

Article

Correlation of Thyroid Gland Functions with Menstrual Patterns amongst Infertile and Fertile Women Attending a Tertiary Care Hospital in North-Central Nigeria

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Abstract: A regular menstrual cycle is important to maintain a woman's fertility. This cycle has been linked to optimal function of the thyroid gland in the production of its hormones. Disturbance of thyroid gland functions could result to female infertility due to changes in menstrual patterns. Aim of this research was to determine the correlation between thyroid gland functions and menstrual patterns amongst infertile and fertile women attending a tertiary care hospital in North-Central Nigeria. This comparative, cross-sectional study recruited 106 women who visited the hospital's Gynecology Clinic and Family Planning Clinic. 53 of the 106 patients were women with a history suggestive of either primary or secondary infertility and the remaining 53 women with no history of infertility served as the control. A well-structured questionnaire was used to obtain data on the patients' menstrual patterns. Anthropometric data were measured and obtained. Collected blood samples were analyzed using Enzyme-Linked Immunosorbent Assay (ELISA) technique to determine the serum levels of thyroid hormones. All obtained data was analyzed, and the level of significance was set at $p < 0.05$, at a 95% confidence interval. 33 patients had menstrual anomalies (78.8% infertile women; 21.2% fertile women who served as control, $p = 0.012$). The incidence of menstrual anomalies in the infertile women group and control group was 7.5% versus 0.0% for amenorrhea; 20.8% versus 5.7% for menorrhagia; 9.4% versus 7.5% for oligomenorrhea; 7.5% versus 0.0% for hypomenorrhea; nil polymenorrhea for both groups; and 50.9% versus 86.8% for normal menstrual patterns. Ten (9.43%) patients were diagnosed with thyroid dysfunctions (80% in infertile group; 20% in control group, $p = 0.046$). Six (18.2%) out of 33 women with menstrual anomalies were diagnosed with thyroid dysfunction. Five (83.3%) out of these 6 women with both menstrual anomalies and diagnosed thyroid dysfunction were infertile while only one (16.7%) was fertile. Thyroid gland dysfunction correlates strongly with abnormal menstrual patterns, which implies that it is vital to evaluate thyroid hormone levels in blood serum in the course of treating menstrual irregularities and female infertility. Early detection of thyroid dysfunction is important in achieving a positive treatment outcome for female infertility.

Keywords: Thyroid Gland, Thyroid Hormones, Menstrual Patterns, Female Infertility, Female Fertility, Reproductive Endocrinology, Reproductive Gynecology

1. Introduction

The menstrual cycle is a natural process in females that is responsible for the development and release of secondary oocyte(s), and vaginal bleeding as a result of the shedding of uterine mucosa, under the influence of hormones to make pregnancy possible [59]. The sperm cell must fertilize an ovum *in vivo* or *in vitro* in order for conception (pregnancy) to occur [5]. Gametes are ova and sperm cells which are haploid and have one copy of each type of chromosome i.e. 1–22 X or 1–22 Y [32]. The menstrual cycle is divided into uterine and ovarian cycles, occurs monthly and is an important factor in maintaining women's fertility as it prepares a woman for pregnancy each month [59]. Menstruation is the bleeding phase of the uterine cycle, and as it commences, the follicular phase in the ovary starts for the growth of another follicle [57].

At menarche, a young girl witnesses her first menstruation. This continues all through her reproductive life and terminates at menopause. The event occurs with associating discomfort but the reproductive benefit outweighs these discomforts. However, there are situations where a female's menstrual cycle experience becomes traumatic, ranging from anovulation to other forms of menstrual disorders [18, 40, 71]. There are instances where these disorders go unnoticed but then, in most cases, they impair a woman's productivity and cause social embarrassment [13]. As these women seek medical attention, their financial burden heightens, however, it is important to note that many of the women are unaware and lack information about these disorders.

The link between menstrual anomalies and other systemic disorders, notably metabolic syndrome diseases (MSDs) is still being studied. MSDs (Hypertension, Adiposity, Diabetes mellitus and Dyslipidemia) are interrelated diseases with very high morbidity and mortality rates [19, 20, 22, 36] and characterized with high levels of blood pressure, glucose and lipid metabolic disorders, asymptomatic hyperuricemia, activation of systemic immune inflammation, fibrogenesis, and contribute to kidney damage [23, 24, 27, 29, 37, 62, 64, 66]. MSDs require new and effective treatment options. Dapagliflozin which is a Sodium-Glucose Linked Transporter 2 (SGLT-2) inhibitor and Liraglutide which is a Glucagon-like Peptide 1 Receptor Agonist (GLP-1 RA) have been found to increase the effectiveness of treatment and improve the clinical course of type 2 diabetes mellitus and hypertension in patients with such comorbidities [21, 25, 26, 30, 34, 67, 68, 69].

Menstrual disorders have also been linked with increased oxidative stress. Major free radicals that are of physiological significance are superoxide anion, hydroxyl radical, and hydroperoxyl radical, while non-radical is hydrogen peroxide [31]. Tobacco use has been reported as teratogenic, while excessive use of both alcohol and tobacco can be lethal [60, 61]. Oxidative stress can also be caused by the imbalance between Reactive Oxygen Species (ROS) produced by the alcohol consumed in the form of free radicals that contain one or more unpaired electrons and antioxidants [10].

The prevalence of menstrual disorders in an Indian population was recorded to be 10.9% [49], and it has been highlighted that 20% of cases reported in the Obstetrics and Gynecology units are related to menstrual disorders [3]. In a study among female university students in Southwestern Nigeria, 82.8% of the students had regular monthly menstrual flow pattern, while others (17.2%) had one or multiple forms of the following menstrual disorders: menorrhagia, oligomenorrhoea, polymenorrhoea, and occasional dysmenorrhoea that disrupted their school activities by preventing them from going to school [1]. This report explains the 25% infertility cases of all reproductive complaints always handled in this study area. In severe cases, other gruesome consequences of menstrual disorders are infertility and an increased risk of death before 70 years of age [14]. Polymenorrhoea described as excessive menstrual bleeding can cause anemia and complicate pregnancy [38, 39]. Infertility is a topic of concern in our society as it has caused several broken homes [5].

Menstruation is regulated by reproductive hormones [57]. However, the thyroid hormones have been identified to have a direct and indirect effect on reproductive physiology [43]. The hormones directly affect various stages of cells in the ovaries, and the indirect function is by elevating prolactin levels, decreasing the binding activity of sex hormone-binding globulin (SHBG), and delaying luteinizing hormone response to gonadotropin-releasing hormone [43, 56]. An optimum secretion of thyroid hormones is the determinant of the efficiency of the thyroid gland, as under- or overproduction of the hormones are termed thyroid gland dysfunctions.

Thyroid gland dysfunctions cause abnormal sexual development and menstrual disorders, and women have been reported to have more cases of thyroid dysfunctions than men [6]. Thyroid gland dysfunctions have been reported by several studies to include subclinical hypothyroidism, overt (clinical) hypothyroidism, subclinical hyperthyroidism, and overt (clinical) hyperthyroidism [17, 43]. These thyroid dysfunctions have been associated with various reproductive anomalies and precisely with menstrual irregularities. As has been documented that thyroid dysfunctions differ from region to region due to the varying iodine intake through salt, other meals and supplements [11], the associating menstrual irregularities are expected to be region-specific. Hence, this study was conducted to correlate thyroid gland dysfunctions with menstrual patterns amongst infertile and fertile women attending a tertiary care hospital in North-Central Nigeria.

2. Materials and Methods

2.1. Study Setting

This comparative, cross-sectional study was conducted at the Gynecology Clinic and Family Planning Clinic of the Department of Obstetrics and Gynecology, University of Ilorin Teaching Hospital (UIH), Ilorin Kwara State, North-Central Nigeria. UIH situated at Oke-Oyi, Old Jebba Road, Kwara State, is a major referral center for Kwara State and other neighboring states and serves as a medical training center for undergraduate and postgraduate students. Approximately 144 female patients visit the clinics weekly.

2.2. Study Population

This study involved women between the ages of 18-45 years visiting the clinics, with a history of infertility (inability to conceive of one year or more duration). This included those with primary infertility and secondary infertility. The control group consisted of fertile women, who had experienced complete gestation within 2 years prior to this study and were new patients at the Family Planning Clinic.

2.3. Sample Size and Sampling Technique

The formula described by Charan & Biswas (2013) [7] for a comparative, cross-sectional study was used.

$$N = \frac{2(Z_{\alpha/2} + Z_{\beta})^2 \times P(1 - P)}{(P_1 - P_2)^2}$$

N = Sample size

$Z_{\alpha/2}$ = 1.96 at type 1 error of 5%

Z_{β} = 1.28 at 90% power

P_1 = Proportion of thyroid disorder in infertile women (47%)

P_2 = Proportion of thyroid disorder in fertile women (16%). P_1 and P_2 were extracted from a previous study by Fatima, *et al* (2014) [12].

P = Pooled prevalence = [prevalence in one group (P_1) + prevalence in another group (P_2)] / 2

P = [(0.47 + 0.16) / 2] = 0.32

$$N = \frac{2(1.96 + 1.28)^2 \times 0.32(1 - 0.32)}{(0.47 - 0.16)^2}$$

$$N = 47.5$$

$N \sim 48$ patients

For attrition, 10% of the sample size was added, making a total of 53 women in each group (infertile group and fertile group). Thus, a total of 106 women constituted the sample size.

2.4. Inclusion and Exclusion Criteria

Inclusions: For the patients, only women who consented and were within 18-45 years of age with primary or secondary infertility were included. Control group consisted of fertile women within the same age range as the subjects and consented to partake in this study. In addition, the fertile women (control group) were new patients at the Family Planning Clinic with no history of infertility, had been pregnant to term, and with no record of contraceptive use 2 years prior to this study.

Exclusions: Women outside 18-45 years of age, with a history of bleeding disorders, on hormonal or intrauterine contraceptives, with co-existing uterine fibroid, with a history of thyroid disorders, on steroids.

2.5. Data Collection Method

This study was conducted over a period of 6 months. Eligible women were briefed about the study in a simple language that they understood. Socio-demographic data, infertility history, anterior neck swelling history, other symptoms suggestive of thyroid disorder, medical conditions, and past surgical procedures were used.

2.6. Menstrual Pattern Assessment

Accurate measurement of menstrual blood loss may be difficult because of its subjectivity. Therefore, for the purpose of this study, cases were assessed by the number of pads used, passage of clots, and duration of bleeding [73]. The study questionnaire was used to assess this aspect of the study. Other menstrual data obtained include age at menarche, duration of flow, cycle length, and history of dysmenorrhea.

The menstrual patterns considered in this study are: normal menses, polymenorrhea, intermenstrual bleeding/metrorrhagia, menorrhagia, hypomenorrhea, oligomenorrhea, and amenorrhea. All consenting patients participating in this study had a pelvic ultrasound scan, at no additional cost to them. Patients with co-existing uterine fibroid were excluded from the study.

2.7. Sample Collection

A sample of blood (4 ml) was collected from each participant after an overnight fast of 8-10 hours. Patients who had fasted coincidentally at their first visit were recruited, while those who ate before coming on their first visit were recruited at their next visit after being pre-informed.

2.8. Laboratory Procedures

Serum concentrations of TSH, fT3 and fT4 were determined by using Enzyme-linked immunosorbent assay (ELISA) kits manufactured by Monobind Ltd using a Rayto micro-well plate reader, as described by Winter, *et al* (2012) [72].

2.9. Criteria for Diagnosis of Thyroid Dysfunction

The reference range of values for thyroid hormones that was used for this study is the range of normal values on the kits used: fT3 - 1.4-4.2 pg/mL, fT4 - 0.7-2.0 ng/dL, and

TSH - 0.39-6.16 mIU/mL [45, 46, 47]. Thyroid gland dysfunctions can be grouped as sub-clinical hypothyroidism (normal fT3, fT4, but elevated TSH), hypothyroidism (decreased fT3, fT4, and elevated TSH), subclinical hyperthyroidism (normal fT3, fT4, but low TSH), and hyperthyroidism (elevated fT3, fT4, and decreased TSH) [17].

2.10. Data Analysis

Collected data were cleaned, entered, hardcoded and analyzed using Statistical Package for Social Sciences (SPSS) version 23. Summary statistics was presented using tables. Age and other anthropometric parameters such as weight, height, BMI, pulse rate, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were categorized and summarized with mean and standard deviation. Continuous variables that are normally distributed (e.g. age) were analyzed using the t-test series while discontinuous variables that are not normally distributed (e.g. levels of thyroid hormones) were analyzed using the Mann-Whitney U test. The normality test was done using the Shapiro-Wilk test. The level of significance was set at $p < 0.05$ and at a confidence interval of 95% for all inferential statistics.

2.11. Ethical Considerations

Approval was obtained from UITH's Ethical Review Committee. Written consent was obtained from all the participants after proper explanation and the data obtained were treated with confidentiality and used solely for the study. This ethical clearance ensured adequate professional work ethics and confidentiality of all patients' data. Patients with thyroid abnormalities were referred for further evaluation, treatment, and were co-managed with endocrinologists. This research was also carried out with due observance of the ethical principles of the Declaration of Helsinki (DoH) in 2013 concerning human research.

3. Results

The socio-demographic variables of the respondents are presented in Table 1. The age bracket of 25-28 years had the highest number of respondents (30.2%), while the age group <25 years had the least (13.2%). The mean age was 32.18 ± 6.47 years for the infertile women and 31.4 ± 5.74 years for fertile women (control group). Most of the infertile women (79.2%) and fertile women (81.1%) were employed. Majority of the respondents (69.8%) had tertiary level of education. Due to the location of the study, most (83%) of the women were from the Yoruba tribe. The socio-demographic variables showed no significant differences.

Figure 1 presents the infertility types among the infertile women. Primary infertility accounted for 24.5% while secondary infertility accounted for 75.5%.

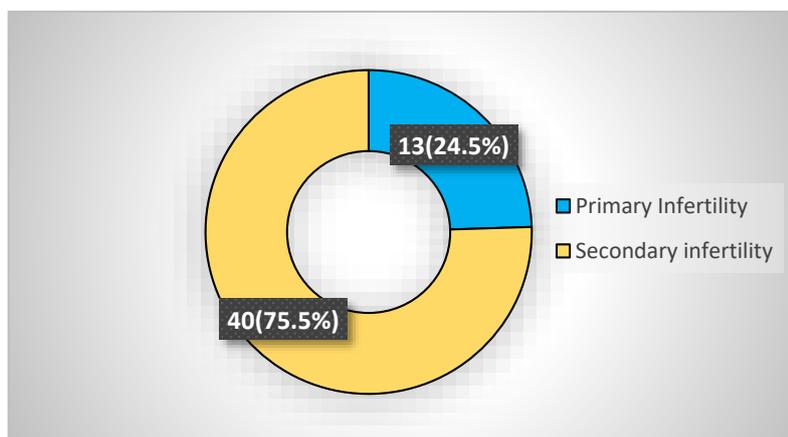


Figure 1. Types of infertility among the infertile women

Table 1. Socio-demographic variables of the infertile women and fertile women (control) groups

Socio-demographic variable	Infertile <i>n</i> (%)	Fertile <i>n</i> (%)	Total <i>n</i> (%)	χ^2/ t	<i>p</i> -value
Age (years)					
< 25	9 (17.0)	5 (9.4)	14 (13.2)	2.932	0.569
25 – 29	14 (26.4)	18 (34.0)	32 (30.2)		
30 – 34	7 (13.2)	11 (20.8)	18 (17.0)		
35 – 39	15 (28.3)	12 (22.6)	27 (25.5)		
≥ 40 – 45	8 (15.1)	7 (13.2)	15 (14.2)		
Total (<i>n</i>)	53	53	106		
Age (Mean ± SD)*	32.18±6.47	31.40±5.74		0.651 ^t	0.516
Occupational status					
Employed	42 (79.2)	43 (81.1)	85 (44.3)	0.509	0.808
Unemployed	11 (20.8)	10 (18.9)	21 (19.8)		
Total (<i>n</i>)	53	53	106		
Educational status					
None	1 (1.9)	1 (1.9)	2 (1.9)	1.784 ^f	0.759
Primary	1 (1.9)	2 (3.8)	3 (2.8)		
Secondary	16 (30.2)	11 (20.8)	27 (25.5)		
Tertiary	35 (66.0)	39 (73.6)	74 (69.8)		
Total (<i>n</i>)	53	53	106		
Ethnicity					
Yoruba	45 (84.9)	43 (81.1)	88 (83.0)	1.137 ^t	0.822
Hausa	2 (3.8)	1 (1.9)	3 (2.8)		
Igbo	2 (3.8)	3 (5.7)	5 (4.8)		
Others	4 (7.5)	6 (11.3)	10 (9.4)		
Total (n)	53	53	106		

χ^2 : Chi square; *t*: Independent Samples T test; *f*: Fisher's exact test

Table 2 summarizes the anthropometric parameters and blood pressure values of women with infertility and fertility. The mean BMI of the infertile women (27.05±5.46 kg/m²) was slightly higher than that of the fertile women (25.47±5.97 kg/m²) with no significant difference between the two groups (*p*=0.156). The pulse rates and blood pressure values were comparable in the two groups with no significant statistical difference.

Table 2. Anthropometric parameters and blood pressure values of women with infertility and fertility

Parameters	Infertile group Mean±SD	Fertile group Mean±SD	T	<i>p</i> -value
Weight (kg)	68.98±14.78	64.51±14.37	1.581	0.117
Height (m)	1.60±0.06	1.59±0.05	0.164	0.870
BMI (kg/m²)	27.05±5.46	25.47±5.97	1.428	0.156
Pulse rate (bpm)	79.84±8.24	81.69±6.20	-1.289	0.200
SBP (mmHg)	113.11±12.18	118.49±17.69	-1.823	0.071
DBP (mmHg)	71.08±11.22	74.06±15.54	-1.132	0.260

t: Independent Samples T-test; *: *p*-value <0.05

Figure 2 depicts the patterns of thyroid dysfunctions among infertile and fertile women. Ten (9.43%) out of all the respondents were diagnosed with thyroid dysfunction. Eight infertile women had some form of thyroid dysfunction: four (7.5%) had subclinical

hypothyroidism, two (3.8%) had overt (clinical) hypothyroidism, and two (3.8%) had overt (clinical) hyperthyroidism. Two fertile women had thyroid dysfunction: one (1.9%) had subclinical hypothyroidism and one (1.9%) had overt (clinical) hyperthyroidism. The majority of the participants were euthyroid - 45 (84.9%) infertile women versus 51 (96.2%) for the fertile women. No significant difference ($p>0.05$) was observed between each thyroid dysfunction in the infertile and fertile women, but the overall difference between infertile and fertile women with thyroid dysfunction was significant, $p=0.046$.

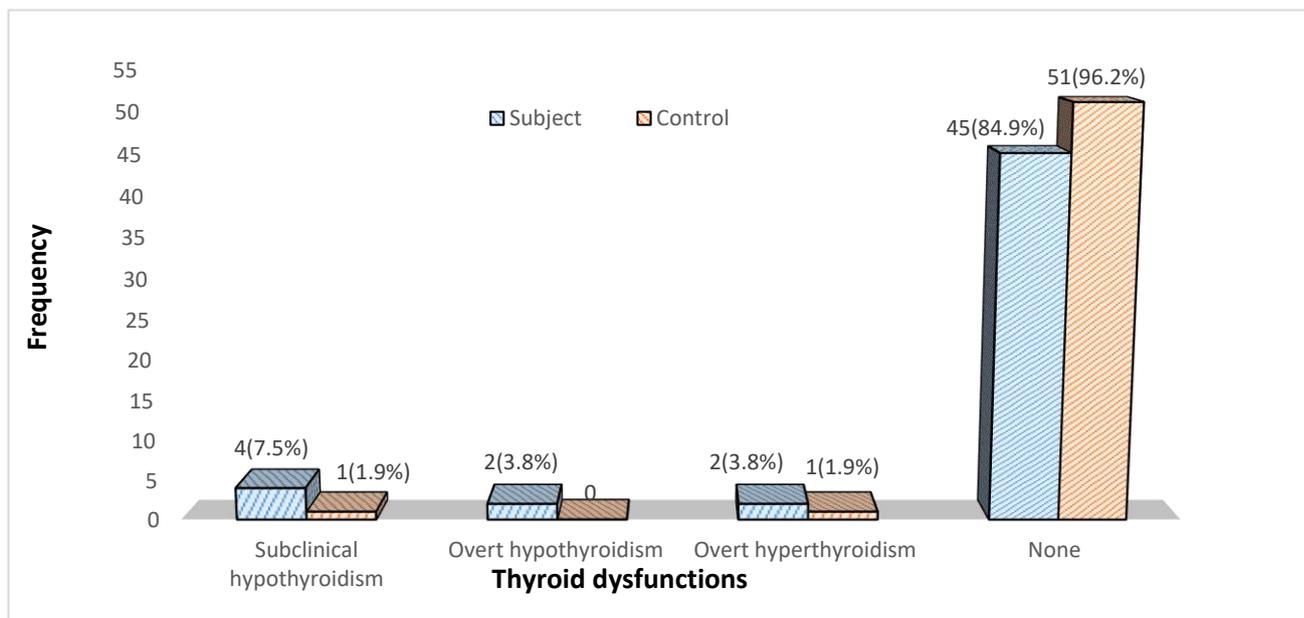


Figure 2. Patterns of thyroid dysfunction among infertile and fertile women

Table 3 shows menstrual patterns and anomalies in women with infertility and the fertile (control) group. Mean age at menarche was similar in the two groups - 14.24±2.26 years in infertile women and 14.43±2.04 years in fertile women ($p=0.669$). The mean cycle length was also comparable - 28.14±1.93 days (infertile group) versus 28.67±1.67 days (fertile group) ($p=0.156$). Menorrhagia was the most predominant menstrual anomaly in the respondents, and was present in 11 (20.8%) of infertile women and in 3 (5.7%) of fertile women. Menorrhagia accounted for the highest (56%) of the total incidence of menstrual anomalies. Five (9.4%) of the infertile women had oligomenorrhea versus four (7.5%) of the fertile women. Hypermenorrhea and amenorrhea accounted for 7.5% each, among the infertile women. Intermenstrual bleeding has a prevalence of 3.8% among the infertile women. None of the 106 study participants reported polymenorrhea. Only menorrhagia showed a significant difference ($p=0.022$) between the infertile and fertile women.

Table 4 shows the prevalence of menstrual anomalies among infertile and fertile women. More infertile women 26 (78.8%) had menstrual anomalies compared with fertile women 7 (21.2%) and this was significantly different ($p=0.012$). Twenty-seven (50.9%) infertile women had normal menses as against 46 (86.8%) fertile women.

Table 5 compares the pattern of thyroid dysfunction among infertile and fertile women. Four (7.5%) of the infertile women had subclinical hypothyroidism while one (1.9%) of the fertile women had subclinical hypothyroidism, and the difference was not significant ($p=0.37$). Overt (clinical) hypothyroidism was present in two of the infertile women but was absent in the fertile women. Overt (clinical) hyperthyroidism was present in two of the infertile women while only one fertile woman had it, and the difference was not significant ($p=1.000$). Majority of the study participants were euthyroid - 45 infertile women (84.9%) versus 51 fertile women (96.2%).

Table 3. Menstrual patterns and anomalies in infertile and fertile women

Variables	Infertile women n (%)	Fertile women n (%)	Total n (%)	χ^2/ t	p-value
Age at menarche (years)					
Mean±SD	14.24±2.26	14.43±2.04		0.429 ^t	0.669
Range	9 –18	9 – 20			
Cycle length (days)					
Mean±SD	28.14±1.93	28.67±1.67		1.430 ^t	0.156
Range	24 – 35	24 – 35			
Polymenorrhea					
No	53 (100.0)	53 (100.0)	106 (100.0)		
Intermenstrual bleeding					
Yes	2 (3.8)	0 (0.0)	2 (1.9)	2.038 ^f	0.495
No	51 (96.2)	53 (100.0)	104 (98.1)		
Menorrhagia					
Yes	11 (20.8)	3 (5.7)	14 (13.2)	5.267	0.022*
No	42 (79.2)	50 (94.3)	92 (86.8)		
Hypomenorrhea					
Yes	4 (7.5)	0 (0.0)	4 (3.8)	4.157 ^f	0.118
No	49 (92.5)	53 (100.0)	102 (96.2)		
Oligomenorrhoea					
Yes	5 (9.4)	4 (7.5)	9 (8.5)	0.121 ^f	1.000
No	48 (90.6)	49 (92.5)	97 (91.5)		
Amenorrhoea					
Yes	4 (7.5)	0 (0.0)	4 (3.8)	4.157 ^f	0.118
No	49 (92.5)	53 (100.0)	102 (96.2)		

χ^2 : Chi square; t: Independent Samples T test; f: Fisher's exact test

Table 4. Prevalence of menstrual anomalies among infertile and fertile women

Variable	Infertile n (%)	Fertile n (%)	Total n (%)	χ^2	p-value	OR (95% CI)
Menstrual anomalies						
Present	26 (49.1)	7 (13.2)	33 (31.1)	6.334	0.012*	3.380 (1.272 – 8.982)
Absent	27 (50.9)	46 (86.8)	73 (68.9)			
Total	53	53	106			

χ^2 : Chi square; OR: Odds ratio; 95% CI: 95% Confidence interval; *: p-value <0.05

Table 5. Patterns of thyroid dysfunction among infertile and fertile women

Thyroid dysfunction	Infertile n (%)	Fertile n (%)	Total n (%)	χ^2/ t	p-value
Subclinical hypothyroidism	4 (7.5)	1 (1.9)	5 (4.7)	0.800	0.371
Overt (clinical) hypothyroidism	2 (3.8)	0 (0.0)	2 (1.9)	NA	
Overt (clinical) hyperthyroidism	2 (3.8)	1 (1.9)	3 (2.8)	0.000	1.000
None	45 (84.9)	51 (96.2)	96 (90.6)	0.260	0.610
Total	53	53	106		

χ^2 : Chi-square; NA: Chi-square not available because of zero '0' value

Table 6 shows the association between menstrual anomalies and the forms of thyroid dysfunction among infertile and fertile women. 3 (16.7%) of the infertile women with men-

strual anomalies had subclinical hypothyroidism, 1 (5.6%) had overt (clinical) hypothyroidism, 1 (5.6%) had overt (clinical) hyperthyroidism, while the remaining 13 (72.2%) were euthyroid. Thirty-five infertile women without menstrual dysfunction had the following distributions of thyroid dysfunction among them: 1 (2.9%) subclinical hypothyroidism, 1 (2.9%) overt (clinical) hypothyroidism, 1 (2.9%) overt (clinical) hyperthyroidism, and 32 (91.3%) were euthyroid. On the other hand, 7 fertile women with menstrual anomalies showed that 1 (14.3%) had overt (clinical) hyperthyroidism and 6 (85.7%) were euthyroid. In addition, the 46 fertile women without menstrual anomalies showed that 1 (2.2%) had subclinical hypothyroidism and 45 (97.8%) were euthyroid.

Table 6. Association between menstrual anomalies and the forms of thyroid dysfunction among infertile and fertile women

Thyroid dysfunction	Menstrual anomalies			χ^2	<i>p</i> -value
	Present <i>n</i> (%)	Absent <i>n</i> (%)	Total <i>n</i> (%)		
Infertile women					
Subclinical hypothyroidism	3 (11.5)	1 (3.7)	4	4.388 ^f	0.155
Overt (clinical) hypothyroidism	1 (3.8)	1 (3.7)	2		
Overt (clinical) hyperthyroidism	1 (3.8)	1 (3.7)	2		
None	21 (80.9)	24 (88.9)	45		
Fertile women					
Subclinical hypothyroidism	0 (0.0)	1 (2.2)	1 (1.9)	4.989 ^f	0.249
Overt (clinical) hypothyroidism	0 (0.0)	0 (0.0)	0		
Overt (clinical) hyperthyroidism	1 (14.3)	0 (0.0)	1 (1.9)		
None	6 (85.7)	45 (97.8)	51 (96.2)		

χ^2 : Chi-square; *f*: Fisher's exact test

4. Discussion

Menstrual anomaly is a topic that has received little attention in society despite its complications and ability to cause infertility in females. Aside from the control of basal metabolic rate and growth functions of the thyroid hormones, the hormones also play a role in maintaining normal menstrual cycle. This therefore means that thyroid gland dysfunction can alter the menstrual cycle and could be associated with infertility [41].

The thyroid hormones are involved in almost all phases of reproduction, from folliculogenesis to placentation [8]. In combination with follicle-stimulating hormone, triiodothyronine (T3) enhances granulosa cell proliferation and inhibits granulosa cell apoptosis by the phosphatidylinositol 3-kinase/Akt (also known as protein kinase B) pathway [74]. Leukemia inhibitory factor (LIF) is involved in embryo implantation and expressed in the mid-secretory endometrium. Thyroid-stimulating hormone (TSH) significantly upregulates LIF expression in endometrial cell cultures, suggesting a potential role of TSH in the implantation process [2].

This study evaluated the anthropometric parameters of the infertile and fertile women. The mean weight of the infertile women was slightly higher, but the two groups had almost the same mean height. Both groups of women had a mean BMI of 25-29.9 making them mostly categorized as overweight. The mean blood pressure for the groups was within the normal range. However, the control group had a slightly higher mean pulse rate. Abnormal BMI and blood pressure levels have adverse effects on the clinical course of MSDs which can be observed on vital body organs such as the heart and kidneys [28, 33, 35, 63, 65, 70].

The menstrual anomalies in this study were significantly more in infertile women than in fertile women. Thirty-three (33) of the study participants had menstrual anomalies, of which infertile and fertile women accounted for 78.8% and 21.2% respectively. The intragroup percentages for women with menstrual anomalies were 49.1% for infertile women and 13.2% for fertile women. This finding is less when compared to the findings that reported menstrual irregularities in 50% of the patients [52], and another finding that reported menstrual anomalies in 61.2% of infertile women [16]. Another study presented a lower incidence of 19.6% menstrual irregularities in the cases examined [48]. Moreover, menstrual anomalies in this study had more occurrence than thyroid dysfunction among the study respondents which supports the fact that the latter precedes the former [58].

This study showed that the most common form of menstrual anomaly was menorrhagia (56%). This finding is similar to the results of other studies in which menorrhagia was also the most common anomaly: 50% [54], 50% [53], and 46.42% [42]. Oligomenorrhea in this present study was the second most prevalent menstrual anomaly (36%). This figure is higher than results reported in other studies: 17.86% [42] and 20% [58]. However, both studies agreed that oligomenorrhea was the second most prevalent anomaly. The fertile women in the present study had no incidence of intermenstrual bleeding, hypomenorrhea or amenorrhea.

Six (18.2%) out of the 33 women with menstrual anomalies were diagnosed with thyroid dysfunction while the remaining were euthyroid. Five (83.3%) of these 6 women with both menstrual anomaly and thyroid dysfunction were infertile while only one (16.7%) was fertile. The incidence of subclinical hypothyroidism was the highest (50%) among the women with menstrual anomalies, while overt (clinical) hyperthyroidism and overt (clinical) hypothyroidism were 33.3% and 16.7% respectively. This result is close to the results of Kumari, *et al* (43.48%) [42]; Sangita, *et al* (45.45%) [58]; Gandi, *et al* (45.45%) [13]; and George, *et al* (55.9%) [15] for the incidence of subclinical hypothyroidism in women with menstrual anomalies, but much lower than the result of Maria, *et al* (66.4%) [44]. Unlike this current study without diagnosis of subclinical hyperthyroidism, subclinical hyperthyroidism was diagnosed with an incidence of 13% [42] and 4.5% [58] among women with both menstrual anomaly and thyroid dysfunction.

The incidence of infertility in this study was 24.5% (primary infertility) and 75.5% (secondary infertility). This shares similarities with the results of another study which found 32.8% (primary infertility) and 67.2% (secondary infertility) [55]. The dominance of secondary infertility in this study agrees with some other African studies [4, 9, 50, 51], but disagrees with results of studies in some Western societies with 63.1 - 80.0% (primary infertility) dominance [17, 48].

Since thyroid dysfunctions have been associated with female infertility, it is important to evaluate thyroid gland function by estimating the serum levels of thyroid hormones rapidly and reliably using modern hormonal assay techniques. This procedure should be incorporated into the diagnostic routines in evaluating women with menstrual irregularities and infertility. It is also very important to note that an early detection of thyroid dysfunction can save patients from treatment costs of overt (clinical) thyroid dysfunction which may include surgery and/or radiotherapy.

Nevertheless, one limitation of this study should be clearly pointed out. The menstrual cycle consists of ovarian cycle and uterine cycle. These cycles are regulated by different hormones including prolactin, estrogen, progesterone, follicle stimulating hormone (FSH), luteinizing hormone (LH), etc. Therefore, these other hormones might have also contributed to the abnormal and normal menstrual patterns observed in this study, apart from thyroid hormones which this study concentrated on.

5. Conclusion

Thyroid gland dysfunctions strongly correlate with abnormal menstrual patterns. Early detection of thyroid gland dysfunction is vital in achieving a positive treatment outcome. Therefore, it is essential to evaluate serum levels of thyroid hormones during treatment of women with menstrual anomalies and infertility.

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