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# Dopamine as a potential diagnostic biomarker in women's sexual dysfunction

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## Abstract

Dopamine and prolactin are the key mediators involved in sexual function in both males and females, but the role of dopamine in female sexual dysfunction (FSD) is still unclear. The aim was to investigate the possible role of dopamine and their relationship with sex steroid hormones (estrogen, progesterone and dehydroepiandrosterone; DHEA) and prolactin levels in Egyptian women suffering from sexual dysfunction. This study included 84 women having sexual dysfunction (FSD group) and 84 normal sexual function (control group). All women were subjected to the questionnaire to assess their demographic and gynecological data as well as female sexual function index (FSFI). Blood samples were collected from all women for measuring serum estradiol, progesterone, DHEA, prolactin and dopamine levels. FSD patients had significantly higher serum progesterone and DHEA and prolactin levels; while significantly lower dopamine and estradiol levels versus controls ($p < 0.001$). In all women, dopamine level appeared as a predictor of FSD at cut-off point $\leq$8.8 ng/mL with sensitivity (75%), specificity (92%) and accuracy (83%) ($p < 0.001$). The low levels of dopamine were associated with significantly higher prevalence in patients with low estradiol ($p < 0.001$) and high progesterone ($p < 0.001$), DHEA ($p < 0.001$) and prolactin ($p = 0.004$). Also, dopamine was significantly positive correlation with arousal score ($r = 0.16$, $p = 0.04$), and negative correlation with age ($r = -0.31$, $p < 0.001$), pain score ($r = -0.19$, $p = 0.01$), DHEA ($r = -0.45$, $p < 0.001$) and prolactin ($r = -0.28$, $p < 0.001$). Low serum dopamine level is a potential diagnostic biomarker in women's sexual dysfunction and their association with high prolactin and sex steroid hormones dysfunction.

## Keywords

Dopamine; Sex hormone; Female sexual dysfunction

# La dopamina como potencial biomarcador diagnóstico en la disfunción sexual de la mujer


## Resumen

La dopamina y la prolactina son los mediadores clave involucrados en la función sexual tanto en hombres como en mujeres, pero el papel de la dopamina en la disfunción sexual femenina (FSD) aún no está claro. El objetivo fue investigar el posible papel de la dopamina y su relación con las hormonas esteroides sexuales (estrógenos, progesterona y dehidroepiandrosterona; DHEA) y los niveles de prolactina en mujeres egipcias que padecen disfunción sexual. Este estudio incluyó a 84 mujeres con disfunción sexual (grupo DSF) y 84 con función sexual normal (grupo control). Todas las mujeres fueron sometidas al cuestionario para evaluar sus datos demográficos y ginecológicos, así como el índice de función sexual femenina (FSFI). Se recolectaron muestras de sangre de todas las mujeres para medir los niveles séricos de estradiol, progesterona, DHEA, prolactina y dopamina. Los pacientes con FSD tenían niveles séricos de progesterona, DHEA y prolactina significativamente más altos; mientras que los niveles de dopamina y estradiol fueron significativamente más bajos que los controles ($p < 0.001$). En todas las mujeres, el nivel de dopamina apareció como predictor de DSF en el punto de corte $\leq$8.8 ng/mL con sensibilidad (75%), especificidad (92%) y precisión (83%) ($p < 0.001$). Los niveles bajos de dopamina se asociaron con una prevalencia significativamente mayor en pacientes con estradiol bajo ($p < 0.001$) y progesterona alta ($p < 0.001$), DHEA ($p < 0.001$) y prolactina ($p = 0.004$). Además, la dopamina tuvo una correlación significativamente positiva con la puntuación de excitación ($r = 0.16$, $p = 0.04$) y una correlación negativa con la edad ($r = -0.31$, $p < 0.001$), la puntuación del dolor ($r = -0.19$, $p = 0.01$), DHEA ($r = -0.45$, $p < 0.001$) y prolactina ($r = -0.28$, $p < 0.001$). El nivel bajo de dopamina sérica es un biomarcador diagnóstico potencial en la disfunción sexual de la mujer y su asociación con la disfunción de hormonas esteroides sexuales y prolactina alta.



## Palabras Clave

Dopamina; Hormonas sexuales; Disfunciones sexuales femeninas


## 1. Introduction

Female sexual dysfunction (FSD) is a complex aetiological integration of biological, hormonal, psychological and social factors that can adverse sexual health and quality of life in women or strain their relationships with their partners [1]. Incidence of FSD has been estimated to range from 6% to 19% and can happen in certain or in all sexual situations [2, 3]. In clinical practice, there is limited understanding of sexual function regarding endocrine disorders in women, whose sexuality is hormone-dependent throughout their life [4].

Sexual function is a complex interaction balance between inhibitory (serotonin and prolactin) and excitatory (dopamine, estrogen, progesterone and testosterone, oxytocin) pathways present centrally in brain and peripherally [1].

Dopamine is a neurotransmitter and synthesized in the central nervous system as well as in the periphery [5]. Dopamine constitutes about 2–4% of the catecholamine released from sympathetic nerves and represents 50–90% of plasma dopamine has a sympathoneural source [6, 7].

Dopamine dysregulation caused by neurological (such as Parkinson's disease, schizophrenia and Alzheimer's disease) or endocrine (such as hyperprolactinemia) disorders has been correlated to dopamine as a regulator of sexuality [8, 9]. Dopamine improved orgasm in women *via* activation the nucleus accumbens of the forebrain [8, 10], although its role in orgasm is still unclear. While, activation of D1 and D2 dopamine receptor subtypes in the preoptic area of the hypothalamus led to sexual desire and sexual arousal [8, 11, 12], Dopaminergic agents such as dextroamphetamine, methylphenidate or bupropion were useful for ameliorating the impaired libido, arousal and orgasm in men and women [5, 9].

Prolactin is a mediator involved in female sexual function [13]. The role of dopamine and a sex-specific dopamine steroid interaction in women suffering sexual disorders are still unclear.

Therefore, the aim of this study was to investigate the possible role of dopamine as a potential marker and their relationship with estrogen, progesterone and dehydroepiandrosterone (DHEA) and prolactin levels in Egyptian women suffering sexual dysfunction.

## 2. Material and method

### 2.1 Patients

This study involved 168 Egyptian females. They were enrolled in outpatient clinics of Gynecology, Andrology and Sexually Transmitted Diseases (STDs), Menoufia University. Women having normal sexual function were selected from employees and medical professionals working in that hospital, in addition to friends, relatives and colleges. The included women were divided into two groups; group 1; include 84 women having sexual dysfunction (FSD group) and group 2; include 84 women having normal sexual function (control group).

The study included sexually active married females ranged from 27 to 43 years [14] (age of legal marriage at 18 years [15], according to "Egypt National Child Protection Legislation") with normal regular menstrual cycle. Any female had one or more of the following was excluded from the study: (1) irregular or any abnormality of menstrual cycles; (2) women less than 18 years [15] or post-menopausal women; (3) evident psychological disorders (*e.g.*, depression, anxiety and schizophrenia) and neurological disorders (*e.g.*, epilepsy,

Alzheimer's disease and ataxia); (4) the hypertensive, diabetes, pregnant, lactating females and those receiving contraceptives or hormonal therapy.

The studied females were subjected to some questionnaires to assess their demographic (age, residence, education, occupation and socioeconomic level); gynecological (level of sexual knowledge, circumcision, having children, number of children, previous marriage and years of marriage) and husband data (marital relation, husband desire and erection) as well as sexual function using female sexual function index (FSFI). The FSFI was utilized to assess FSD which has validated by Arabic language to evaluate six domains throughout the previous 4 weeks: (a) desire, (b) arousal, (c) lubrication, (d) orgasm, (e) satisfaction and (f) pain. The scale for each domain was range between 0 to 6. The total score was calculated by summation of all domain scores. It had range from 2 to 36. Total score $\leq$23 means sexual dysfunction (patient group), and >23 means normal sexual function (control group) [15–17].

## 2.2 Laboratory analysis

At 21 days after the first day of the last menstrual cycle of each participant (the mid-luteal phase), under complete aseptic conditions, morning 5 mL of venous blood was withdrawn after 10–12 hours fasting. The samples were transferred into a plain tube left to clot for 30 minutes, then centrifuged at 3000 rpm for 10 minutes. The obtained sera were kept frozen at −20 °C till time of analysis.

Estrogen [18], progesterone [19] and DHEA [20] were assayed by the IMMULITE 2500 (Diagnostic Products Corp., Los Angeles, CA, USA), which is an automated, random-access immunoassay analyzer with a solid phase washing process and a chemiluminescence detection system [14]. Prolactin was measured by electro-chemiluminescence immunoassay analyzer (ECLIA) from Roche Diagnostics (Elecsys® Prolactin II, cobas e402/801, Indianapolis, IN, USA) [13, 21]. Dopamine assay was investigated by the competitive Dopamine Enzyme Linked Immunosorbent Assay (ELISA) Kit from Abcam (ab285238) (Boston, MA, USA) according to the manufacturer instruction [22].

## 2.3 Statistical analysis

Statistical analysis of the present study was conducted with SPSS Version 23 (IBM Corp., Armonk, NY, USA). Quantitative data were appeared as mean ± standard deviation (SD) [14], where student *t*-test was used for comparison of two groups with normally distributed data, while Mann Whitney (U test) was used for not normally distributed data. Number and percentages (%) were used to express qualitative data where Chi-square ($\chi^2$) and fisher exact test were used. Correlation test (*r*-test) was used to test association between quantitative data. Receiver operator characteristic (ROC) curve with respective points of maximal accuracy for sensitivity and specificity were generated. Area under the ROC curve measures the accuracy of the test. An area of 1 represents a perfect result; an area of 0.5 represents a worthless result. Differences were considered significant at two-sided *p*-value $< 0.05$.

# 3. Results

## 3.1 Socio-demographic, gynaecological and husband data of all subjects

The age of the studied women sexually active married with normal regular menstrual cycle (n = 168) ranged from 27 to 43 years (FSD, 36.76 ± 6.79 and normal sexual function, 36.71 ± 6.36 years; Table 1). More than half were from urban (102/168, 60.7%). Most of our participants were low educated (148/168, 88%) and had moderate socioeconomic level (113/168, 67.3%) and 109 of them had a professional occupation (47.4%). Regarding gynaecological data most of studied women had children (153/168, 91%) with a mean number of two children. About half of them were with low sexual knowledge (79/168, 47%). Most of them were circumcised (123/168, 73.2%) and 4 of them were previously married. More than half of the studied women (93/168, 55%) had excellent marital relationship. Most of the studied women reported no abnormality regarding their husband desire (141/168, 84%) and erection (150/168, 89%).

Women with longer marriages, parity, more children, circumcision, greater husband desire and erection difficulties were all found to be potential risk factors for FSD when compared to controls ($p < 0.05$) (Table 1).

## 3.2 FSFI domains of all women

Sexual desire, sexual arousal, lubrication, sexual orgasm and satisfaction scores were significantly lower in female having FSD than controls ($p < 0.001$ for all). However, pain score was significantly higher in those having FSD than controls ($p = 0.004$). The FSFI total score was significantly lower in women having FSD than those with normal sexual function ($p < 0.001$) (Fig. 1I).

## 3.3 Serum dopamine and sex hormones levels of all women

Serum estradiol levels were significantly lower in women having sexual dysfunction (33.92 ± 5.45 pg/mL *vs.* 57.97 ± 2.87 pg/mL, $p < 0.001$) than those with normal sexual function. However, serum progesterone (1.62 ± 0.52 ng/mL *vs.* 1.38 ± 0.05 ng/mL, $p < 0.001$), DHEA (3.47 ± 0.06 ng/mL *vs.* 1.16 ± 0.07 ng/mL, $p < 0.001$) and prolactin (13.45 ± 1.89 ng/mL *vs.* 5.00 ± 0.34 ng/mL, $p < 0.001$) levels were significantly higher in women having sexual dysfunction than those with normal sexual function. Serum dopamine levels were significantly lower in women having sexual dysfunction (6.68 ± 0.45 ng/mL *vs.* 11.48 ± 0.27 ng/mL, $p < 0.001$) than those with normal sexual function (Fig. 1IIA–E).

## 3.4 Diagnostic validity of estradiol, progesterone, DHEA, prolactin and dopamine levels in women's with sexual dysfunction

In FSD group, a predictor of FSD was diagnosed when women had a cut-off point value of estradiol (31.7 pg/mL) with sensitivity (99%) and specificity (87%); progesterone (0.125 ng/mL) with sensitivity (74%) and specificity (1%); DHEA (4.025 ng/mL) with sensitivity (99%) and specificity

**TABLE 1. Sociodemographic, gynecological and husband data of all participants.**

| | Sexual dysfunction (FSD group) (n = 84) | Normal sexual function (Control group) (n = 84) | Test of significant | *p* value |
|---|---|---|---|---|
| Age group (yr) | 36.76 ± 6.79 | 36.71 ± 6.36 | $t = 0.05$ | 0.960 |
| Menstrual cycle (d) | 28.60 ± 3.10 | 29.10 ± 3.60 | $t = 0.96$ | 0.341 |
| Years of marriage | 11.69 ± 5.68 | 5.96 ± 3.69 | U = 7.75 | <0.001* |
| Parity (no. of children) | 2.51 ± 1.06 | 1.85 ± 1.06 | U = 4.04 | <0.001* |
| Residence n (%) | | | | |
| Rural | 31 (36.9%) | 35 (41.7%) | $\chi^2 = 0.40$ | 0.532 |
| Urban | 53 (63.1%) | 49 (58.3%) | | |
| Female's education n (%) | | | | |
| High | 3 (3.6%) | 2 (2.4%) | | |
| Moderate | 10 (11.9%) | 5 (5.9%) | $\chi^2 = 2.11$ | 0.351 |
| Low | 71 (84.5%) | 77 (91.7%) | | |
| Female's occupation n (%) | | | | |
| Housewife | 22 (26.2%) | 13 (15.5%) | | |
| Nonprofessional | 15 (17.9%) | 9 (10.7%) | $\chi^2 = 5.88$ | 0.053 |
| Professional | 47 (56.0%) | 62 (73.8%) | | |
| Social class n (%) | | | | |
| High | 1 (1.2%) | 0 (0.0%) | | |
| Moderate | 63 (75.0%) | 50 (59.5%) | $\chi^2 = 6.13$ | 0.052 |
| Low | 20 (23.8%) | 34 (40.5%) | | |
| Sexual knowledge n (%) | | | | |
| High | 5 (6.0%) | 5 (6.0%) | | |
| Moderate | 43 (51.2%) | 36 (42.9%) | $\chi^2 = 1.24$ | 0.540 |
| Low | 36 (42.9%) | 43 (51.2%) | | |
| Circumcision n (%) | | | | |
| Yes | 72 (85.7%) | 51 (60.7%) | $\chi^2 = 13.39$ | <0.001* |
| No | 12 (14.3%) | 33 (39.3%) | | |
| Have children n (%) | | | | |
| Yes | 81 (96.4%) | 72 (85.7%) | $\chi^2 = 5.93$ | 0.012* |
| No | 3 (3.6%) | 12 (14.3%) | | |
| Previous marriage n (%) | | | | |
| Yes | 3 (3.6%) | 1 (1.2%) | $F = 1.02$ | 0.310 |
| No | 81 (96.4%) | 83 (98.8%) | | |
| Marital relation n (%) | | | | |
| Excellent | 49 (58.3%) | 44 (52.4%) | | |
| Good | 24 (28.6%) | 34 (40.5%) | $\chi^2 = 3.46$ | 0.182 |
| Bad | 11 (13.1%) | 6 (7.1%) | | |
| Problem with husband desire n (%) | | | | |
| Yes | 20 (23.8%) | 7 (8.3%) | $F = 7.46$ | 0.006* |
| No | 64 (76.2%) | 77 (91.7%) | | |
| Problem with erection of the husband n (%) | | | | |
| Yes | 13 (15.5%) | 5 (6.0%) | $F = 3.98$ | 0.041* |
| No | 71 (84.5%) | 79 (94.0%) | | |

*FSD: Female sexual dysfunction; $\chi^2$: chi square test; t: t-test; F: Fisher exact; U: Mann-Whitney; Data were presented as numbers (%) and mean ± SD. *p value is significant < 0.05.*

(94%), prolactin (4.025 ng/mL) with sensitivity (77%) and specificity (55%); and dopamine (8.8 ng/mL) with sensitivity of (75%) and specificity of (92%) ($p < 0.001$ for all) (Fig. 1IIIA–C). Also, other parameters such as the accuracy with area under the curve (AUC) and 95% confidence interval (CI) for all hormones as shown in Fig. 1IIIC.

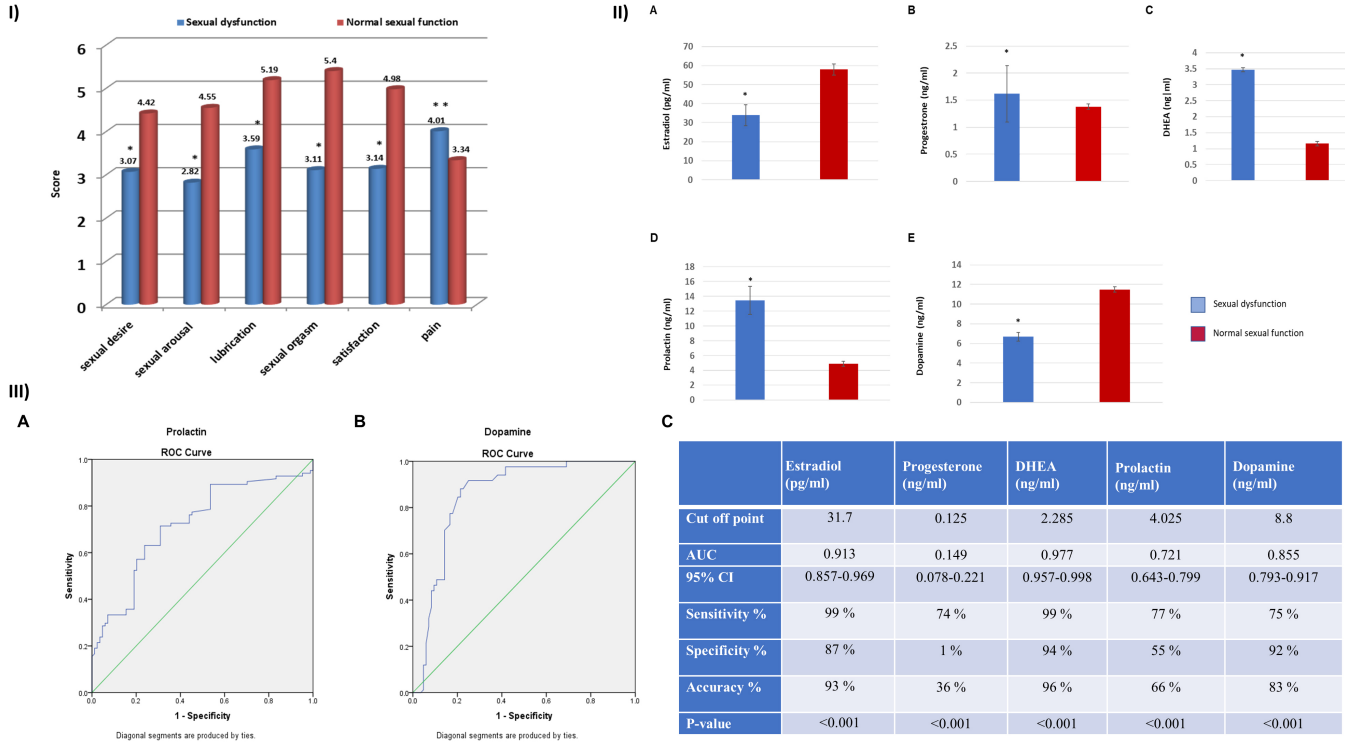
In the entire studied participants, all women were classified according to serum prolactin and dopamine levels into four quartiles depending on statistically cut-off points the level of prolactin and dopamine (Fig. 2A). The analysed data showed that the highest quartile levels of prolactin (quartile-3 and quartile-4 groups) (Fig. 2B) and lowest quartile levels of dopamine (quartile-1 and quartile-2 groups) (Fig. 2C) were associated with women's with sexual dysfunction versus controls.

## 3.5 Serum level of dopamine and risk of women's sexual dysfunction

In the entire studied participants, all women were classified according to serum dopamine levels (cutoff point, 8.8 ng/mL) into low and high groups (Fig. 2A,D). Therefore, 70 women had low levels of dopamine, while 98 women had high levels of dopamine. The age of women based on low dopamine group (36.4 ± 6.56) versus high dopamine group (35.91 ± 7.21) were not show any significant difference ($p = 0.65$). The other laboratory hormonal levels based on low dopamine levels (<8.8 ng/mL, $p < 0.001$) showed a significantly higher prevalence in patients with low level of estradiol ($p < 0.001$) and high levels of serum progesterone ($p < 0.001$), DEHA ($p < 0.001$) and prolactin ($p = 0.004$) (Fig. 2D).

## 3.6 Correlation of serum dopamine to age, FSFI domains and other hormones

In all participant women, serum dopamine levels were significant negative correlations with age ($r = -0.31$, $p < 0.001$) (Fig. 3I). There was a significant positive correlation between serum DHEA level and arousal domain ($r = 0.16$, $p = 0.04$), but negatively with pain domain ($r = -0.19$, $p = 0.01$) (Fig. 3I). There was a significant positive correlation between serum prolactin level and orgasm domain ($r = 0.37$, $p < 0.001$) but negatively with arousal ($r = -0.49$, $p < 0.001$), lubrication ($r = -0.49$, $p < 0.001$), satisfaction ($r = -0.46$, $p < 0.001$), pain domain ($r = -0.40$, $p < 0.001$) and total scores ($r = -0.05$, $p < 0.001$) (Fig. 3I). On the other hand, there was a significant positive correlation between serum dopamine level and arousal domain ($r = 0.16$, $p = 0.04$), and significant negative correlation regarding pain domain ($r = -0.19$, $p = 0.01$) (Fig. 3I).




| | Estradiol (pg/ml) | Progesterone (ng/ml) | DHEA (ng/ml) | Prolactin (ng/ml) | Dopamine (ng/ml) |
|---|---|---|---|---|---|
| Cut off point | 31.7 | 0.125 | 2.285 | 4.025 | 8.8 |
| AUC | 0.913 | 0.149 | 0.977 | 0.721 | 0.855 |
| 95% CI | 0.857-0.969 | 0.078-0.221 | 0.957-0.998 | 0.643-0.799 | 0.793-0.917 |
| Sensitivity % | 99 % | 74 % | 99 % | 77 % | 75 % |
| Specificity % | 87 % | 1 % | 94 % | 55 % | 92 % |
| Accuracy % | 93 % | 36 % | 96 % | 66 % | 83 % |
| P-value | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

**FIGURE 1. Female sexual function index (FSFI) and sex hormones and dopamine levels in women's with sexual dysfunction.** (I) FSFI domains in all women. (II) Comparison of serum sex-steroid hormones, prolactin and dopamine hormone levels in all women. This figure showed serum estradiol (IIA), progesterone (IIB), dehydroepiandrosterone (DHEA, IIC), prolactin (IID) and dopamine (IIE) levels in female sexual dysfunction (FSD) and normal sexual function (control group). (III) The area under the receiver operating characteristics (ROC) curve for prolactin (IIIA) and dopamine (IIIB) levels in all participant women. Diagnostic validity, cut-off points, sensitivity and specificity of estradiol, progesterone, dehydroepiandrosterone (DHEA), prolactin and dopamine levels were assessed in all participant women (IIIC). Data were presented as mean ± SD. *$p$ value is significant < 0.001. **$p$ value is significant < 0.05; AUC: area under the curve; CI: confidence interval.

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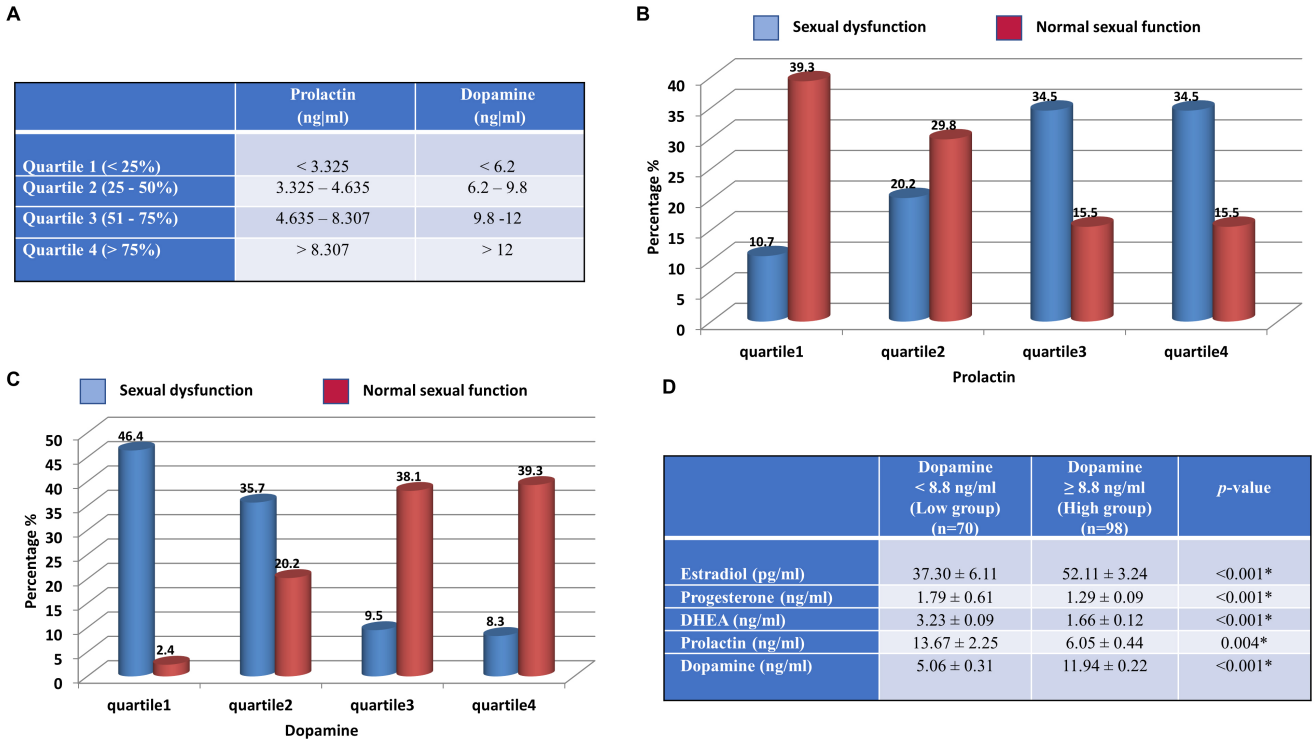
| | Prolactin (ng|ml) | Dopamine (ng|ml) |
|---|---|---|
| Quartile 1 (< 25%) | < 3.325 | < 6.2 |
| Quartile 2 (25 - 50%) | 3.325 – 4.635 | 6.2 – 9.8 |
| Quartile 3 (51 - 75%) | 4.635 – 8.307 | 9.8 -12 |
| Quartile 4 (> 75%) | > 8.307 | > 12 |




| | Dopamine < 8.8 ng/ml (Low group) (n=70) | Dopamine ≥ 8.8 ng/ml (High group) (n=98) | *p*-value |
|---|---|---|---|
| Estradiol (pg/ml) | 37.30 ± 6.11 | 52.11 ± 3.24 | <0.001* |
| Progesterone (ng/ml) | 1.79 ± 0.61 | 1.29 ± 0.09 | <0.001* |
| DHEA (ng/ml) | 3.23 ± 0.09 | 1.66 ± 0.12 | <0.001* |
| Prolactin (ng/ml) | 13.67 ± 2.25 | 6.05 ± 0.44 | 0.004* |
| Dopamine (ng/ml) | 5.06 ± 0.31 | 11.94 ± 0.22 | <0.001* |

**FIGURE 2. The incidence of female sexual dysfunction (FSD) among all subjects.** All women were classified according to quartiles levels of prolactin and dopamine (A). Distribution of percentage % of female sexual dysfunction (FSD) among the different quartiles of prolactin (B) and dopamine (C) in FSD and normal sexual function (control group). Laboratory hormonal data of all participants according to cutoff value of dopamine levels (D). DHEA: dehydroepiandrosterone. Data were presented as a percentage %, mean ± SD. *$p$ value is significant $< 0.05$.

In all participant women, there was a non-significant positive correlation between serum dopamine regarding estradiol and progesterone levels ($r = 0.03$, $p = 0.69$; $r = 0.045$, $p = 0.56$) respectively (Fig. 3IIA,B). On other hand, a significant negative correlation between serum dopamine with DHEA ($r = -0.45$, $p < 0.001$) and prolactin ($r = -0.28$, $p < 0.001$) levels was observed (Fig. 3IIC,D).

## 4. Discussion

Normal sexual function in female are 4 sexual phases: excitement/arousal and plateau, then orgasm and finally resolution [23]. Women's sexual dysfunction is hypoactive sexual function disorders leading to failure of sexual fantasies and interpersonal distress [1, 24].

Our data showed women with sexual dysfunction had recurrent and persistent symptomatic disturbances of normal sexual function phases such as low in sexual desire, arousal, lubrication, satisfaction and orgasm with discomfort or painful sexual intercourse. Our results were in agreement with other studies [1, 2].

Our data showed women with sexual dysfunction had significantly low serum estradiol and dopamine levels, while high serum progesterone, DHEA and prolactin levels. These results were in agreement with other studies showing high progesterone [14], DHEA [25, 26] and prolactin [13, 27], while low estrogen [14] and dopamine [10].

Our data showed sex steroid hormones (estradiol, progesterone and DEHA) dysfunction in women with sexual dysfunction, and serum DHEA level was significantly positive correlated with arousal but negatively with pain domain. Supporting our results, the low estradiol levels associated with vaginal dryness and vulvovaginal atrophy and dyspareunia; and local or systemic use of estrogen improved the women complaining FSD [28, 29]. Additionally, estradiol is a modulator of serotonergic function in the brain to regulate desire and mood, which could affect sexual function [30]. Also, high DHEA serum levels were reported in women FSD having polycystic ovaries with low arousal [26].

Our data showed serum prolactin level was significantly positive correlated with orgasm but negatively with arousal, lubrication, satisfaction, pain and total scores in FSD patients. These data agreed with other studies showing hyperprolactinemia associated with sexual dysfunction in women [13, 27].

Our data showed the low levels of dopamine (≤8.8 ng/mL) were significantly associated with higher prevalence in patients with low estradiol and high progesterone, DHEA and prolactin. Dopamine was significantly positive correlation with arousal score, and negative correlation with age, pain score, DHEA and prolactin levels in FSD patients. Supporting our results, lower dopamine with aging impaired sexual function in old women [31]. Dopamine agonist enhances activation of sexual motivation, arousal, orgasm and sexual reward behaviors (desire and wanting) in many studies [9, 32, 33]. The interaction pathway between dopamine and prolactin was shown as feedback mechanism affecting both male and

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| | Estradiol (pg/ml) | | Progesterone (ng/ml) | | DHEA (ng/ml) | | Prolactin (ng/ml) | | Dopamine (ng/ml) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* |
| **Age (years)** | 0.12 | 0.14 | -0.02 | 0.82 | -0.09 | 0.27 | 0.09 | 0.24 | -0.31 | <0.001* |
| **Female sexual function index score** | | | | | | | | | | |
| **Desire** | 0.04 | 0.59 | 0.04 | 0.61 | 0.11 | 0.16 | -0.07 | 0.40 | 0.11 | 0.16 |
| **Arousal** | 0.08 | 0.31 | 0.07 | 0.34 | 0.16 | 0.04* | -0.49 | <0.001* | 0.16 | 0.04* |
| **Lubrication** | 0.11 | 0.15 | 0.09 | 0.23 | 0.09 | 0.21 | -0.49 | <0.001* | 0.09 | 0.21 |
| **Orgasm** | 0.06 | 0.41 | 0.06 | 0.39 | 0.09 | 0.22 | 0.37 | <0.001* | 0.09 | 0.22 |
| **Satisfaction** | 0.08 | 0.33 | 0.04 | 0.58 | 0.05 | 0.50 | -0.46 | <0.001* | 0.05 | 0.50 |
| **Pain** | 0.04 | 0.58 | 0.05 | 0.50 | -0.19 | 0.01* | -0.40 | <0.001* | -0.19 | 0.01* |
| **Total score** | 0.09 | 0.23 | 0.07 | 0.31 | 0.13 | 0.10 | -0.05 | <0.001* | 0.13 | 0.10 |

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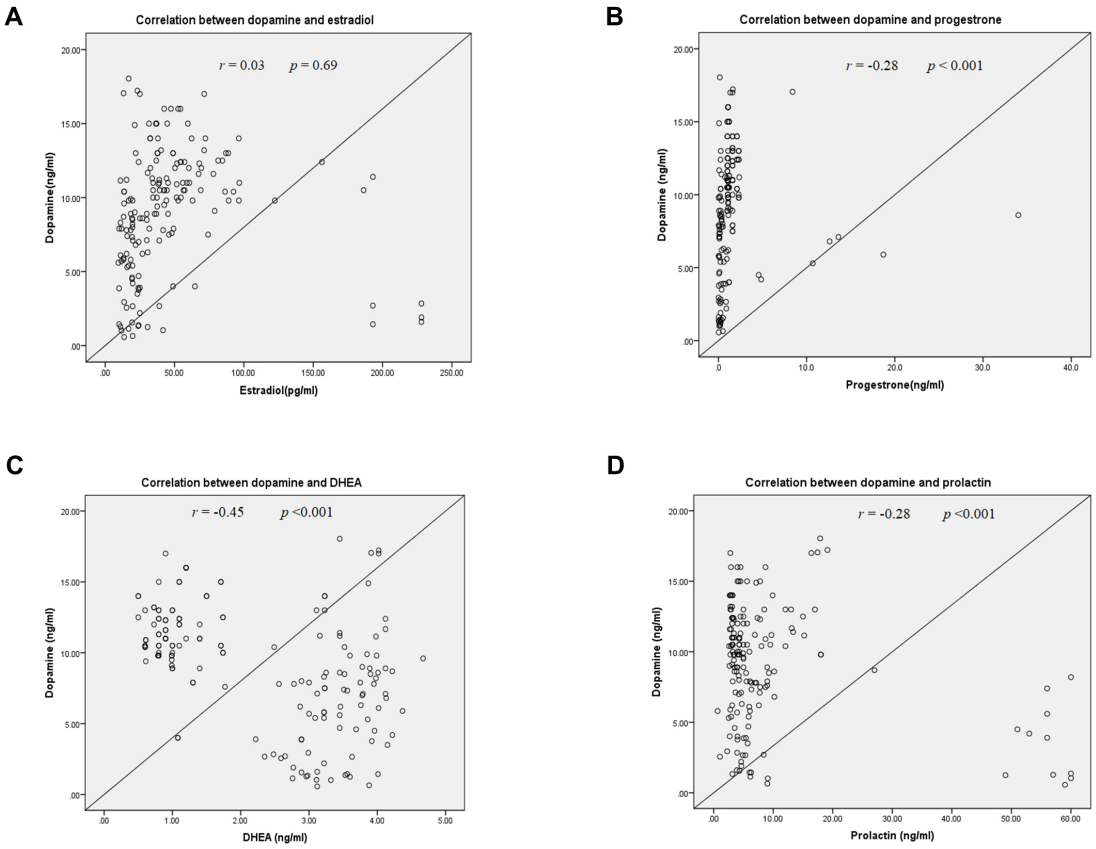


**FIGURE 3. Correlation of serum dopamine to age, FSFI domains and sex hormones.** (I) Correlations between studied hormones and different domains among all participant women. (II) Correlation of dopamine and other sex hormonal levels in all participant women: Correlation between dopamine and estradiol level (IIA); correlation between dopamine and progesterone level (IIB); correlation between dopamine and dehydroepiandrosterone (DHEA) level (IIC); and correlation between dopamine and prolactin level (IID). DHEA: dehydroepiandrosterone; *r*: Spearman correlation; **p* value is significant < 0.05.

female sexual arousal and orgasmic disorders [10]. Decreased dopamine levels were associated with painful symptoms during sexual intercourse in women [34]. However, there is no clear study showing lowering of serum dopamine in FSD, but their lowering evidence during administration of specific drugs such as antipsychotic agents that impair orgasm *via* blocking dopamine receptors or dopamine antagonist drugs [32, 35]. In contrast, dopamine agonist, releasers or reuptake inhibitors improved the sexual orgasm in men and women [36]. The role of dopamine in facilitating orgasm was detected during several brain-imaging studies that provide evidence that the dopaminergic "reward" system is activated during sexual arousal and orgasm *via* activation in the ventral midbrain area [37]. In contrast, another studies showed there was no evidence to the effect of dopamine antagonism on conditioned sexual response in women [32], or lack of sexual drive and function on healthy women with dopamine agonist [5].

Taken together, mediobasal hypothalamus (MBH) and hypothalamic pituitary gonadal (HPG) axis have role in regulation of estrogen, progesterone and testosterone for modulating sexual arousal, interest and desire sexual response [11]. Additionally, dopamine interacts with ovarian hormones and neuronal excitability in the ventromedial area in the hypothalamus [5]. Dopamine binds to the G protein of dopamine receptors and induces signaling pathway of many physiological processes including motor control, motivation, arousal, reinforcement and reward [5, 6, 10].

Our recommendation to increase the number of patients including their clinical data and complaints in further study to get a better evaluation and to clarify the correlation of dopamine in women suffering sexual dysfunction that may be targeted during FSD management.

## 5. Conclusions

In Egyptian women suffering from sexual dysfunction, low serum dopamine and estradiol levels, together with high serum progesterone, DHEA and prolactin levels, were potential diagnostic hormonal profiles and may play active roles in the pathophysiology of FSD and should be targeted during FSD management.

### AVAILABILITY OF DATA AND MATERIALS

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### AUTHOR CONTRIBUTIONS

AGF, EAB, IE, WAT and SYA—shared the idea. WAT, ZE and ME—collected clinical data and blood samples of the patients. EAB and IE—performed the laboratory investigation. SYA—performed the statistic of the study. All authors participate in writing, reading, and approve the final manuscript.

### ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was permitted by the Ethical Committee of Faculty of Medicine, Menoufia University before conduction. A written informed consent was gotten from every participant before joining the study.

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### CONFLICT OF INTEREST

The authors declare no conflict of interest.

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