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The Effect of Female Sex Hormones and Prolactin on Female Sexual Function and Their Association with Psoriasis Severity

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Abstract

Background: Psoriasis is a common, immune mediated chronic inflammatory skin disease, affecting individuals of all ages with prevalence rates of 0.1–5.1% have been reported worldwide causing discomfort, disfigurement and disability. Sex hormones and prolactin have been suggested to play a role in the pathogenesis of psoriasis. The effect of psoriasis on sexual health may be linked to several factors. The study aimed to assess the female sexual function in female patients with psoriasis and the role of some hormones (Estradiol, progesterone and prolactin) in female sexual dysfunction.

Methods: This study was case-control study which conducted on 30 female patients with a diagnosis of psoriasis (psoriasis group), in addition to 20 female healthy volunteers of matched age and sex as a control group. Determining the sexual function through female sexual function index (FSFI): All studied subjects were tested for (Estradiol, progesterone and prolactin).**Results:** The clinical data of psoriatic group showed that most of the patients presented with psoriasis vulgaris (76.7%), (40%) presented with genital involvement, PASI scores varied from (1.8 to 47.4) with a mean of (17.49±13.9). 13 patients presented with mild PASI , 6 patients with moderate PASI while 11patients presented with sever PASI score. Comorbidities were presented in 40% of the psoriasis group (2 cases with obesity, 2 cases with hypertension, 4 cases with DM, 1 case with dyslipidemia and 3 cases with PsA) while presented in 35% of the control group. Female sexual dysfunction was reported in (90 %) of psoriatic patients vs (65%) of control groups. The mean of FSFI was statistically lower in psoriatic group (20.42±4.21) than control group (23.76±4.85).The result of the present study showed a significant relation between female sexual dysfunction(FSFI) and associated comorbidities Regarding assessment of serum level of Estradiol, Progesterone and Prolactin; this study revealed significantly higher level of prolactin and progesterone level in psoriatic patients than control group. Estradiol was higher in psoriatic group with no statistically significant between both groups.

Conclusion: The female sexual dysfunction was significantly high in psoriatic cases. Female sexual dysfunction was reported more in psoriatic group associated with comorbidities and in patients presented with psoriasis involvement of genital area than psoriasis group without comorbidities or genital area affection. Both prolactin and progesterone serum level were increased in psoriatic patients.

Key words: Female Sex Hormones- Female Sexual Function- Psoriasis.

Introduction:

Psoriasis is a common, immune mediated chronic inflammatory skin disease, affecting individuals of all ages with prevalence rates of 0.1–5.1% have been reported worldwide causing discomfort, disfigurement and disability **(1)**.

Psoriasis is characterized by the presence of sharply demarcated, red plaques with adherent silvery white scales and a tendency for symmetrical distribution over the body **(2).**

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While the exact etiology is still not fully understood, it may be related to both genetic and environmental factors such as injury, infection, stress and drugs. Immune defect take part in autoimmune pathogenesis of the disease. In addition, it has been reported that some hormones may also have a role in the pathogenesis of psoriasis, due to their effects on keratinocytes proliferation [(3)].
Sex hormones and prolactin have been suggested to play a role in the pathogenesis of psoriasis. The role of sex hormones is implicated from their influence on the course of the disease with a peak during puberty, postpartum, and menopause, while improvement may occur during pregnancy. Also the severity of psoriasis in female patients may fluctuate with hormonal changes [(4)].
In vivo and in vitro studies suggest that sex steroid hormones including estrogen and progesterone may regulate a variety of pathophysiological condition in the skin [(5)].
Estrogen has been hypothesized to contribute to immunological changes by creating a shift from Th1 and Th17 to Th2 immunity [(6)].
Psoriasis vulgaris is often triggered or exacerbated by psycho- emotional stress. Prolactin(PRL) represents a classic neuro-endocrine mediator of stress responses, given that the PRL has been hypothesized that effects of stress on psoriasis are controlled by modifications in serum PRL levels [(7)].

Husakova et al. [(8)] demonstrated correlation between increased PRL serum levels and psoriatic arthritis, therefore elevated PRL serum levels might represent a marker of inflammatory joint disease in patients suffering from psoriasis vulgaris.
Multiple comorbidities such as diabetes mellitus, atherosclerotic disease, metabolic syndrome and psychological disorder such as anxiety and depression, have been associated with psoriasis [(9)].
Furthermore, the physical, social, and psychological impact of psoriasis is considerable, and as in other chronic diseases, this negative impact may contribute to sexual dysfunction [(10)].
The effect of psoriasis on sexual health may be linked to several factors, including the detrimental effect of the condition on the individual's physical appearance, decreased libido, and the inconvenience caused both by skin desquamation and by topical treatment [(11)].
According to the World Health Organization (WHO), sexuality is a basic human need, as well as an important aspect of human beings. This need cannot be separated from others. WHO highlights that sexuality is extremely important in maintaining good mental health [(12)].
The study aimed to assess the female sexual function in female patients with psoriasis and the role of some hormones (Estradiol, progesterone and prolactin) in female sexual dysfunction.

Patients and Methods

Type of study:

Case-control study

Study population

This study included 30 female patients with a diagnosis of psoriasis (psoriasis group), in addition to 20 female healthy volunteers of matched age and sex as a control group. All patients were selected from the outpatient clinic of Dermatology, venerology and Andrology Department of Zagazig University Hospitals from March 2019 to January 2020.

Ethical considerations: An informed consent was obtained from all participants. The present study was approved by the ethics committee on research involving human subjects of Faculty of Medicine, Zagazig University.

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Inclusion criteria

Females with ranging age between 18 to 60 years old and have active sexual life.

For psoriatic group:

1. Clinically typical psoriatic lesions with different clinical varieties of psoriasis.

Exclusion criteria:

1- Age less 18 or more than 60.

2- Receiving topical therapy for 2 weeks or systemic therapy for 1 month before being enrolled in our study.

3- Receiving hormonal therapy as oral contraceptive pills.

4- Presence of gynecological disorders potentially affecting sexual function including (vaginitis, chronic pelvic pain, malignant neoplasm, vaginismus and alteration of Pelvic anatomy).

5- Pregnancy, breast-feeding, renal, hepatic or endocrinopathic diseases.

6- Patient diagnosed with primary psychiatric disorder such as (depression or anxiety).

All patients were subjected to the followings:

A. Full history taking

1. **Personal history:** The patient's name, age, sex, marital status.
2. **Present history:** onset, course and duration of psoriasis.
3. **Past history of medication intake:** Type and duration of medication intake and dose.
4. **Previous treatment of psoriasis:** Systemic or topical, duration and dose.
5. **Family history of** Psoriasis, or other skin or systemic diseases.
6. **History of associated comorbidities** as: Diabetes, hypertension dyslipidemia, liver and renal diseases.

B. Examination:

1. Clinical assessment of cases

a. Type of psoriasis and site of lesions were recorded.

b. Presence of arthritis, genital involvement and exposed skin areas (scalp, face, hand).

c. Clinical Assessment of female sexual function by female sexual function Index (FSFI) **[13].**

2- Determining the sexual function through female sexual function index (FSFI):

FSFI, a self-reported questionnaire measured the female sexual function during the previous 4 weeks, which has been previously validated in the Arabic language **[13].**

The FSFI is a valid and accurate method to measure the female sexual function. This questionnaire comprises of 19 questions that evaluate six different domains of sexual function including desire, arousal, lubrication, orgasm, satisfaction and pain. The answer is rated on a 5-point

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Likert scale between 0 and 5. Each domain score was obtained by adding individual items of the domain and multiplying this result by the domain factor (i.e. desire, 0.6; arousal and lubrication, 0.3; orgasm, satisfaction and pain, 0.4) **(14).**

The FSFI total score is determined by the sum of the six domains. The score varies from 2 to 36, where higher scores are associated with the lower degree of sexual dysfunction **(14).**

A total score of 26.5 is the cutoff point for women with sexual dysfunction **(15).**

Six FSFI sexual domains have cutoffs in each of their domains. Desire has a domain value with a cutoff of 2.4. Values below 2.4 fall into the category of dysfunction, and above 2.4 falls into normal category. The other five domains, (the arousal, lubrication, orgasm, satisfaction and pain), have a cutoff value of 3.6. Values below3.6 belong to dysfunction category, while above 3.6 is considered normal **(15).**

Laboratory investigations:

All studied subjects were tested for:

1. Serum level of Estradiol.
2. Serum level of progesterone.
3. Serum level of prolactin.
4. Routine investigation as complete blood picture, lipid profile, liver functions.

The included subjects were submitted to a hematic hormonal evaluation on the third day of their menstrual cycle for estradiol and prolactin, the blood samples were taken in the morning between 08.00 and 10.00 hours, in both patients and controls.

In addition, progesterone hormone was measured on the 20–21 day of their menstrual cycle. Patients with amenorrhea had all hormones tested through only one random blood drawing. Methods for measuring blood hormones were electro-chemiluminescence immunoassay analyzer (ECLIA).

Statistical Analysis: Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) **(**Statistical Package for the Social Sciences) software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD, the following tests were used to test differences for significance;. Difference and association of qualitative variable by Chi square test (X^2). Differences between quantitative independent groups by t test or Mann Whitney, correlation by Pearson's correlation or Spearman's. P value was set at <0.05 for significant results & <0.001 for high significant result.

Results:

The mean age (years) of psoriatic group was (40.53 ±12.18) vs (39.4 ±12.33) of control group with no significant difference between them. More than half of both groups were less than 40 years old **Table (1).**

2-Associated comorbidities distribution between cases and controls

The cases and controls were nearly matched regard distribution of co-morbidities as 40% of cases had co-morbidities vs 35% of control group with no statistical significant difference between

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both groups (p value =0.72). Among cases, 13.3% were diabetic, 10% had Psoriatic arthritis and 6.7% were hypertensive and obese **Table (2).**

3-Clinical data of the psoriatic group

The majority of patients (76.7%) presented with psoriasis vulgaris. Genital involvement were reported in 40% of patients. The duration of psoriasis was less than 5 years in 60%. The mean of PASI score was 17.49±13.9. The mild cases represented 43.3%, moderate cases represented 20% and sever cases represented 36.7% .10% of patients had positive family history of psoriasis **Table (3).**

4-Female sexual dysfunction distribution among cases and controls

According to FSFI; 90% of cases have sexual dysfunction vs 65% of controls. Among cases impaired arousal was reported in (56.7%), impaired orgasm in (46.7%), impaired satisfaction in (40%), impaired desire in (33.3%) and impaired lubrication in (26.7%) while pain was reported in (6.7%). The impairment of desire, arousal, lubrication, satisfaction and orgasm were more frequent in cases than controls ;however the difference wasn't statistically significant except for orgasm (p value = 0.049) **Table (4)**.

The mean FSFI was significantly lower among psoriasis group with genital area involvement (18.77±3.0) vs (23.51±3.83) among patients without genital involvement (p value = 0.001) **Table (5) and Figure (1).**

6- Relation between FSFI score and associated comorbidities in psoriasis patients

The mean FSFI was significantly lower among psoriatic group associated with comorbidities (19.39±3.43) vs (23.10±4.01) among psoriatic group without comorbidities (p value = 0.015) **Table (6).**

7-Estradiol and Progesterone serum levels of the studied groups:

The mean serum level of progesterone (ng/ml) was significantly higher among cases (5.84 ±5.21) vs (2.33 ±2.11) among the control (p value = 0.027). The mean estradiol serum level was higher in psoriatic patients (53.75 ±38.6 pg/ml) vs (44.71±35.2 pg/ml) in controls. However, the difference between both groups wasn't statistically significant **Table (7) and Fig (2).**

8-Prolactin distribution between studied groups:

The mean serum level of prolactin (ng/ml) was significantly higher in case group (16.15 ±14.4) than control group (8.81 ±2.85) (p value = 0.038). Female patients with psoriatic arthritis (PsA) associated with high level of serum prolactin (PRL>29 ng/ml) **Table (8) Fig (3)**.

Table (1): Age distribution between cases and controls

			Psoriasis group	Control group	t/X^2	P
Age(years) Mean ±SD			40.53±12.18	39.4±12.33	0.321	0.750
Age	**<40**	**N**	16	11		
		%	53.3%	55.0%		

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	>40	N	14	9	0.013	0.908
		%	46.7%	45.0%		
Total		N	30	20		
		%	100.0%	100.0%		

P value >0.05 non-significant.

Table (2): Associated comorbidities distribution between cases and controls

			Group		Total	X^2	P
			Psoriasis group	Control group			
Associated co-morbidities	Absent	N	18	13	31		
		%	60.0%	65.0%	62.0%		
	Present	N	12	7	19	0.12	0.72
		%	40.0%	35.0%	38.0%		
Obesity BMI>30	Absent	N	28	17	45		
		%	93.3%	85.0%	90.0%		
	Present	N	2	3	5	0.92	0.33
		%	6.7%	15.0%	10.0%		
Hypertension	Absent	N	28	19	47		
		%	93.3%	95.0%	94.0%		
	Present	N	2	1	3	0.059	0.808
		%	6.7%	5.0%	6.0%		
Diabetes Mellitus (DM)	Absent	N	26	18	44		
		%	86.7%	90.0%	88.0%		
	Present	N	4	2	6	0.12	0.72
		%	13.3%	10.0%	12.0%		
Dyslipidemia	Absent	N	29	17	46		
		%	96.7%	85.0%	92.0%		
	Present	N	1	3	4	2.21	0.13
		%	3.3%	15.0%	8.0%		
Associated rhumatological	Absent	N	27	20	47		
		%	90%	100	88.0%		
	Psoriatic arthritis	N	3	0	3	5.01	0.17
		%	10.0%	0.0%	6.0%		
Total		N	30	20	50		
		%	100.0%	100.0%	100.0%		

P value > 0.05non significant. X^2 = the chi square test. N: number of patients. BMI: body mass index

Table (3): Clinical data of the psoriatic group

		N	%
+ve family history	No	27	90.0
	Yes	3	10.0

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Type Psoriasis		**Psoriasis vulgaris**	23	76.7
		Erythrodermic	3	10.0
		Palmo plantar	2	6.7
		Flexural	1	3.3
		Guttate	1	3.3
Genital involvement		**No**	18	60.0
		Yes	12	40.0
Duration of disease(years)		**<5**	18	60.0
		5-10	7	23.3
		>10	5	16.7
PASI score		**Mild**	13	43.3
		Moderate	6	20.0
mean± SD **median (Range)**	**17.49±13.9** **12.9 (1.8-47.4)**	**Sever**	11	36.7
		Total	30	100.0

Mild =PASI(<10), moderate=PASI(10-20), sever= PASI(>20).

Table (4): Female sexual dysfunction distribution among cases and control

			Group		Total	X^2	P
			Psoriasis group	Control group			
FSFI Cut off value 26.55	**Normal**	**N**	3	7	10		
		%	10.0%	35.0%	20.0%		
	Dysfunction	**N**	27	13	40	4.68	0.03*
		%	90.0%	65.0%	80.0%		
Desire Cut off value 2.4	**Normal**	**N**	20	17	44		
		%	66.6%	85.0%	88.0%		
	Abnormal	**N**	10	3	6	0.28	0.59
		%	33.3%	15.0%	12.0%		
Arousal Cut off value 3.6	**Normal**	**N**	13	11	24		
		%	43.3%	55.0%	48.0%		
	Abnormal	**N**	17	9	26	0.65	0.41
		%	56.7%	45.0%	52.0%		
Lubrication Cut off value 3.6	**Normal**	**N**	22	15	37		
		%	73.3%	75.0%	74.0%		
	Abnormal	**N**	8	5	13	0.017	0.89
		%	26.7%	25.0%	26.0%		
Orgasm Cut off value 3.6	**Normal**	**N**	16	16	32		
		%	53.3%	80.0%	64.0%		
	Abnormal	**N**	14	4	18	3.81	0.049*
		%	46.7%	20.0%	36.0%		

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Satisfaction Cut off value 3.6	**Normal**	**N**	18	15	33		
		%	60.0%	75.0%	66.0%		
	Abnormal	**N**	12	5	17	1.21	0.27
		%	40.0%	25.0%	34.0%		
Pain Cut off value 3.6	**Normal**	**N**	28	19	47		
		%	93.3%	95.0%	94.0%		
	Abnormal	**N**	2	1	3	0.059	0.808
		%	6.7%	5.0%	6.0%		
Total		**N**	30	20	50		
		%	100.0%	100.0%	100.0%		

*****P value< (0.05) significant. X^2 = chi square test. FSD=FSFI≤26.55

Table (5): Relation between FSFI and genital area involvement in psoriatic patients

	Group with genital affection	**Group without genital affection**	**t**	**P**
FSFI Mean ±SD	18.77±3.0	23.51±3.83	3.60	0.001*

*(P value < 0.05) significant t: t-test

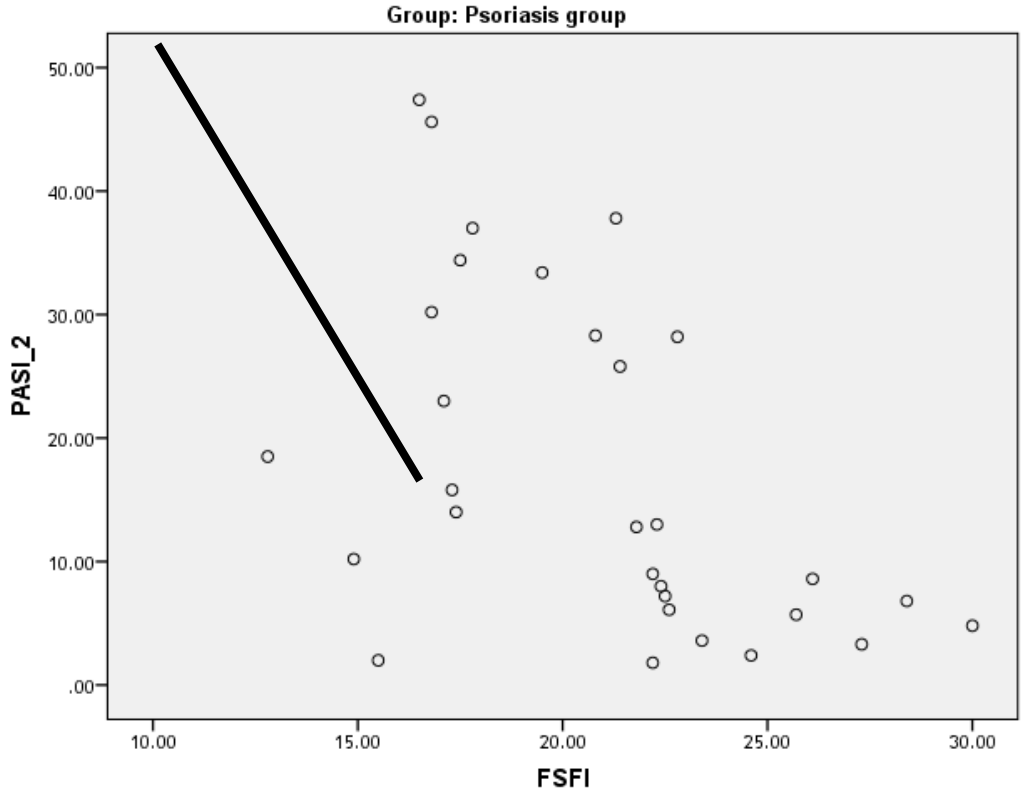

Figure (1): Significant negative correlation between FSFI and PASI in psoriatic patients.

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Table (6): Relation between FSFI and associated comorbidities in psoriatic patients

	Psoriasis group with comorbidities	Psoriasis group without comorbidity	t	P
FSFI Mean±SD	19.39±3.43	23.10±4.01	2.59	0.015*

*(P value<0.05) significant t: t-test

Table (7): Estradiol and Progesterone serum levels of the studied groups:

			Psoriasis group	Control group	Mann Whitney/ X^2	P
Estradiol (pg/ml) Mean ±SD			53.75±38.6	44.71±35.2	0.892	0.373
Median (Range)			41.75 (5-167.3)	33.55 (5-170)		
Progesterone(ng /ml) Mean ±SD			5.84±5.21	2.33±2.11	2.287	0.027***
Median (Range)			3.95 (0.04-19.1)	1.8 (0.04-6.1)		
Estradiol	**Normal ***	**N**	28	19		
		%	93.3%	95.0%		
	Abnormal	**N**	2	1	0.059	0.808
		%	6.7%	5.0%		
Progesterone	**Normal ****	**N**	20	13		
		%	66.7%	65.0%		
	Abnormal	**N**	10	7	0.015	0.903
		%	33.3%	35.0%		
Total		**N**	30	20		
		%	100.0%	100.0%		

***** Normal estradiol level: 12.5-166 pg/ml (follicular phase), 5-54.7pg/ml (post –menopausal)

******Normal progesterone level: 1.7-27ng/ml (luteal phase), up to .8 ng/ml (post –menopausal)

*** (P value<0.05) significant.

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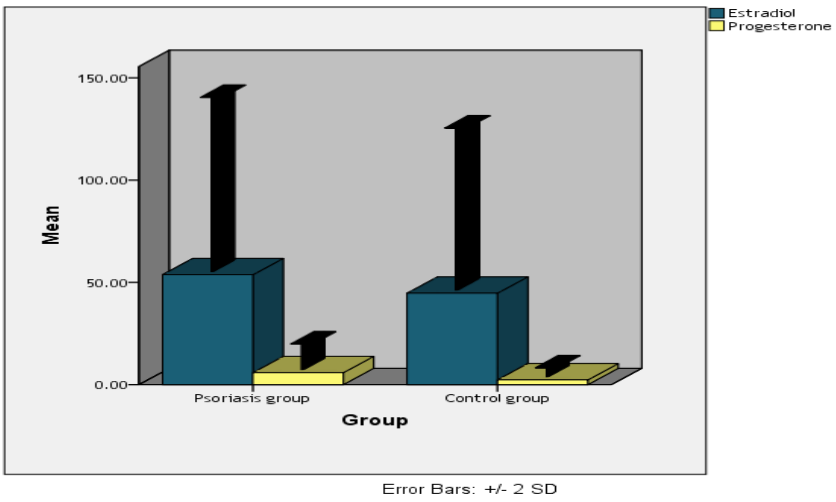

Figure (2): Bar chart show estradiol and progesterone distribution between studied groups:

Table (8): Prolactin distribution between studied groups:

			Psoriasis group	Control group	Mann Whitney/ X^2	P
Prolactin (ng/ml) Mean ±SD Median (Range)			16.15±14.4 10.75 (1.9-65.8)	8.81±2.85 8.45 (3.2-13.7)	2.147	0.038**
Prolactin	**Normal ***	**N**	25	20		
		%	83.3%	100.0%		
	Abnormal	**N**	5	0	3.42	0.062
		%	16.7%	0.0%		
Total		**N**	30	20		
		%	100.0%	100.0%		

***Normal prolactin level= (2.9-29 ng/ml), Abnormal = (PRL>29ng/ml)

**** P value (<0.05) significant.

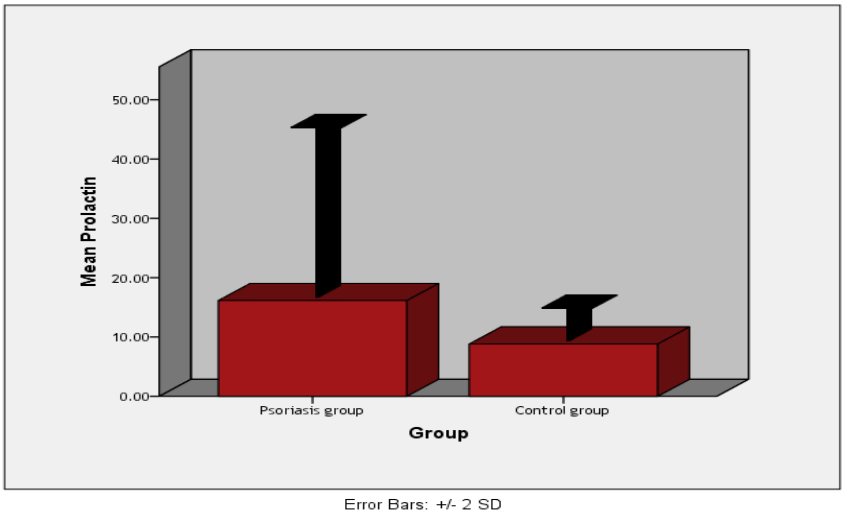

Figure (3): Bar chart shows prolactin distribution between studied groups.

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Discussion

The clinical data of psoriatic group showed that most of the patients presented with psoriasis vulgaris (76.7%), (40%) presented with genital involvement, PASI scores varied from (1.8 to 47.4) with a mean of (17.49±13.9). 13 patients presented with mild PASI , 6 patients with moderate PASI while 11patients presented with sever PASI score.

Comorbidities were presented in 40% of the psoriasis group (2 cases with obesity, 2 cases with hypertension, 4 cases with DM, 1 case with dyslipidemia and 3 cases with PsA) while presented in 35% of the control group.

Female sexual dysfunction was reported in (90 %) of psoriatic patients vs (65%) of control groups. The mean of FSFI was statistically lower in psoriatic group (20.42±4.21) than control group (23.76±4.85). This came in agreement with **Mercan et al.** [16] and **Abul Maaty et al.** [17]**;** all reported increased incidence of female sexual dysfunction and decreased FSFI in psoriatic female than among healthy control.

The mean FSFI was significantly lower among psoriasis group with genital area involvement (18.77±3.0) vs (23.51±3.83) among patients without genital involvement. This came in agreement with **Meeuwis et al.** [18]**, Hariram et al.** [19] and **Abul Maaty et al.** [17]. However, this run counter to a study conducted by **Dorssen et al.** [20] who stated absence of correlation between genital area affection and sexual dysfunction in psoriatic patients.

The result of the present study showed a significant relation between female sexual dysfunction(FSFI) and associated comorbidities such as (obesity, hypertension,DM, dyslipidimia and PsA) in psoriatic patients. This result come in agrement with **Laumann et al.** [21] and **West et al.** [22] who reported a relationship between chronic disease, especially rhumatic comorbidities and sexual dysfunction. **Boone et al.** [23] also revealed that, the women with PsA and rheumatoid arthritis have higher rates of sexual dysfunction, across each of the FSFI domains, compared with women without inflammatory arthritis. However **Kurizky et al.** [24] reported absence of significant relation between female sexual dysfunction and associated comorbidities in psoriatic patients.

Regarding assessment of serum level of Estradiol, Progesterone and Prolactin; this study revealed significantly higher level of prolactin and progesterone level in psoriatic patients than control group.Estradiol was higher in psoriatic group with no statistically significant between both groups. This came in agreement with **Giasuddin et al.** [25]**, Keen and Iffat,** [26] and **Pawan et al.** [27], who reported higher serum prolactin level in psoriatic patients than controls. On the other hand, these results disagree with **Azizzadeh et al.** [28] who reported absence of significant difference in the serum prolactin level between psoriatic and control group.

To the best of our knowledge, no published studies were found to discuss the serum level of estrogen or progesterone in non-pregnant psoriatic patients. **Murase et al.** [29] reported that, the increased levels of estrogen relatively to progesterone correlate with improvement of psoriasis. They found that progesterone levels alone did not correlate with change in psoriasis and therefore it can be assumed that patients who experience an improvement of psoriasis have higher levels of estrogen relative to progesterone during pregnancy, whereas those who have lower ratio levels will remain unchanged or potentially worsen.

Conclusion:

The female sexual dysfunction was significantly high in psoriatic cases. Female sexual dysfunction was reported more in psoriatic group associated with comorbidities and in patients presented with psoriasis involvement of genital area than psoriasis group without comorbidities or genital area affection. Both prolactin and progesterone serum level were increased in psoriatic patients.

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