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## **Sexual function assessment in women with rheumatoid arthritis: Correlation with psychological states and hormonal profile**

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**Abstract**---Background: Rheumatoid arthritis (RA) is a common disabling joint disease affecting both males and females. Sexual dysfunction (SD) is a common association with RA. Aim and objectives: The aim of this study was to assess the frequency rates of sexual problems and associated factors in a cohort of married females with Rheumatoid arthritis (RA), and to investigate the correlation between hormonal profile (serum testosterone level, estrogen and progesterone level) and female sexual function in RA patients. Subjects and methods: This cross-sectional analytical study included 100 female RA patients and 80 age matched healthy control female from Rheumatology and Rehabilitation Clinic in Qena University Hospital. Results: there were a highly statistically significant negative correlation between Female Sexual Function Index (FSFI) and each of DAS, VAS, MHAQ, HAM-A and Testosterone level while it showed statistically significant positive correlation between Female Sexual Function Index (FSFI) and each of Estrogen and Progesterone. Conclusion: Our study suggests that rheumatoid arthritis has a

negative impact on patients' sexuality. Age of patients and partners, pain, and tender joints appear to be the main factors influencing sexual function.

**Keywords**---rheumatoid arthritis, sexual problems, physical disability, depression, anxiety.

## **Introduction**

Rheumatoid arthritis (RA) is a chronic, progressive, debilitating autoimmune disease that is most prevalent in middle-aged and old women, with incidence rate in the range 0.32–0.38%. This illness is characterized by joint pain, stiffness, and deformity in different joints, particularly the hands and feet, resulting in irreversible joint deformities, physical disability, and functional impairment. (Huskisson et al., 2013) Furthermore, reports from Africa note an increasing incidence; e.g. in Egyptian population, the prevalence of RA is approximately 0.3%. (Chopra et al., 2008) RA inevitably leads to pain, various degrees of disability, and profound impact on individual's physical, psychological, and socioeconomic aspects of life. (Ziarko et al., 2019)

Sexuality is a complex aspect of the human's life and is more than the sexual act only. Sexual activity has an impact on sexual satisfaction of patients, several aspects of their personal lives and relationships. Normal sexual functioning consists of sexual activity with transition through the phases from arousal to relaxation with no problems, and with a feeling of pleasure, fulfillment, and satisfaction. Patients with RA experience different aspects of sexual problems such as difficulties in sexual performance and diminution of sexual desire, arousal, lubrication, orgasm and satisfaction, which are directly or indirectly caused by the disease. (Josefsson et al., 2012) The cause of sexual problems with RA is multifactor due to chronic disease aspects such as disease activity, pain, reduced physical activities, fatigue, and poor sleep and psychiatric comorbidities such as depression, anxiety, poor self-esteem, and altered body image and rarely drugs used for treatment. (Zhanga et al., 2018) Researches are needed to identify and understand the mechanisms of sexual problems in RA to determine different types of interventions to support a satisfactory quality of life for patients with RA. The aim of this study was to assess the frequency rates of sexual problems and associated factors in a cohort of married females with Rheumatoid arthritis (RA), and to investigate the correlation between hormonal profile (serum testosterone level, estrogen and progesterone level) and female sexual function in RA patients.

## **Patients and Methods**

This study was a quasi-experimental pre-post-test single group design. This study was performed at the Outpatient Clinic of Dermatology, Venerology and Andrology department, South Valley University on 43 women complaining of sexual dysfunction were recruited at period from November 2015 till June 2017 to evaluate efficacy of sildenafil citrate in the treatment of female sexual dysfunction. The experimental design was approved by the Institutional Ethics and Research Committee of Faculty of Medicine, South Valley University, Egypt. Informed

written consent was obtained from each woman before enrollment in the study.

### **Inclusion criteria included**

Sexually active women who were 18 -60 years of age, patients who clinically diagnosed having female sexual dysfunction, patients who had sexual activity at least once weekly. Patients were in a stable, heterosexual relationship that is secure and communicative, patients should be reliable, honest, compliant and agree to co-operate with all trial evaluations as well as to be able to perform them, normal sexual function of male partner was evaluated by using the International Index of Erectile Function (IIEF-5) and normal hormonal profile as regard testosterone and estrogen.

### **Exclusion criteria included**

Women with a history of hypertension and on anti-hypertensive treatment, women with Coronary heart disease, patient on treatment with vasodilator (nitrates and alpha blocker), impaired hepatic function or neoplasia, taking any medication with a known influence on sexual function (e.g Anti-Depressant and Anti-Psychotic drugs) and pregnancy or breast feeding for last 6 month.

All patients were subjected to:

### **A-Full history taking including**

Personal history: Age of the patient and occupation, duration of marriage, number of children, age of younger child and age of older child , special habits of medical importance e.g. smoking. Complaint and present history: Onset, course, duration, precipitating factors, relation to menstrual cycle. Menstrual history: last menstrual period, regularity, length of cycle, dysmenorrhoea. contraceptive history: type of contraceptive methods. Sexual history: relationship status, history of sexual abuse, frequency of intercourse, pain during or after intercourse and infection (sexually transmitted infections). Obstetric history: number of pregnancies, losses and type of delivery. Past and family history: chronic medical illness, previous medications (as antihypertensive, antipsychotic drugs), previous surgeries.

### **B-Sexual function questionnaire (SFQ)**

The duration of the study 6 weeks, based on the results of the factor analysis of the 19 -items Female Sexual Function Index (FSFI ) questionnaire, which its individual items were assigned to six separate domains of female sexual function. Each male partner has completed the 5-items international index of erectile function (IIEF-5) questionnaire for assessment of erectile function and ED severity the arabic version. The questions were about erection confidence, erection firmness, maintenance ability, maintenance frequency and satisfaction. The score ranges between "5-25" as follow: 5-7 (severe ED), 8-11 (moderate ED), 12-16 (mild to moderate), 17-21 (mild ED), 22 -25 (no ED) before his wife taking the treatment to make sure normal male sexual factor.

### **C-Physical examination: including**

General examination including full general examination. Local examination including: inspection of external genitalia for pupic hair amount / distribution, swelling, degree of circumcision (1st degree partial or total removal of the clitoris, 2nd degree removal of the clitoris, labia minora 3rd degree, previous scars, episiotomy) and per vaginal examination to exclude infection, cervical erosion, cervical mass, state of the vagina and fixed Retro-Verted- Flexed uterus.

### **D-Treatment**

Women who accepted to participate in the study received sildenafil 25 mg tablet (Silden 25mg EIPICO company) once daily on empty stomach for six week duration and detection of side effects of the drug on participated and evaluate safety of sildenafil citrate.

### **E-Ethical approval**

The study was approved by scientific and ethical committees at Faculty of Medicine South Valley University. All women were informed about the nature of the study and the treatment they received and they signed an informed consent before starting the study.

### **F- Statistical Methodology**

Analysis of data was done by IBM computer using SPSS (statistical program for social science version 20) as follows; Description of quantitative variables as mean, SD and range, Description of qualitative variables as number and percentage. Paired T-test: was used to compare the difference in means between the two groups. Correlation coefficient test (r): was used to rank variables against each other either positively or inversely. Correlation is significant at the 0.05 level (-tailed) based on normal approximation.

### **Results**

Table (1) shows demographic data of the studied group. Age was ranged between 26 – 56 years with mean value  $39.95 \pm 9.213$  years. Duration of Marriage was ranged between 2 – 36 years with mean value  $17.70 \pm 10.675$  years. About three quarter of the studied patients were housewife (74.0%). 23(23.0%) were diabetic while 36(36.0%) had a history with hypertension. Disease Duration was ranged between 1 month – 26 years with mean value  $8.53 \pm 8.600$  years.

Table (1): Distribution of studied sample according to demographic data

	Number	Percent
Age (years)		
Range	26 – 56	
Mean±S.D.	39.95±9.213	
Duration of Marriage		
Range	2 – 36	

Mean±S.D.	17.70±10.675	
Occupation		
Housewife	74	74.0
Employed	18	18.0
Teacher	6	6.0
Nurse	2	2.0
Medical history		
DM	23	23.0
HTN	36	36.0
Disease Duration		
Range	1 month – 26 years	
Mean±S.D.	8.53±8.600	

Table (2) shows hormones test results of the studied group. Testosterone level was ranged between 0.6 – 8.10 ng/ml with a mean value of 3.31±2.704 ng/ml. Estrogen was ranged between 94.8 – 193.10 pg/ml with a mean value of 128.91±32.088 pg/ml. Progesterone was ranged between 5.08 – 18.90 ng/ml with a mean value of 10.87±3.938 ng/ml.

Table (2): Distribution of studied sample according to Hormones

	Range	Mean±S.D.
Testosterone level (ng/ml)	0.6 – 8.10	3.31±2.704
Estrogen (pg/ml)	94.8 – 193.10	128.91±32.088
Progesterone (ng/ml)	5.08 – 18.90	10.87±3.938

Table (3) shows Female Sexual Function Index (FSFI) of the studied group and it show that FSFI final score was ranged between 9.60 – 26.40 with mean value 19.40±3.394 and it show that all patients had classified as FSD ( $\leq 26.5$ ).

Table (3): Distribution of studied sample according to Female Sexual Function Index (FSFI)

	Number	Percent
Desire		
Range	1.2 – 4.8	
Mean±S.D.	2.95±1.348	
Arousal		
Range	2.4 – 4.8	
Mean±S.D.	3.80±0.981	
Lubrication		
Range	1.2 – 4.8	
Mean±S.D.	3.06±1.336	
Orgasm		
Range	1.2 – 6.0	
Mean±S.D.	3.79±1.642	

Satisfaction	
Range	1.2 – 4.8
Mean±S.D.	2.71±1.328
Pain	
Range	1.2 – 6.0
Mean±S.D.	3.08±1.409
FSFI final score	
Range	9.60 – 26.40
Mean±S.D.	19.40±3.394

Table (4) shows DAS score of the studied group and it show that it was ranged between 2.0 – 5.5 with mean value 3.14±1.278 and it show that more than one third of the patients classified as Remission (37.0%).

Table (4): Distribution of studied sample according to DAS score

	Number	Percent
DAS Score		
Range	2.0 – 5.5	
Mean±S.D.	3.14±1.278	
DAS Score Classifications		
Low Disease Activity	30	30.0
Moderate Disease Activity	13	13.0
High Disease Activity	20	20.0
Remission	37	37.0

Table (5) shows VAS score of the studied group and it show that it was ranged between 2 – 8 with mean value 4.80±2.156 and it show that the most of the patients classified as Mild Pain (39.0%).

Table (5): Distribution of studied sample according to VAS score

	Number	Percent
VAS Score		
Range	2 – 8	
Mean±S.D.	4.80±2.156	
VAS Score Classifications		
Mild Pain	39	39.0
Moderate Pain	18	18.0
Severe Pain	31	31.0
Very Severe Pain	12	12.0

Table (6) shows Modified Health Assessment Questionnaire score (MHAQ) score of the studied group and it show that it was ranged between 0.13 – 1.5 with mean value 0.73±0.497 and it show that the most of the patients classified as moderate (40.0%).

Table (6): Distribution of studied sample according to Modified Health Assessment Questionnaire score (MHAQ)

	Number	Percent
MHAQ Score		
Range	0.13 – 1.5	
Mean±S.D.	0.73±0.497	
MHAQ Score Classifications		
Mild	38	38.0
Mild to Moderate	21	21.0
Moderate	40	40.0
Moderate to Severe	1	1.0

Table (7) shows Hamilton Anxiety Rating Scale (HAM-A) of the studied group and it show that it was ranged between 10 – 26 with mean value 18.36±4.284 and it show that more than half of the patients classified as mild to moderate (67.0%).

Table (7): Distribution of studied sample according to Hamilton Anxiety Rating Scale (HAM-A)

	Number	Percent
HAM-A		
Range	10 – 26	
Mean±S.D.	18.36±4.284	
HAM-A Classifications		
Mild	30	30.0
Mild to Moderate	67	67.0
Moderate to Severe	3	3.0

Table (8) show correlation between Female Sexual Function Index (FSFI) and other parameters and it show highly statistically significant negative correlation between Female Sexual Function Index (FSFI) and each of DAS, VAS, MHAQ, HAM-A and Testosterone level while it show statistically significant positive correlation between Female Sexual Function Index (FSFI) and each of Estrogen and Progesterone.

Table (8): Correlation between Female Sexual Function Index (FSFI) and other parameters

	Female Sexual Function Index (FSFI)													
	Desire		Arouse		Lubricatio n		Orgasm		Satisfactio n		Pain		Full Scale Score	
	r	P	r	P	r	P	r	P	r	P	r	P	r	P
DAS	- 0.4 28	<0. 001 *	- 0.3 52	<0. 001 *	- 0.4 62	<0. 001 *	- 0.2 95	0.0 03*	- 0.3 47	<0.0 01*	- 0.2 53	0.0 11	- 0.8 37	<0.0 01*
VAS	- 0.4	<0. 001	- 0.3	<0. 001	- 0.4	<0. 001	- 0.3	<0. 001	- 0.3	<0.0 01*	- 0.1	0.0 13*	- 0.8	<0.0 01*

	75	*	59	*	17	*	65	*	83		59		49	
MHAQ	- 0.4 71	<0. 001 *	- 0.3 72	<0. 001 *	- 0.4 34	<0. 001 *	- 0.3 95	<0. 001 *	- 0.3 53	<0.0 01*	- 0.1 79	0.0 15*	- 0.8 69	<0.0 01*
HAM-A	- 0.4 61	<0. 001 *	- 0.3 58	<0. 001 *	- 0.4 23	<0. 001 *	- 0.3 91	<0. 001 *	- 0.4 65	<0.0 01*	- 0.2 46	0.0 14*	- 0.9 26	<0.0 01*
Testosterone	- 0.4 83	<0. 001 *	- 0.3 61	<0. 001 *	- 0.4 41	<0. 001 *	- 0.3 83	<0. 001 *	- 0.3 49	<0.0 01*	- 0.1 93	0.0 14*	- 0.8 72	<0.0 01*
Estrogen	0.3 31	0.0 01*	0.3 08	0.0 02*	0.2 83	0.0 04*	0.1 52	0.1 32	0.3 00	0.0 02*	0.3 14	0.0 01*	0.6 53	<0.0 01*
Progesterone	0.1 81	0.0 71	0.1 66	0.0 98	0.1 37	0.1 74	- 0.0 15	0.8 85	0.1 46	0.1 46	0.3 08	0.0 02*	0.3 52	<0.0 01*

## Discussion

Sexual health is a state of physical, emotional, mental and social wellbeing related to sexuality, not merely the absence of disease, dysfunction or infirmity. In humans, sexual desires are one of the biggest problems that affect their personal as well as social lives and satisfaction of such desires plays a decisive role in the creation of a human's personality. Separation of these desires from behavior is inevitable (Gopal et al., 2021). This cross-sectional analytical study included 100 female RA patients and 80 age matched healthy control female from Rheumatology and Rehabilitation Clinic in Qena University Hospital.

Analysis of our findings revealed that Age was ranged between 26 – 56 years with mean value  $39.95 \pm 9.213$  years. Duration of Marriage was ranged between 2 – 36 years with mean value  $17.70 \pm 10.675$  years. About three quarter of the studied patients were housewife (74.0%). 23(23.0%) were diabetic while 36(36.0%) had a history with hypertension. Disease Duration was ranged between 1 month and 26 years with mean value  $8.53 \pm 8.600$  years.

In agreement with our findings the cross sectional study of Abda et al., 2016 which included 200 female RA patients (mean age  $44.2 \pm 9.1$  years; range 18 to 55 years) and 100 age matched healthy control females (mean age  $42.5 \pm 6.3$  years; range 18 to 55 years) recruited from the general population. Furthermore, Azab et al., 2021 reported that the mean age of studied women was  $32.1 \pm 8.3$  years, mean duration of marriage was  $7.8 \pm 6.4$  years, 41.9% of them were not working, the mean number of children was  $2.3 \pm 1.8$ , 10.5 % were smokers, and mean BMI was  $27.1 \pm 4.5$ .

As regard hormones test results of the studied group, we found that testosterone level was ranged between 0.6 – 8.10 ng/ml with a mean value of  $3.31 \pm 2.704$  ng/ml. Estrogen was ranged between 94.8 – 193.10 pg/ml with a mean value of  $128.91 \pm 32.088$  pg/ml. Progesterone was ranged between 5.08 – 18.90 ng/ml with a mean value of  $10.87 \pm 3.938$  ng/ml. Lashkari et al., 2018 reported that the mean serum testosterone level was not significantly different between the groups. But in subgroup analysis, mean serum testosterone level in females of the control group

was significantly higher than in females of the case group.

In the current study; Female Sexual Function Index (FSFI) of the studied group showed that FSFI final score was ranged between 9.60 – 26.40 with mean value of  $19.40 \pm 3.394$  and it show that all patients had classified as FSD ( $\leq 26.5$ ). This comes in comparison with the study of Yilmaz et al., 2012 where Patients reported significantly lower sexual function (SF) total and domain scores compared with controls. Moreover, patients showed significantly higher frequency of abnormality related to FSFI total (94 vs. 30%) and domain scores compared with controls. The FSFI total scores were insignificantly different among patients as rated by residence, occupational status, educational level, and age groups. However, significantly lower SF scores were reported among patients with morning stiffness (14/100).

Others of Coskun et al., 2014; Hari et al., 2014 found that all sexuality dimensions were affected in women with RA except pain. One study of van Berlo et al., 2007 showed that satisfaction and pain among women with RA were not statistically different compared with controls. Lubrication and orgasm domains were impaired in all patients, whereas desire was the least affected dimension (91%). El Miedany et al., 2012 found that pain was the least contributing domain in patients with RA with SD (73%), whereas orgasmic disorder was the most prevalent (96.8%).

In addition to above findings, we assessed the DAS score of the studied group and it showed that it was ranged between 2.0 – 5.5 with mean value  $3.14 \pm 1.278$  and it show that more than one third of the patients classified as Remission (37.0%). In the study done by Azab et al., 2021 reported that DAS score was higher insignificantly in females than males  $5.5 \pm 8.2$  versus  $4.1 \pm 1.9$  respectively but the severity of DAS was statistically significant. Pain is a core complaint among rheumatoid arthritis (RA) patients, and persistent pain requires treatment adjustments according to current strategies. VAS score of the studied women were assessed, and showed that it was ranged between 2 – 8 with mean value  $4.80 \pm 2.156$  and the most of the patients classified as Mild Pain (39.0%).

Ono et al., 2016 reported that the Disease Activity Score-28 was 3.3. While, Azab et al., 2021 reported that the mean HAQ score was also higher but insignificantly in female than male patients  $1.3 \pm 1$  versus  $1.2 \pm 1.1$  respectively. Moreover; Hamilton Anxiety Rating Scale (HAM-A) of the studied women was ranged between 10 – 26 with mean value  $18.36 \pm 4.284$  and it show that more than half of the patients classified as mild to moderate (67.0%). Azab et al., 2021 reported that mean HADs A score was higher in females than males,  $4.1 \pm 3.2$  versus  $3.3 \pm 2.1$  respectively ( $P > 0.05$ ). Mean HADs D score was higher significantly also in females than males,  $8.9 \pm 5.8$  versus  $7.1 \pm 4.9$  respectively.

In the present study, the correlation between Female Sexual Function Index (FSFI) and other parameters were assessed, and it showed highly statistically significant negative correlation between Female Sexual Function Index (FSFI) and each of DAS, VAS, MHAQ, HAM-A and Testosterone level while it showed statistically significant positive correlation between Female Sexual Function Index (FSFI) and each of Estrogen and Progesterone. Nearly similar to our findings, The

study of Azab et al., 2021 reported that the predictors of SD prevalence in RA patients revealed that in female patients; The prevalence of FSD was significantly related to disease duration ( $U = 1654.0 - P < 0.001$ ), DAS score ( $U = 11416.0 - P < 0.001$ ), HADs D score ( $U = 12128.0 - P < 0.001$ ), HAQ score ( $U = 12250.0 - P < 0.001$ ), VAS score ( $U = 12064.0 - P < 0.001$ ), joint deformity ( $\chi^2 = 92.39 - P < 0.001$ ) and the number of drugs ( $\chi^2 = 119.8 - P < 0.001$ ).

In the same line, FSD was found in 64 of 140 Egyptian women (45.7%) with RA in an Egyptian study by El Miedany et al., 2012. Coskun and colleagues in 2014 studied the relation between SD and RA on 32 females and 20 controls and reported that all sexual domains of FSFI including desire, arousal, lubrication, orgasm, and satisfaction were lower in the RA group than controls except for pain which was higher in controls than the RA group. In 2021 Zhou et al., studied sexual functions on 151 Chinese mainland female patients with RA (mean age:  $46.3 \pm 8.6$  years) and 146 healthy control subjects (mean age  $45.7 \pm 7.6$  years). The prevalence of FSD was 67.5% in RA patients versus 54.1% in controls ( $P < 0.05$ ). Marital dysfunction, postmenopausal status, BMI, physical component summary, and resignation coping style were significant predictive factors.

In the study of Alia et al., 2019; a significant association was found between sexual dysfunction and pain ( $p = 0.001$ ), tender joint counts ( $p = 0.04$ ), DAS28 ESR ( $p = 0.043$ ), fatigue ( $p = 0.028$ ), and functional disability ( $p = 0.02$ ). No association was found between sexual dysfunction and treatment. In multivariate analysis, only pain was a predictive factor of sexual dysfunction in patients ( $p = 0.05$ , OR = 1.26 [1.16–1.3]).

## Conclusion

There was high prevalence of sexual dysfunction and depression in RA patients. Sexual dysfunction and depression might be present concomitantly in RA patients and are suggested to be associated with worse clinical aspects. There is no association of the aspects of sexual function with depression or with the intensity of depression symptoms. Our study suggests that rheumatoid arthritis has a negative impact on patients' sexuality. Age of patients and partners, pain, and tender joints appear to be the main factors influencing sexual function.

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