuaciones obtenidas en estos estudios indican que la afectación de la calidad de vida en pacientes con HS es comparable a la de pacientes con enfermedad pulmonar obstructiva crónica, diabetes mellitus, enfermedad cardiovascular o cáncer(143).

Múltiples estudios han relacionado la HS con mayor riesgo de depresión y ansiedad(136, 137, 139, 140, 146-148). La prevalencia de depresión oscila entre un 1,6% y un 42,9%, según la investigación, y la de ansiedad entre un 0,8% y un 3,9%. El principal factor de riesgo identificado para la presencia de depresión es la gravedad de la enfermedad(137, 139, 140, 146); también se ha observado una asociación con la localización anogenital de las lesiones(139). Se ha postulado que las citoquinas proinflamatorias de la HS o los niveles elevados de proteína C reactiva puedan ser mecanismos que subyacen a la aparición de la depresión(146, 147).

Asimismo, en los pacientes con HS se ha encontrado una mayor tendencia al aislamiento y la soledad, medidos con la escala *UCLA Loneliness Scale*, una menor autoestima, medida con la escala *Rosenberg Self-Esteem Scale*, y una mayor estigmatización, medida con la escala de 6 ítems de Evers(137, 139). En este caso, las peores puntuaciones se asociaron con localizaciones en áreas expuestas y visibles como cabeza y cuello(139), pero no con la gravedad de la enfermedad(137).

También se ha observado en un estudio basado en registros en Dinamarca un mayor riesgo de suicidio en los pacientes con HS que en la población general, incluso tras ajustar por posibles factores de confusión como la edad, el sexo, el nivel socioeconómico o el consumo de tabaco o alcohol(149).

La HS también puede afectar a la vida laboral de los pacientes. En una investigación se estimó una prevalencia de desempleo del 25,1% de los pacientes con respecto al 6,2% de la población general(144). En otro estudio con 2 años de seguimiento, el 10% de los pacientes perdieron su empleo debido al absentismo laboral causado por la enfermedad, mientras que un 23,3% refirió dificultad para obtener ascensos laborales o progresión en sus trabajos(150).

A pesar de la gran cantidad de investigaciones que han intentado objetivar el impacto en diversas esferas de la calidad de vida de los pacientes con HS, solo tres se habían dirigido específicamente a la esfera sexual utilizando herramientas validadas(138, 151, 152). En estas investigaciones se ha determinado una correlación de la afectación de la función sexual y la calidad de vida de los pacientes con HS(138, 151). Otros estudios han empleado herramientas como la novena pregunta del DLQI, que hace referencia a si la patología dermatológica afecta a la vida sexual; sin embargo, este ítem está diseñado para ser valorado en conjunto con el resto de las preguntas del test, no de forma aislada.

2. JUSTIFICACIÓN E HIPÓTESIS

La HS es una enfermedad inflamatoria cutánea crónica con repercusión sistémica, debilitante, de difícil manejo y con una profunda afectación de la calidad de vida de los pacientes. El dermatólogo es el especialista con el papel central en la asistencia de los pacientes con HS moderada-grave. En muchos casos, conseguir un control total de la enfermedad es complejo. Por ello, estimamos que considerar el control completo de la HS como variable de resultado final de éxito terapéutico puede ser desalentador para el paciente y el dermatólogo, por la dificultad que implica alcanzar este objetivo.

Sin embargo, sí puede ser factible mejorar diversos aspectos de la calidad de vida de los pacientes. Uno de ellos, como es la función sexual, ha sido escasamente investigado en la HS. Por ello, nos planteamos las siguientes cuestiones:

- ¿Con qué frecuencia presentan disfunción sexual las mujeres y disfunción eréctil los varones con HS?
- ¿Cuáles son los factores asociados a dicha disfunción?
- ¿Qué grado de distrés sexual experimentan estos pacientes y cuáles son los factores asociados?
- ¿Qué dificultades y necesidades presentan estos pacientes en sus relaciones sexuales?
- ¿Cuál es la evidencia científica disponible acerca de la sexualidad de los pacientes con HS?

2. JUSTIFICATION AND HYPOTHESES

HS is a chronic, debilitating, inflammatory skin disease with systemic involvement, which is difficult to manage and profoundly affects patients' quality of life. The dermatologist is the specialist with the central role in the care of patients with moderate-to-severe HS. In many cases, it is difficult to achieve complete control of the disease. We therefore believe that considering complete remission of HS as the endpoint of therapeutic success can be discouraging for both the patient and the dermatologist, due to the difficulty of achieving this goal.

However, it may be possible to improve several aspects of patients' quality of life. One of these aspects, sexual functioning, has been poorly investigated in patients with HS. Thus, we asked ourselves the following questions:

- How often do women with HS present sexual dysfunction? How often do men with HS present erectile dysfunction?
- What are the factors associated with such dysfunction?
- What degree of sexual distress do these patients experience and what are the associated factors?
- Do these patients have difficulties and needs in their sexual relationships?
- What is the available scientific evidence about sexuality in patients with HS?

3. OBJETIVOS

OBJETIVO GENERAL

Evaluar la función sexual de los pacientes con HS

OBJETIVOS ESPECÍFICOS

OBJETIVO 1. Explorar la prevalencia de disfunción sexual en mujeres y de disfunción eréctil en varones con HS, así como los potenciales factores clínicos y/o epidemiológicos asociados a dicha disfunción.

OBJETIVO 2. Explorar el distrés que sufren los pacientes con HS en sus relaciones sexuales y los potenciales factores clínicos y/o epidemiológicos asociados a dicho distrés.

OBJETIVO 3. Explorar las creencias, comportamientos y necesidades de los pacientes con HS en sus relaciones sexuales.

OBJETIVO 4. Evaluar la evidencia científica disponible acerca de la afectación de la vida sexual de los pacientes con HS para generar una evidencia científica sólida de cara a la toma de decisiones en la práctica clínica habitual y para definir futuras líneas de investigación.

3. OBJECTIVES

OVERALL OBJECTIVE

To assess the sexual function of patients with HS.

SPECIFIC OBJECTIVES

OBJECTIVE 1. To explore the prevalence of sexual dysfunction in women and erectile dysfunction in men with HS, as well as potential clinical and/or epidemiological factors associated with such dysfunction.

OBJECTIVE 2. To explore the distress experienced by patients with HS in their sexual relationships and the potential clinical and/or epidemiological factors associated with this distress.

OBJECTIVE 3. To explore the beliefs, behaviours and needs of patients with HS in their sexual relationships.

OBJECTIVE 4. To evaluate the available scientific evidence on the impact on the sex life of patients with HS in order to generate solid scientific evidence for decision-making in routine clinical practice and to define future lines of research.

4. PACIENTES Y MÉTODOS

4.1 OBJETIVOS 1, 2 Y 3

4.1.1 Marco temporal

Se llevó a cabo un estudio transversal mediante un cuestionario online *crowdsourced* sobre HS y sexualidad entre el 1 de marzo y el 1 de abril de 2018.

El *crowdsourcing* se define como "un tipo de actividad en línea participativa en la que una persona, institución, organización sin ánimo de lucro o empresa, propone a un grupo de individuos, mediante una convocatoria abierta y flexible, la realización libre y voluntaria de una tarea"(153).

4.1.2 Canal de difusión

La encuesta se difundió por medio de la asociación española de enfermos de hidradenitis supurativa ASENDHI. ASENDHI es una entidad sin ánimo de lucro fundada en 2008 e inscrita en el Registro Nacional de Asociaciones con el número 593.089. Sus objetivos son ayudar a la divulgación de la HS, promoviendo la sensibilización social, fomentar el conocimiento y la formación de especialistas y profesionales de la salud en la enfermedad, así como la investigación acerca de la misma para el desarrollo de tratamientos específicos, y servir de apoyo a los pacientes afectos favoreciendo su bienestar. La difusión se realizó a través de: *emailing* a grupo de socios, página web de ASENDHI y grupo de ASENDHI en la red social Facebook(154).

4.1.3 Población de referencia

La población diana fue el conjunto de pacientes con HS. La población accesible fueron los pacientes con HS con acceso a Internet y en contacto con ASENDHI. La muestra final fueron los pacientes que completaron la encuesta facilitada.

4.1.4 Criterios de inclusión y exclusión

El criterio de inclusión fue el diagnóstico referido por los pacientes de padecer HS. Se excluyeron aquellos pacientes que presentaran patología maligna activa, discapacidad intelectual o incapacidad para completar un cuestionario. Los participantes tenían conocimiento de la anonimidad del cuestionario y del posterior uso de los datos facilitados en la encuesta para fines de investigación y su consecuente difusión. El protocolo del estudio fue aprobado por el Comité de Ética de la Investigación de la Provincia de Granada.

4.1.5 Cuestionario

El cuestionario fue diseñado con la tecnología de Google Forms® que cuenta con las siguientes características(155):

- Navegación sencilla
- Multi-página
- Campos obligatorios
- Múltiples tipos de pregunta (texto, párrafo, respuesta múltiple, *checkbox*, gradiente, matriz)
- Redirección según selección
- Recogida automática de resultados en hoja de cálculo en Google Docs
- Aviso de respuesta a email

En el cuestionario se recogió información acerca de diversas variables de interés:

- Características sociodemográficas de los pacientes: año de nacimiento, país de residencia y nivel de estudios.
- Datos biométricos: talla y peso.
- Hábito tabáquico.
- Variables clínicas: antecedentes médicos de interés, medicación para otras comorbilidades, edad de debut de la HS, localizaciones afectadas por lesiones activas, localizaciones afectadas por cicatrices, tiempo recibiendo atención médica por la HS, tratamiento recibido para la HS.
- Daño estructural: se empleó el sistema de estadificación de Hurley referido por los pacientes. La ventaja de este sistema respecto a otros sistemas de estadificación es la buena concordancia existente entre la clasificación en estadios de Hurley por parte de médicos y pacientes, con un coeficiente kappa ponderado de 0,63(156). Así, en nuestro cuestionario se mostraron imágenes de cada uno de los estadios de la HS para que el paciente dijera a cuál se parecía más su enfermedad.

- Intensidad de los síntomas (dolor, supuración, mal olor y prurito): mediante *Numeric Rating Scales* (NRS), consistentes en una escala numérica graduada del 0 al 10 en la que el paciente señalaba la intensidad del síntoma, siendo 0 la ausencia del síntoma y 10 la máxima intensidad del mismo (60). Estas escalas evalúan la afectación subjetiva del individuo, con igual importancia o mayor que las escalas objetivas(157).
- La evaluación global de la actividad de la enfermedad se realizó por medio del *Patient´s Global Assessment* (PtGA), que incluye 5 categorías (inactivo, muy leve, leve, moderado y grave)(158).
- Disfunción sexual en mujeres: se empleó el cuestionario validado *Female Sexual Function Index-6* (FSFI-6). El cuestionario FSFI contiene 19 preguntas que puntúan la función sexual femenina, evaluándola en 6 esferas: deseo, excitación, lubricación, orgasmo, satisfacción y dolor(159, 160) siguiendo las 6 principales categorías de disfunción sexual definidas en el *Diagnostic and Statistical Manual of Mental Disorders* (DSM-V)(161) y en la *International Classification of Diseases* (ICD-10)(162). En 2010, Isidori *et al.*(163) desarrollaron y validaron un cuestionario simplificado con 6 ítems, el FSFI-6, que explora cada una de las esferas con una sola pregunta. Una puntuación igual o inferior a 19 indica la existencia de disfunción sexual con una sensibilidad del 96,1% y una especificidad del 90,9%.
- Disfunción eréctil en varones: se empleó el cuestionario validado *International Index of Erectile Function-5* (IIEF-5). El IIEF es un cuestionario desarrollado y validado por Rosen *et al.*(164) que contiene 15 preguntas que evalúan 5 factores de la función sexual en el varón: función eréctil, orgasmo, deseo sexual, penetración y satisfacción global. Posteriormente, los mismos autores desarrollaron un cuestionario resumido con 5 ítems, el IIEF-5(165). Una puntuación igual o inferior a 21 indica la presencia de disfunción eréctil con una sensibilidad del 98% y una especificidad del 88%.
- Distrés causado por la HS en las relaciones sexuales: el distrés sexual hace referencia al impacto o angustia que sufren los pacientes con HS en sus relaciones sexuales. Para evaluarlo se empleó una NRS en la que se pedía al paciente que indicara cuánto consideraba que le afectaba la enfermedad en sus relaciones sexuales en una escala numérica graduada del 0 al 10, siendo 0 la ausencia de afectación y 10 la máxima afectación posible.

- Por último, ante la falta de instrumentos validados, se elaboraron específicamente preguntas para indagar en la afectación de la sexualidad y vida privada de los pacientes más allá de la mera presencia o no de disfunción sexual. Estas preguntas se elaboraron en base a la evidencia científica disponible mediante guías clínicas de evaluación de la función sexual(166). Posteriormente, se remitieron a la Junta Directiva de ASENDHI para su evaluación y sugerencias. Por parte de ASENDHI, se estimaron oportunas todas las preguntas, y tras su *feedback,* se incluyó la variable "pareja estable: sí/no" y una pregunta adicional para cada una de las respuestas posibles. Los investigadores reformularon las cuestiones en base a las guías clínicas para la evaluación de la función sexual. Se remitió nuevamente el cuestionario a ASENDHI estimando oportunas las modificaciones realizadas y las preguntas incluidas. Así, se preguntó acerca de cómo la enfermedad interfería en las relaciones sexuales de los pacientes (por los síntomas, por las curas, por los tratamientos, etc.), si se consideraban atractivos, su orientación sexual, sobre si les gustaría compartir sus problemas sexuales con personal médico y con quién y si tenían pareja. En el caso de pacientes con pareja estable, se preguntó acerca del rol de sus parejas y cuánto consideraban que afectaba la HS a su relación de pareja. En el caso de pacientes solteros, se indagó sobre cómo se sentían al conocer nuevas personas con las que podrían mantener relaciones sexuales/de pareja y cuánto consideraban que afectaba la HS a sus posibilidades de mantener relaciones sexuales/tener una relación de pareja. Al no ser preguntas validadas, para comprobar si la afectación de los pacientes con HS era significativa, se recogió un grupo control de sujetos sanos a los que se les hicieron todas las preguntas que no estaban directamente relacionadas con la enfermedad. Para ello, ASENDHI pidió a sus socios que distribuyeran un cuestionario, que contenía únicamente dichas preguntas, entre sus conocidos sin HS. En este cuestionario también se incluyó un apartado de datos sociodemográficos, biométricos, antecedentes médicos de interés y medicación para otras comorbilidades; se excluyeron los participantes en el caso de que estuviera presente alguna de las comorbilidades que suponía un criterio de exclusión para los pacientes (patología maligna activa, discapacidad intelectual o incapacidad para completar un cuestionario).

4.1.6 Análisis estadístico

La normalidad de las variables se comprobó mediante el test de Shapiro-Wilk e histogramas, la homogeneidad de varianzas mediante el test de Levene y la independencia de las observaciones mediante gráficos de residuos estandarizados. Cuando hubo datos faltantes para alguna de las variables de interés, los pacientes fueron excluidos. Cuando hubo datos faltantes para alguna otra variable, éstos fueron imputados. Se determinaron estadísticos descriptivos para explorar las características de la muestra.

Las puntuaciones de los cuestionarios FSFI-6 e IIEF-5 se categorizaron como disfunción sexual sí o no según los puntos de corte previamente mencionados (FSFI-6 ≤19 e IIEF-5 ≤21, disfunción sexual/eréctil sí; FSFI-6>19 e IIEF-5>21, disfunción sexual/eréctil no). Para explorar los factores asociados a disfunción sexual/eréctil, las variables cuantitativas continuas se analizaron mediante regresión logística, y las variables cualitativas mediante el test $\chi 2$; cuando >20% de las casillas tuvieron un valor esperado inferior a 5, se utilizó el test exacto de Fisher. La asociación de las variables con la NRS de afectación de la vida sexual se analizó mediante regresión lineal simple cuando las variables fueron cuantitativas continuas, mediante la t de Student cuando las variables fueron dicotómicas y mediante análisis de la varianza de una vía cuando las variables tuvieron más de una categoría. Las variables para las que se halló significación estadística ($p<0,05$) o indicios de significación estadística ($p<0,20$) en los análisis univariantes fueron incluidas en modelos de análisis multivariante (regresión logística en el caso de variables dicotómicas y regresión lineal múltiple en el caso de variables continuas).

Se analizó la correlación entre las puntuaciones de la NRS de afectación de la vida sexual y las puntuaciones del FSFI-6 y del IIEF-5 mediante regresión lineal simple, así como las diferencias en las puntuaciones de la NRS de afectación de la vida sexual en participantes con y sin disfunción sexual/eréctil mediante la t de Student. Los puntos de corte para detectar disfunción sexual/eréctil utilizando la NRS de afectación de la vida sexual se evaluaron mediante el análisis de curvas ROC.

También se exploraron los factores asociados al miedo al rechazo/reacción de la pareja sexual, al atractivo percibido, a la interferencia de la HS en las relaciones y a la interferencia de la HS en conocer gente nueva mediante regresiones logísticas multivariantes, incluyendo como variables aquellas que se habían identificado como factores de riesgo de disfunción sexual/eréctil y de distrés sexual. Las variables atractivo percibido, interferencia en las relaciones e interferencia en conocer gente nueva se codificaron de forma dicotómica (sí/no) para este análisis.

En todos los análisis, la significación estadística se consideró para valores de $p < 0,05$, considerándose todos los test de dos colas.

4.2 OBJETIVO 4

En febrero de 2020 se llevó a cabo una revisión sistemática de la literatura científica disponible acerca de la HS y la función sexual, con el objetivo de contextualizar nuestros resultados y responder a las siguientes preguntas: ¿Coinciden nuestros datos de prevalencia de disfunción sexual y disfunción eréctil en pacientes con HS con otras investigaciones? ¿Y los de distrés sexual? ¿Hay más factores asociados a estas alteraciones sexuales? ¿Cómo influyen estos trastornos en la calidad de vida de los pacientes? ¿Cuáles son los mecanismos subyacentes a la disfunción y distrés sexual en estos pacientes? ¿Qué papel juegan los trastornos del estado de ánimo como la depresión o la ansiedad? ¿Y otras comorbilidades como la hipertensión o la diabetes? ¿Hay alguna evidencia de que el tratamiento de la enfermedad pueda mejorar la función sexual de estos pacientes? ¿En qué aspectos debe centrarse la investigación futura sobre la sexualidad de los pacientes con HS? El algoritmo de búsqueda empleado en las bases de datos de Medline y Embase fue el siguiente: (“Hidradenitis suppurativa” OR “acne inversa”) AND (“sex” OR “sexual” OR “sexuality” OR “erectile”).

Los criterios de inclusión fueron: 1) artículos con datos en humanos, 2) artículos escritos en inglés, español, alemán o polaco y 3) artículos publicados después del primer año incluido en las bases de datos. Todos los tipos de estudios epidemiológicos fueron incluidos; las revisiones narrativas, guías, protocolos, resúmenes de congresos y casos clínicos fueron excluidos.

Dos revisores independientes analizaron los títulos y resúmenes de los artículos obtenidos en la búsqueda. Se revisó el texto completo de los artículos que cumplían los criterios de inclusión, así como sus referencias bibliográficas para identificar fuentes adicionales. Los artículos considerados relevantes por ambos revisores fueron incluidos en el análisis; en caso de discordancia, un tercer revisor analizó el artículo.

Las variables analizadas fueron: diseño epidemiológico, nivel de evidencia científica de acuerdo con el *Centre for Evidence-Based Medicine* (CEBM), tamaño muestral, herramientas empleadas para analizar la sexualidad de los pacientes, análisis estadísticos y resultados.

5. RESULTADOS

5.1 DISFUNCIÓN SEXUAL Y DISFUNCIÓN ERÉCTIL EN PACIENTES CON HIDRADENITIS SUPURATIVA

En marzo de 2018, ASENDHI difundió el cuestionario online. Éste tuvo una gran acogida por parte de los pacientes. Recurrir al *crowdsourcing* permitió contar con un alto número de participantes de hasta 16 nacionalidades distintas. El canal de difusión permitió que los pacientes se expresaran libremente venciendo las barreras psicológicas que puede conllevar el abordaje de este tema en persona.

La función sexual se define según la CIE-10 como "las diversas formas en las que un individuo es capaz de participar en una relación sexual como desea"(167). La disfunción sexual puede estar causada por factores orgánicos o psicológicos, o una combinación de ambos, y puede afectar a cualquier elemento de la respuesta sexual, como el deseo, la excitación o el orgasmo(168). Por su parte, la disfunción eréctil es un subtipo de disfunción sexual que se define como "la incapacidad constante o recurrente de lograr y/o mantener una erección del pene suficiente para la satisfacción sexual"(168).

Identificar dicha disfunción y los factores de riesgo que están relacionados a ella en pacientes con HS es un paso fundamental a la hora de plantear acciones estratégicas dirigidas a mejorar la salud sexual de estos pacientes.

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Risk factors of sexual dysfunction in patients with hidradenitis suppurativa: a cross-sectional study

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Short title: Risk Factors of Sexual Dysfunction in Hidradenitis Suppurativa Patients

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Key message: There is a high prevalence of sexual dysfunction and erectile dysfunction in patients with hidradenitis suppurativa. Related factors in women were disease activity, intensity of pain and unpleasant odour and education status, while in men they were the presence of active lesions in the genital area, the number of areas affected by active lesions and increasing age. Being in a stable relationship was a protective factor in women.

Keywords: hidradenitis suppurativa; Sexual dysfunction; Risk factors; Cross-sectional study; Sexual health; Quality of life.

1. Abstract

Background: Hidradenitis suppurativa (HS) has a high impact on quality of life. However, sexual health has scarcely been investigated.

Objective: To describe the frequency of sexual dysfunction (SD) in women and erectile dysfunction (ED) in men with HS and to explore potential risk factors.

Patients and Methods: We conducted a cross-sectional study using a crowd-sourced online questionnaire spread by the Spanish hidradenitis suppurativa patients' association (ASENDHI).

Results: In total, 393 participants answered the questionnaire. SD was found in 51% (95% CI 45%-57%) of women and ED in 60% (95% CI 49%-70%) of men. Factors related to SD were education status, patient's global assessment for disease activity, numeric rating scale for pain and unpleasant odour and the absence of a stable relationship. Factors related to ED were increasing age, the presence of active lesions in the genital area and the number of areas affected by active lesions.

Conclusions: There is a high prevalence of SD and ED in HS patients. Being in a stable relationship has been a protective factor of SD in women. The results suggest that sexual impairment in HS patients is due, at least in part, to disease activity, symptoms and active lesions.

2. Introduction

Hidradenitis suppurativa (HS) is a chronic auto-inflammatory skin disease with an estimated worldwide prevalence ranging from 0.5 to 4% [1-5]. It is characterized by recurrent nodules, abscesses and fistulae that involve hair follicles, predominantly in intertriginous areas [6]. These lesions cause pain, unpleasant odour, itch and suppuration, and they may result in a permanent disturbance of corporal self-image and functional limitation due to pain or scars.

Several studies indicate that patient's quality of life disturbance is one of the highest among dermatological patients [7,8] and comparable to other illnesses such as chronic obstructive pulmonary disease, diabetes mellitus, cardiovascular disease or cancer [9]. Disease symptoms, like pain or pruritus, may have an impact on quality of life in patients with HS [10,11]. Numerous publications have associated HS with different psychological and social problems, including depression, anxiety, low self-esteem, loneliness, stigmatization, suicide risk or impact on working life [7,8,12-17].

Sexuality is a basic need and an element that cannot be separated from other aspects of human life, being extremely important for maintaining good mental health [18]. Multiple investigations indicate a direct relationship between sexual function and quality of life [19,20]. Chronic diseases can decrease sexual functionality, due to factors related to the disease itself, with its treatments or with alterations in body image [21]. Due to the chronic course of HS, with unpredictable spontaneous recurrences, and the characteristics of the disease, with lesions that can be disfiguring and dysfunctional, apart from the classic symptoms of pain, unpleasant odour and suppuration, HS is expected to affect patients' sexuality.

However, only three investigations have explored the impact of HS on patients' sexual life. Kurek *et al*. [22] found out that patients with HS had higher sexual dysfunction (SD) and sexual distress than matched control subjects, particularly women; there was also a correlation between SD and sexual distress with quality of life in women, but the authors did not find any factor related to SD. Janse *et al*. [23] found a prevalence of SD of 62% in women and 52% in men, with late age at onset and disease activity as risk factors of SD in women. They also found a correlation between SD and poor quality of life in women. Alavi *et al*. [24] corroborated that SD was correlated with poor quality of life, in both women and men. Other studies have made an approach to the issue, finding that HS has the highest impact on sexuality among several dermatological diseases, but using the ninth question of the Dermatology Life Quality Index, which has not been validated to use separated from the rest of the questionnaire to assess SD [25].

The aims of this study are to describe the frequency of SD in patients with HS and to explore epidemiological and clinical factors potentially associated, in order to identify patients with a higher risk of SD.

3. Patients and Methods

For further details, see the online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000501905) (Fig. 1) [3, 25–27].

4. Results

Baseline

In total, 393 participants answered the questionnaire, 7 of them incompletely for at least one of the main outcome variables, so they were excluded from the study. The final sample consisted of 386 participants, 79.27% (306) women and 20.73% (80) men, resulting in a ratio of 3.8:1. Their sociodemographic characteristics and comorbidities are shown in Table 1, HS baseline characteristics in Table 2 and received treatments in Table 3.

Six-item Female Sexual Function Index

According to scores obtained in the 6-item Female Sexual Function Index (FSFI-6) questionnaire, 51% (95% CI 45%-57%) of women suffered from SD (normal values >19). The worse score was obtained in the second question, in which the participant was asked to rate her sexual arousal during sexual activity or intercourse (2.55 ± 1.66).

Five-item International Index of Erectile Function

Erectile dysfunction (ED) was found in 60% (95% CI 49%-70%) of male participants, according to scores from the 5-item International Index of Erectile Function (IIEF-5) questionnaire (normal values >21). The worse score was obtained in the fifth question, which enquires about global satisfaction in sexual intercourse (3.28 ± 1.86).

Clinical and Epidemiological Factors Associated with SD in Women with HS

Results from univariant analysis of factors associated with SD are shown in Table 4. There were no differences according to body distribution of HS. Factors significantly associated with SD according to FSFI-6 scores were higher education level, patient's global assessment, numeric rating scale for pain and unpleasant odour and the absence of a stable relationship.

Clinical and Epidemiological Factors Associated with ED in Men with HS

Results from univariant analysis of factors possibly associated with ED in men are shown in Table 5. Increasing age, the presence of active lesions in the genital area and the number of areas affected by active lesions were significantly associated with a higher risk of ED.

5. Discussion

In this cross-sectional study we investigated sexual health and related factors in patients with HS. Sociodemographic characteristics, such as sex ratio, actual age, mean body mass index, current smoking or comorbidities, and disease characteristics, such as age of onset or affected areas, were in general terms similar to those reported in other investigations, and representative of the general HS population [2-4,26-30].

We observe that HS probably produces a profound impact on sexual function, with high prevalence of SD in women (51%) and ED in men (60%), as has been previously reported in HS [23]. These percentages are higher than those reported in other investigations using FSFI-6 and IIEF-5, either in the general population [31-34], in a population attending a screening programme for prostate cancer [35] or in patients suffering from other dermatological diseases such as psoriasis [36,37].

Previous investigations indicate higher sexual distress in women than in men with HS [22] or with other dermatological diseases such as psoriasis [38]. These differences have been related to an early onset of HS in women (in our sample it was 4.5 years earlier) or even with cultural aspects and differences in emotional and neuroendocrine response to disfigurement [22]. It has also been associated with a higher prevalence of lesions at the lower abdomen [22]; nevertheless, in our sample the groins were the only region below the abdomen more frequently affected in women than in men.

Despite the fact that in other dermatological diseases, such as psoriasis, involvement of several areas, e. g. anogenital, has been related to SD [39-41], in HS anogenital involvement has been related to impairment in quality of life [7,23] but not to SD [22,23]. In our investigation, we found an association between genital active lesions and ED. The number of areas affected by active lesions was also associated with ED. In previous investigations about SD and related factors in patients with HS, samples were taken from hospital departments [22,23] and from a patient's association [23], without important differences in baseline patient's characteristics regarding our sample, with the exception of a more prevalent Hurley III stage in our sample. Therefore, probably these findings were made possible due to the larger size of our sample.

Furthermore, subjective symptoms and disease activity seem to cause an important impact on sexual life. In fact, a worse sexual function has been demonstrated in other dermatological diseases causing genital symptoms, as lichen sclerosus, but the prevalence of SD was not determined in these investigations [42,43]. In HS patients, although disease activity was previously associated with lower FSFI scores [23], for the first time to our knowledge subjective intensity of symptoms has been identified as a risk factor of SD. Thereby, the intensity of pain and unpleasant odour, as well as disease activity, were associated with lower FSFI-6 scores. This relation could be due to factors directly related to the nature of the sexual act and/or to psychological factors that may be associated with disease activity [7], and indicate the need for symptom control in order to improve sexual health in patients with HS. Unfortunately, there are no definitive and curative treatments for HS. In fact, we have not observed that treatments with oral antibiotics, oral contraceptives, adalimumab or infliximab were associated with lesser SD or ED. Clinical management of this disease is challenging, and patients should receive medical/surgical individualized therapies, depending on disease features (inflammatory load, scars, phenotype, menstrual worsening…), in order to relieve their symptoms, achieve disease control and improve their sexual function, among other spheres.

Other factors such as antidepressant or benzodiazepine consumption were not statistically associated with SD, suggesting that sexual impairment in patients with HS is directly related to symptoms and disease activity. However, benzodiazepine consumption showed a trend toward statistical significance in women, indicating the importance of anxiety in SD. Taking into account that there are no curative treatments for HS, psychological help may have a great importance in the management of these patients. Moreover, patients may suffer from SD or ED even when symptoms are under control, because of previous bad experiences or no sexual experience in the youngest, so psychological support should be a mainstay of the management of these patients.

Prior investigations did not find differences in sexual function in patients with or without a relationship [22,23]. However, our results show that being in a stable relationship is an important protective factor in women for SD. Since having a partner is associated with less self-consciousness and less orgasm difficulty in both men and women [44], probably, apart from commented disease activity, symptoms and severity, feelings of shame, distrust, shyness and rejection influence SD, which could be relieved by the confidence generated in a relationship. Nevertheless, future investigations should explore to what extent the disease affects sexual health of partners (stable or sporadic), whether their desires are fulfilled or whether an unwilling attitude causes impairment in their HS partners.

Higher education status was also related to SD in women, as previously reported [45]. This association could be explained because of different lifestyles and expectations about sexuality between different degrees of education, which may lead to feelings of failure and frustration.

Finally, we observed a positive association between age and ED, as occurs in the general population, due to decline in dehydroepiandrosterone levels and atherosclerosis associated with ageing [46].

We acknowledge some methodological weaknesses in our study. Firstly, a possible selection bias, since it only represents patients in contact with support groups and Internet access. The elderly, who could use the Internet with less frequency, or those with low sociocultural status or fear of new technologies, could be underrepresented [47]. Moreover, patients with severer disease or those more concerned about their disease, as well as those with sexual difficulties, could have been more prone to answer the questionnaire. Nevertheless, baseline characteristics of our sample are similar to those reported in other investigations, either in hospital-based or population-based studies. Given the scarce information about HS and sexuality and the embarrassment that sexual issues usually produce in patients, we consider that this study is a good approximation to the problem, facilitating patients to express themselves anonymously, and could lay the foundation for future research. Secondly, a possible classification bias, since it was an online questionnaire, so we could not confirm HS diagnosis, and HS characteristics were self-referred. However, an informed population can properly identify HS, because of its apparent clinical manifestations. Given the questionnaire dissemination by means of a patient's association, it is expected that the participants suffered from the disease.

In conclusion, we have presented the results from the study about HS and sexual health with the largest sample size to date. We observed an important impact on the sexual life of patients with HS, with a high prevalence of SD and ED. Being in a stable relationship was an important protective factor of SD in women. HS features related to SD in women were disease activity and intensity of pain and unpleasant odour. HS features related to ED in men were the presence of active lesions in the genital area and the number of areas affected by active lesions. These results suggest that SD and ED in HS patients are due, at least in part, to disease activity, symptoms and active lesions, and highlight the importance of adequate individualized treatment to improve the patient's sexual function. Future prospective studies should confirm the improvement of sexual health when disease control is achieved, explore the impact of HS on sentimental partners and investigate the role of psychological intervention.

6. Appendix

Tables 1-5 are submitted in separate files.

7. Supplementary Material

Full text of Patients and methods is submitted as supplementary material.

8. Statements

8.1 Acknowledgements

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8.2 Statement of Ethics

Participants were aware of the questionnaire anonymity and of the use of their data for research purposes. The study was approved by the Hospital Universitario San Cecilio ethics committee and is in accordance with the Helsinki Declaration.

8.3 Disclosure Statement

The authors have no conflicts of interest to declare

8.4 Funding Sources

The authors have no funding sources to declare

8.5 Author Contributions

Study concept and design: A.M.-L. *Acquisition, analysis and interpretation of data*: C.C.-B., A.M.-L. *Drafting of the manuscript*: C.C.-B. *Critical revision of the manuscript for important intellectual content*: A.M.-L. *Statistical analysis*: C.C.-B. *Study supervision*: A.M.-L.

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Table 1. Sociodemographic characteristics and comorbidities

	Men (*n* = 80)	Women (*n* = 306)	All (*n* = 386)
Age, years	39.21 (11.15)	37.44 (8.69)	37.81 (9.26)
Residence country			
Spain	90% (72)	80.7% (247)	82.6% (319)
Other	8.7% (7)	19.3% (50)	14.8% (57)
Not referred	1.3% (1)	2.9% (9)	2.6% (10)
Education status			
Basic	16.3% (13)	11.8% (36)	12.7% (49)
Medium	32.5% (26)	35.6% (109)	35% (135)
Superior	51.2% (41)	52.6% (161)	52.3% (202)
BMI	28.12 (5.03)	29.67 (7.05)	29.35 (6.71)
Current smoking			
No	35% (28)	44.1% (135)	42.2% (163)
Yes	65% (52)	55.9% (171)	57.8% (223)
Comorbidities			
HBP	5% (4)	6.9% (21)	6.5% (25)
DM2	2.5% (2)	6.5% (20)	5.7% (22)
Dyslipidaemia	3.8% (3)	2.9% (9)	3.1% (12)
IBD	1.3% (1)	0.7% (2)	0.8% (3)
Antidepressant consumption	5% (4)	10.1% (31)	9.1% (35)
Benzodiazepine consumption	5% (4)	5.9% (18)	5.7% (22)
Levothyroxine consumption	–	7.8% (24)	6.2% (24)
Hyperuricaemia	3.8% (3)	0.7% (2)	1.3% (5)
Asthma/seasonal allergy	–	1.6% (5)	1.3% (5)
Stable relationship	67.5% (54)	77.1% (236)	75.1% (290)

Continuous variables are expressed as means (standard deviation) and qualitative variables as proportion (absolute frequencies). BMI, body mass index; HBP, high blood pressure; DM2, diabetes mellitus type 2; IBD, inflammatory bowel disease.

Table 2. HS patients' baseline characteristics

	Men (*n* = 80)	Women (*n* = 306)	All (*n* = 386)
Age of onset, years	23.57 (9.45)	19.09 (7.1)	20.02 (7.85)
Time of evolution, years	15.64 (10.53)	18.33 (9.3)	17.77 (9.62)
Time under medical attention, years	6.79 (7.21)	7.1 (7.29)	7.03 (7.27)
Diagnosis delay, years	8.86 (9.13)	11.23 (9.55)	10.74 (9.51)
Locations			
Axilla			
Active lesions	50% (40)	47.1% (144)	47.7% (184)
Scars	47.5% (38)	43.8% (134)	44.6% (172)
Groins			
Active lesions	53.8% (43)	65.7% (201)	63.2% (244)
Scars	42.5% (34)	57.2% (175)	54.1% (209)
Genitals			
Active lesions	38.8% (31)	36.3% (111)	36.8% (142)
Scars	35% (28)	26.8% (82)	28.5% (110)
Buttocks			
Active lesions	43.8% (35)	31% (95)	33.7% (130)
Scars	35% (28)	32.4% (99)	32.9% (127)
Breast			
Active lesions	2.5% (2)	29.4% (90)	23.8% (92)
Scars	6.3% (5)	27.1% (83)	22.8% (88)
Abdomen			
Active lesions	11.3% (9)	10.1% (31)	10.4% (40)
Scars	10% (8)	11.8% (36)	11.4% (44)
Perianal region			
Active lesions	43.8% (35)	16.3% (50)	22% (85)
Scars	31.3% (25)	18% (55)	20.7% (80)
Neck			
Active lesions	13.8% (11)	4.6% (14)	6.5% (25)
Scars	11.3% (9)	4.6% (14)	6% (23)
Active regions, *n*	2.73 (1.79)	2.5 (1.57)	2.55 (1.62)
Regions with scars, *n*	2.34 (2.29)	2.31 (2.06)	2.31 (2.1)
Hurley stage			
I	16.3% (13)	18% (55)	17.6% (68)
II	31.3% (25)	48.7% (149)	45.1% (174)
III	52.5% (42)	33.3% (102)	37.3% (144)
PtGA score	3.73 (1.04)	3.65 (1.11)	3.66 (1.09)
NRS pain score	6.64 (2.81)	6.52 (2.98)	6.54 (2.95)
NRS pruritus score	6.24 (2.67)	6.48 (3.03)	6.43 (2.96)
NRS unpleasant odour score	6.11 (3.05)	5.47 (3.45)	5.6 (3.38)
NRS suppuration score	6.84 (3.04)	6.39 (3.21)	6.48 (3.18)

Continuous variables are expressed as means (standard deviation) and qualitative variables as proportion (absolute frequencies). PtGA, patient's global assessment; values range from 1 (inactive disease) to 5 (severe disease); NRS, numeric rating scale; values range from 0 (no symptoms) to 10 (maximum intensity of symptoms).

Table 3. Received treatments for HS

	Men (*n* = 80)	Women (*n* = 306)	All (*n* = 386)
Topical antibiotic	41.3% (33)	41.8% (128)	41.7% (161)
Oral antibiotic	33.8% (27)	27.1% (83)	28.5% (110)
Contraceptives	–	19.6% (60)	15.5% (60)
Adalimumab	22.5% (18)	13.7% (42)	15.5% (60)
Infliximab	3.8% (3)	0.7% (2)	1.3% (5)
Metformin	1.3% (1)	2.3% (7)	2.1% (8)
Isotretinoin	5% (4)	2.6% (8)	3.1% (12)
Acitretin	1.3% (1)	0.3% (1)	0.5% (2)
Resorcinol	–	0.7% (2)	0.5% (2)
Corticosteroids	–	1.3% (4)	1% (4)
Dapsone	–	0.7% (2)	0.5% (2)
Anakinra	–	0.3% (1)	0.3% (1)
Laser	–	0.3% (1)	0.3% (1)
NSAID	–	0.3% (1)	0.3% (1)
Finasteride	1.3% (1)	–	0.3% (1)

Variables are expressed as proportion (absolute frequencies). NSAID, non-steroidal anti-inflammatory drugs.

Table 4. Univariant analysis of factors associated with sexual dysfunction in women

Age	$p = 0.0863$
BMI	$p = 0.93$
Education status	
Superior vs. medium	OR = 1.82 (1.11–3)
Superior vs. basic	OR = 1.02 (0.48–2.11)
Basic vs. medium	OR = 1.8 (0.83–3.91)
	$p < 0.05$
Current smoking	$p = 0.58$
Antidepressant consumption	$p = 0.22$
Benzodiazepine consumption	$p = 0.059$
HBP	$p = 0.89$
DM2	$p = 0.71$
Dyslipidaemia	$p = 0.78$
Age of onset	$p = 0.88$
Time of evolution	$p = 0.14$
Time under medical attention	$p = 0.17$
Diagnosis delay	$p = 0.69$
Active lesions in axilla	$p = 0.93$
Scars in axilla	$p = 0.7$
Active lesions in groins	$p = 0.71$
Scars in groins	$p = 0.84$
Active lesions in genitals	$p = 0.29$
Scars in genitals	$p = 0.8$
Active lesions in buttocks	$p = 0.7$
Scars in buttocks	$p = 0.97$
Active lesions in breast	$p = 0.83$
Scars in breast	$p = 0.37$
Active lesions in abdomen	$p = 0.29$
Scars in abdomen	$p = 0.33$
Active lesions in perianal region	$p = 0.88$
Scars in perianal region	$p = 0.35$
Active lesions in neck	$p = 0.64$
Scars in neck	$p = 0.62$
Number of active lesions	$p = 0.72$
Number of regions with scars	$p = 0.65$
Hurley stage	$p = 0.77$
Treatment with oral antibiotics	$p = 0.49$
Treatment with oral contraceptives	$p = 0.057$
Treatment with adalimumab	$p = 0.6$
Treatment with infliximab	$p = 0.5$
PtGA	$\beta = -0.25$ (0.11) **$p < 0.05$**
NRS of pain	$\beta = 0.1$ (0.04) **$p < 0.05$**
NRS of pruritus	$p = 0.36$
NRS of unpleasant odour	$\beta = 0.07$ (0.03) **$p < 0.05$**
NRS of suppuration	$p = 0.29$
Stable relationship	OR = 0.36 (0.2; 0.63) **$p < 0.001$**

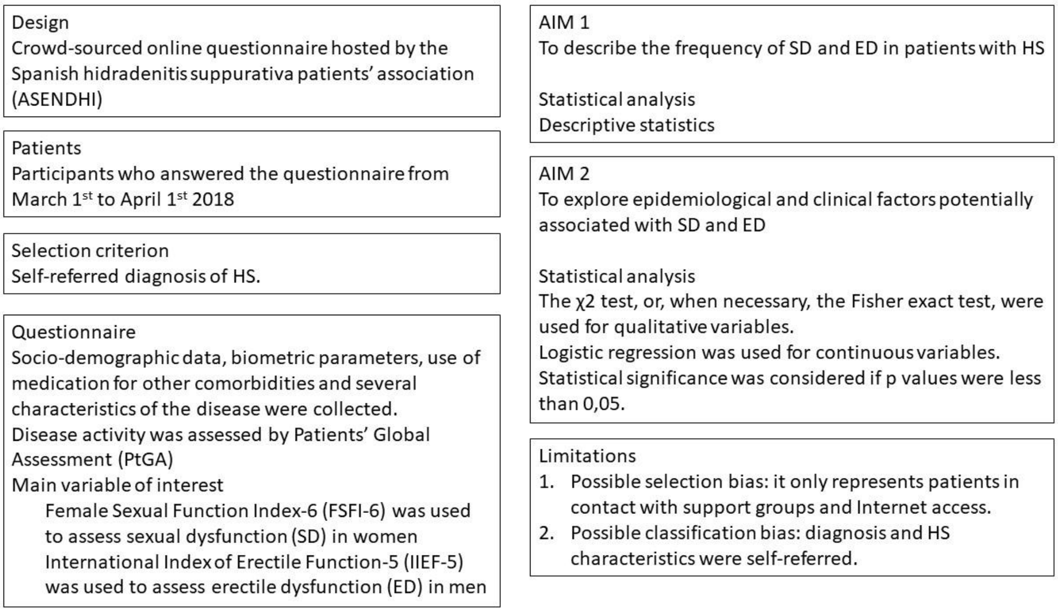
p values are shown for all variables; significant *p* values are in bold. Variables significantly associated are expressed as odds ratio (95% confidence interval), when qualitative variables, or as regression slope (standard deviation), when continuous variables. BMI, body mass index; HBP, high blood pressure; DM2, diabetes mellitus type 2; PtGA, patient's global assessment; NRS, numeric rating scale.

Table 5. Univariant analysis of factors associated with erectile dysfunction in men

Age	β = 0.05 (0.02) ***p* < 0.05**
BMI	*p* = 0.8
Education status	*p* = 0.42
Current smoking	*p* = 0.7
Antidepressant consumption	*p* = 0.15
Benzodiazepine consumption	*p* = 0.15
HBP	*p* = 0.68
DM2	*p* = 0.24
Dyslipidaemia	*p* = 0.15
Age of onset	*p* = 0.09
Time of evolution	*p* = 0.47
Time under medical attention	*p* = 0.21
Diagnosis delay	*p* = 0.86
Active lesions in axilla	*p* = 0.36
Scars in axilla	*p* = 0.2
Active lesions in groins	*p* = 0.054
Scars in groins	*p* = 0.46
Active lesions in genitals	OR = 3.57 (1.3; 9.82) ***p* < 0.01**
Scars in genitals	*p* = 0.29
Active lesions in buttocks	*p* = 0.17
Scars in buttocks	*p* = 0.7
Active lesions in breast	*p* = 0.51
Scars in breast	*p* = 0.64
Active lesions in abdomen	*p* = 1
Scars in abdomen	*p* = 0.88
Active lesions in perianal region	*p* = 0.17
Scars in perianal region	*p* = 0.62
Active lesions in neck	*p* = 0.18
Scars in neck	*p* = 0.81
Number of active lesions	β = 0.32 (0.15) ***p* < 0.05**
Number of regions with scars	*p* = 0.93
Hurley stage	*p* = 0.37
Treatment with oral antibiotics	*p* = 0.7
Treatment with adalimumab	*p* = 0.22
Treatment with infliximab	*p* = 1
PtGA	*p* = 0.63
NRS of pain	*p* = 0.97
NRS of pruritus	*p* = 0.28
NRS of unpleasant odour	*p* = 0.52
NRS of suppuration	*p* = 0.98
Stable relationship	*p* = 0.0926

p values are shown for all variables; significant *p* values are in bold. Variables significantly associated are expressed as odds ratio (95% confidence interval), when qualitative variables, or as regression slope (standard deviation), when continuous variables. BMI, body mass index; HBP, high blood pressure; DM2, diabetes mellitus type 2; PtGA, patient's global assessment; NRS, numeric rating scale.

Figure 1. Flow chart of Patients and Methods.



Design
Crowd-sourced online questionnaire hosted by the Spanish hidradenitis suppurativa patients' association (ASENDHI)

Patients
Participants who answered the questionnaire from March 1st to April 1st 2018

Selection criterion
Self-referred diagnosis of HS.

Questionnaire
Socio-demographic data, biometric parameters, use of medication for other comorbidities and several characteristics of the disease were collected.
Disease activity was assessed by Patients' Global Assessment (PtGA)
Main variable of interest
Female Sexual Function Index-6 (FSFI-6) was used to assess sexual dysfunction (SD) in women
International Index of Erectile Function-5 (IIEF-5) was used to assess erectile dysfunction (ED) in men

AIM 1
To describe the frequency of SD and ED in patients with HS

Statistical analysis
Descriptive statistics

AIM 2
To explore epidemiological and clinical factors potentially associated with SD and ED

Statistical analysis
The χ2 test, or, when necessary, the Fisher exact test, were used for qualitative variables.
Logistic regression was used for continuous variables.
Statistical significance was considered if p values were less than 0,05.

Limitations
1. Possible selection bias: it only represents patients in contact with support groups and Internet access.
2. Possible classification bias: diagnosis and HS characteristics were self-referred.

HS, hidradenitis suppurativa; SD, sexual dysfunction; ED, erectile dysfunction.

Supplemental material: Patients and methods

Patients and design

We conducted a cross-sectional study by means of a crowdsourced online questionnaire. Participants were recruited from March 1st to April 1st 2018. The Spanish hidradenitis suppurativa patients' association (ASENDHI) spread the questionnaire and invited people with HS to participate in the study.

Selection criterion was self-referred diagnosis of HS. Participants were aware of the questionnaire anonymity and of the use of their data for research purposes. The study was approved by the Hospital Universitario San Cecilio ethics committee and is in accordance with the Helsinki Declaration.

Questionnaire

The questionnaire was developed with Google Forms® suite. Socio-demographic data, biometric parameters, use of medication for other comorbidities and several characteristics of the disease, such as age of onset, time under medical attention or affected areas, were collected. Disease severity was assessed by patients' self-reported Hurley, since patients with HS are capable of self-assessing their Hurley stage with a good correlation with physician assessment.

Disease activity was assessed by Patients' Global Assessment (PtGA), including five categories (inactive, very low, low, mild and severe), and intensity of symptoms by Numeric Rating Scales (NRS). These scales show subjective impact of the disease on patients, with equal or greater importance than objective scales.

SD was evaluated using two tools: 1) Female Sexual Function Index-6 (FSFI-6), a validated questionnaire that explores the six domains of the female sexual function (desire, arousal, lubrication, orgasm, overall satisfaction and pain), each one with a single question. A score of 19 or less indicates SD with 96,1% of sensitivity and 90,9% of specificity. 2) International Index of Erectile Function-5 (IIEF-5), a validated questionnaire with 5 questions about erectile function. A score of 21 or less indicates erectile dysfunction (ED) with 98% of sensitivity and 88% of specificity.

Statistical analysis

Statistical analyses were performed using IBM software Statistical Package for Social Science version 23.0 (SPSS Inc, Chicago, IL). Descriptive statistics were used to explore the characteristics of the sample. Continuous variables were expressed as means and standard deviation (SD). For qualitative variables, absolute and relative frequencies were estimated.

The main outcome of interest, SD, was binary codified as either SD (FSFI-6 ≤19 for women and IIEF-5 ≤21 for men) or no SD (FSFI-6 >19 for women and IIEF-5 >21 for men). To explore factors associated with SD, logistic regression was used for continuous variables, and the χ^2 test, or, when necessary, the Fisher exact test, were used for qualitative variables. Statistical significance was considered if p values were less than 0,05.

5.2 DISTRÉS DE LOS PACIENTES CON HIDRADENITIS SUPURATIVA EN SUS RELACIONES SEXUALES

Aparte de la disfunción sexual y de la disfunción eréctil, en el cuestionario también exploramos el distrés que experimentan los pacientes con HS en sus relaciones sexuales, el cual se refiere al impacto emocional y al sufrimiento o angustia que las dificultades sexuales causan al individuo(168). Es importante para el clínico distinguir entre distrés sexual y disfunción sexual, ya que la primera revela el sufrimiento subjetivo del sujeto, mientras que la segunda puede suponer una peor experiencia sexual para ambos miembros de la relación.

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Article

Sexual Distress in Patients with Hidradenitis Suppurativa: A Cross-Sectional Study

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Abstract: Hidradenitis suppurativa (HS) is a chronic auto-inflammatory skin disease with a great impact in quality of life. However, there is little research about the impact of HS on sex life. The aims of this study are to describe the frequency of sexual distress (SD) in patients with HS and to explore potentially associated epidemiological and clinical factors. We conducted a cross-sectional study by means of a crowd-sourced online questionnaire hosted by the Spanish hidradenitis suppurativa patients' association (ASENDHI). Sexual distress (SD) was evaluated with a Numeric Rating Scale (NRS) for HS impact on sex life. A total of 393 participants answered the questionnaire. The mean NRS for HS impact on sex life was 7.24 (2.77) in women and 6.39 (3.44) in men ($p < 0.05$). Variables significantly associated ($p < 0.05$) with SD in the multiple linear regression model were sex, with a higher risk in females, the presence of active lesions in the groin and genitals and NRS for pain and unpleasant odor; being in a stable relationship was an important protector factor. Regarding these results, it seems that SD in HS patients is due, at least in part, to disease symptoms and active lesions in specific locations, emphasizing the importance of disease control with a proper treatment according to management guidelines. Women and single patients are more likely to suffer from sexual distress.

Keywords: sexuality; mental health; mental disorder; sexual dysfunction; hidradenitis suppurativa

1. Introduction

Hidradenitis suppurativa (HS) is a chronic auto-inflammatory skin disease characterized by recurrent nodules, abscesses and fistulae and which involves hair follicles, predominantly in intertriginous areas [1]. These lesions cause pain, unpleasant odor, itching and suppuration. When the disease progresses to advanced stages, there may be a permanent negative effect on body image due to scarring.

According to recent studies, the reduction in HS patients' quality of life is one of the most significant among dermatological patients [2,3] and similar to other non-dermatological illnesses such as chronic obstructive pulmonary disease, diabetes mellitus, cardiovascular disease and cancer [4]. Some research indicates that pain or pruritus may negatively affect quality of life [5,6].

Sexuality is a basic need and one which cannot be separated from other aspects of human life, being extremely important for maintaining good mental health [7]. Several studies show a direct relationship between sexual function and quality of life [8,9]. Sexual functionality can be impaired by chronic diseases because of factors related to the disease itself, its treatments, or alterations in body image [10]. Due to the chronic relapsing course of HS and the disease's characteristics, HS may affect patients' sexuality. Numerous publications have associated HS with depression, anxiety, low self-esteem, loneliness, stigmatization, suicide risk, or impact on working life [2,3,11–16]. However, there is little research about the impact of HS on sex life.

The aims of this study are to describe the frequency of sexual distress (SD) in patients with HS and to explore potentially associated epidemiological and clinical factors.

2. Experimental Section

2.1. Patients and Design

We conducted a cross-sectional study by means of a crowd-sourced online questionnaire. Participants were recruited from 1 March to 1 April 2018. The Spanish hidradenitis suppurativa patients' association (ASENDHI) hosted the questionnaire and invited people with HS to participate in the study [17].

The selection criterion was self-referred diagnosis of HS. Participants were aware of the questionnaire's anonymity and the use of their data for research purposes. The study was approved on May 2017 by the ethics committee of Hospital Universitario San Cecilio and is in accordance with the World Health Organization Declaration of Helsinki.

2.2. Questionnaire

The questionnaire was developed with Google® Forms suite. Socio-demographic data, biometric parameters, use of medication for other comorbidities and several characteristics of the disease, such as age of onset, time under medical attention and affected areas were collected. Disease severity was assessed by patients' self-reported Hurley stage, since patients with HS are capable of self-assessing their Hurley stage with a good correlation with physician assessment [18].

Disease activity was assessed by Patients' Global Assessment (PtGA), including five categories (inactive, very low, low, mild and severe) [19], and intensity of symptoms by Numeric Rating Scales (NRS) [20]. These scales show the subjective impact of the disease on patients, with equal or greater importance than objective scales.

SD was evaluated with a NRS for HS impact on sex life, in which participants were asked to measure from 0 to 10 how much the disease affects their sex life. This scale reflects the subjective suffering and distress caused by the disease to patients' sex lives. Its concordance with the Female Sexual Function Index-6 (FSFI-6) and the International Index of Erectile Function-5 (IIEF-5), two validated questionnaires that explore female sexual dysfunction and erectile dysfunction respectively, was also assessed.

2.3. Statistical Analysis

Statistical analyses were performed using JMP version 9.0.1 (SAS institute, Inc., Cary, North Carolina, USA). When there were missing data in any of the variables of interest, patients were excluded from the study. When missing data were found in other variables, they were imputed. To explore the characteristics of the sample, descriptive statistics were used. Continuous variables were expressed as means and standard deviations. Qualitative variables were expressed as absolute and relative frequencies.

The main outcome of interest was SD, measured by the NRS for HS impact on sex life. To explore possibly associated factors, simple linear regression was used for continuous variables, Student's t-test for dichotomous variables, and one-way analysis of variance for nominal variables with two or more categories (Levene's test was used to assess the equality of variances, standardized residual plots to check independence and Normality was assumed because of the sample size). Significantly associated variables ($p < 0.05$) or those showing trends towards statistical significance ($p < 0.20$) were included in a multiple linear regression model to assess the factors associated with SD. Statistical significance was considered if *p* values were less than 0.05.

The correlation of NRS for HS impact on sex life with FSFI-6 and IIEF-5 was checked with simple linear regression. Student's *t*-test was used to assess differences between NRS for HS impact in sex life means in participants with and without sexual or erectile dysfunction according to the FSFI-6 or IIEF-5 scores, respectively. The cut-off point for sexual dysfunction using the NRS for HS impact on sex life was assessed by ROC curve analysis.

3. Results

3.1. Baseline

Three hundred and ninety three participants answered the questionnaire. Seven of them filled out the questionnaire incompletely, so the final sample consisted of 386 participants (319 (82.6%) from Spain, 57 (14.8%) from abroad, and 10 (2.6%) did not provide their country of residence). The ratio of women to men was 3.8:1 (306 (79.27%) women and 80 (20.73%) men). Their socio-demographic characteristics and comorbidities are shown in Table 1; current smoking was higher among men, body mass index was 1.5 greater in women, and the prevalence of diabetes mellitus type II and antidepressant consumption was higher among women, but these differences did not reach statistical significance. HS baseline characteristics are shown in Table 2. Age of onset was earlier in women (19.09 ± 7.1 vs. 23.57 ± 9.45, $p < 0.0001$), with a medium diagnosis delay of 11.23 ± 9.55 in women and 8.86 ± 9.13 in men. The groin was the location most affected in women, either by active lesions (65.7%) or scars (57.2%). In men, groin was the location more frequently affected by active lesions (53.8%), and axilla by scars (47.5%). Genitals were affected by active lesions in 111 (36.3%) of women and in 31 (38.8%) of men, and by scars in 82 (26.8%) of women and in 28 (35%) of men. The presence of active lesions in the perianal region (35 (43.8%) vs. 50 (16.3%), $p < 0.0001$) and on the buttocks (35 (43.8%) vs. 95 (31%), $p < 0.05$) were higher among men, while the breast region was more frequently affected in women (90 (29.4%) vs. 2 (2.5%), $p < 0.0001$).

Table 1. Socio-demographic characteristics and comorbidities.

	Men (*n* = 80)	**Women (*n* = 306)**	**All (*n* = 386)**
Age	39.21 ± 11.15	37.44 ± 8.69	37.81 ± 9.26
BMI	28.12 ± 5.03	29.67 ± 7.05	29.35 ± 6.71
Current smoker			
No	28 (35%)	135 (44.1%)	163 (42.2%)
Yes	52 (65%)	171 (55.9%)	223 (57.8%)
Comorbidities			
HBP	4 (5%)	21 (6.9%)	25 (6.5%)
DM2	2 (2.5%)	20 (6.5%)	22 (5.7%)
Dyslipidemia	3 (3.8%)	9 (2.9%)	12 (3.1%)
Antidepressant use	4 (5%)	31 (10.1%)	35 (9.1%)
Benzodiazepine use	4 (5%)	18 (5.9%)	22 (5.7%)

Stable relationship	54 (67.5%)	236 (77.1%)	290 (75.1%)

Continuous variables are expressed as means ± standard deviation and qualitative variables as absolute (relative) frequencies. BMI: body mass index. HBP: high blood pressure. DM2: diabetes mellitus type 2.

Table 2. Hidradenitis suppurativa (HS) patients' baseline characteristics.

	Men (*n* = 80)	**Women (*n* = 306)**	**All (*n* = 386)**
Time of evolution	15.64 ± 10.53	18.33 ± 9.3	17.77 ± 9.62
Time under medical attention	6.79 ± 7.21	7.1 ± 7.29	7.03 ± 7.27
Number of active regions	2.73 ± 1.79	2.5 ± 1.57	2.55 ± 1.62
Number of regions with scars	2.34 ± 2.29	2.31 ± 2.06	2.31 ± 2.1
Hurley state			
I	13 (16.3%)	55 (18%)	68 (17.6%)
II	25 (31.3%)	149 (48.7%)	174 (45.1%)
III	42 (52.5%)	102 (33.3%)	144 (37.3%)
PtGA	3.73 ± 1.04	3.65 ± 1.11	3.66 ± 1.09
NRS pain	6.64 ± 2.81	6.52 ± 2.98	6.54 ± 2.95
NRS pruritus	6.24 ± 2.67	6.48 ± 3.03	6.43 ± 2.96
NRS unpleasant odor	6.11 ± 3.05	5.47 ± 3.45	5.6 ± 3.38
NRS suppuration	6.84 ± 3.04	6.39 ± 3.21	6.48 ± 3.18

Continuous variables are expressed as means ± standard deviation and qualitative variables as absolute (relative) frequencies. PtGA: Patient's Global Assessment; values range from 1 (inactive disease) to 5 (severe disease). NRS: Numeric Rating Scale; values range from 0 (no symptoms) to 10 (maximum intensity of symptoms).

3.2. Sexual Distress and Related Factors in Patients with Hidradenitis Suppurativa

The mean NRS for HS impact on sex life was 7.24 (2.77) in women and 6.39 (3.44) in men ($p < 0.05$). Results from univariate analysis of factors possibly related to NRS for HS impact on sex life are shown in Table 3.

Table 3. Univariate analysis of factors associated with sexual distress in patients with HS.

	Univariate Analysis	***p*-Value**
Sex		
Female	$\bar{X}$= 7.24 (0.17)	0.021 *
Male	$\bar{X}$= 6.39 (0.33)	
Age	β= −0.01 (0.02)	0.738
Current smoker		
Yes	$\bar{X}$= 7.35 (0.2)	0.023 *
No	$\bar{X}$= 6.66 (0.23)	
Antidepressant use		
Yes	$\bar{X}$= 7.37 (0.5)	0.51
No	$\bar{X}$= 7.03 (0.16)	
Benzodiazepine use		
Yes	$\bar{X}$= 6.82 (0.63)	0.692
No	$\bar{X}$= 7.07 (0.15)	
Age of onset	β= −0.01 (0.02)	0.667
Time under medical attention	β= 0.04 (0.02)	0.042 *
Active lesions in axilla		
Yes	$\bar{X}$= 7.16 (0.22)	0.532
No	$\bar{X}$= 6.97 (0.21)	
Scars in axilla		0.607
Yes	$\bar{X}$= 7.15 (0.22)	

No	$\bar{X}$= 6.99 (0.2)	
Active lesions in groin		
Yes	$\bar{X}$= 7.63 (0.18)	<0.0001 *
No	$\bar{X}$= 6.09 (0.24)	
Scars in groin		
Yes	$\bar{X}$= 7.25 (0.2)	0.169
No	$\bar{X}$= 6.84 (0.22)	
Active lesions on genitals		
Yes	$\bar{X}$= 7.99 (0.24)	<0.0001 *
No	$\bar{X}$= 6.16 (0.18)	
Scars on genitals		
Yes	$\bar{X}$= 7.6 (0.28)	0.022 *
No	$\bar{X}$= 6.84 (0.18)	
Active lesions on buttocks		
Yes	$\bar{X}$= 7.45 (0.26)	0.065
No	$\bar{X}$= 6.86 (0.18)	
Scars on buttocks		
Yes	$\bar{X}$= 6.94 (0.26)	0.566
No	$\bar{X}$= 7.12 (0.18)	
Active lesions on breast		
Yes	$\bar{X}$= 7.65 (0.3)	0.026 *
No	$\bar{X}$= 6.87 (0.17)	
Scars on breast		
Yes	$\bar{X}$= 7.33 (0.31)	0.327
No	$\bar{X}$= 6.98 (0.17)	
Active lesions on abdomen		
Yes	$\bar{X}$= 7.6 (0.46)	0.219
No	$\bar{X}$= 7 (0.16)	
Scars on abdomen		
Yes	$\bar{X}$= 7.18 (0.44)	0.77
No	$\bar{X}$= 7.04 (0.16)	
Active lesions in perianal region		
Yes	$\bar{X}$= 7.47 (0.32)	0.144
No	$\bar{X}$= 6.94 (0.17)	
Scars in perianal region		
Yes	$\bar{X}$= 7.46 (0.33)	0.168
No	$\bar{X}$= 6.95 (0.17)	
Active lesions on neck		
Yes	$\bar{X}$= 7.2 (0.59)	0.805
No	$\bar{X}$= 7.05 (0.16)	
Scars on neck		
Yes	$\bar{X}$= 7.22 (0.61)	0.791
No	$\bar{X}$= 7.05 (0.15)	
Number of regions with active lesions	β= 0.48 (0.09)	<0.0001 *
Number of regions with scars	β= 0.1 (0.07)	0.182
Hurley stage		
I	$\bar{X}$= 6.21 (0.35)	0.01 *
II	$\bar{X}$= 7.02 (0.22)	
III	$\bar{X}$= 7.51 (0.24)	
Treatment with oral antibiotics		
Yes	$\bar{X}$= 7.48 (0.28)	0.074
No	$\bar{X}$= 6.89 (0.18)	
Treatment with oral contraceptives		0.833

Yes	X̄= 7.13 (0.38)	
No	X̄= 7.05 (0.16)	
Treatment with adalimumab		
Yes	X̄= 7.82 (0.38)	0.03 *
No	X̄= 6.92 (0.16)	
PtGA	β= 0.87 (0.13)	<0.0001 *
NRS for pain	β= 0.32 (0.05)	<0.0001 *
NRS for pruritus	β= 0.27 (0.05)	<0.0001 *
NRS for unpleasant odor	β= 0.25 (0.04)	<0.0001 *
NRS for suppuration	β= 0.25 (0.05)	<0.0001 *
Stable relationship		
Yes	X̄= 6.88 (0.17)	0.032 *
No	X̄= 7.62 (0.3)	

p-values of variables significantly associated are marked with * PtGA: Patient's Global Assessment; values range from 1 (inactive disease) to 5 (severe disease). NRS: Numeric Rating Scale; values range from 0 (no symptoms) to 10 (maximum intensity of symptoms).

Variables that were significantly associated or showed trends towards statistical significance ($p < 0.20$) were included in the multiple linear regression model, whose results are shown in Table 4. Variables significantly associated with SD were sex, with a higher risk in females, the presence of active lesions in the groin and genitals and NRS for pain and unpleasant odor; being in a stable relationship was an important protector factor for SD. Current smoking, PtGA, time under medical attention and treatment with adalimumab showed trends toward statistical significance.

Table 4. Multivariate analysis of factors associated with sexual distress in patients with HS.

	Multivariate Analysis	***p*-Value**
Sex (female)	β= 0.57 (0.19)	0.003 *
Current smoker	β= 0.27 (0.14)	0.059
Time under medical attention	β= 0.03 (0.02)	0.088
Active lesions in groin	β= 0.44 (0.18)	0.015 *
Scars in groin	β= 0.15 (0.19)	0.449
Active lesions on genitals	β= 0.4 (0.19)	0.033 *
Scars on genitals	β= 0.05 (0.21)	0.812
Active lesions on buttocks	β= 0.19 (0.18)	0.296
Active lesions on breast	β= 0.09 (0.21)	0.666
Active lesions in perianal region	β= 0.15 (0.21)	0.463
Scars in perianal region	β= 0.23 (0.21)	0.28
Number of regions with active lesions	β= 0.15 (0.19)	0.44
Number of regions with scars	β= 0.14 (0.12)	0.24
Hurley stage		
III vs. I	β= 0.07 (0.26)	0.804
III vs. II	β= 0.03 (0.19)	0.866
Treatment with oral antibiotics	β= 0.02 (0.16)	0.9
Treatment with adalimumab	β= 0.38 (0.2)	0.054
PtGA	β= 0.3 (0.19)	0.115
NRS for pain	β= 0.15 (0.08)	0.049 *
NRS for pruritus	β= 0.03 (0.06)	0.615
NRS for unpleasant odor	β= 0.13 (0.06)	0.035 *
NRS for suppuration	β= 0.05 (0.07)	0.489
Stable relationship	β= −0.56 (0.16)	<0.001 *

p values of variables significantly associated are marked with * PtGA: Patient's Global Assessment; values range from 1 (inactive disease) to 5 (severe disease). NRS: Numeric Rating Scale; values range from 0 (no symptoms) to 10 (maximum intensity of symptoms).

3.3. Correlation between NRS for HS Impact on Sex Life and FSFI-6/IIEF-5 Scores

Scores from NRS for HS impact on sex life and FSFI-6 showed a negative correlation ($\beta = -0.15 \pm 0.02$, $r^2 = 0.16$, $p < 0.0001$), indicating a good concordance between both questionnaires. Scores from NRS for HS impact on sex life and IIEF-5 also showed a negative correlation ($\beta = -0.21 \pm 0.05$, $r^2 = 0.15$, $p < 0.001$). The mean score on the NRS for HS impact on sex life was 8.27 ± 0.21 in women with sexual dysfunction, and 6.16 ± 0.21 in women without sexual dysfunction ($p < 0.0001$). In men, the mean score on the NRS for HS impact on sex life was 7.31 ± 0.47 in those with erectile dysfunction, and 5 ± 0.58 in those without erectile dysfunction ($p < 0.01$).

In women, a score of 8 or more on the NRS for HS impact on sex life was indicative of sexual dysfunction according to FSFI-6 scores, with a sensitivity of 73% and a specificity of 64% (Figure 1). In men, a score of 9 or more on the NRS for HS impact on sex life was indicative of erectile dysfunction according to IIEF-5 scores, with a sensitivity of 52% and a specificity of 81% (Figure 2).

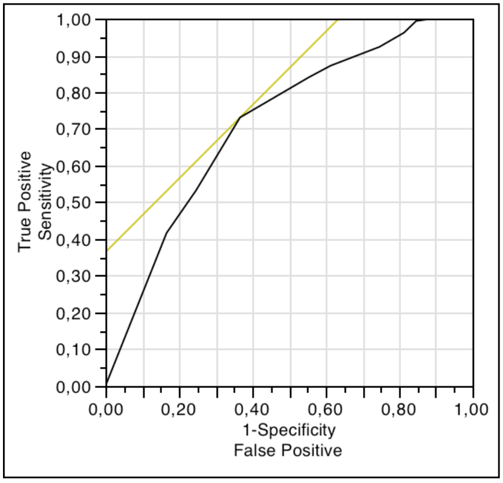

Figure 1. ROC curve analysis for comparison between scores of NRS of HS impact on sex life and FSFI-6.

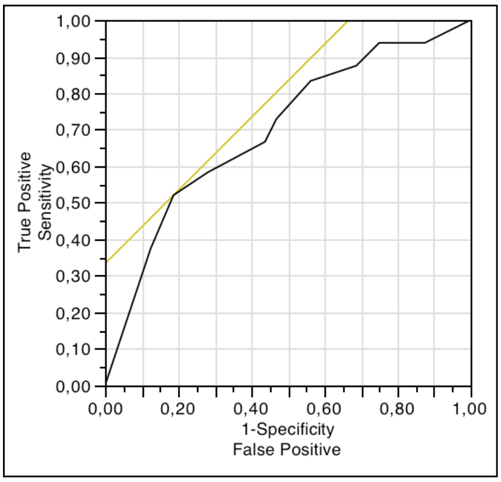

Figure 2. ROC curve analysis for comparison between scores of NRS of HS impact on sex life and IIEF-5.

4. Discussion

To our best knowledge, this is the largest cross-sectional study about the impact of HS on sexuality. Socio-demographic and disease characteristics did not differ from those previously reported in the literature, and were representative of the general HS population [21–28].

The mean NRS score for HS impact on sex life was significantly higher in women, which tallies with previous research that indicates higher sexual distress in women than in men with HS [29] or psoriasis [30]. These differences have been associated with cultural aspects and differences in emotional and neuroendocrine responses to disfigurement, and with the earlier onset of HS in women (4.5 years earlier in our sample) [29]. A higher prevalence of lesions at the lower abdomen has also been posed as a reason for this higher distress in women [29], but in our sample we only observed more involvement below the abdomen in the groin.

Although in psoriasis the involvement of the anogenital area has been related to sexual dysfunction [31–33], in HS anogenital involvement has been related to a reduction in quality of life [2,34], but there are no locations related to sexual dysfunction or to sexual distress [29,34]. In our investigation, we found an association between active lesions in the groin and genitals and SD, so a properly medical/surgical intervention at this level could turn into a better sexual life. In previous research about sexual health in patients with HS, samples were taken from hospital departments [29,34] and from a patient's association [34], and there were no important differences in patients' baseline characteristics, with the exception of a more prevalent Hurley III stage in our sample. Therefore, these findings were probably made possible due to the larger size of our sample.

Moreover, subjective symptoms caused sexual distress. The intensity of pain and unpleasant odor were related with higher scores on NRS for HS impact on sex life. This association may be due to factors directly related to the nature of the sexual act and/or to psychological factors that could be related to disease activity [2], highlighting the importance of symptom management to improve sexual health in patients with HS. Other factors such as antidepressant or benzodiazepine use were not statistically associated with SD, suggesting that SD is directly related to organic symptoms.

The absence of a stable relationship was not associated with sexual dysfunction in previous research [29,34]. Nevertheless, we observed that the presence of a stable partner was importantly related to lower SD. Since having a partner is associated with less self-consciousness and less orgasm difficulty in both men and women [35], probably feelings of shame, distrust, shyness and rejection influence SD, which could be lessened by the trust built in a relationship.

There were other factors that showed trends toward statistical significance in the multiple linear regression model: (1) PtGA, pointing to the importance of disease activity in sexual distress and the need to control the inflammatory load; (2) current smoking, because it is related to greater disease activity, since it favors follicular occlusion, a proinflammatory state with activation of neutrophils and Th17 lymphocytes, induces biofilm formation and suppresses notch signaling, among other effects [36]; moreover, smoking cessation is associated with clinical improvement [37]; (3) time under medical care, since it reflects time of disease evolution, with cumulative life course impairment [38]; and (4) Treatment with adalimumab, probably because in our sample it is a better predictor of severity than Hurley, since the patients treated with adalimumab are the most severe.

Finally, we found a good correlation between the scores on NRS for HS impact on sex life and those of FSFI-6 and IIEF-5, which indicates an association between the subjective and objective involvement of the sexual sphere in participants. However, despite this concordance, the ROC curve analyses revealed that the NRS for HS impact on sex life was not a good tool to assess sexual dysfunction in women or erectile dysfunction in men, because the cut-off points reach neither an acceptable sensitivity nor specificity. It is important to the clinician to distinguish between sexual distress and sexual dysfunction, because the first reveals the suffering of the subject, whereas the second may mean a worse sexual experience for both members of the stable/sporadic relationship. Therefore, clinicians should assess both aspects when patients' sexuality is addressed.

There are some methodological weaknesses in our study: (1) A possible selection bias, since it only represents patients in contact with support groups and Internet access. The elderly, who may use the Internet less frequently, or those with low sociocultural status or fear of new technologies, could be under-represented [39]. Moreover, people already concerned about sexual problems may have been more likely to answer the questionnaire. Nonetheless, the baseline characteristics of our sample did not differ from those previously reported in the literature, either in hospital-based or population-based studies. Given the scarcity of information about HS and sexuality we consider that this study is a good introduction to the problem, and could lay the foundation for future research. (2) A possible classification bias, because it was an online questionnaire and HS diagnosis could not be confirmed; HS characteristics were also self-referred. Nevertheless, an informed population can properly identify HS, because of its apparent and distinctive clinical manifestations. Since a patients' association hosted the questionnaire, it is expected that the participants did suffer from the disease.

5. Conclusions

This is the largest cross-sectional study about HS and sexuality. We have observed important sexual distress in patients with HS. Factors related to SD were female sex, the presence of active lesions in the groin and genital areas, and the intensity of pain and unpleasant odor. Being in a stable relationship has been an important protector factor against SD. Regarding these results, it seems that SD in HS patients is due, at least in part, to disease symptoms and active lesions in specific locations, emphasizing the importance of proper control of the disease based on management guidelines to improve their sexual health. Women and single patients are more likely to suffer from sexual distress, so special medical care should be given to them.

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5.3 CREENCIAS, COMPORTAMIENTOS Y NECESIDADES DE LOS PACIENTES CON HIDRADENITIS SUPURATIVA EN SUS RELACIONES SEXUALES

Por último, también quisimos explorar en el cuestionario otros aspectos de la vida sexual y de la vida privada/en pareja de estos pacientes. Conocer qué dificultades experimentan los pacientes con HS en su vida sexual, sus sentimientos de miedo o vergüenza en las relaciones sexuales, el atractivo percibido por ellos mismos, el rol de sus parejas o cómo afrontan conocer a una nueva pareja o iniciar una nueva relación puede ayudar a identificar necesidades desatendidas en estos pacientes y la posibilidad de recibir apoyo psicológico para mejorar su confianza, así como identificar el personal sanitario más apropiado para abordar los problemas de la esfera sexual.

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Article

Sexuality in Patients with Hidradenitis Suppurativa: Beliefs, Behaviors and Needs.

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Abstract: Little is known about the impact of hidradenitis suppurativa (HS) on patients' sexuality. The aim of this research is to investigate the impact of HS on several previously unexplored aspects of sexuality. In March 2018, we conducted a crowd-sourced cross-sectional online survey hosted by the Spanish association of patients with HS (ASENDHI) and available in Spanish. A panel of experts and patients from ASENDHI designed various questions in order to explore the extent to which HS influenced participants' sex lives. The final sample consisted of 386 participants, 79.27% (306/386) of which were women and 20.73% (80/306) of which were men. Seventy-seven point one percent (236/306) of women and 67.5% (54/80) of men were in stable relationships; the rest of the participants were single. Forty-seven point nine percent (185/386) admitted to feeling fear of rejection. Pain was the symptom that most interfered with sexual relations in women and suppuration in men. Forty-four point three percent (171/386) of the participants considered themselves to be less attractive than average. Considering the participants in a stable relationship, women described receiving more emotional support from their partners, while men received more help with lesion dressing in intimate areas. Seventy-one point four percent (207/290) of participants stated that HS negatively affected their relationship. Among single patients, women experienced greater fear of rejection and were less willing to meet new people because of HS. Ninety-four point three percent (66/70) of women and 80.8% (21/26) of men stated that HS had a negative influence on their chances of having a relationship or sexual relations. In conclusion, HS has a significant, unrecognized and misunderstood impact on sexuality which must be addressed.

Keywords: hidradenitis suppurativa; cross-sectional studies; sexual health; sexual behavior; quality of life

1. Introduction

Hidradenitis suppurativa (HS)/acne inversa is a recurrent, chronic, inflammatory, debilitating skin disease of the hair follicle that usually presents after puberty with painful, deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body [1]. As the disease progresses, permanent scarring occurs in the form of sinus tracts. These lesions, besides pain, can cause suppuration, unpleasant odor and pruritus.

The World Health Organization (WHO) defines quality of life as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns [2]. It is a broad-ranging concept affected in a complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment [2]. Recent studies show that the reduction in quality of life in patients with HS is one of the most significant among dermatological patients and comparable to other diseases such as cancer, diabetes, cardiovascular disease and chronic obstructive pulmonary disease [3-5].

According to WHO, sexual health is a state of physical, mental and social wellbeing in relation to sexuality [6]. Sexuality is considered to be quite important for maintaining good mental health and a basic need that cannot be separated from other aspects of human life [7]. Several studies indicate that sexual function is directly related to quality of life [8, 9]. Chronic diseases can have a negative impact on sex life through different mechanisms [10].

Psoriasis is the most investigated chronic dermatological disease in terms of its impact on patients' sexuality. Measured using validated questionnaires, the prevalence of sexual dysfunction varies between research from 40% to 55.6%, with patients with psoriasis having a risk of sexual dysfunction 5.5-fold higher than healthy controls [11]. The presence of anxiety or depression, female sex, increasing age, psoriatic arthritis, genital psoriasis and psoriasis severity are factors possibly associated with sexual dysfunction [11]. Several biologic drugs seem to improve sexual dysfunction in psoriasis patients [11].

In a multicentric study in 13 European countries, 23.1% of 3485 patients reported sexual difficulties, with hidradenitis suppurativa, prurigo, blistering disorders, psoriasis, urticaria, eczema and skin infections being the diseases with highest impairment [12]. This impact was associated with anxiety, depression and suicidal ideation [12]. However, the research did not use validated questionnaires to explore sexual dysfunction, but instead used question 9 of the Dermatology Life Quality Index.

Regarding HS, the prevalence of sexual dysfunction in women measured using validated tools ranges from 51% to 62%, and that of erectile dysfunction in men from 52% to 60% [13]. Factors associated with sexual dysfunction in women with HS are higher educational status, disease activity, intensity of pain and unpleasant odor, absence of a stable relationship and older age at HS onset, while in men, the factors are ageing, active lesions on the genitals and increased number of active lesions [13]. Patients with HS also suffer from more sexual distress than the healthy population; factors related to sexual distress are female sex, active lesions in the groin and on the genitals, intensity of unpleasant odor and pain and the absence of a stable relationship [13]. Sexual function is correlated with quality of life and with mood status disturbances (anxiety and depression) [13]. However, there is no information about how HS hinders sex life, how patients perceive themselves, whether they experience interference in their relationships or opportunities to find a partner and, if so, what this interference is. We hypothesize that HS has a high impact on these unexplored aspects of sexuality, and the aim of this study is to investigate this and to answer the following questions: Which difficulties do patients with HS experience in sexual activity? Would they like to share these difficulties with healthcare staff? What is their sexual orientation? How attractive do they feel? How does HS influence patients who are in relationships? How does HS influence patients who are single?

2. Materials and Methods

2.1. Patients and Methods

We conducted a cross-sectional study by means of a crowd-sourced online survey from 1 March to 1 April 2018. The Spanish hidradenitis suppurativa patients' association (ASENDHI) hosted the survey on its website and posted the survey on its social media networks [14].

The selection criterion was self-referred diagnosis of HS. The study was approved by the Institutional Review Board of Hospital Universitario San Cecilio (Granada, Spain, IRB code 0105-N-20) and is in accordance with the Declaration of Helsinki. Participants were informed about the survey's anonymity and the use of their data for research purposes, and they received no compensation for participating in the survey.

2.2. Questionnaire

The questionnaire was developed with Google Forms® suite, and was provided in Spanish. The data presented belong to a research project about sexuality and HS. Results regarding sexual and erectile dysfunction, sexual distress and associated factors have been already published elsewhere [15, 16].

In this study, questions were created both by a panel of experts and a group of patients from ASENDHI in order to evaluate the extent to which the disease has an influence on participants' sex lives. The survey included questions about difficulties in their sex life due to HS, which healthcare professional they would trust to share their sexual problems with, perceived attractiveness and sexual orientation. In the case of patients in a stable relationship, there were also questions about the role of their partners and how HS affects their relationships. In the case of single patients, there were also questions about their feelings when they meet new people and how HS affects their opportunities to meet people/establish a relationship. We did not use validated questionnaires because there are no tools available to explore these important factors related to sexuality and private life, since other questionnaires merely explore the presence or absence of sexual dysfunction and, as mentioned above, they have already been used on HS [15, 17-19].

Since the questions used were new and not validated, a control group of healthy acquaintances was also recruited by ASENDHI and a survey with all the questions not directly related to HS was distributed among them. The questions used in the present manuscript for both patients with HS and healthy controls are available as supplementary material in the original Spanish version and in an English translation (Supplementary Material File 1).

Sociodemographic data, biometric parameters, use of medication for other comorbidities and several characteristics of the disease were also collected. Disease severity was assessed by patients' self-reported Hurley stage since patients with HS are capable of self-assessing their Hurley stage with a good correlation with physician assessment [20].

Disease activity was assessed by the Patients' Global Assessment (PtGA) scale, consisting of five categories (inactive, very low, low, mild and severe) [21] and intensity of symptoms by Numeric Rating Scales (NRS) [22], where 0 is the lowest and 10 the highest intensity of the symptom. These scales show the subjective impact of the disease on patients, with equal or greater importance than objective scales [23, 24].

2.3. Statistical Analyses

Statistical analyses were performed using the IBM software Statistical Package for Social Science version 23.0 (SPSS Inc, Chicago, IL, USA). When data were missing from any of the variables of interest, patients were excluded from the study. When missing data were found in other variables, they were imputed. We used the Shapiro-Wilk test and histograms to assess if the variables were normally distributed. Descriptive statistics were used to explore the characteristics of the sample. Continuous variables were expressed as means and standard deviations (SD) or as medians and interquartile ranges (IR). Qualitative variables were expressed as absolute and relative frequencies.

We explored factors associated with fear of rejection/reaction of the sexual partner, perceived attractiveness, interference in relationships and interference in meeting new people by means of multivariate logistic regressions, including as variables age, sex, body mass index (BMI), educational status, age at HS onset, PtGA, NRS for pain, suppuration and unpleasant odor, self-reported Hurley, the number of areas affected by active lesions, the number of areas affected by scars, the presence of active lesions in the groin and genitals and, in the case of fear of rejection/the reaction of the sexual partner and perceived attractiveness, the presence of a stable relationship. Perceived attractiveness, interference in relationships and interference in meeting new people were binary codified (yes/no) for this analysis. Significance was set for all tests at two tails, $p<0.05$.

3. Results

3.1. Baseline Characteristics

Three hundred and ninety-three participants with HS completed the questionnaire, seven of them incompletely. The final sample therefore consisted of 386 participants, 79.27% (306/386) of which were women and 20.73% (80/386) men, resulting in a female-male ratio of 3.8:1. Their mean age was 37.81 (9.26) years old. Seventeen point six percent (68/386) of the patients were in Hurley stage I, 45.1% (174/386) in stage II and 37.3% (144/386) in stage III (Table 1). We also collected 157 healthy controls, with no statistically significant differences from patients with HS in terms of sex (73.25% (115/157) were women and 26.75% (42/157) men, $p=0.16$) or age (mean age= 37.5 (12.03) years old, $p=0.74$). BMI was significantly lower in healthy controls (24.66 (4.47) kg, $p<0.001$).

Table 1. Sociodemographic characteristics, comorbidities and baseline characteristics of patients with HS and healthy controls.

Baseline characteristics	Men (*n*=80)	Women (*n*=306)	All (*n*=386)	Controls (*n*=157)	*p* value*
Age (years)	39.21 (11.15)	37.44 (8.69)	37.81 (9.26)	37.05 (12.03)	0.74
Residence country					
Spain	90% (72)	80.7% (247)	82.6% (319)	89.2% (140)	0.13
Other**	8.7% (7)	19.3% (50)	14.8% (57)	10.2% (16)	
Not answered	1.3% (1)	2.9% (9)	2.6% (10)	0.6% (1)	
Educational status					
Basic	16.3% (13)	11.8% (36)	12.7% (49)	8.3% (13)	0.14
Medium	32.5% (26)	35.6% (109)	35% (135)	31.8% (50)	
Superior	51.2% (41)	52.6% (161)	52.3% (202)	59.9% (94)	
BMI (kg)	28.12 (5.03)	29.67 (7.05)	29.35 (6.71)	24.66 (4.47)	**<0.001**
Current smoker					
No	35% (28)	44.1% (135)	42.2% (163)	47.1% (74)	0.15
Yes	65% (52)	55.9% (171)	57.8% (223)	52.9% (83)	
Comorbidities					
HBP	5% (4)	6.9% (21)	6.5% (25)	4.5% (7)	0.11
DM2	2.5% (2)	6.5% (20)	5.7% (22)	3.1% (5)	
Dyslipidemia	3.8% (3)	2.9% (9)	3.1% (12)	1.3% (2)	
IBD	1.3% (1)	0.7% (2)	0.8% (3)	0% (0)	
Antidepressant use	5% (4)	10.1% (31)	9.1% (35)	5.7% (9)	
Benzodiazepine use	5% (4)	5.9% (18)	5.7% (22)	5.1% (8)	
Levothyroxine use	-	7.8% (24)	6.2% (24)	4.5% (7)	
Hyperuricemia	3.8% (3)	0.7% (2)	1.3% (5)	0.5% (1)	
Asthma/Seasonal allergies	-	1.6% (5)	1.3% (5)	2.6% (4)	
Stable relationship	67.5% (54)	77.1% (236)	75.1% (290)	74.5% (117)	0.88
Age of onset (years)	23.57 (9.45)	19.09 (7.1)	20.02 (7.85)		
Time of disease evolution (years)	15.64 (10.53)	18.33 (9.3)	17.77 (9.62)		
Time under medical attention (years)	6.79 (7.21)	7.1 (7.29)	7.03 (7.27)		
Diagnosis delay (years)	8.86 (9.13)	11.23 (9.55)	10.74 (9.51)		

Locations			
Axilla			
Active lesions	50% (40)	47.1% (144)	47.7% (184)
Scars	47.5% (38)	43.8% (134)	44.6% (172)
Groin			
Active lesions	53.8% (43)	65.7% (201)	63.2% (244)
Scars	42.5% (34)	57.2% (175)	54.1% (209)
Genitals			
Active lesions	38.8% (31)	36.3% (111)	36.8% (142)
Scars	35% (28)	26.8% (82)	28.5% (110)
Buttocks			
Active lesions	43.8% (35)	31% (95)	33.7% (130)
Scars	35% (28)	32.4% (99)	32.9% (127)
Breast			
Active lesions	2.5% (2)	29.4% (90)	23.8% (92)
Scars	6.3% (5)	27.1% (83)	22.8% (88)
Abdomen			
Active lesions	11.3% (9)	10.1% (31)	10.4% (40)
Scars	10% (8)	11.8% (36)	11.4% (44)
Perianal region			
Active lesions	43.8% (35)	16.3% (50)	22% (85)
Scars	31.3% (25)	18% (55)	20.7% (80)
Neck			
Active lesions	13.8% (11)	4.6% (14)	6.5% (25)
Scars	11.3% (9)	4.6% (14)	6% (23)
Nº of active regions	2.73 (1.79)	2.5 (1.57)	2.55 (1.62)
Nº of regions with scars	2.34 (2.29)	2.31 (2.06)	2.31 (2.1)
Hurley stage			
I	16.3% (13)	18% (55)	17.6% (68)
II	31.3% (25)	48.7% (149)	45.1% (174)
III	52.5% (42)	33.3% (102)	37.3% (144)
PtGA	3.73 (1.04)	3.65 (1.11)	3.66 (1.09)
NRS pain	6.64 (2.81)	6.52 (2.98)	6.54 (2.95)
NRS pruritus	6.24 (2.67)	6.48 (3.03)	6.43 (2.96)
NRS unpleasant odor	6.11 (3.05)	5.47 (3.45)	5.6 (3.38)
NRS suppuration	6.84 (3.04)	6.39 (3.21)	6.48 (3.18)

Continuous variables are expressed as means (standard deviation) and qualitative variables as relative (absolute) frequencies. HS: hidradenitis suppurativa. BMI: body mass index. HBP: high blood pressure. DM2: diabetes mellitus type 2. IBD: inflammatory bowel disease. PtGA: Patient's Global Assessment; values range from 1 (inactive disease) to 5 (severe disease). NRS: Numeric Rating Scale; values range from 0 (no symptoms) to 10 (maximum intensity of symptoms). *p value for the difference between HS patients and healthy controls. Significant values ($p<0.05$) are in bold. **Other includes: Germany, Argentina, Australia, Chile, Colombia, Costa Rica, Ecuador, USA, Italy, Mexico, Peru, Portugal, Switzerland, Uruguay and Venezuela.

When comparing patients with HS with and without a stable partner, there were no differences in genital involvement (35.5% (103/290) vs. 40.6% (39/96) respectively, p=0.37 for the difference), inguinal involvement (64.1% (186/290) vs. 60.4% (58/96), p=0.51), PtGA (3.7 vs. 3.6, p=0.62), number of active regions (2.5 (0.1) vs. 2.7 (0.2), p=0.4), NRS for pain (6.7 (0.2) vs. 6.2 (0.3), p=0.18) or Hurley stage (I: 16.2% (47/290), II: 44.1% (128/290), III: 39.7% (115/290) vs. I: 21.9% (21/96), II: 47.9% (46/96), III: 30.2% (29/96), p=0.2). NRS for unpleasant odor was higher among patients with a stable partner (5.9 (0.2) vs. 4.8 (0.3), p<0.01).

3.2. Perceived Difficulties in Sexual Activity

When participants were asked how HS affected their sexual relationships (Table 2), almost half reported feeling fear of rejection or of the reaction of their sexual partner, while in the healthy control group, 37.6% (59/157) reported feeling fear of rejection at some point in their lives ($p<0.05$), mainly due to insecurity (27.39%, 43/157) and concerns about physical appearance (26.12%, 41/157). Factors significantly associated with this feeling in patients with HS were younger age (OR=1.05 (95% CI: 1.02-1.08), $p<0.001$), the absence of a stable relationship (OR=7.72 (4.24-14.06), $p<0.0001$) and the number of areas affected by scars (OR=1.14 (1.02-1.28), $p<0.05$). We found trends toward statistical significance in self-reported Hurley (III vs. I, OR=2.06 (0.97-4.38), p=0.059). Patients also felt that symptoms significantly affected their relationships, with pain being the most important symptom in women (65.4%, 200/306) and suppuration in men (56.3%, 45/80). Some participants also thought that treatment made sexual relations difficult (10.6%, 41/386).

Table 2. Perceived difficulties in sexual relations.

Perceived Difficulties in Sexual Relations	Men (*n*=80)	Women (*n*=306)	All (*n*=386)
How does HS affect your sexual relations?			
"I experience fear of rejection or of the reaction of my sexual partner"	47.5% (38)	48% (147)	47.9% (185)
"Pain interferes with my sexual relations"	48.8% (39)	65.4% (200)	61.9% (239)
"Suppuration interferes with my sexual relations"	56.3% (45)	43.5% (133)	46.1% (178)
"Odor interferes with my sexual relations"	40% (32)	31.4% (96)	33.2% (128)
"Treatment interferes with my sexual relations"	13.8% (11)	9.8% (30)	10.6% (41)
"None of the above"	18.8% (15)	9.5% (29)	11.4% (44)
Would you like to share your sexual problems with healthcare staff?			
"No"	46.3% (37)	35.3% (108)	37.6% (145)
"Yes, with my GP"	8.8% (7)	15.7% (48)	14.2% (55)
"Yes, with my dermatologist"	31.3% (25)	26.8% (82)	27.7% (107)
"Yes, with nursing staff"	2.5% (2)	5.6% (17)	4.9% (19)
"Yes, with a psychologist/ sexologist"	27.5% (22)	41.2% (126)	38.3% (148)

Results are expressed as relative (absolute) frequencies. HS: hidradenitis suppurativa. GP: general practitioner.

Regarding the healthcare staff they would share their sexual problems with, a considerable percentage of participants with HS would not talk with anyone (37.6%, 145/386); women preferred a psychologist or a sexologist (41.2%, 126/306), and men felt most comfortable with their dermatologist (31.3%, 25/80) (Table 2). This is the opposite to the healthy control group, where most would like to share their sexual problems (95.5%, 150/157, $p<0.0001$), mainly with a psychologist or a sexologist (82.2%, 129/157).

3.3. Sexual Orientation

Regarding sexual orientation, most participants were heterosexual (87.5% (70/80) of men and 94.8% (290/306) of women). Eleven point three percent (9/80) of men and 1.3% (4/306) of women were homosexual and 1.3% (1/80) of men and 3.9% (12/306) of women were bisexual. Sexual orientation was similar in the control group: 88.1% (37/42) of men and 89.57% (103/115) of women were heterosexual, 11.9% (5/42) of men and 3.48% (4/115) of women were homosexual, and 6.95% (8/115) of women were bisexual.

3.4. Perceived Attractiveness

Participants were also asked to rate their perceived sexual attractiveness (Table 3). The differences with the control group were again significant ($p<0.0001$). It is noteworthy that 38.75% (31/80) of men and 45.75% (140/306) of women with HS considered themselves as "less attractive than average" or "not at all attractive". Factors related to lower perceived attractiveness in patients with HS were NRS for unpleasant odor (OR=1.14 (1.04-1.26), $p<0.01$), NRS for suppuration (OR=1.14 (1.01-1.27), $p<0.05$) and the absence of a stable relationship (OR=1.81 (1.1-2.96), $p<0.05$); the presence of active lesions in the groin showed trends toward statistical significance (OR=1.62 (0.97-2.7), $p=0.07$).

Table 3. Perceived attractiveness in patients with HS and healthy controls.

Perceived Attractiveness	**Patients with HS (*n*=386)**		**Healthy controls (*n*=157)**	
	Men (*n*=80)	**Women (*n*=306)**	**Men (*n*=42)**	**Women (*n*=115)**
Do you consider yourself sexually attractive?				
Not at all	26.25% (21)	26.14% (80)	-	6.09% (7)
Less than average	12.5% (10)	19.61% (60)	7.14% (3)	12.17% (14)
Average	48.75% (39)	39.22% (120)	42.86% (18)	56.52% (65)
More than average	10% (8)	12.75% (39)	45.24% (19)	13.91% (16)
Very attractive	2.5% (2)	2.28% (7)	4.76% (2)	11.3% (13)

Results are expressed as relative (absolute) frequencies. HS: hidradenitis suppurativa.

3.5. Sexuality in Patients with HS in a Stable Realtionship

Sixty-seven point five percent (54/80) of men and 77.1% (236/306) of women were in a stable relationship. Although it was not statistically significant, women reported more support ($p=0.22$) and greater help with overcoming the fear of rejection ($p=0.09$) than men, whereas help with lesion dressing in intimate areas was higher in men ($p<0.05$).

It is significant that around 70% of participants, regardless of sex, state that HS negatively affects their relationship (Table 4). PtGA was related to the perception of relationships being negatively affected (OR=1.45 (1.01-2.08), $p<0.05$); the number of areas affected by active lesions showed trends toward statistical significance (OR=1.3 (0.98-1.72), $p=0.06$).

Table 4. Sexuality in patients with HS in a stable relationship.

Sexuality in Patients in a Stable Relationship	**Men (*n*=54)**	**Women (*n*=236)**	**All (*n*=290)**
Your partner			
Helps you overcome the fear of rejection	37% (20)	49.6% (117)	47.2% (137)
Supports you	64.8% (35)	73.3% (173)	71.7% (208)
Helps with lesion dressing in intimate areas	63% (34)	47% (111)	50% (145)
None of the above	9.3% (5)	10.6% (25)	10.3% (30)
Do you think that HS negatively influences your relationship?			
0: Not at all	31.5% (17)	28% (66)	28.6% (83)
1: A little	35.2% (19)	44.9% (106)	43.1% (125)
2: Somewhat	18.5% (10)	18.6% (44)	18.6% (54)
3: Very much	14.8% (8)	8.5% (20)	9.7% (28)

Results are expressed as relative (absolute) frequencies. HS: hidradenitis suppurativa.

3.6. Sexuality in Single Patients with HS

Thirty-two point five percent (26/80) of men and 22.9% (70/306) of women were single. When patients were asked how they felt when they meet someone they could have a relationship or sexual relations with, women experienced greater fear of rejection (p=0.11) than men, and the percentage of women who did not want to meet people because of HS was also higher (p=0.22). Less than a quarter of participants felt excited when they met new people. On the other hand, in the control group, 77.5% (31/40) of the participants felt excited when meeting new people (p<0.0001) and 22.5% (9/40) stated fear of rejection of the new partner for whatever reason (p<0.0001).

A striking fact is that almost 95% of women and more than 80% of men stated that HS had a negative influence on their chances of having a relationship or sexual relations (Table 5). We did not find any significant association of the explored factors with this feeling.

Table 5. Sexuality in single patients with HS.

Sexuality in Single Patients	Men (*n*=26)	Women (*n*=70)	All (*n*=96)
How do you feel when you meet someone you could have a relationship or sexual relations with?			
"I feel good, excited"	34.6% (9)	20% (14)	24% (23)
"I am afraid of rejection and the reaction of the other person because of HS"	53.8% (43)	71.4% (50)	66.7% (64)
"I prefer not to meet anyone because of HS"	15.4% (4)	27.1% (19)	24% (23)
"I prefer not to meet anyone for other reasons"	15.4% (4)	5.7% (4)	8.3% (8)
Do you think that HS negatively influences your chances of having a relationship or sexual relations?			
0: Not at all	19.2% (5)	5.7% (4)	9.4% (9)
1: A little	19.2% (5)	37.1% (26)	32.3% (31)
2: Somewhat	38.5% (10)	25.7% (18)	29.2% (28)
3: Very much	23.1% (6)	31.4% (22)	29.2% (28)

Results are expressed as relative (absolute) frequencies. HS: hidradenitis suppurativa.

4. Discussion

In this study, several previously unexplored factors related to sexuality in patients with HS have been assessed. Previous research has shown that sexual and erectile dysfunction have a high prevalence in patients with HS, that they suffer greatly from sexual distress and that this is related to a lower quality of life [13]. In this investigation, we have seen that HS has an important, unrecognized and misunderstood impact on sexuality which must be addressed. Most patients experience feelings of fear in their relationships, and factors such as symptoms or the absence of a stable partner play an important role in this impact on sexuality. However, both single patients and those in a stable relationship are affected.

4.1. Baseline Characteristics

In general terms, the baseline characteristics of the sample, such as disease or sociodemographic features, including the male-female ratio, were similar to those reported in other studies, and representative of the general HS population [25-32]. As expected, BMI was significantly higher in patients with HS than in healthy controls, given the association of this disease with being overweight and obesity [33]. However, BMI was considered in multivariate analyses, and no association was found with any of the explored aspects of sexuality.

4.2. Perceived Difficulties in Sexual Activity

Symptoms seem to play an important role in the sexual impairment of patients with HS. Women perceived pain as the symptom which most affected their sexual relations. This is consistent with several studies indicating that women have a greater perception of pain and an increased risk of developing chronic pain, based on various mechanisms such as endogenous opioid activity, sex hormones, genetic factors and psychosocial factors [34-36]. On the other hand, suppuration was identified by men as the symptom which most affected their sexual relations. The interference of suppuration in sexual relations is probably due to factors related to the nature of the sexual act and/or to psychological factors that could be associated with disease activity [3] and probably also the reason for the observed association between the NRS for suppuration and unpleasant odor with a lower perceived attractiveness.

Several treatments for HS can affect patients' sex lives, such as surgical procedures, topical ointments and lesion dressings. We found a lower percentage of sexual impairment due to HS treatment than Janse *et al.* [18], maybe because their sample came in part from a hospital setting.

It should be noted that almost 1 in 3 participants would share their sexual problems with their dermatologist, and almost 2 in 5 with a psychologist or sexologist. According to Janse *et al.* [18], only 6% of patients with HS reported receiving enough attention from their doctor about their sexual problems, probably due to the complexity of sexual problems, embarrassment about tackling the issue, difficulty of treatment and lack of time. Given the profound impact of HS on sexuality, it would be advisable to routinely screen these patients for sexual problems, offering them follow-up attention in a specialized unit if they so require. Moreover, it is necessary to create an atmosphere of trust with these patients, since 1/3 do not want to talk about their sexual problems, in contrast to more than 95% of the healthy controls who would discuss their sexual problems. It seems that patients are so embarrassed by their disease that they prefer not to share their problems, so it is important to create a relationship which allows them to freely express their concerns.

4.3. Sexual Orientation

As far as we know, this is the first study evaluating the sexual orientation of patients with HS. We did not observe any differences compared to the healthy controls, as has been observed in previous research on patients with psoriasis [37, 38].

4.4. Perceived Attractiveness

More than 2/5 of participants considered themselves less attractive than average, and almost half reported being afraid of rejection and of the reaction of their sentimental/sexual partner, probably due to the impact of HS on self-body image [39], as also occurs in psoriasis [40]. These results were significantly higher than those found in healthy people. Younger patients were at greater risk of experiencing these feelings, probably because they had not yet developed coping mechanisms. The relation observed between fear of rejection and the number of areas affected by scars, as well as the trend towards significance for self-reported Hurley, is in concordance with this impact on self-body image. Like patients with burns, body image disturbances may be due to dysfunctional coping strategies, and appropriate intervention in this area could lead to an improvement in these feelings [41]. These alterations are associated with sexual impairment due to inhibition and shyness, generating less excitability and less ability to achieve orgasm, regardless of sex and whether or not in a stable relationship [42]. However, we observed that the absence of a stable relationship was related to greater fear of rejection and to lower perceived attractiveness, probably because the trust generated in a relationship could alleviate the negative feelings previously described, with less self-consciousness and less orgasm difficulty in both men and women [42].

4.5. Sexuality in Patients with HS in a Stable Relationship

Even when body image alterations have a lower impact on sexual health in people with a stable partner [42], they can still influence the relationship quality as perceived by the subject [43]. Around 70% of patients in a stable relationship referred to support from their partners and around half help them to overcome fear of rejection and help with lesion dressing in intimate areas. In addition, around 70% of the patients stated that the disease has little or no influence on their relationships, reflecting the importance of partner support in the feelings experienced by the patients. However, around 1/3 thought that HS had a significant negative influence on their relationship. These data agree with previous studies showing lower quality of life in the cohabitants of patients with psoriasis [44] and HS [45, 46]. Another investigation observed a higher prevalence of intimate partner violence, but no increased risk of sexual assault, in patients with HS than in patients with acne, indicating a possible deterioration of life as a couple [47]. Therefore, the disease seems to have a significant impact on relationships. Disease activity was related to this impact and the number of areas affected by active lesions showed trends towards statistical significance, so proper individualized treatment could improve patients' relationships.

4.6. Sexuality in Single Patients with HS

We observed that patients with factors related to sexual dysfunction or sexual distress in HS (genital and inguinal involvement, higher PtGA, higher number of affected areas or higher NRS for pain and for unpleasant odor) [15, 16], as well as those with a higher Hurley stage, were not more likely to be single. The percentages of single women who felt fear of rejection when meeting a possible sexual partner and of people who preferred not to meet anyone because of the disease were higher than single men with HS, although not statistically significant. On the other hand, the differences between patients and healthy controls in terms of feelings of excitement or fear of rejection when meeting new people were significant. More than 90% of participants thought that HS influenced their ability to find a stable/sporadic partner, and more than half reported that it influenced this ability "somewhat" or "very much", this percentage again being higher in women. These data are worrying and reflect the profound impact of the disease on sexuality and patients' confidence. Several studies indicate that young adults with chronic illnesses are less likely to get married [48-50]. It seems that people with chronic diseases have less self-confidence, decreasing their chances of finding a partner and thus getting into a vicious cycle of sexual distress.

4.7. Limitations

Our investigation has some limitations. Firstly, there is a possible selection bias, since it only represents patients in contact with support groups and with internet access. Elderly patients who might use the internet less frequently, or those with low socio-cultural status or fear of new technologies, might be under-represented [51]. However, the baseline characteristics of our sample do not differ significantly from those reported in other research about HS, either in hospital-based or population-based studies. Secondly, there was a possible classification bias, since it was an online questionnaire so we could not confirm the HS diagnosis and HS characteristics, which were self-reported. Nevertheless, an informed population can properly identify HS due to its apparent and distinctive clinical manifestations. Given the questionnaire's dissemination through a patients' association, it is expected that the participants did in fact suffer from the disease. Finally, the questions used in this study are not validated; however, as discussed above, there are no validated tools available to assess the aspects of sexuality explored in this research, and we have compared many of the questions (all those which did not ask directly about the disease) with a healthy control group.

5. Conclusions

In conclusion, HS has a significant impact on important aspects of quality of life, such as sexuality and private life. Symptoms, and sometimes treatment, affect sexual activity. Many patients experience greater feelings of rejection and lower perceived attractiveness than healthy people. Body image alteration may play an important role, as it demonstrates the association between fear of rejection and the number of areas affected by scars. The absence of a stable relationship is also an important risk factor. However, there is also a noticeable impact on stable relationships, in part due to disease activity. A high percentage of single participants thought that the disease decreased their possibilities of having a sexual/sentimental partner, reflecting their sexual distress and lack of confidence. A considerable number of participants would like to share their sexual problems with health professionals, so patients should be asked about their sexual difficulties and specialized attention should be provided when necessary.

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5.4 REVISIÓN DE LA EVIDENCIA CIENTÍFICA DISPONIBLE SOBRE HIDRADENITIS SUPURATIVA Y SEXUALIDAD

Una vez determinada la frecuencia de disfunción sexual en mujeres y de disfunción eréctil en varones con HS, los altos niveles de distrés sexual, la afectación de otras áreas de la sexualidad y de la vida en pareja y los factores asociados a todas estas alteraciones y dificultades que nos permiten identificar pacientes con alto riesgo de padecer trastornos sexuales, nos preguntamos: ¿cuáles deben ser las siguientes líneas de investigación en relación con la sexualidad en pacientes con HS? ¿Qué evidencia científica existe sobre la materia en la literatura médica que nos pueda orientar, así como ayudar a contextualizar nuestros resultados y en la toma de decisiones en la práctica clínica habitual? Para ello, realizamos una revisión sistemática sobre HS y sexualidad.

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Abstract

Hidradenitis suppurativa (HS) can cause considerable impact on several aspects of quality of life. Sexuality is a central aspect of quality of life. In recent years, there has been an increase in the number of articles on HS and sexuality. To achieve our aim of synthesizing the available scientific evidence on HS and sexual health, we conducted a systematic review in February 2020. The clinical databases used included Medline and Embase. All types of epidemiological articles were included; reviews, guidelines, protocols, conference abstracts and case report articles were excluded. Eleven studies were included for review, representing 42 729 patients with HS. The most common study design was cross-sectional with or without comparison group(s), conducted in an outpatient setting or through surveys. Prevalence of sexual dysfunction ranged between 51-62%, and in the case of erectile dysfunction, a specific kind of sexual dysfunction affecting penile erection, it ranged from between 52% and 60% of patients studied using validated questionnaires. Potential risk factors for sexual dysfunction among men and women were identified, mainly related to disease activity, symptoms and partners. Mood disorders like depression and anxiety appear to be associated with sexual dysfunction. Women were more affected by sexual distress. HS patients with sexual dysfunction had a decreased overall quality of life. With respect to treatment, surgery did not improve sexual function and there is no scientific evidence regarding medical treatments. Patients stated that they would like to treat their sexual problems with healthcare professionals. In conclusion, sexual and erectile dysfunction are common in HS patients, and negatively affect their quality of life. There are clinical factors potentially associated with this which should be identified and treated by dermatologists in the comprehensive care of HS patients. Prospective studies are needed to provide more scientific evidence on this unmet need.

Introduction

Hidradenitis suppurativa (HS) is a chronic, inflammatory, recurrent, debilitating skin disease of the hair follicle that usually presents after puberty with painful, deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body.[1] In the absence of disease control, it can cause uncomfortable symptoms and tissue damage with the appearance of fistulae and scars.[2] HS has an estimated prevalence of about 0.5-1% in Western countries.[3-5] It is associated with several comorbidities, such as metabolic syndrome, cardiovascular risk or inflammatory bowel disease.[6-8]

HS has a profound impact on patients' quality of life, more than other dermatoses and comparable to diseases such as diabetes, cancer, cardiovascular disease or chronic obstructive pulmonary disease, at least in part due to its uncomfortable symptoms, like pain, mal odour, suppuration and pruritus.[9,10] HS is related to depression, anxiety, sleep disturbances, isolation, loneliness, stigmatization, suicide risk and unemployment, among other issues.[10-16]

According to the World Health Organization (WHO), 'sexual health is a state of physical, mental and social well-being in relation to sexuality'. Sexuality is important for maintaining good mental health, and a basic need that cannot be separated from other aspects of human life.[17] Quality of life is significantly influenced by sexual function,[18,19] but the latter can be impaired by chronic diseases.[20]

In recent years, there has been increased interest in and research on the impact of HS on sex life, which is directly related to quality of life.[18,21] However, the scientific evidence available on this subject is limited and heterogeneous in terms of design, tools used and results. The aim of this systematic review is to synthesize the available scientific evidence on HS and sexual health in order to serve as a basis for future research and facilitate the integration of new scientific findings into clinical practice.

Methods

Definitions

Sexual function is defined by ICD-10 as 'the various ways in which an individual is able to participate in a sexual relationship as he or she wishes'.[22] Sexual dysfunction (SD) may be caused by organic or psychological factors, or a combination of both, and can involve any element of the sexual response, such as desire, arousal or orgasm.[23]

Erectile dysfunction (ED) is a subtype of SD defined as 'consistent or recurrent inability to attain and/or maintain penile erection sufficient for sexual satisfaction'.[23]

Sexual distress refers to the emotional impact and suffering that sexual difficulties cause the individual.[23]

Inclusion and exclusion criteria

The search was limited to: (i) human data, (ii) articles written in English, German, Polish or Spanish, (iii) articles published after the first year included in the databases. All types of epidemiological studies (clinical trials, cohort studies, case-control studies and cross-sectional studies) regarding sexuality and sexual function in patients with HS were included and analysed. Reviews, guidelines, protocols, conference abstracts and case reports were excluded.

Bibliographic search

A literature search of major clinical databases including Medline and Embase was conducted on 10 February 2020 using the following search term: ('Hidradenitis suppurativa' OR 'acne inversa') AND ('sex' OR 'sexual' OR 'sexuality' OR 'erectile'). Two researchers (CCB and AML) independently reviewed the titles and abstracts of the articles obtained in the first search to assess relevant studies. The full texts of all articles meeting the inclusion criteria were reviewed, and their bibliographic references were checked for additional sources. The articles considered relevant by both researchers were included in the analysis; in the case of disagreement, a third researcher (TMV) analysed the article.

Variables

The variables assessed were as follows: study design, level of scientific evidence according to the Centre for Evidence-Based Medicine,[24] sample size, tools used to assess sexuality or sexual function, statistical analysis and results.

Results

Study design

The results of the bibliographic search are shown in Fig. 1. A total of 556 articles were identified from the electronic database search. After eliminating duplicates, reviewing titles and abstracts, and applying inclusion and exclusion criteria, 11 epidemiological studies representing 42 729 patients with HS were considered relevant and included for review.[25-35] Their main characteristics are summarized in Table 1. Most studies had a cross-sectional design with or without comparison group(s), were conducted in an outpatient setting or through surveys and included patients with mild to moderate HS. One study presented level of evidence 2b and 10 were classified as scientific level of evidence 4. The most frequently used tools for assessing sexual function were the Female Sexual Function Index (FSFI), and its short variant (FSFI-6), and the International Index of Erectile Function (IIEF), and its short variant (IIEF-5).

Sexual dysfunction

The prevalence of SD in women assessed using FSFI and FSFI-6 ranged from 51% to 62%.[28,34] Janse *et al.*[28] also estimated the presence of SD in both sexes with the Arizona Sexual Experience Scale (ASEX), finding slightly lower prevalence, with women having worse scores than men. In another study, prevalence was 3.5% using self-reported data without any questionnaires.[35] Many studies compared questionnaire scores between patients with HS and healthy controls or with patients with other dermatological diseases, finding worse scores in HS without using the validated cut-offs points[25,27,29,31] (Table 2).

One study evaluated the incidence of SD in patients with HS and found that it was higher compared to the general population.[30] The odds of incident SD was 38% higher in patients with HS controlling for age, sex and depressive and anxiety disorders (OR = 1.38, 95% CI 1.28 - 1.48, $P < 0.001$). Regarding socio-demographic characteristics, there was higher incidence in men than in women. Although ageing was associated with increased incidence of SD, HS was associated with SD only in the group of 18 - 44 years old (OR = 1.7, 95% CI 1.52 - 1.9; Table 2).

Erectile dysfunction

The prevalence of ED in men with HS using IIEF and IIEF-5 ranged from 52% to 60%.[28,34] Other studies compared the IIEF scores of patients with HS with healthy controls, finding significantly worse scores in patients with HS without using the validated cut-offs points[25,29] (Table 2).

Factors associated with sexual dysfunction and erectile dysfunction

Factors related to a higher frequency of SD in women were higher educational status, increased disease activity, intensity of pain and unpleasant odour, the absence of a stable relationship and an older age at HS onset.[28,34] On the other hand, factors related to ED in men were ageing, active lesions on the genitals and increased number of active lesions[34] (Table 3).

Sexual distress and associated factors

Three studies investigated the presence of sexual distress in patients with HS. They found that patients with HS had higher sexual distress than healthy controls,[25,29] and that women had higher sexual distress than men.[25,32] Sexual distress correlated with both SD and ED.[32] Factors associated with sexual distress in patients with HS were female sex, active lesions in the groin and on the genitals, increasing intensity of pain and unpleasant odour as well as the absence of a stable relationship.[32]

Janse *et al.*[28] determined that 59.7% of patients experienced a decline in sexual activity after HS onset. Among these patients, the main reasons for this decline were the influence on their physical appearance (79% of men and 89% of women), their diminished sexual desire (87% of men and 91% of women) and the inconvenience caused by inflammation (89% of men and 99% of women). Garg *et al.*[35] also found a large impact on sexual activity (Table 4).

Sexual function and quality of life

A correlation between the FSFI and the Dermatology Quality of Life Index (DLQI) has been found,[25,28] and also between the Frankfurt Self-Concept Scale for Sexuality (FKKS SSEX) and the DLQI.[25] Alavi *et al.*[29] concluded that scores from the IIEF and the Sexual Quality of Life Questionnaire for Use in Men explained 42% of the variance in DLQI in men, and scores from the FSFI and the Female Sexual Distress Scale-Revised explained 46% of the variance in DLQI in women.

Sex and psychological comorbidities

Kurek *et al.*[26] observed a correlation between the HADS-depression (Hospital and Anxiety Depression Scale) score and the FKKS SSEX. Slyper *et al.*[30] reported that the incidence of SD over 5 years was higher among patients with HS who suffered depressive disorder (2.4% vs 1.4%) and anxiety disorder (2.4% vs 1.5%).

Effect of treatment on sexual dysfunction

Only one study evaluated the effect of HS treatment on SD: 'major surgery under general anesthesia' (the exact type of surgery or wound closure technique was not specified). A consistent improvement in sexual function 3 and 6 months later was not observed. Only patients ≥36 years old showed improvement in ASEX scores at 6 months (18 vs 13.5 points, $P = 0.02$).[33]

Are patients satisfied with their physicians?

Janse *et al.*[28] reported that only 6% of patients thought that doctors paid enough attention to their sexual problems, and 34% of patients believed that doctors should pay more attention to their sexual problems, although the first question was not answered by 50% of the participants and the second by 37%.

Discussion

In recent years, there has been an increase in the number of scientific articles on HS. All epidemiological articles on HS and sexuality have been published from 2013 onwards. Most of the designs are cross-sectional with or without a comparison group, which limits the quality of the evidence. Many studies are also hospital-based, so estimates may not be representative of the general population.

SD and ED in HS patients appear to be present in around half the patients.[28,34] This prevalence is higher than the general population[36-38] and also slightly higher than patients with psoriasis[39] or in a population attending a screening program for prostate cancer[40] using the same validated questionnaires. The incidence over 5 years is estimated at 1.7%, with HS associated with the incidence of SD in younger people, probably because they are more sexually active and their expectations are higher.[30] The studies with a comparison group did not use the validated cut-off points of the different tools used to assess SD or ED. The use of nominal outcomes offers clinically relevant results, but requires larger sample sizes to observe statistically significant differences. In opposition, the clinical relevance of an average score in a questionnaire is in most situations very limited but statically significant differences require lower numbers of subjects.[25,29,31]

The exact mechanism by which SD or ED occurs in patients with HS is unclear. It may be a combination of organic and psychological factors. Sexual function may be impaired by uncomfortable symptoms,[34,41] by lesions in specific areas which make sexual activity difficult[34] or by disease activity,[28,34] as proinflammatory cytokines and systemic inflammation can both alter sex hormone levels and cause vascular dysfunction.[42] As occurs in the general population, ageing can also cause ED,[34] due to a decline in dehydroepiandrosterone levels and atherosclerosis.[43] Some cultural factors may also be involved in SD, such as educational status, which may be explained by different lifestyles and expectations between people with different levels of education.[34] Psychological factors may also play a role. HS is related to alterations in body image[44] and stigmatization,[11] feelings that can be relieved by the confidence created in a relationship, since having a partner is associated with less self-consciousness and less orgasm difficulty.[34] Although there is some research on HS patients' partners, finding a moderate impact on their quality of life,[45] there are no studies evaluating their sexuality. A higher incidence of SD has been reported among HS patients with both depressive and anxiety disorders.[30] This increased frequency of anxiety and depression in patients with HS, as occurs with other dermatological diseases such as psoriasis, could represent a vicious circle in which SD and ED can be both cause and consequence of mood disorders.[39]

The impact on the sexual function of patients with HS is reflected negatively in their quality of life. Alavi *et al.*[29] demonstrated that around half the changes in DLQI depended on SD/ED and sexual distress, giving some idea of the magnitude of its impact on quality of life. A correlation has also been found between FSFI and DLQI scores,[25,28] although these studies did not evaluate the influence of HS itself on quality of life, so, as HS can be the cause of both sexual difficulties and impairment of quality of life, the causal chain between HS, SD and quality of life is not clear.

Patients with HS also experience more sexual distress than a healthy population.[25,29] This impact seems to be higher for women with HS,[25,32] as occurs with psoriasis.[46] Some factors such as changes in body image may affect women more at this level,[47] since their arousal mechanisms and sexual function are more complex. Reported gender differences in symptom notification, due to different social roles and responsibilities, psychosocial and cultural factors, and physiological differences, such as women's greater sensitivity to the external environment, may also play a role, independent of possible psychiatric comorbidities.[48] Other factors associated with sexual distress were the presence of active lesions in the groin and on the genitals, the intensity of pain and unpleasant odour and the absence of a stable relationship,[32] highlighting the importance of organic factors and partners in patients' sexuality.

The onset of the disease seems to have an impact on the sexual activity of most patients, more than happens with psoriasis,[46,49] mainly due to concerns about physical appearance, embarrassment, lack of desire or inflammation and consequent symptoms such as pain.[28,35] However, unlike psoriasis,[39,50] there are no studies on the possible improvement of patients' sexual function after systemic immunosuppressive treatment. Only one investigation evaluated changes in sexual function after surgical procedures in patients with HS, but found no clear improvement. The mean time for wound closure was almost 3 months, and sexual function was evaluated at month 3 and 6 after surgery.[33] Surgical treatment may take longer to improve complex life activities such as sexual function. Moreover, other factors which may influence sexual function, such as overall disease severity and activity, symptoms and the presence of a relationship, were not reported.

Finally, patients complained about the lack of attention given to their sexual problems by doctors, and thought they should focus more on this issue.[28] Dermatologists must be primarily responsible for the care of HS patients, so we must pay attention to these problems in order to manage the disease with a holistic approach, since it is currently still not possible to achieve a cure or a complete control of HS in most patients. We should facilitate patients expressing themselves, initiate treatment according to the origin of the problem and refer patients to the appropriate specialists when required. The presence of sexual impairment could even be considered a criterion of severity when choosing a treatment.

Our systematic review has some limitations. Most studies were cross-sectional, so the scientific evidence they provide is limited. They may have been affected by selection biases, as the samples came from hospital settings or through questionnaires distributed by patient associations, so more severe patients may have been included. Some research included a comparison group, but cannot be considered case-control studies according to their designs. In addition, some investigations did not use validated questionnaires or did not use their cut-off points to assess sexual function. We encourage researchers to use validated questionnaires and to report both cut-off (nominal) and average (continuous) data of these questionnaires in future studies. The lack of data and the heterogeneity of the information prevent us from conducting a meta-analysis.

In conclusion, patients with HS are at higher risk of SD, ED and sexual distress compared to a healthy population, and probably compared to other dermatological diseases such as psoriasis. Women seem to be more affected than men. Organic and psychological factors may play a role in these dysfunctions, which have a negative impact on quality of life. Dermatologists must be aware of these problems and address them, since potential factors related to SD or ED are related to disease activity. More prospective studies, such as clinical trials, cohort studies and case-control studies are needed to provide more scientific evidence on the subject, clearly define risk factors, the importance of psychological comorbidities, the impact on quality of life, on other aspects of sexuality and on partners and especially, the role of medical and surgical treatment for HS in improving sexual function.

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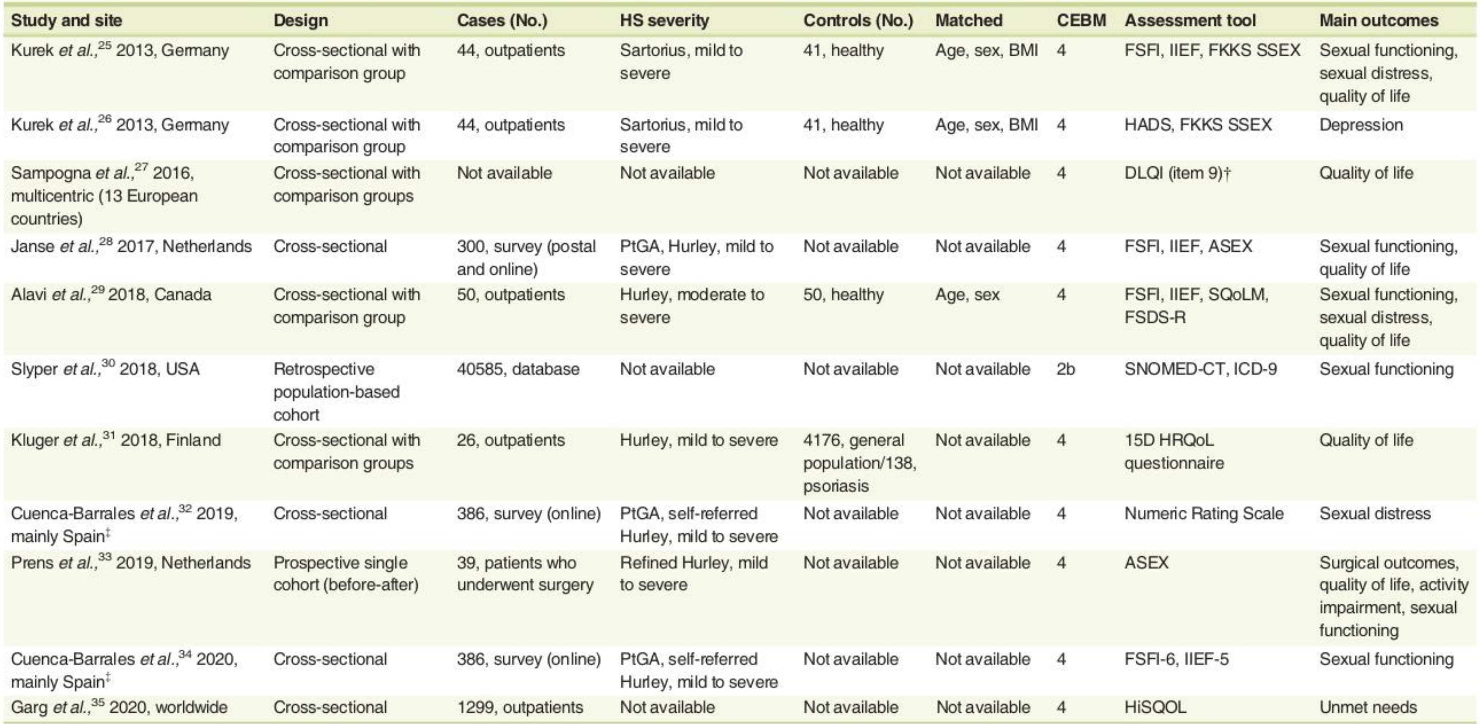
Table 1 Main characteristics of epidemiological studies on HS and sexuality



Study and site	Design	Cases (No.)	HS severity	Controls (No.)	Matched	CEBM	Assessment tool	Main outcomes
Kurek *et al.*,[25] 2013, Germany	Cross-sectional with comparison group	44, outpatients	Sartorius, mild to severe	41, healthy	Age, sex, BMI	4	FSFI, IIEF, FKKS SSEX	Sexual functioning, sexual distress, quality of life
Kurek *et al.*,[26] 2013, Germany	Cross-sectional with comparison group	44, outpatients	Sartorius, mild to severe	41, healthy	Age, sex, BMI	4	HADS, FKKS SSEX	Depression
Sampogna *et al.*,[27] 2016, multicentric (13 European countries)	Cross-sectional with comparison groups	Not available	Not available	Not available	Not available	4	DLQI (item 9)†	Quality of life
Janse *et al.*,[28] 2017, Netherlands	Cross-sectional	300, survey (postal and online)	PtGA, Hurley, mild to severe	Not available	Not available	4	FSFI, IIEF, ASEX	Sexual functioning, quality of life
Alavi *et al.*,[29] 2018, Canada	Cross-sectional with comparison group	50, outpatients	Hurley, moderate to severe	50, healthy	Age, sex	4	FSFI, IIEF, SQoLM, FSDS-R	Sexual functioning, sexual distress, quality of life
Slyper *et al.*,[30] 2018, USA	Retrospective population-based cohort	40585, database	Not available	Not available	Not available	2b	SNOMED-CT, ICD-9	Sexual functioning
Kluger *et al.*,[31] 2018, Finland	Cross-sectional with comparison groups	26, outpatients	Hurley, mild to severe	4176, general population/138, psoriasis	Not available	4	15D HRQoL questionnaire	Quality of life
Cuenca-Barrales *et al.*,[32] 2019, mainly Spain‡	Cross-sectional	386, survey (online)	PtGA, self-referred Hurley, mild to severe	Not available	Not available	4	Numeric Rating Scale	Sexual distress
Prens *et al.*,[33] 2019, Netherlands	Prospective single cohort (before-after)	39, patients who underwent surgery	Refined Hurley, mild to severe	Not available	Not available	4	ASEX	Surgical outcomes, quality of life, activity impairment, sexual functioning
Cuenca-Barrales *et al.*,[34] 2020, mainly Spain‡	Cross-sectional	386, survey (online)	PtGA, self-referred Hurley, mild to severe	Not available	Not available	4	FSFI-6, IIEF-5	Sexual functioning
Garg *et al.*,[35] 2020, worldwide	Cross-sectional	1299, outpatients	Not available	Not available	Not available	4	HiSQOL	Unmet needs

15D HRQoL questionnaire, 15-dimensions Health-Related Quality of Life questionnaire; ASEX, Arizona Sexual Experience Scale; BMI, body mass index; CEBM, level of scientific evidence according to the Centre for Evidence-Based Medicine (24); DLQI, Dermatology Quality of Life Index; FKKS SSEX, Frankfurt Self-Concept Scale for Sexuality; FSDS-R, Female Sexual Distress Scale-Revised; FSFI, Female Sexual Function Index (FSFI-6 indicates short variant); HADS, Hospital Anxiety and Depression Scale; HiSQOL, Hidradenitis Suppurativa Quality of Life instrument; IIEF, International Index of Erectile Function (IIEF-5 indicates short variant); PtGA, Patient's Global Assessment; SQoLM, Sexual Quality of Life Questionnaire for Use in Men.

†Item 9: Over the last week, how much has your skin caused any sexual difficulties? The responses are scored as 0, not at all; 1, a little; 2, a lot; and 3, very much.

‡14.8% of participants were from Germany, Argentina, Australia, Chile, Colombia, Costa Rica, Ecuador, USA, Italy, Mexico, Peru, Portugal, Switzerland, Uruguay and Venezuela.

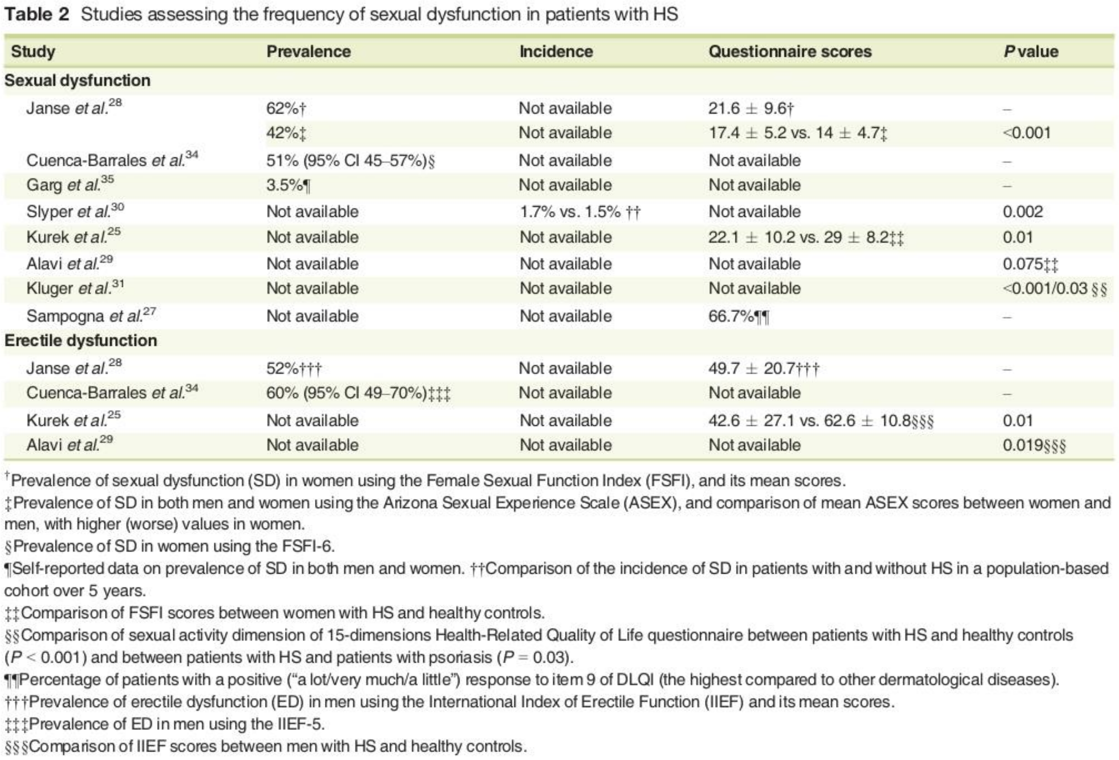


Table 2 Studies assessing the frequency of sexual dysfunction in patients with HS

Study	Prevalence	Incidence	Questionnaire scores	*P* value
Sexual dysfunction				
Janse *et al.*[28]	62%†	Not available	21.6 ± 9.6†	–
	42%‡	Not available	17.4 ± 5.2 vs. 14 ± 4.7‡	<0.001
Cuenca-Barrales *et al.*[34]	51% (95% CI 45–57%)§	Not available	Not available	–
Garg *et al.*[35]	3.5%¶	Not available	Not available	–
Slyper *et al.*[30]	Not available	1.7% vs. 1.5% ††	Not available	0.002
Kurek *et al.*[25]	Not available	Not available	22.1 ± 10.2 vs. 29 ± 8.2‡‡	0.01
Alavi *et al.*[29]	Not available	Not available	Not available	0.075‡‡
Kluger *et al.*[31]	Not available	Not available	Not available	<0.001/0.03 §§
Sampogna *et al.*[27]	Not available	Not available	66.7%¶¶	–
Erectile dysfunction				
Janse *et al.*[28]	52%†††	Not available	49.7 ± 20.7†††	–
Cuenca-Barrales *et al.*[34]	60% (95% CI 49–70%)‡‡‡	Not available	Not available	–
Kurek *et al.*[25]	Not available	Not available	42.6 ± 27.1 vs. 62.6 ± 10.8§§§	0.01
Alavi *et al.*[29]	Not available	Not available	Not available	0.019§§§

†Prevalence of sexual dysfunction (SD) in women using the Female Sexual Function Index (FSFI), and its mean scores.

‡Prevalence of SD in both men and women using the Arizona Sexual Experience Scale (ASEX), and comparison of mean ASEX scores between women and men, with higher (worse) values in women.

§Prevalence of SD in women using the FSFI-6.

¶Self-reported data on prevalence of SD in both men and women. ††Comparison of the incidence of SD in patients with and without HS in a population-based cohort over 5 years.

‡‡Comparison of FSFI scores between women with HS and healthy controls.

§§Comparison of sexual activity dimension of 15-dimensions Health-Related Quality of Life questionnaire between patients with HS and healthy controls ($P < 0.001$) and between patients with HS and patients with psoriasis ($P = 0.03$).

¶¶Percentage of patients with a positive ("a lot/very much/a little") response to item 9 of DLQI (the highest compared to other dermatological diseases).

†††Prevalence of erectile dysfunction (ED) in men using the International Index of Erectile Function (IIEF) and its mean scores.

‡‡‡Prevalence of ED in men using the IIEF-5.

§§§Comparison of IIEF scores between men with HS and healthy controls.

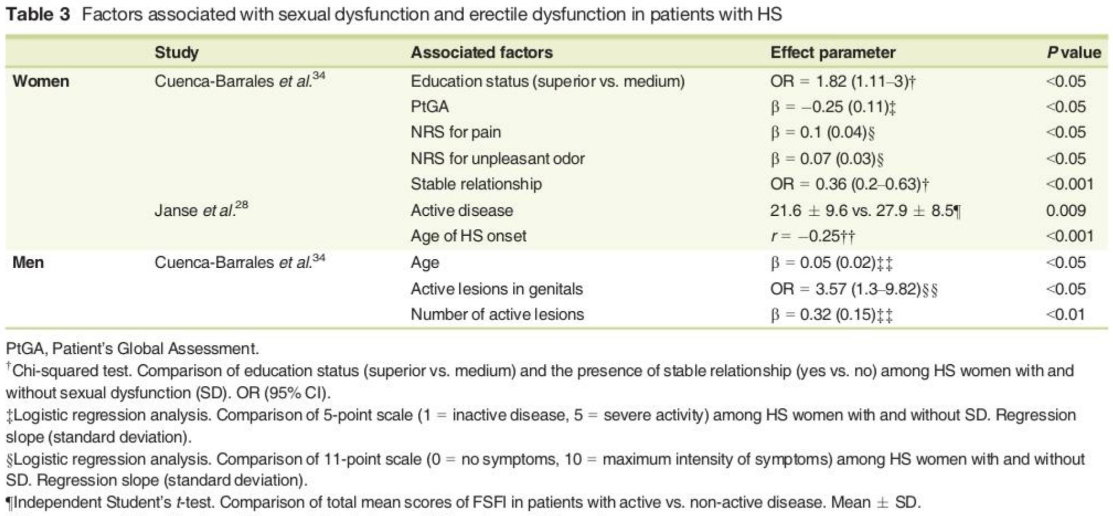


Table 3 Factors associated with sexual dysfunction and erectile dysfunction in patients with HS

	Study	Associated factors	Effect parameter	*P* value
Women	Cuenca-Barrales *et al.*[34]	Education status (superior vs. medium)	OR = 1.82 (1.11–3)†	<0.05
		PtGA	β = −0.25 (0.11)‡	<0.05
		NRS for pain	β = 0.1 (0.04)§	<0.05
		NRS for unpleasant odor	β = 0.07 (0.03)§	<0.05
		Stable relationship	OR = 0.36 (0.2–0.63)†	<0.001
	Janse *et al.*[28]	Active disease	21.6 ± 9.6 vs. 27.9 ± 8.5¶	0.009
		Age of HS onset	*r* = −0.25††	<0.001
Men	Cuenca-Barrales *et al.*[34]	Age	β = 0.05 (0.02)‡‡	<0.05
		Active lesions in genitals	OR = 3.57 (1.3–9.82)§§	<0.05
		Number of active lesions	β = 0.32 (0.15)‡‡	<0.01

PtGA, Patient's Global Assessment.

†Chi-squared test. Comparison of education status (superior vs. medium) and the presence of stable relationship (yes vs. no) among HS women with and without sexual dysfunction (SD). OR (95% CI).

‡Logistic regression analysis. Comparison of 5-point scale (1 = inactive disease, 5 = severe activity) among HS women with and without SD. Regression slope (standard deviation).

§Logistic regression analysis. Comparison of 11-point scale (0 = no symptoms, 10 = maximum intensity of symptoms) among HS women with and without SD. Regression slope (standard deviation).

¶Independent Student's *t*-test. Comparison of total mean scores of FSFI in patients with active vs. non-active disease. Mean ± SD.

††Pearson correlation. *R* values of the correlation between FSFI and age of HS onset.

‡‡Logistic regression analysis. Comparison of age and number of active lesions among HS men with and without SD. Regression slope (standard deviation).

§§Chi-squared test. Comparison of the presence of active lesions in genitals (yes vs. no) among HS women with and without SD. OR (95% CI).

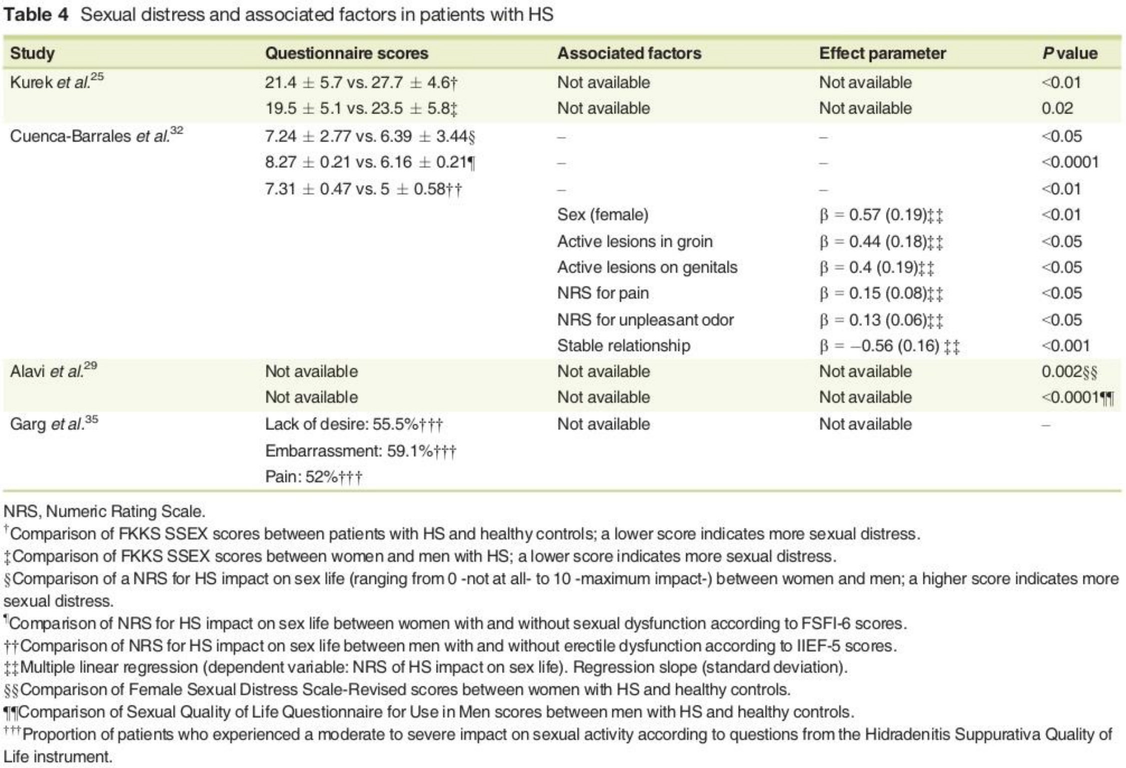


Table 4 Sexual distress and associated factors in patients with HS

Study	Questionnaire scores	Associated factors	Effect parameter	*P* value
Kurek *et al.*[25]	21.4 ± 5.7 vs. 27.7 ± 4.6†	Not available	Not available	<0.01
	19.5 ± 5.1 vs. 23.5 ± 5.8‡	Not available	Not available	0.02
Cuenca-Barrales *et al.*[32]	7.24 ± 2.77 vs. 6.39 ± 3.44§	–	–	<0.05
	8.27 ± 0.21 vs. 6.16 ± 0.21¶	–	–	<0.0001
	7.31 ± 0.47 vs. 5 ± 0.58††	–	–	<0.01
		Sex (female)	β = 0.57 (0.19)‡‡	<0.01
		Active lesions in groin	β = 0.44 (0.18)‡‡	<0.05
		Active lesions on genitals	β = 0.4 (0.19)‡‡	<0.05
		NRS for pain	β = 0.15 (0.08)‡‡	<0.05
		NRS for unpleasant odor	β = 0.13 (0.06)‡‡	<0.05
		Stable relationship	β = −0.56 (0.16) ‡‡	<0.001
Alavi *et al.*[29]	Not available	Not available	Not available	0.002§§
	Not available	Not available	Not available	<0.0001¶¶
Garg *et al.*[35]	Lack of desire: 55.5%††† Embarrassment: 59.1%††† Pain: 52%†††	Not available	Not available	–

NRS, Numeric Rating Scale.

†Comparison of FKKS SSEX scores between patients with HS and healthy controls; a lower score indicates more sexual distress.

‡Comparison of FKKS SSEX scores between women and men with HS; a lower score indicates more sexual distress.

§Comparison of a NRS for HS impact on sex life (ranging from 0 -not at all- to 10 -maximum impact-) between women and men; a higher score indicates more sexual distress.

¶Comparison of NRS for HS impact on sex life between women with and without sexual dysfunction according to FSFI-6 scores.

††Comparison of NRS for HS impact on sex life between men with and without erectile dysfunction according to IIEF-5 scores.

‡‡Multiple linear regression (dependent variable: NRS of HS impact on sex life). Regression slope (standard deviation).

§§Comparison of Female Sexual Distress Scale-Revised scores between women with HS and healthy controls.

¶¶Comparison of Sexual Quality of Life Questionnaire for Use in Men scores between men with HS and healthy controls.

†††Proportion of patients who experienced a moderate to severe impact on sexual activity according to questions from the Hidradenitis Suppurativa Quality of Life instrument.

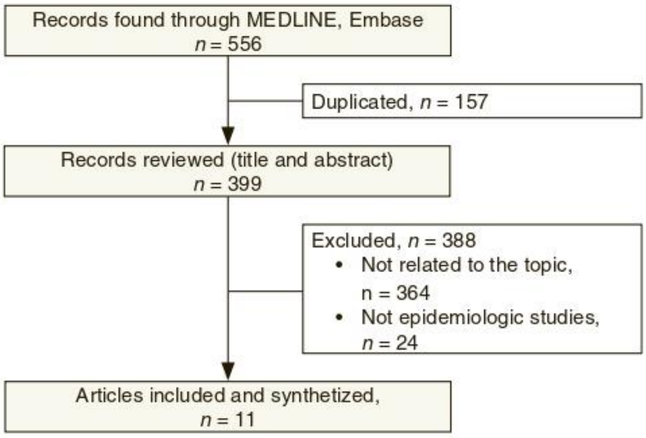


Figure 1 Search algorithm.

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6. DISCUSIÓN

6.1 METODOLOGÍA

6.1.1 Cuestionario online *crowdsourced*

Dado el carácter exploratorio de nuestra investigación, elegimos el diseño epidemiológico más factible y adecuado para responder a nuestras hipótesis: el transversal. Las características inherentes a este diseño nos impiden evaluar el sentido de las asociaciones encontradas. El abordaje de la sexualidad de los pacientes con HS mediante un cuestionario online *crowdsourced* presenta una serie de ventajas e inconvenientes.

La privacidad y anonimato que ofrece Internet son la principal ventaja, puesto que el abordaje de un tema como la sexualidad mediante entrevista clínica puede resultar complejo y embarazoso tanto para el paciente como para el médico(169). Además, el *crowdsourcing* permitió alcanzar a un amplio número de personas alrededor del mundo y reclutar un gran tamaño muestral (el mayor hasta la fecha en investigaciones sobre disfunción sexual en HS utilizando cuestionarios validados), lo cual resulta ventajoso en una investigación de características exploratorias como la nuestra y puede haber sido determinante a la hora de hallar factores de riesgo no identificados en estudios anteriores.

En cuanto a las desventajas, la disponibilidad del cuestionario quedó restringida a personas con acceso a Internet y que además estuvieran en contacto con grupos de apoyo, dado el canal de difusión a través de la asociación de pacientes ASENDHI. Los pacientes de edad avanzada, que podrían utilizar Internet con menos frecuencia, o aquellos con un estatus sociocultural bajo o con miedo a las nuevas tecnologías, podrían estar infrarrepresentados, así como aquellos que no tengan contacto con asociaciones de pacientes(170). Además, la participación fue voluntaria, por lo que los pacientes con una enfermedad más grave o aquellos más preocupados por su enfermedad, así como los que tuvieran dificultades sexuales, podrían haber sido más propensos a responder al cuestionario. Todo ello podría haber dado lugar a sesgos de selección. Sin embargo, las características basales de nuestra muestra, tanto sociodemográficas como clínicas, no difieren significativamente de las que se han comunicado en otras investigaciones en HS, tanto en estudios de base hospitalaria como poblacional(7-9).

Por otro lado, el diagnóstico de HS fue referido por los pacientes y no se pudo confirmar, así como las características clínicas de la enfermedad, lo que podría haber ocasionado sesgos de selección (en el caso del diagnóstico referido) y/o de clasificación (en el caso de las características clínicas referidas). No obstante, una población informada puede identificar adecuadamente la HS debido a sus manifestaciones clínicas aparentes y distintivas. Dada la difusión del cuestionario a través de una asociación de pacientes, es esperable que los participantes sufrieran realmente la enfermedad. Además, la mayoría de las preguntas reflejan la opinión subjetiva del paciente tal y como ocurre en la entrevista clínica habitual, y para el Hurley, un parámetro objetivo, existe una buena concordancia entre médicos y pacientes(156).

Por último, algunas de las preguntas empleadas en el cuestionario no estaban validadas. Sin embargo, no existen herramientas validadas para explorar los aspectos de la sexualidad y vida privada de los pacientes en cuanto a creencias y comportamientos recogidos en dichas preguntas. Éstas se crearon en base a la evidencia científica disponible y las guías clínicas para la evaluación de la función sexual(166), y posteriormente se presentaron a un grupo de pacientes con HS para valorar su comprensibilidad y pertinencia. Además, todas aquellas que no hacían referencia directa a la HS fueron comparadas con un grupo control de sujetos sanos. Recoger a estos controles a través de los propios socios de ASENDHI podría resultar en la selección de sujetos no representativos de la población general dado que podrían ser familiares o convivientes de los pacientes que se vieran afectados por su enfermedad. En contra de ello, observamos diferencias significativas entre las respuestas dadas por estos controles y los pacientes con HS.

6.1.2 Revisión sistemática de la literatura científica

Debido a la escasez de literatura científica sobre la materia de estudio, elegimos parámetros amplios para el algoritmo de búsqueda a fin de incluir todas las investigaciones al respecto. Sin embargo, dado que la sexualidad es una esfera compleja de la vida del ser humano con diversidad de abordajes y enfoques, no se puede descartar que hayamos obviado alguna investigación no incluida en las bases de datos analizadas. Nuestra revisión sistemática se ve limitada por no haber contactado con los autores de las investigaciones finalmente incluidas y por la calidad general de los estudios publicados. Algunas investigaciones no emplearon herramientas validadas para la evaluación de la función sexual, y la mayoría de las que lo hicieron no utilizaron los puntos de corte validados sino las puntuaciones de los cuestionarios. Además, muchos estudios pudieron sufrir sesgos de selección, al provenir las muestras de ámbito hospitalario o de asociaciones de pacientes, por lo que se podrían haber incluido los pacientes más graves. La mayoría de las investigaciones fueron transversales, por lo que la evidencia que aportan es limitada. Algunas investigaciones incluyeron un grupo de comparación, pero no pueden considerarse estudios de casos y controles de acuerdo con sus diseños.

6.2 RESULTADOS

6.2.1 Disfunción sexual y disfunción eréctil en pacientes con hidradenitis supurativa

En nuestra investigación observamos una alta prevalencia de disfunción sexual en las mujeres (51% de acuerdo con las puntuaciones del FSFI-6) y de disfunción eréctil en los hombres (60% de acuerdo con las puntuaciones del IIEF-5). Esta prevalencia es mayor que la observada en otras investigaciones empleando los mismos cuestionarios en población general(171-174), en población acudiendo a un programa de cribado de cáncer de próstata(175) o en pacientes con otras enfermedades dermatológicas como la psoriasis(176, 177).

Aunque en otras enfermedades dermatológicas, como la psoriasis, la afectación de varias zonas, como por ejemplo la anogenital, se ha relacionado con disfunción sexual(178), en la HS la afectación anogenital se ha relacionado con peor calidad de vida(139, 152), pero no con disfunción sexual. En nuestra investigación, encontramos una asociación entre la presencia de lesiones activas en los genitales y de disfunción eréctil, así como con el número de áreas afectadas por lesiones activas. En investigaciones previas sobre disfunción sexual y factores asociados en pacientes con HS, las muestras se reclutaron de servicios hospitalarios(138, 151, 152) y de una asociación de pacientes(152), sin diferencias importantes en las características basales de los pacientes con respecto a nuestra muestra, con la excepción de un estadio Hurley III más prevalente en nuestra investigación. Por lo tanto, probablemente estos hallazgos han sido posibles gracias a nuestro mayor tamaño muestral.

Los síntomas subjetivos y la actividad de la enfermedad también parecen causar un impacto importante sobre la función sexual. Otras enfermedades dermatológicas que causan síntomas genitales, como el liquen escleroso, se han asociado a peor función sexual, si bien la prevalencia de disfunción sexual no se determinó en estas investigaciones(179, 180). En nuestro estudio, observamos que la intensidad del dolor y del mal olor, así como la actividad de la enfermedad, estaban asociadas a disfunción sexual en las mujeres. Esta relación podría deberse a factores directamente relacionados con la naturaleza del acto sexual y/o a factores psicológicos que pueden estar asociados con la actividad de la enfermedad(139), e indican la necesidad de controlar los síntomas para mejorar la función sexual de los pacientes con HS. Desafortunadamente, no existen tratamientos definitivos y curativos para la HS. De hecho, no observamos que el tratamiento con antibióticos orales, anticonceptivos orales, adalimumab o infliximab se asociara a menor disfunción sexual. El manejo clínico de esta enfermedad es un reto, y los pacientes deben recibir terapias médicas/quirúrgicas individualizadas, dependiendo de las características de su enfermedad (carga inflamatoria, cicatrices, fenotipo, empeoramiento menstrual...), con el fin de aliviar sus síntomas, lograr el control de la enfermedad y mejorar su función sexual, entre otras esferas de su salud.

Otros factores como el consumo de antidepresivos o benzodiacepinas no se asociaron estadísticamente a disfunción sexual, lo que sugiere que el deterioro sexual en los pacientes con HS está directamente relacionado con los síntomas y la actividad de la enfermedad. Sin embargo, el consumo de benzodiacepinas mostró una tendencia a la significación estadística en las mujeres, apuntando a una potencial importancia de la ansiedad en la disfunción sexual. Teniendo en cuenta que no existen tratamientos curativos para la HS, y que los pacientes podrían sufrir disfunción sexual incluso cuando los síntomas están bajo control, debido a malas experiencias previas o a la ausencia de experiencia sexual en los más jóvenes, la ayuda psicológica puede tener una gran importancia en el manejo de estos pacientes.

Por otro lado, aunque en investigaciones previas en HS no se hubiera encontrado relación entre la función sexual y la presencia de pareja estable(138, 151, 152), nuestros resultados muestran que tener una relación estable es un importante factor protector de disfunción sexual en las mujeres con HS. Dado que tener una pareja estable se asocia con una menor cohibición y mayor facilidad para alcanzar el orgasmo tanto en hombres como en mujeres(181), es probable que, aparte de los factores orgánicos de la enfermedad comentados como los síntomas, la actividad de la enfermedad, las lesiones activas o la afectación de ciertas localizaciones, sentimientos de vergüenza, desconfianza, timidez y rechazo influyan sobre la disfunción sexual, los cuales pueden ser mitigados por el clima de confianza que se genera en una relación estable.

Un nivel educativo más elevado también se asoció a disfunción sexual en las mujeres en nuestra investigación, tal y como ha sido comunicado previamente en otros estudios en población general(182). Esta asociación podría explicarse por los diferentes estilos de vida y expectativas sobre la sexualidad entre los distintos niveles educativos, que pueden conducir a sentimientos de fracaso y frustración.

Por último, observamos una asociación positiva entre la edad y la disfunción eréctil, como ocurre en la población general debido a factores como, por ejemplo, la disminución de los niveles de dehidroepiandrosterona y la aterosclerosis asociada al envejecimiento(183).

6.2.2 Distrés de los pacientes con hidradenitis supurativa en sus relaciones sexuales

La NRS de impacto de la enfermedad en las relaciones sexuales reveló niveles altos de distrés sexual en los pacientes con HS, siendo estos niveles mayores en las mujeres, lo cual concuerda con investigaciones previas en HS que indican mayor distrés sexual en mujeres que en hombres(138), al igual que ocurre en otras enfermedades dermatológicas como la psoriasis(184). En HS, estas diferencias se han atribuido a factores como un debut de la enfermedad más temprano en mujeres (en nuestra muestra el inicio de la HS fue 4,5 años anterior en las mujeres), e incluso a factores culturales y a una mayor respuesta emocional y neuroendocrina a la desfiguración(138). También se ha relacionado con la mayor frecuencia de lesiones por debajo del abdomen en las mujeres(138), aunque en nuestra muestra la única localización infraabdominal más frecuente en las mujeres fue las ingles, siendo más frecuente en los varones la afectación de las regiones glútea y perianal.

Aparte del sexo femenino, otros factores de riesgo de padecer mayor distrés sexual estuvieron relacionados principalmente con la actividad y los síntomas de la enfermedad, al igual que ocurría en el caso de la disfunción sexual y la disfunción eréctil. De este modo, la presencia de lesiones activas en ingles y genitales y la intensidad del dolor y del mal olor se relacionaron con mayor distrés sexual, resaltando una vez más la importancia del tratamiento para el control de la enfermedad. Asimismo, la presencia de pareja estable fue nuevamente un importante factor protector.

Hubo otros factores que mostraron tendencia hacia la significación estadística: 1) PtGA, que señala la importancia de la actividad de la enfermedad en el distrés sexual y la necesidad de controlar la carga inflamatoria; 2) el tabaquismo, probablemente porque se relaciona con una mayor actividad de la enfermedad(29); 3) el tiempo recibiendo atención médica, ya que refleja el tiempo de evolución de la enfermedad, con un deterioro acumulado a lo largo de la vida(185); y 4) el tratamiento con adalimumab, probablemente porque en nuestra muestra es un mejor predictor de la gravedad/de la carga inflamatoria que el estadio de Hurley, ya que los pacientes tratados con adalimumab son los más graves.

Por último, observamos una buena correlación entre las puntuaciones en la NRS de impacto de la HS en la vida sexual y las del FSFI-6 y el IIEF-5, lo que indica una asociación entre la afectación subjetiva y objetiva de la esfera sexual de los pacientes. Sin embargo, a pesar de esta concordancia, los análisis mediante curvas ROC mostraron que la NRS de impacto de la HS en la vida sexual no era una buena herramienta para evaluar la disfunción sexual en las mujeres ni la disfunción eréctil en los hombres, porque los puntos de corte no alcanzaron una sensibilidad ni una especificidad aceptables.

6.2.3 Creencias, comportamientos y necesidades de los pacientes con hidradenitis supurativa en sus relaciones sexuales

Las respuestas a las preguntas elaboradas específicamente para este cuestionario mostraron que la HS tiene una repercusión importante, no reconocida e incomprendida en la sexualidad de los pacientes que debe ser atendida.

Muchos pacientes percibían dificultades en sus relaciones sexuales. Varios tratamientos para la HS pueden causar dificultades en la vida sexual, como los procedimientos quirúrgicos, los tratamientos tópicos o las curas locales para las lesiones. En nuestra muestra observamos un porcentaje menor de pacientes que percibía dificultades sexuales debido al tratamiento de la HS que Janse *et al.*(152), quizá porque su muestra procedía en parte de ámbito hospitalario, con tratamientos que por tanto podían ser más complejos. Los síntomas también causaban dificultades en la vida sexual de los pacientes. La supuración fue identificada como el síntoma que más interfería en las relaciones en los varones, mientras que el dolor lo fue en las mujeres. Esto puede deberse a que las mujeres tienen una mayor percepción del dolor y un mayor riesgo de desarrollo de dolor crónico, en base a diversos mecanismos, como la actividad de opioides endógenos, hormonas sexuales, factores genéticos o factores psicosociales(186-188).

Más de 2/5 de los participantes se consideraban menos atractivos de lo normal, y casi la mitad afirmaba tener miedo al rechazo y a la reacción de su pareja sentimental/sexual. Estos porcentajes fueron mayores que los encontrados en los controles sanos. Los pacientes más jóvenes tenían mayor riesgo de experimentar estos sentimientos, probablemente porque aún no han desarrollado mecanismos de afrontamiento. El bajo atractivo percibido y el miedo al rechazo posiblemente se deban al impacto de la HS en la imagen corporal(189), al igual que ocurre en la psoriasis(190). La relación observada entre el miedo al rechazo y el número de zonas afectadas por las cicatrices, así como la tendencia a la significación del Hurley referido, está en concordancia con ello. Al igual que en los pacientes quemados, las alteraciones de la imagen corporal pueden deberse a estrategias de afrontamiento disfuncionales, y una intervención adecuada a este nivel podría conducir a una mejora de estos sentimientos(191). Estas alteraciones de la imagen corporal se asocian a un deterioro sexual debido a cohibición y timidez, generando una menor excitabilidad y capacidad de alcanzar el orgasmo, independientemente del sexo y de la existencia o no de una relación estable(181). Sin embargo, observamos que la ausencia de relación estable se relaciona con un mayor miedo al rechazo y con un menor atractivo percibido, probablemente porque la confianza generada en una relación podría aliviar los sentimientos negativos previamente descritos, con una menor cohibición y dificultad para alcanzar el orgasmo tanto en hombres como en mujeres(181).

Aunque las alteraciones de la imagen corporal tienen un menor impacto en la salud sexual de las personas con pareja estable(181), pueden influir en la calidad de la relación percibida por el sujeto(192). Así, aunque alrededor del 70% de los pacientes refirieron sentir apoyo de sus parejas y en torno a la mitad ayuda para superar el miedo al rechazo y ayuda con las curas en las zonas íntimas, alrededor de 2/3 pensaba que la HS tenía una influencia negativa en su relación, siendo en 1/3 de los casos una influencia alta o muy alta. Estos datos coinciden con estudios previos que muestran una menor calidad de vida en los convivientes de los pacientes con psoriasis(193) y HS(194, 195). En otra investigación se observó una mayor prevalencia de violencia de género en pacientes con HS que en pacientes con acné, pero no un mayor riesgo de agresión sexual(196), lo que indica un posible deterioro de la vida en pareja. Por tanto, la enfermedad parece tener un impacto significativo en las relaciones de pareja. La actividad de la enfermedad se relacionó con este impacto, y el número de áreas afectadas por lesiones activas mostró tendencia hacia la significación estadística, por lo que un tratamiento individualizado adecuado podría mejorar también las relaciones de pareja de los pacientes.

En cuanto a los pacientes sin relación estable, observamos que aquellos que presentaban factores de riesgo de disfunción sexual, disfunción eréctil o distrés sexual, así como los que tenían un mayor estadio de Hurley, no tenían más probabilidad de estar solteros. Entre las mujeres solteras con HS, los porcentajes que sentían miedo al rechazo cuando conocían a una posible pareja sexual y que preferían no conocer a nadie a causa de la enfermedad eran mayores que en los hombres, aunque las diferencias no fueron estadísticamente significativas. Por otro lado, sí fueron significativas las diferencias entre los pacientes y los controles sanos en cuanto a los sentimientos de ilusión o miedo al rechazo al conocer a gente nueva. Más del 90% de los pacientes solteros pensaban que la HS influía en sus posibilidades para encontrar pareja estable/esporádica, afirmando más de la mitad que influía "bastante" o "mucho", siendo este porcentaje, de nuevo, mayor en las mujeres. Estos datos son preocupantes y reflejan el profundo impacto de la enfermedad en la sexualidad y en la confianza de los pacientes. Varios estudios indican que los adultos jóvenes con enfermedades crónicas tienen menos probabilidades de casarse(197-199). Parece por tanto que las personas con enfermedades crónicas tienen menos confianza en sí mismas, lo que disminuye sus posibilidades de encontrar pareja, entrando en un estado mantenido de distrés o angustia sexual.

En cuanto a la orientación sexual, nuestra investigación es la primera que la evalúa en pacientes con HS. No observamos ninguna diferencia en comparación con los controles sanos, tal y como se ha comunicado en investigaciones previas en psoriasis(200, 201).

Por último, cabe destacar que casi 1 de cada 3 participantes compartiría sus problemas sexuales con su dermatólogo, y casi 2 de cada 5 con un psicólogo o sexólogo. Según Janse *et al.*(152), sólo el 6% de los pacientes con HS refería haber recibido suficiente atención de su médico sobre sus problemas sexuales, quizás debido entre otros factores a la complejidad de estos, la vergüenza de abordar el tema, la dificultad de su tratamiento y la falta de tiempo. Dada la profunda repercusión de la HS en la sexualidad, sería recomendable realizar un cribado rutinario de estos pacientes en busca de problemas sexuales, ofreciéndoles atención en unidades especializadas si así lo requieren. Además, es necesario crear un ambiente de confianza con estos pacientes, ya que 1/3 referían no querer hablar de sus problemas sexuales, en contraste con más del 95% de los controles sanos, que sí hablarían de ellos. Parece que los pacientes se sienten tan avergonzados por su enfermedad que prefieren no compartir sus problemas, por lo que es importante crear una relación de confianza que les permita expresar libremente sus preocupaciones.

6.2.4 Revisión de la evidencia científica disponible sobre hidradenitis supurativa y sexualidad

En nuestra revisión sistemática encontramos un interés creciente en la investigación de la sexualidad de los pacientes con HS, pues todos los estudios epidemiológicos al respecto se habían publicado desde 2013 en adelante. La mayoría de los estudios eran transversales, algunos con grupo de comparación, lo que limita la calidad de la evidencia científica generada. Además, muchas de las investigaciones se llevaron a cabo en el ámbito hospitalario, por lo que los pacientes incluidos podrían no ser representativos del conjunto general de pacientes con HS. En algunos casos, no se emplearon herramientas validadas para la evaluación de la función sexual, sino preguntas específicas sobre sexualidad dentro de cuestionarios globales de calidad de vida, como el *Dermatology Life Quality Index* (DLQI), el *15D Health-Related Quality of Life* (15D HRQoL) o el *Hidradenitis Suppurativa Quality of Life Instrument* (HiSQOL). Aunque el uso de estas preguntas podría resultar útil para el cribado de problemas sexuales, los cuestionarios no han sido diseñados para ello y podrían obviar casos de disfunción sexual que los pacientes no relacionen de manera directa con su patología dermatológica, por lo que es recomendable el uso de herramientas validadas(202, 203).

La prevalencia de disfunción sexual y de disfunción eréctil en pacientes con HS se situó entre el 50% y el 60%(152, 204). En cuanto a la incidencia de disfunción sexual, en un estudio de cohortes retrospectivo de base poblacional basado en registros (el único de los estudios incluidos cuyo diseño no era transversal) se determinó que era de 1,7% a lo largo de 5 años en pacientes con HS, con una odds de incidencia un 38% mayor que en población sin HS (OR 1,38, IC 95% 1,28-1,48, p<0,001). La HS se asoció con una mayor incidencia de disfunción sexual en el grupo de edad más joven de los estudiados (18-44 años)(205), quizás por ser un grupo de edad sexualmente más activo y con mayores expectativas que los otros. Los estudios con grupos de comparación no utilizaron los puntos de corte validados de las diferentes herramientas empleadas para evaluar la disfunción sexual o la disfunción eréctil. El uso de resultados nominales ofrece resultados clínicamente relevantes, pero requiere tamaños de muestra mayores para observar diferencias estadísticamente significativas. Por el contrario, la relevancia clínica de una puntuación media en un cuestionario es en la mayoría de las situaciones muy limitada, pero las diferencias estadísticamente significativas requieren un número menor de sujetos. Por tanto, es recomendable que se comuniquen siempre los resultados nominales en base a los puntos de corte establecidos, pudiendo acompañarse también estos resultados de las puntuaciones medias de los cuestionarios.

El mecanismo exacto por el que se producen la disfunción sexual y la disfunción eréctil en pacientes con HS permanece sin clarificar. ¿Es consecuencia de las lesiones y de los síntomas de la enfermedad? ¿Se debe a otros factores orgánicos como la presencia de mediadores inflamatorios o ciertas comorbilidades como la diabetes mellitus o la hipertensión arterial, de mayor prevalencia en la HS y asociadas con disfunción sexual y disfunción eréctil? ¿Tienen un papel relevante los trastornos del estado de ánimo como la depresión y la ansiedad? Posiblemente, la génesis de la disfunción sexual y eréctil de estos pacientes sea una conjunción de todos/varios de estos factores, en función de cada caso. La presencia de lesiones activas en genitales en los hombres y la intensidad de síntomas desagradables como el dolor y el mal olor en las mujeres se asociaron a disfunción sexual(204). La actividad de la enfermedad también se relacionó con disfunción sexual(152, 204), lo que puede explicarse porque las citoquinas proinflamatorias y los estados de inflamación sistémica pueden alterar los niveles de hormonas sexuales y la función del endotelio vascular(206). Por otro lado, se encontró una mayor incidencia de disfunción sexual en pacientes con HS con diagnóstico tanto de depresión como de ansiedad(205). Sin embargo, debido al diseño de los estudios, no es posible establecer una cadena de causalidad clara, ya que, por ejemplo, la disfunción sexual/eréctil puede ser tanto causa como consecuencia de trastornos del estado de ánimo como depresión o ansiedad. Otros factores asociados a disfunción sexual fueron el nivel educativo elevado, la ausencia de pareja estable y un inicio temprano de la enfermedad en las mujeres y el envejecimiento en los varones(152, 204).

La afectación de la sexualidad de estos pacientes se ve reflejada en su calidad de vida. Alavi *et al.*(151) demostraron que en torno al 50% de los cambios en el DLQI se debían a la presencia de disfunción sexual, disfunción eréctil y/o distrés sexual, lo que da una idea de la magnitud del impacto negativo que tienen estas alteraciones sobre la salud del sujeto. Otros estudios encontraron una asociación entre las puntuaciones del DLQI y del FSFI en las mujeres(138, 152), aunque no se evaluó la influencia en sí de la HS en las puntuaciones del DLQI, por lo que, dado que la HS puede ser causa tanto de disminución en la calidad de vida como de dificultades en la esfera sexual, nuevamente y debido al diseño de los estudios la causalidad no puede establecerse con claridad.

La revisión sistemática también mostró que los pacientes con HS sufren mayor distrés en sus relaciones sexuales que la población sana(138, 151). Este impacto parece ser mayor en las mujeres con HS(138, 207), al igual que ocurre en la psoriasis(208). Algunos factores, como los cambios en la imagen corporal, pueden afectar más a las mujeres a este nivel(209), ya que sus mecanismos de excitación y función sexual son más complejos. Las diferencias por sexos en cuanto a notificación de síntomas, debidas a los diferentes roles y responsabilidades sociales, a factores psicosociales y culturales, y a diferencias fisiológicas, como la mayor sensibilidad de las mujeres al entorno externo, también pueden desempeñar un papel relevante, con independencia de otros factores(210). También se encontró una asociación entre el distrés sexual y factores como la presencia de lesiones activas en ingles y genitales, la intensidad del dolor y el mal olor y la ausencia de una relación estable, lo que pone de manifiesto una vez más la importancia de los factores orgánicos y de las parejas en la sexualidad de los pacientes(207).

A pesar de haberse observado estas alteraciones en la sexualidad de los pacientes en relación con la actividad de la enfermedad, la presencia de lesiones activas en ciertas localizaciones y la intensidad de los síntomas, no existen investigaciones sobre la posible mejora de la función sexual en los pacientes con HS tras el tratamiento biológico/inmunosupresor sistémico, a diferencia de lo que ocurre en la psoriasis(178, 184). Sólo en una investigación se evaluaron los cambios en la función sexual después de procedimientos quirúrgicos (no especificados) con anestesia general en pacientes con HS, pero no se encontró una clara mejoría. El tiempo medio de curación de la herida quirúrgica fue de casi 3 meses, y la función sexual se evaluó 3 y 6 meses después de la cirugía(211). El tratamiento quirúrgico, debido a sus características, puede tardar más tiempo en mejorar actividades vitales complejas, como es la función sexual. Además, no se informó sobre otros factores que pueden influir en la función sexual, como la gravedad y la actividad de la enfermedad, los síntomas o la presencia pareja estable.

Por último, los pacientes aquejaron una falta de atención a sus problemas sexuales por parte de los médicos, y pensaban que éstos debían centrarse más en esta esfera de su salud(152). Los dermatólogos son los principales especialistas responsables del cuidado de los pacientes con HS, por lo que deben prestar atención a estos problemas para poder manejar la enfermedad con un enfoque holístico, ya que actualmente todavía no es posible lograr una cura o un control completo de la HS en la mayoría de los pacientes. Por ello, se debe facilitar que expresen libremente las preocupaciones de su vida sexual, iniciar el tratamiento según el origen del problema y remitir a los pacientes a unidades especializadas cuando sea necesario. La presencia de alteraciones sexuales podría incluso considerarse un criterio de gravedad a la hora de elegir el tratamiento.

7. PERSPECTIVAS

Esta Tesis Doctoral es el punto de partida para la realización de futuras investigaciones acerca de la sexualidad en pacientes con HS. Es primordial llevar a cabo estudios longitudinales de carácter prospectivo para poder analizar con precisión los mecanismos que subyacen a la disfunción sexual en estos pacientes. El papel que juegan factores psicológicos y trastornos del estado de ánimo, así como ciertas comorbilidades, debe ser dilucidado. También es fundamental analizar la posible mejoría de la función sexual de los pacientes tras el tratamiento de la HS, en vista del impacto que causan la actividad de la enfermedad, la presencia de lesiones activas en ciertas localizaciones y los síntomas. El rol de las parejas debe ser determinado, dada la gran importancia que tienen en la sexualidad de los pacientes, y sería recomendable analizar hasta qué punto la enfermedad afecta a la salud sexual de las parejas (estables o esporádicas), si sus deseos se ven satisfechos o si una falta de deseo sexual puede provocar una afectación de la sexualidad de los pacientes.

Todo ello permitirá establecer con un nivel de evidencia científico adecuado si es necesario hacer un cribado rutinario de la función sexual de los pacientes con HS, si la disfunción sexual puede considerarse un criterio a la hora de iniciar un determinado tratamiento como por ejemplo fármacos biológicos, y el potencial beneficio del apoyo psicológico tanto para pacientes como para sus parejas. Mejorar la salud sexual de los pacientes implica mejorar su calidad de vida y dar un enfoque holístico a la atención sanitaria.

7. PERSPECTIVES

This Doctoral thesis is the starting point for future research on sexuality in patients with HS. It is essential to carry out prospective longitudinal studies to be able to accurately analyse the mechanisms underlying sexual dysfunction in these patients. The role of psychological factors and mood disorders, as well as certain comorbidities, needs to be clarified. It is also crucial to analyse the possible improvement in sexual function in patients after treating the disease, in view of the impact of disease activity, the presence of active lesions in certain locations and symptoms. The role of partners must be determined, given the great importance they have in patients' sexuality, and it would be advisable to analyse to what extent the disease affects the sexual health of partners (stable or sporadic), whether their desires are fulfilled or whether an unwilling attitude can lead to sexual impairment in patients with HS.

This will allow us to establish with an adequate level of scientific evidence whether there is a need for routine screening of sexual function in patients with HS, whether sexual dysfunction can be considered a criterion for initiating a particular treatment such as biologic drugs, and the potential benefit of psychological support for both patients and their partners. Improving the sexual health of patients involves improving their quality of life and a holistic approach to healthcare.

8. CONCLUSIONES

OBJETIVO 1

- La frecuencia de disfunción sexual en las mujeres y de disfunción eréctil en los varones con HS es elevada.
- Los factores clínico-epidemiológicos asociados a la presencia de disfunción sexual en las mujeres se relacionan con los síntomas y la gravedad de la enfermedad. La presencia de pareja estable es un factor protector.
- Los factores clínico-epidemiológicos asociados a disfunción eréctil en los varones se relacionan con el envejecimiento y con la distribución y la gravedad de la enfermedad.

OBJETIVO 2

- Los pacientes con HS presentan altos niveles de distrés sexual.
- Los factores clínico-epidemiológicos asociados con un mayor distrés sexual se relacionan con la distribución de la enfermedad, los síntomas y el sexo femenino. La presencia de pareja estable es un factor protector.
- Existe una correlación entre los niveles de distrés sexual y la presencia de disfunción sexual y disfunción eréctil.

OBJETIVO 3

- Los pacientes con HS sufren con frecuencia síntomas de miedo al rechazo de sus parejas sexuales y un bajo atractivo percibido, experimentando estos sentimientos en mayor proporción que los sujetos sanos.
- La HS causa un importante impacto en las relaciones de pareja, en parte debido a la gravedad de la enfermedad.
- Un alto número de pacientes solteros consideran que la HS dificulta sus posibilidades de encontrar pareja sentimental/sexual.
- A un elevado número de pacientes les gustaría compartir sus problemas sexuales con personal sanitario.

OBJETIVO 4

- Los resultados de la revisión sistemática indican una elevada frecuencia de disfunción sexual, disfunción eréctil y distré*s* sexual en los pacientes con HS, siendo mayor que en la población general.
- Aunque se han identificado factores de riesgo, existe una falta de estudios longitudinales prospectivos que permita establecer los mecanismos subyacentes a esta disfunción sexual, el rol de los factores psicológicos y los trastornos del estado de ánimo y la posible mejoría de la función sexual tras el tratamiento de la enfermedad.

GLOBAL

La sexualidad es una necesidad desatendida de los pacientes con HS. Es frecuente la presencia de una profunda afectación de la función sexual y de altos niveles de distrés en relación a diversas características clínico-epidemiológicas. La enfermedad limita las relaciones personales, tanto de las personas en pareja como de los solteros. Con frecuencia, los pacientes tienen la necesidad de compartir sus problemas sexuales con personal sanitario. El dermatólogo es el profesional sanitario central en la atención de esta enfermedad, por lo que debe considerar la afectación de esta dimensión de la calidad de vida y coordinar el abordaje del problema.

8.CONCLUSIONS

OBJECTIVE 1

- The frequency of sexual dysfunction in women and erectile dysfunction in men with HS is high.
- The clinical-epidemiological factors associated with sexual dysfunction in women are related to the symptoms and severity of the disease. The presence of a stable partner is a protective factor.
- The clinical-epidemiological factors associated with erectile dysfunction in men are related to aging and to the distribution and severity of the disease.

OBJECTIVE 2

- Patients with HS have high levels of sexual distress.
- The clinical-epidemiological factors associated with greater sexual distress are related to the distribution of the disease, symptoms and female sex. The presence of a stable partner is a protective factor.
- There is a correlation between the level of sexual distress and the presence of sexual dysfunction and erectile dysfunction.

OBJECTIVE 3

- Patients with HS frequently suffer from symptoms of fear of rejection by sexual partners and low perceived attractiveness, experiencing these feelings in greater proportion than healthy people.
- HS has a major impact on relationships, partly due to the severity of the disease.
- A large number of single patients feel that HS decreases their possibilities of finding a sentimental/sexual partner.
- A considerable number of patients would like to share their sexual problems with healthcare staff.

OBJECTIVE 4

- The results of the systematic review indicate a high frequency of sexual dysfunction, erectile dysfunction and sexual distress in patients with HS, with higher figures than in the general population.
- Although risk factors have been identified, there is a lack of prospective longitudinal studies to establish the mechanisms underlying this sexual dysfunction, the role of psychological factors and mood disorders and the possible improvement of sexual function after treatment.

OVERALL

Sexuality is an unmet need in patients with HS. The presence of profound impairment to sexual function and high levels of distress in relation to various clinical-epidemiological features is frequent. The disease limits personal relationships, both in patients with a partner and in single patients. Patients often feel the need to share their sexual problems with healthcare professionals. The dermatologist is the central healthcare professional in the management of this disease and should therefore consider the impact of this dimension of quality of life and coordinate the approach to the issue.

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GLOSARIO DE ABREVIATURAS

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15D HRQoL: 15D Health-Related Quality of Life

APP: Amyloid precursor protein

ASENDHI: Asociación de Enfermos de Hidrosadenitis

ASEX: Arizona Sexual Experience Scale

BLC: B lymphocyte chemoattractant

BMI: Body mass index

BSA: Body Surface Area

CCL 3, 5, 27: Chemokine ligand 3, 5, 27

CEBM: Centre for Evidence-Based Medicine

CI: Confidence interval

CIE-10: Clasificación Internacional de Enfermedades, 10ª edición

CXCL2: Chemokine ligand 2

DAMPs: Damage-associated molecular patterns

DLQI: Dermatology Life Quality Index

DM2: Diabetes mellitus tipo 2

DSM-V: Diagnostic and Statistical Manual of Mental Disorders

ED: Erectile dysfunction

EQ-5D: EuroQol-5 Dimensions questionnaire

Fenotipos LC1, 2 y 3: Fenotipos latent class 1, 2 y 3

FKKS SSEX: Frankfurt Self-Concept Scale for Sexuality

FSDS-R: Female Sexual Distress Scale-Revised

FSFI: Female Sexual Function Index

GP: General practitioner

HADS: Hospital Anxiety and Depression Scale

hBD: human Beta-defensin

HBP: High blood pressure

HiSCR: Hidradenitis Suppurativa Clinical Response

HiSQOL: Hidradenitis Suppurativa Quality of Life Instrument

HLA: Human Leukocyte Antigen

HS: Hidradenitis supurativa

IBD: Inflammatory bowel disease

IBM: International Business Machines Corporation

IC: Intervalo de confianza

ICAM-1: Intercellular adhesion molecule 1

ICD-10: International Classification of Diseases, 10th revision

IFN: Interferón

IHS4: International Hidradenitis Suppurativa Severity Score System

IIEF: International Index of Erectile Function

IL: Interleucina

IL-6R: Interleukin 6 receptor

IL-36RA: Interleukin 36 receptor antagonist

IMC: Índice de masa corporal

IR: Interquartile range

IRB: Institutional review board

LC2: Lipocalin-2

Linfocitos Th: Linfocitos T Helper

MMP2: Matrix metalloproteinase-2

mTOR: mammalian target of rapamicyn

NCSTN: Nicastrina

NRS: Numeric Rating Scale

OMS: Organización Mundial de la Salud

OR: Odds ratio

PAMPs: Pathogen-associated molecular patterns

PAPASH: artritis piógena, pioderma gangrenoso, acné e hidradenitis supurativa

PASH: pioderma gangrenoso, acné e hidradenitis supurativa

PASS: pioderma gangrenoso, acné conglobata, hidradenitis supurativa y espondiloartropatía axial

PCR: Proteína C reactiva

PG: Pioderma gangrenoso

PGE2: Prostaglandina E2

PsAPASH: artritis psoriásica, pioderma gangrenoso, acné e hidradenitis supurativa

PSTPIP1: Proline-serine-threonine phosphatase interacting protein 1

PtGA: Patient´s Global Assessment

SAPHO: sinovitis, acné, pustulosis, hiperostosis y osteítis

SD: Sexual dysfunction (excepto en el epígrafe 5.2 donde significa sexual distress)

SPSS: Statistical Package for the Social Sciences

SQoLM: Sexual Quality of Life Questionnaire for Use in Men

sTNFR: soluble Tumour Necrosis Factor Receptor

TGF: Transforming growth factor

TLR: Toll-like receptor

TNF: Tumour Necrosis Factor

UCLA: University of California, Los Angeles

VSG: Velocidad de sedimentación globular

WASp: Wiskott-Aldrich syndrome protein

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