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Original Research

Evaluation of sex hormone profiles and seminal fluid analysis in psoriatic patients and their correlation with psoriasis severity

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Abstract

Background and objective: Psoriasis is a chronic inflammatory skin condition characterized by thick silvery plaques, commonly involving the elbow, knees, lower back, and scalp. Psoriasis also affects the reproductive systems of patients. Males with untreated psoriasis are at risk of impaired fertility due to chronic systemic inflammation, which might affect the hormonal profile and sexual accessory glands. In females, having psoriasis does not affect the chances of getting pregnant. This study aims to assess the effect of psoriasis, as a chronic inflammatory condition, on sex hormone profiles and seminal fluid parameters. **Methods**: 87 male patients aged 18−50 with psoriasis who fulfilled the inclusion criteria were included in the study and matched with healthy controls. Demographic and clinical data, including age, severity, duration, and body mass index (BMI) were recorded. All patients underwent a complete physical exam, including a skin and andrological exam, in addition to ultrasound scrotum and seminal fluid analysis. Blood sample tests were conducted for a complete hormonal profile, including luteinizing hormone (LH), follicular stimulating hormone (FSH), testosterone, and estradiol. **Results**: The mean age of the case group was 39.5 $\pm$ 5.6 years, and the mean BMI was 24.0 $\pm$ 2.2. The mean duration of psoriasis was 6.5 $\pm$ 3.5 years. The mean levels of testosterone and LH of cases were lower than those of controls, whereas FSH and estradiol were abnormally higher among case groups. Sperm concentration, normal sperm motility, and normal sperm morphology were also found to be lower than in the case group. Age, psoriasis area, and severity index (PASI) scores were significant predictors of sperm concentration (P = 0.000). The BMI was negatively correlated with sperm concentration (−0.249, P = 0.01), motility (−0.198, P = 0.05), and morphology (−0.205, P = 0.05). A negative correlation was found between the PASI score and sperm concentration (−0.519, P = 0.01). **Conclusion**: The evaluation of seminal fluid analysis and hormone profiles among psoriasis patients showed marked variability. However, it was evident that the levels of sex hormones and seminal parameters were lower among patients with psoriasis than the healthy controls; this may indicate the possibility of developing sexual dysfunction and infertility among patients with untreated psoriasis. The level of estradiol was found to be abnormally high among psoriasis cases, which may account for a possible compensatory mechanism in ongoing sexual dysfunction among psoriasis patients.

Keywords: Psoriasis; Semen analysis; Sexual functions; Sex hormones

1. Introduction

Psoriasis is a chronic relapsing and recurrent autoimmune disease that affects the skin and joints [1,2]. It is a worldwide disease affecting approximately 2% of the population [3], and more than 50% of psoriatic patients experience the disease after age 40 [4].

Psoriasis dramatically impairs quality of life and well-being, and in addition to skin manifestations, it carries a variety of emotional and psychological consequences [5].

The disease has an unpredictable course with variable features, including its distribution, course, and severity [2]. A psoriatic lesion is typically a well-demarcated circular silver-to-white plaque or red papule with a scaly surface [6], and joint involvement may coexist, resulting in psoriatic arthritis. It is evident now that psoriasis carries a multisystemic pathology that affects many areas other than the skin, including the eyes, cardiovascular system, renal system, reproductive system, and psychological states [7]. Additional epidemiologic reports have suggested that immune-mediated inflammation, such as in psoriasis, is associated with other comorbidities, including metabolic syndrome, cardiovascular disease, diabetes mellitus, and liver disease [8].

There is growing concern that methotrexate, used as a treatment for psoriasis and other systemic diseases, is involved in developing infertility [9]. Recent reports have emphasized that being in a state of chronic inflammation, such as psoriasis, may lead to the development of male infertility, and the effect of tumor necrosis factor (TNF) indicates the pathology behind this, a cytokine that plays an essential role in both the pathogenesis of psoriasis and the regulation of the spermatogenesis process, as it is secreted

by germ cells [9–11]. It has been found that the level of TNF-α found in seminal plasma is low in normal physiologic status, but a marked increase in the level of this cytokine is noted in some inflammatory conditions, which in turn alters the genomic constitution and integrity of spermatozoa [12,13]. Notably, other inflammatory cytokines (IFN-γ) and proinflammatory cytokines (TNF-α, IL-6, and IL-1) have been found to play a significant role in the inhibition of reproductive functions during such conditions in the seminal fluid of patients with these diseases. This inhibition is mainly considered to occur at the hypothalamic-pituitary axis [14]. Another effect that may compound this negative outcome and impact male fertility is that serum testosterone levels are significantly lower during systemic inflammation due to their inhibitory effect on Leydig cells [15–17].

2. Materials and methods

2.1 Study design

This is a matched case-control study conducted in Jerash governmental hospital, affiliated with the Faculty of Medicine, Yarmouk University, from April 2018 to July 2020. An ethical approval number 12/1/2285 was provided by the institutional review board at King Abdullah University Hospital.

2.2 Population

The study included male patients with psoriasis, aged between 18 and 50 years, who attended the dermatology clinic.

2.3 Inclusion and exclusion criteria

The included subjects had to have not been receiving topical treatment for at least eight weeks or active systemic treatment, including phototherapy, in the three months before enrollment; this applies to cases and controls. The study excluded patients with chronic medical conditions (e.g., diabetes mellitus and hypertension), smokers, alcoholics, and those with a history of infertility, as well as patients with testicular diseases (e.g., cryptorchidism, orchitis, scrotal trauma, genital tumors, and gross varicocele).

2.4 Methods

Of the 430 male psoriasis patients who attended the dermatology clinic during the study period, only 87 patients who fulfilled the inclusion criteria and agreed to participate in the study were assigned to the case group. Another 87 healthy individuals who were admitted for follow-up for various dermatological reasons were matched with the cases, according to age and sex, and considered controls. Information about age, BMI, psoriasis severity (using PASI score), and disease duration were recorded. The psoriasis area and severity index (PASI) is a quantitative rating score for measuring the severity of psoriatic lesions, based on area coverage and plaque appearance, including erythema, thickness, and scaling on the head, trunk, and upper and lower limbs, respectively. The maximum score was 72, and the minimum was 0. Additionally, all patients were subjected to physical examinations, including dermatologic and andrological examinations. A complete hormonal profile, including luteinizing hormone (LH), follicular stimulating hormone (FSH), testosterone, and estradiol, was also performed using seminal fluid analysis and blood tests. Psoriasis was clinically diagnosed, and severity was assessed using the PASI score. Scrotal ultrasounds were also performed to assess testicular volume and homogeneity and exclude any testicular disease.

Data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS) version 21 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were applied, and continuous data were presented as means and standard deviations. Differences between cases and controls were assessed using independent sample *t*-tests. Correlations between psoriasis parameters (PASI score and disease duration), sperm, hormonal parameters, and BMI were determined using Pearson correlation and expressed as *P*-values and correlation coefficients (r). A *P*-value of $\leq$0.05 was considered significant for all purposes.

3. Results

The study included 176 male patients (88 cases and 88 controls). The mean age of the case group was 30.5 $\pm$ 5.6 years, while the control group's mean age was 39.2 $\pm$ 5.7 years (P = 0.793). The mean BMI of the cases was 24 $\pm$ 2.2, while it was 22.6 $\pm$ 2.9 for the control group (P = 0.001). In the case group, psoriasis duration ranged from 1–12 years, with a mean of 6.5 $\pm$ 3.5 years (Table 1).

The mean testosterone levels were 3.8 $\pm$ 0.7 ng/mL and 5.6 $\pm$ 0.9 ng/mL for the cases and control groups, respectively ($P < 0.001$). In comparison, estradiol levels were 39.7 $\pm$ 6.2 pg/mL and 25.8 $\pm$ 3.7 pg/mL for the cases and the control groups, respectively ($P < 0.001$). The mean levels of LH were 3.8 $\pm$ 1.1 mIU/L and 4.1 $\pm$ 0.2 mIU/L for the case and control groups, respectively (P = 0.009). In comparison, FSH was 5.1 $\pm$ 1.6 mIU/L and 4.0 $\pm$ 1 mIU/L for the cases and control groups, respectively ($P < 0.001$). The mean of sperm concentrations in the case group was found to be (21.7 $\pm$ 4.8) n $\times$ 10^6/mL, while it was (65.9 $\pm$ 12.6) n $\times$ 10^6/ML in the control group ($P < 0.001$). The recorded percentages of normal motility and morphology of sperm samples from the case group were 28.3% $\pm$ 9.7% and 14.3% $\pm$ 4.4% for normal motility and morphology, respectively, compared to 61.6% $\pm$ 5.7% and 34.3% $\pm$ 4.3% for normal motility and morphology, recorded from sperm samples of the control group ($P < 0.001$ for both parameters). The overall PASI score of the cases was 17.4 $\pm$ 7.9 (Table 1).

Regression analysis demonstrated that age and PASI scores were significant predictors of sperm concentration ($P < 0.001$ for both parameters). Age was found to be a significant predictor of sperm motility (P = 0.005) (Table 2).

Table 1. Demographic, clinical, and sperm and hormonal parameters of psoriasis patients.

	Study group		*P* (*t*)
	Case	Control	
Demographic and clinical information			
Age	39.5 ± 5.6	39.2 ± 5.7	0.793* (0.26)
Duration of psoriasis	6.5 ± 3.5	0	0
BMI	24.0 ± 2.2	22.6 ± 2.9	0.001* (3.26)
PASI score	17.4 ± 7.9	0	0
Hormonal profile			
Testosterone level ng/mL (NV 2.5–8.4)	3.8 ± 0.7	5.6 ± 0.9	<0.001* (−13.3)
LH level mIU/L (NV 2.5–10)	3.8 ± 1.1	4.1 ± 0.2	0.009* (−2.7)
FSH level mIU/L (NV 2.5–11)	5.1 ± 1.6	4.0 ± 1	<0.001* (4.5)
Estradiol level pg/mL (NV 10–35)	39.7 ± 6.2	25.8 ± 3.7	<0.001* (15.6)
Sperm parameters			
Sperm concentration n × 10 to power of 6/mL (NV >15)	21.7 ± 4.8	65.9 ± 12.6	<0.001* (−26.4)
Normal motility percent (NV >40)	28.3 ± 9.7	61.6 ± 5.7	<0.001* (−23.9)
Normal morphology percent (NV >4)	14.3 ± 4.4	34.3 ± 4.3	<0.001* (−26.2)

PASI, Psoriasis area and severity index; NV, normal value; E2, estradiol; FSH, follicle-stimulating hormone; LH, luteinizing hormone; **P* value; n × 10, sperm concentration.

Among patients with psoriasis, age was significantly negatively correlated with testosterone (−0.352, $P = 0.01$), sperm motility (−0.240, $P = 0.01$), and morphology (−0.202, $P = 0.01$). BMI was positively correlated with FSH (0.193, $P = 0.01$), and estradiol (0.203, $P = 0.01$) levels, and negatively correlated with sperm concentration (−0.249, $P = 0.01$), motility (−0.198, $P = 0.05$), and morphology (−0.205, $P = 0.05$). In addition, testosterone level showed a negative correlation with both FSH (−0.279, $P = 0.01$) and estradiol (−0.658, $P = 0.01$) levels, while there was a negative correlation between PASI score and sperm concentration (−0.519, $P = 0.01$).

4. Discussion

This study explored semen analysis and sex hormonal profiles in male patients with psoriasis and their relationship to BMI and disease severity. It revealed an increased level of estradiol and decreased level of testosterone in the psoriasis group compared to the control group, which is similar to evidence reported by Caldarola *et al.* [18] and Cemil *et al.* [19], who pointed out an inverse correlation between PASI score and level of estradiol.

It is postulated that this hormonal imbalance of testosterone and estradiol may be accounted for by the evidence that the proinflammatory state and cytokines stimulate the aromatase enzyme, which converts androgens to estrogens [20,21]. This hormonal imbalance was also reported by Tsilidis *et al.* [22] and was associated with high C-reactive protein levels, a systemic marker of inflammation, which supports the proinflammatory theory. The relationship between sex hormones and the etiology of psoriasis studied by Ozir *et al.* [23] found that estrogen and testosterone imbalance was an independent risk factor regarding psoriasis etiology in males. Some studies further mentioned a possible responsibility of sex hormones in reducing psoriasis severity, as supported by a marked reduction of C-reactive protein levels and improvement of psoriatic skin manifestations in 15 patients with psoriasis, and hypogonadism after treatment with a long-acting testosterone replacement therapy [24].

This sex hormonal disparity in proinflammatory conditions is not limited to testosterone. Tengstrand *et al.* [25] reported abnormalities in all sex hormones measured, including DHEAS, estrone, and estradiol in patients with rheumatoid arthritis. Furthermore, estrogen has been reported to have both pro-and anti-inflammatory roles [26].

The proinflammatory state, along with its sex hormonal disparity, has been indicated by the low level of seminal parameters in psoriasis patients, resulting in inflammation of the male genital accessory glands, as indicated by high seminal suPAR levels [18].

Semen analysis parameters of the case group were also noted to be lower than those of the control group, as shown in Table 1. Caldarola *et al.* [18] reported similar findings. Impaired testicular function in the form of a reduction in sperm morphology and motility in psoriasis settings was described in a study about testicular function and spondyloarthritis, where five participants had psoriatic arthritis [27].

Ataseven *et al.* [28] reported a significant decrease in proinflammatory indicators in patients with psoriasis treated with anti-TNF inhibitors compared to patients treated with interleukin antagonists. However, it is not yet evident whether the decrease in sperm production in pa-

Table 2. Regression analysis of demographic and clinical characteristics and parameters of semen analysis.

Model (R^2)		B	SE	Beta	t	Sig.	95% CI for B	
							Lower bound	Upper bound
Sperm conc. (0.565)	Age	−0.460	0.074	−0.539	−6.187	0.000	−0.609	−0.311
	Duration of psoriasis	−0.041	0.120	−0.030	−0.341	0.734	−0.282	0.200
	BMI	0.155	0.193	0.070	0.803	0.425	−0.231	0.541
	PASI score	−0.275	0.053	−0.453	−5.228	0.000	−0.381	−0.170
Sperm motility (0.192)	Age	−0.603	0.205	−0.349	−2.945	0.005	−1.012	−0.193
	Duration of psoriasis	−0.205	0.331	−0.074	−0.620	0.538	−0.868	0.458
	BMI	0.904	0.531	0.202	1.704	0.094	−0.158	1.966
	PASI score	−0.137	0.145	−0.111	−0.944	0.349	−0.427	0.153
Sperm morphology (0.07)	Age	−0.111	0.101	−0.140	−1.097	0.277	−0.312	0.091
	Duration of psoriasis	0.112	0.163	0.088	0.686	0.496	−0.215	0.439
	BMI	0.313	0.262	0.152	1.196	0.236	−0.210	0.836
	PASI score	0.062	0.071	0.110	0.873	0.386	−0.081	0.205

tients with untreated psoriasis is primarily due to the effect of the disease itself on sperm production, or if it arises from the effect of the accompanying inflammatory status with high levels of proinflammatory cytokines that are tumor necrosis factor alpha, interleukin1 alpha and beta. Oxidative stress has been shown to decrease spermatogenesis, sperm motility, and membrane integrity of testicular somatic cells [10,29]. Therefore, genital tract inflammation has been described as a significant comorbidity in psoriasis patients [30].

Data analysis showed a predictive effect of PASI scores on sperm concentration, which may reflect the effect of the disease on sexual functions. This was evident in another report that linked psoriasis with the development of sexual dysfunction, abnormal sperm parameters, and hypogonadism [31].

The study demonstrated a correlation between BMI and semen and hormonal parameters, and BMI was positively correlated with FSH and estradiol levels. Moreover, it was negatively correlated with sperm concentration, motility, and morphology, in contrast to what was reported by Caldarola *et al*. [18], who reported no association, but supported previous evidence of an inverse relationship between BMI and sperm motility [32].

It is evident that the longer the duration of untreated psoriasis, the higher the chances of developing infertility [33]. However, it is not clear whether the treatment of psoriasis can improve or worsen sexual dysfunction, as the treatment for psoriasis is linked to the development of sexual dysfunction in both males and females [34]. The average time within which a patient seeks psoriasis treatment is around five to six months [35], and beyond that, permanent and irreversible infertility may develop [36]. However, although the disease duration reported by Caldarola *et al*. [18] ($M = 15.8 \pm 10.6$) was longer than that obtained from our study participants ($M = 7 \pm 4$), our resulting semen analysis parameters and overall PASI scores of the cases were less than what they found. Moreover, the PASI score was negatively correlated with sperm concentration, which is consistent with what was found by Lambert *et al*., who identified the presence of a relationship between the two parameters that directly affected the sexual functions of males.

5. Conclusions

The evaluation of seminal fluid analysis and hormone profiles among psoriasis patients showed marked variability. However, it was evident that the levels of sex hormones and seminal parameters were lower in patients with psoriasis than in the healthy controls. This may uncover the possibility of developing sexual dysfunction and infertility among patients with untreated psoriasis. Estradiol levels were found to be abnormally high in the case group, which may account for a possible compensatory mechanism of ongoing sexual dysfunction among psoriasis patients.

Author contributions

MA, KS, BJ, AA, YR, and SD contributed to study concept and design. MA, KS, and YR performed the data collection. MA, SD, BJ, and AA performed data analysis and interpretation. MA, KS, SD, and YR drafted the manuscript. MA, KS, BJ, AA, YR, and SD completed the critical revision of the manuscript. All authors read and approved the final version of the manuscript and contributed to the editorial changes of the manuscript.

Ethics approval and consent to participate

Informed written consent was obtained from all participants after explaining the objectives and benefits of the research. Participants had the right to refuse participation or withdraw from the study at any point without any detriment to their health care. The study was conducted in accordance with the Declaration of Helsinki, and the proto-

col was approved by the Ethics Committee of 13-1_2720. Meanwhile, an ethical approval number 12/1/2285 was provided by the institutional review board at King Abdullah University Hospital.

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Conflict of interest

The authors declare no conflict of interest.

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