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Research Article

INVESTIGATING THE ENDOCRINE DISORDERS IN WOMEN WITH MENSTRUAL DISTURBANCES IN BAYELSA STATE, NIGER DELTA REGION OF NIGERIA

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ABSTRACT

Background: Many women in Bayelsa State, South-South Nigeria have been presenting with different menstrual disturbances and some with infertility problems that are associated with abnormal uterine bleeding, amenorrhea, dysmenorrhea, premature menopause and premature syndrome. Menstruation is an important indication of possible pregnancy as well as the reproductive health women and it is recognized universally that menstrual disturbances may accompany and most times, succeed endocrine disorders. **Objective:** The aim of the study was to investigate the various endocrine disorders associated with women of reproductive age experiencing different menstrual disturbances attending the different specialist hospitals in Yenagoa, Bayelsa State, Nigeria. This was with the interest of establishing the different hormone disorders and its prevalence in these women of Bayelsa State. **Method:** A total of 1852 subjects (women with menstrual disturbances) were randomly selected using a questionnaire design containing the information of age, last menstrual date, degree of irregularity, whether on medication for any infertility problem or preventive measures and have had any form of surgery. Excluded from the study were pregnant women, women above 45 years of age, those on infertility and contraceptive medication. Women who had undergone hysterectomy or have had abortion in the last three months. Analyses of the different hormones of the hypothalamic – pituitary- gonadal reproductive axis were measured using Enzyme Linked Immunosorbent Assay (ELISA). **Results:** From the study, it was observed that the menstrual disturbances were accompanied with female reproductive hormone fluctuations; with a high significant 79.97% of the women having one form of the endocrine disorders (P=0.012). The study has shown that 63.17% of the studied subjects had hypoestrogenism (P=0.019), 38.66% had hypergonadotropic hypogonadism (P=0.037) and a non-significant (P=0.063) 1.35% with hypogonadotropic hypogonadism. Analysis of the results also showed 15.12% of the subjects had hypothalamic amenorrhea (P=0.047), 30.62% with hyperprolactinaemia (P=0.033) and non-significant value of 1.30% with hypoprolactinaemia (P=0.064). From the study, 10.91% of the women with menstrual disturbances studied in Bayelsa State had hyperthyroidism (P=0.048), 4.75% with hypothyroidism (P=0.061), 3.73% with T3 thyrotoxicosis (P=0.060) and 2.37% with TBG excess (P=0.062). **Conclusion:** This study therefore concluded that a significant number ($p<0.05$) of women in Bayelsa State, Nigeria with menstrual disturbances are associated with different endocrine disorders, especially hypoestrogenism and hypergonadotropic hypogonadism probably due to life style (diet, obesity, stress), environmental factors and an underlying illness(infections, cancer and polycystic ovarian syndrome).

INTRODUCTION

Worldwide, reproductive ill health constitutes about 32% of total burden of disease among the reproductive age group women (1). It has been reported that endocrine dysfunction or disorder is frequently associated with menstrual disturbances (1, 3).The endocrine system is composed of endocrine glands and hormone-producing tissues and hormone receptors. These are series of glands that produce and secrete hormones that the body uses for a wide range of functions (4). The endocrine glands produce hormones (chemical messengers) that are secreted into the interstitial fluid, diffuse into blood capillaries and are carried via the circulatory system to target organs (5). Menstruation, is the periodical flow of blood from the uterus through the cervix and out through the vagina (6).The normal menstrual cycle occurs every 28±7 days, with duration of flow of 2 to 7 days and a loss of less than 80ml of menstrual blood (7) and is divided into menstrual phase, follicular phase, ovulation phase and luteal phase (8).Menstrual disturbances

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also called dysfunctional uterine bleeding (DUB) is an abnormal bleeding from the uterus in the absence of organic genital tract disorders and demonstrable extrogenital cause, accounts for 12 percent of the gynecology oriented complaints(9).They are predominantly a result of dysfunction at any point in the hypothalamic–pituitary (hypophyseal)–ovarian–endometrial axis (10). The common menstrual disorders in adolescents are amenorrhea - the absence of menstruation, abnormal/excessive uterine bleeding – heavy flow > 80ml, polymenorrhea – describes cycles with intervals of ≤ 21 days, dysmenorrhea – refers to excessive menstrual pain which is severe enough to limit normal activity or require medication, and premenstrual syndrome – these are reported pre-menstrual complaints that typically do not cause functional impairment (10, 11).

Reproductive morbidity comprises of contraceptive morbidity, obstetric morbidity, and gynaecological morbidity. Gynaecological morbidity includes reproductive tract infections (RTIs) and other types of non-infectious morbidities like menstrual disorders, infertility, gynaecological cancer, congenital malformations or birth defects or injuries, sexual dysfunctions and menopausal symptoms (12). Globally among the reproductive age group gynaecological morbidity leads to about 20% loss of healthy life in total years (13).

Endocrine disorders involve the body's over- or under-production of certain hormones. They include hypothyroidism, hyperthyroidism, hyperprolactinemia, congenital adrenal hyperplasia, diseases of the parathyroid gland, diabetes mellitus, diseases of the adrenal glands (including Cushing's syndrome and Addison's disease), and ovarian dysfunction (including polycystic ovary syndrome), etc. (14,15). In hypergonadotropic hypogonadism, reduced levels of estrogen in women lead to increased pituitary gonadotropin secretion in a negative feedback mechanism (16).In hypogonadotropic hypogonadism, deficiency of pituitary gonadotropins (FSH and LH)leads to secondary ovaries/testes failure, manifested by menstrual disorders in women (17, 18). In Dysfunction of the hypothalamic-pituitary-gonadal axis, impaired activation of the hypothalamic-pituitary-gonadal axis results in alterations of pulsatile GnRH secretion(usually reduced frequency and amplitude of GnRH pulses) and in women, there is no gonadotropin surge, without which ovulation does not occur, or too low FSH and LHconcentrations, which result in disturbances in maturation of Graafian follicles or luteal phase insufficiency (19. 20).In obese subjects, because of higher estradiol levels, FSH concentration is more reduced, but not very low, so that the new follicle is growing, but does not reachfull maturity and the ability to ovulate (15). The most important cause of menstrual cycle irregularity is functional hypothalamic amenorrhea associated with decreased gonadotropin – releasing hormone secretion and hypothalamic-pituitary – adrenal (HPA) axis dysregulation (20, 21)

Hyperprolactinemia impairs pulsatile secretion of GnRH by the hypothalamus, and thus pulsatile LH and FSH release from thepituitary. This in women, results in reduction of estradiol and progesterone concentrations andinhibition of follicular maturation thus leading to anovulation (16).

Thyroid disorders are among the commonest endocrine disorders worldwide with females having higher dysfunction rate than males (22). Thyroid dysfunctions interfere with numerous aspects of reproduction and pregnancy and an association of hyperthyroidism or hypothyroidism with menstrual disturbance, anovulatory cycles, decreased fecundity and increased morbidity during pregnancy has been observed (23).These hormonal disorders result in oligoovulation or anovulation (24).

Complex interactions among hormones control the start of menstruation during puberty, the rhythms and duration of menstrual cycles during the reproductive years and the end of menstruation at menopause. The hormonal interactions that control menstruation occur in the hypothalamus (GnRH), pituitary (LH,FSH) ovarian (E2,Prog) pattern and hormones produced by other glands, such as the adrenal and thyroid glands can also affect the functioning of the ovaries and menstruation. This means that a variety of hormones affects the menstrual cycle. Irregular menstrual cycle is a major symptom of anovulation, a phenomenon that is accompanied by decreased ovarian steroid secretion and production (18)Evaluating the levels of female reproductive hormone therefore, in women with menstrual disturbances is important in the identification and management of endocrine disorders (25), particularly in Bayelsa State, Niger Delta Region of Nigeria where studies on gynaecological morbidity are very scanty. Establishing the nature and the rate of occurrence of endocrine disorders in women with menstrual disturbancesis vital in ascertaining if endocrine disorders are the cause of the disturbances. When established, if there is an underlying condition causing the hormone imbalance, management of the condition will help to ensure hormonal balance. This cross sectional regional based study was conducted to establish the association of the hormones among the population of women (married and not married) of reproductive age group with menstrual disturbances.

MATERIALS AND METHOD

Study Area

This study was carried out in Bayelsa State, Niger Delta region of Nigeria with a population of 1,704,515 inhabitants and 830,432 are females (26). This isgeographically located within latitude $04°15^{1}$ North, $05°23^{1}$South, and longitude $05°22^{1}$West and $06°45^{1}$ East. The hospitals involved in the study include the Specialist Hospitals, Niger Delta University Teaching Hospital, Okolobiri, Federal Medical Center Yenagoa, Diette-koki Memorial Hospital, Yenagoa, allin the State.

Study Population

A total of one thousand eight hundred and fifty two (1852) consented subjects were randomly recruited for this studyusing a questionnaire design containing the information of about age, last menstrual date, degree of irregularity, whether on contraceptives medication/medication for any infertility problem or suffering from any known illness. This comprised of women with different menstrual disturbances that reported to the hospitals for evaluation and treatment and were willing to participate in the study. The demographic, medical and occupational data were collected through interviews, medical records and questionnaire. Excluded from the study were pregnant and breast feeding women, women who were above 45 years of age and those who were on certain infertility or contraceptive medication for family planning, women who had undergone hysterectomy or have had abortion in the last 3 months. Also excluded were women with established PCOS and Diabetes mellitus.

Ethical Clearance

Ethical clearance was obtained from the Ethical Committee responsible for Human Research at Federal Medical Center Yenagoa, with the clearance certificate number FMC/REC/ECC/2014/JAN/145. The subject's consent was gotten from them during the period of questionnaire administration.

Sample Collecting and Processing

Blood samples were collected from women with various menstrual disturbances following the standard operating procedure of venipuncture between 2nd and4th day of menses and randomly in cases of amenorrhea and transferred into a plain container. Menstrual disorders were defined as any of four menstrual cycle characteristics, short cycle, long cycle, irregular cycle bleeding or spotting between periods (27, 14). The collected samples in the plain container were allowed to clot and dislodged carefully from the sides of the tubes to avoid haemolysis. The samples were then centrifuged at 3500rpm for 10 minutes. Using an automatic pipette, the serum was carefully aspirated and transferred into another plain containers which were properly labeled and stored frozen at -20°C until analysis.

The measurement for the various hormone parameters were done within 7 days of sample collection. The study was carried out between the periods of January, 2014 to January, 2019.

Method of the study

Analyses of the different hormones of the hypothalamic – pituitary- gonadal reproductive axis were measured using Enzyme Linked Immunosorbent Assay (ELISA)(28, 29, 30). The ELISA kits were purchased from Elabscience biotechnology Co. LTD (USA). It uses the sandwich and competitive ELISA principle and the Biotechnology Awareness plate reader was used to read the sample absorbance at 450nm (31, 32).

Statistical Analysis

Data analysis was performed using Microsoft Excel version 10 and IBM Statistical Package for Social Science (SPSS) version 20. Descriptive statistics was used to determine the mean and prevalence of common menstrual disorders. Tabular representation, frequency and percentage analysiswas applied to analyze the data and95% confidence interval, P<0.05 was considered to be statistically significant.

RESULTS

The number of women involved in the study was 1852. Those unwilling to participate and those not suitable were excluded from the study. The result of investigating the endocrine disorders in women with menstrual disturbances in Bayelsa State, Niger Delta Region of Nigeria shows that menstrual disturbances in the studied subjects were accompanied with female reproductive hormone fluctuations with a high significant (P<0.05) percentage, 79.97% of the women having one form of the endocrine disorders and this might be because of pressure or tension that results from demanding situation, stress which can be physical, emotional, psychological or combination of these (14).The findings from this study was compared with the normal published work (33) to enable the interpretations in this study. The results is as presented in the tables below

Table 1 The Percentage of abnormal GnRH, FSH, LH, E2, Prog.& Prolactin in serum of Women with Menstrual Disturbances.

Parameter measured (n = 1852)	Normal (%)	High (%)	Low (%)	Total % abnornmal	P-value
GnRH	84.88	0.92	14.20	15.12*	P=0.047
FSH	60.26	38.35	1.39	39.74*	P=0.030
LH	62.64	36.71	0.65	37.36*	P=0.032
E2	36.83	0.59	62.58	63.17*	P=0.019
PROG	28.67	1.24	70.09	71.33*	P=0.015
PROL	67.98	30.67	1.35	32.02*	P= 0.033

(GnRH- Gonadotropin-releasing hormone, FSH – Follicle stimulating hormone, LH – Luteinizing hormone, E2 – Estradiol,, Prog – Progesterone, Prol - Prolactin)

The **table 1** shows the percentage of abnormally high/low levels of the hormones of the hypothalamus – pituitary-gonadal axis and prolactinin serum of women with menstrual disturbances. From the results, the percentage of the gonadotropins, E2, Prog, and Prol that were abnormal, were statistically (P<0.05) significant.

Table The Percentage of abnormal Triiodothyronine (T3), Thyroxine (T4) Thyroid stimulating hormone (TSH) and Thyroid binding globulin (TBG) levels in serum of women with menstrual disturbances.

parameter measured n=1852	normal (%)	high (%)	low (%)	total % abnormal	p-value
T3	80.03	14.66	5.31	19.97*	P=0.045
T4	70.60	16.22	8.70	24.92*	P=0.036
TSH	78.67	9.34	11.99	21.33*	P=0.038
TBG	96.98	2.37	1.57	3.94	P= 0.060

Table 2 shows the percentage of abnormal levels ofthyroid hormones inwomen with menstrual disorders. The percentage values for T3, T4 and TSH from the study were statistically (P<0.05) significant except the TBG with a non-significant value (P=0.060)

Table 3 Frequency distribution of Disorders of Gonadal Function in Women with Menstrual Disturbances in Bayelsa State

Endocrine disorder	Frequency (n)	Percentage (%)	P-value
Hypothalamic Amenorrhea	280	15.12*	P= 0.047
Hypergonadism	25	1.35	P= 0.063
Hypogonadism	1028	55.51*	P= 0.021
Hypergonadotropic Hypognadism	716	38.66*	P= 0.031
Hypogonadotropic Hypogonadism	25	1.35	P= 0.063
Hypoestrogenism	1159	63.17*	P= 0.019

*Percentage statistically significant.

Total will not tally for 100 as women had multiple cases of dysfunctions.

Table 4 Frequency distribution ofdisorders of thyroidfunction in women with menstrual disorders in Bayelsa State.

Endocrine disorder	Frequency (n)	Percentage (%)	P-value
Hyperthyroidism	202	10.91*	P= 0.048
Hypothyroidism	88	4.75	P= 0.061
Goitre	98	5.30	P= 0.059
T3 Thyrotoxicosis	69	3.73	P= 0.061
T4 thyrotoxicosis	98	5.30	P= 0.059
TBG Excess	44	2.37	P= 0.062
TBG Deficiency	34	1.57	P= 0.063

*Percentage statistically significant

Table 5 Frequency distribution of Disorders of Prolactin Secretion in Bayelsa State Women with Menstrual Disturbances

Endocrine disorder	Frequency (n)	Percentage (%)	P-value
Hyperprolactinaemia	604	30.62*	P = 0.033
Hypoprolactinaemia	24	1.30	P = 0.064

*Significantly different at P<0.05

DISCUSSION

This study demonstrates the dependence of menstrual disturbance on endocrine disorder of female reproductive hormones of the hypothalamus – pituitary – gonadal axis, the thyroids and prolactin in women of Bayelsa State of Nigeria. Menstrual disturbances are conditions common in females in their reproductive years that interferes with normal menstrual cycle causing pain, unusual uterine bleeding and other menstrual irregularities. (34). Menstrual health is essential to women's sexual and reproductive health. Changes in the normal menstrual patterns of women in reproductive age group may affect physical and gynaecological well-being (35). Endocrine disorders are conditions resulting from the body's over- or underproduction of certain hormones that can lead to infertity (14). The impact of menstrual disorder on women's reproductive health is particularly serious in developing regions like the Bayelsa State, Niger Delta Region of Nigeria where the health care especially in public sector is not well equipped to make the diagnosis and treatment of these menstrual dysfunctions.

The result from this study (**table 1**) showed that the level of estradiol was greatly decreased in most women, which is in line with the increased follicle stimulating hormone and luteinizing hormone levels in agreement with earlier published works(31,32,36). It is however presumed that the significant reduction in the estradiol levels have caused the increase in the follicle stimulating hormone and luteinizing hormone levels, resulting in menstrual disturbances caused by deficiency of the gonadal hormones (estradiol) due to ovarian failure (37). The women who had normal values of follicle stimulating hormone, luteinizing hormone, estradiol and prolactin (60.26%, 62.64%, 36.83% and 67.98% respectively) in the presence of menstrual disturbance as shown in**table 1**, suggests that it is not of hypothalamic-pituitary-gonadal origin but due to other causes such as thyroid dysfunction, infections, excessive exercise, stress, eating disorders, hormonal birth control pills, polycystic ovarian syndrome, etc (38).

From the results, 55.51%% of the subjects had hypogonadism (**table 3**) which may be as a result of the gonads not responding to the secreted gonadotropins or as a result of problem with the hypothalamic-pituitary axis where there is a deficiency in the secretion of gonadotropin releasing hormone or gonadotropins (FSH & LH) and is believed to have caused their menstrual disturbance such as amenorrhea, oligomenorrhea which is in line with the study by Richard – Eaglin (37). 38.66% of the women had hypergonadotropic hypogonadism suggesting that their menstrual disturbances are caused by hormonal imbalance of elevated FSH & LH with concomitant reduction in E2 and/or Progesterone.

In hypergonadotrotropic hypogonadism, reduced levels of estrogen in women lead to increased pituitary gonadotropin secretion in a negative feedback mechanism but the gonads do not respond to the gonadotropins (31).In the study, 63.17% of the women had hypoestrogenism that are mostly responsible for the anovulation in women of reproductive age (39) and 15.12% had hypothalamic amenorrhea which according to Liu (20) is believed to be the most important cause of menstrual cycle irregularity that is associated with decreased gonadotropin – pituitary – adrenal (HPA) axis dysregulation.
From **table 5**,30.62% of the subjects had hyperprolactinaemia which is a major cause of menstrual disturbance such as amenorrhea, because high prolactin levels indicates ovarian failure in some women leading to lack of ovulation and eventually amenorrhea (40).

From the result in **table 4**, Hyperthyroidism (10.91%) is significant and it may be due to the fact that these women have an autoimmune disorder called Graves's disease which makes the body produce antibody that causes the thyroid to make too much thyroid hormone. It might be also due to lumps, nodules, inflammation in the thyroid gland or a problem with the immune system causing an excessive production of thyroid hormones (Table 2).Thyroid dysfunction is an important causative etiology of menstrual abnormalities. Assessment of thyroid function should be done in all patients with menstrual disorders to avoid unnecessary interventions like curettage and hysterectomy (41). While activity of the thyroid is closely linked with the process of ovarian maturation, the thyroid gland is itself dependent on direct and indirect stimuli from the ovary to discharge its own function.

According to the work by Sharme and Sharme, 2012(7), the prevalence of hyperthyroidism is 14.00% in women with Dysfunctional Uterine Bleeding and in this study, the prevalence of Hyperthyroidism is 10.91% for women with menstrual disturbances. The results in **table 2**, has shown that 14.66% and 16.22% of the women had T3, T4 significantly (P<0.05) elevated values respectively. These conditions generally are seen in cases of T3 toxicosis, hyperthyroidism and generalized thyroid hormone resistance (41).

More than half of the women had hormone associated menstrual disorders which are very high, especially hypoestrogenism and hypogonadism that are more common than other hormone associated menstrual problems. Some of the women were suffering from more than one menstrual disorder and therefore need urgent medical intervention to take care of the problem (42). The endocrine disorders are probably due to life style (diet, obesity, and stress), environmental factors and an underlying illness (infections, cancer and polycystic ovarian syndrome) (43).

CONCLUSION

The study concluded that menstrual disturbances were accompanied with female reproductive hormone fluctuations; with a high significant (P<0.005) percentage of the women in Bayelsa State, Nigeria having one form of the endocrine disorders especially hypoestrogenism and hypergonadotropic hypogonadism which were more common with other menstrual disorders.

Limitations about the study

1. Getting enough patient samples was a challenge because women with menstrual disturbances are not always available and some of them were very reluctant and needed a lot of conviction.
2. During questionnaire administration, the study attempted to compare the subject's history with medical records, which were not readily available or were incomplete. Interpreting the results sometimes were

complex because of the nature of information supplied from the subjects.

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Conflict of Interest

Nil

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