Avens Publishing Group
J Androl Gynaecol
April 2021 Vol.:9, Issue:1

Gonadotropins Disorder among Reproductive Age Women that Attended Fertility Clinics in Delta State University Teaching Hospital, Oghara, Delta State, Nigeria

Keywords: Gonadotropins; Hypergonadotropic; Hypogonadotropic; Adenomas; Hypogonadism; Infertility

Abstract

The inability of couples of reproductive age women to conceive after a year of regular sexual Intercourse is term infertility. Hormonal abnormality of the hypothalamic-pituitary- gonadal axis is one of the cause of infertility. Thus, the measurement of peptide and steroid hormones in serum is an essential aspect of the evaluation of infertility.

Method: This is a retrospective study of gonadotropin disorder of 268 reproductive age women between 20-45 years and with infertility duration between 2-7 years, who attended fertility clinics at the Delta State University Teaching Hospital, Oghara, Delta State, Nigeria between 2015-2020.

Results: The mean age of 268 reproductive age women is 33.50 ± 5.3 which accounts for 85.5 % menstruating while 14.5 % non- menstruating and with infertility duration of 2 to 7 years. Hypergonadotropic hypogonadism accounts for12.3 % with mean FSH, LH, Progesterone of 48.39±31.28, 30.91±-16.4, 0.34±0.14, p-value ,0.05 while hypogonadotropic hypogonadism accounts for 2.2 % with mean FSH, LH of 0.62±0.56, 0.46± 0.5, p-value .>0.05 and progesterone of 0.33 ±0.22 with p-value <0.04. In addition, isolated FSH group account for the functional gonadotropin secreting tumors which represent 11.6% and mean FSH, LH values of 15.55±8.6, 6.84±2.4 with p-value of < 0.05. Also, normal gonadotropins group accounts for 73.9% with a mean for FSH, LH of 5.61±1.5, 5.16±2.2 and with p-value <0.05.

Conclusion: One of the causes of infertility among reproductive age women in this study are hypergonadotropic hypogonadism, hypogonadotropic hypogonadism and gonadotropin secreting adenomas which accounts for 26.1 % of gonadotropins disorder and this findings need early intervention by the clinical team in our setting.

Introduction

The inability to conceive after a year of regular unprotected sexual intercourse in couples of reproductive age is term infertility [1]. In addition, it can also be defined as the inability to carry a pregnancy to term (delivery of a live baby) [2].

The age between 15 and 45 is considered to be the reproductive age for women [3] and infertility is a common social problem that affects more than 10-15% of marriage couples [4]. According to research, fertility in women is at its maximum in the mid-twenties and decline after the age of 30 years [5] and fertility is halved in women who are 35 years or above and declines sharply after the age of 37 [6].

Open Access Research Article

Journal of Androlgy & Gynaecology

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Submission: 1 March, 2021
Accepted: 5 April, 2021
Published: 10 April, 2021

Furthermore, the leading reason for gynecological consultation in Nigeria is infertility [7] and the factors that cause infertility vary from country to country and for different social groups. Hormonal dysfunction of the hypothalamic-Pituitary-Gonadal axis is one of the causes of infertility among other causes and thus the measurement of peptide and steroid hormones in serum is therefore an essential aspect of the evaluation of infertility [8]. Furthermore, the gonadotropins, prolactine, steroid (progesterone and estradiol) must be at the optimal level to control reproduction and alteration of these hormones results in infertility among women of child bearing age [9]. Thus the objectives of this retrospective study are:

A. To determine Hypergonadotropic Hypogonadism

B. To determine Hypogonadotropic Hypogonadism

C. To determine isolated increase of Follicle Stimulating Hormone with normal Luteinizing Hormone in reproductive age women.

Materials and Methods

This is a retrospective study of gonadotrophins disorder among reproductive age women between 20-45 years old and who attended the fertility Clinics at Delta State University Teaching Hospital, Oghara, between 2015-2020 for infertility investigation. Ethical approval was sought for from the Health and Research Ethic Committee of the hospital and it was given approval.

Only two hundred and sixty eight women of the above reproductive age and who came for infertility investigation with duration of 2-7 years of infertility were included in this study.

5ml of blood was collected from two hundred and sixty eight women in the first three days of menstruation for those menstruating and blood was collected the first day of visitation for those not menstruating. The blood was allowed to clot for 30 minutes and centrifuged for 5 minutes at 3000 revolutions per minute. The serum gotten were transferred to another bottle and then stored frozen at 20 degree Celsius until the time for hormonal analysis.

Furthermore, serum Luteinizing Hormone (LH) , Follicle

ISSN: 2332-3442

Table 1: Infertile female's serum hormonal characteristics.
Average age of women is 33.50±5.3

GROUP	N	FSH miu/ml	P-value	LH miu/ml	P-value	Prog ng/ml	P-value	%
Hypergonadotropic hypogonadism	33	48.39±31.28	<0.05	30.91±16.4	<0.05	0.34±0.14	<0.05	12.3
Hypogonadotropic hypogonadism	6	0.62±0.56	0.06	0.46±0.5	0.08	0.33±0.22	<0.04	2.2
Isolated FSH increase with normal LH	31	15.55±8.6	<0.05	6.84±2.4	<0.05			11.6
Normal gonadotropins	198	5.61±1.5	<0.05	5.16±2.2	<0.05			73.9
Menstruating								85.5
Non-menstruating								14.5

Table 2: Gonadotropins ratio of the Isolated FSH group.

GROUP	N	FSH Mean	LH Mean	Ratio FSH/LH	LH Mean	FSH Mean	Ratio LH/FSH
Isolated FSH group	31	15.55	6.84	2.3	6.64	15.55	0.43

Table 3: Normal values for gonadotropins and progesterone.

LH miu/ml	1.8-11.78
FSH miu/ml	3.03-8.08
Progesterone ng/ml	1.2-16

Stimulating Hormone (FSH), Progesterone were measured by using Architect Abboti 1000 analyzer that work with the principle of chemiluminescent micro plate immunoassays.

The data was analyzed using SPSS version 22.mean and standard deviations (SD) were calculated for FSH, LH, Progesterone, and Age. 95% confidence interval was calculated for the proportion and means and mean values were compared for statistical significance using t-value with level of significance < 0.05 (p-value).

Results

A total of 268 blood samples from reproductive age women were analyzed for FSH, LH, and Progesterone for this retrospective study. The mean of these women age is 33.50± 5.3 and with infertility duration between 2-7 years. From Table 1, hypergonadotropic hypogonadism which accounts for 12.3% with a mean for FSH,LH, Progesterone as 48.38±31.28, 30.91±16.4, 0.34±0.14 and with a significant p-value <0.05. Also, hypogonadotropic hypogonadism group which accounts for 2.2 % with a mean for FSH, LH as 0.60±0.56, 0.46±0.5 with a non significant p-value >0.05 and mean progesterone of 0.33±0.22 with a significant p-value <0.04 In addition, isolated FSH group which accounts for 11.6% with a mean value for FSH,LH as 15.55+8.6, 6.84±2, 4 and a significant p-value <0.05.Also, normal gonadotropic group which accounts forfor 73.9% with a mean value for FSH, LH as 5.61 ±1.5, 5.16±2.2 and with a significant p-value<0.05. Also 85.5 % accounts for the menstruating group while 14.5% accounts for non-menstruating group in this study.

In Table 2, FSH/LH and LH/FSH mean ratios for the isolated FSH group are 2.3 and 0.43.

In Table 3, indicate the normal values of FSH, LH and progesterone used for this study.

Discussion

In this study, the mean age of reproductive age women that came for infertility assessment is 33.5 years and this is in agreement with previous authors who reported that majority of infertile women are in the age group between 30-36 years [10]. It was also revealed in this study that 14.5% women were non menstruating while 85.5% were menstruating. This is in contrast with work done by Kester AD et al where 3.3% of infertile women were non-menstruating and 96.7% were menstruating. This could be as a result of difference in environmental exposure of the studied population. In addition, the infertility duration of infertile women this study is between 2-7 years which is in agreement with previous authors who observed mean duration of 6.8 and two years [10].

The outcome of this study further indicated that there was 12.3% occurrence of hypergonadotropic hypogonadism among the reproductive age women investigated and is comparable to the work done in Bida, Niger state where it was reported to be 13.3% [11] but lower than the 26.5% reported in Kano [12] and higher than 5.9% reported in Zaria [13]. Furthermore, hypergonadotropic hypogonadism in female (low progesterone with high FSH and LH) occurs as a result of primary ovarian hypofunction, an indication of the inability to conceive lie in the ovary. Also other causes of hypergonadotropic hypogogadism include testicular feminization, Turner 's syndrome and menopause [11].

Also, it was observed in this study that 2.2% of infertile women had hypogonadotropic hypogonadism which is comparable to 1.7% reported by Isah I A, [13] and lower than 3% reported by Emokpae MA et al [12]. Low FSH, LH and Progesterone level (Hypogonadotropic Hypogonadism) indicate that there may be inadequate secretion of gonadotropins to stimulate the ovaries in this women and this is as a result of dysfunction of the hypothalamus or the pituitary gland in this women. The causes of hypogonadotropic hypogonadism include Kallmans Syndrome, Cerebral tumor, Head trauma cerebral infection, cerebral radiation, malnutrition, hyperprolactinemia, Diabetes mellitus and marijuana [11]

The hypergonadotropins level of infertile women in this study is consistent with studies done by Adegoke et al [14] and Braide et al [15] while the hypogonadotrophins level in this study is consistent with the study by Eniola et al [16]. This shows that the above low and high gonadotropins in the reproductive age women in this study may be the cause of female infertility and menstrual irregularities in this

ISSN: 2332-3442

group of patients in our setting.

In addition, 73.9% of infertile women in this study indicated normal gonadotropins level and this is higher than the one recorded in Pakistan of 55.9% [17] and 42% recorded by Onyenekwe CC et al [18]. The difference in this outcome could be due to different sets of studied population and geographical location.

Functional and non-functional Pituitary adenomas can be classified depending on hormonal secretion. Gonadotrophs adenomas accounts for approximately 64% of clinically non-functional pituitary adenomas through immunohistochemistry [19] and while the clinical functional ones that produce an active form of gonadotropins which represent the minority of these tumors [20]. Furthermore, gonadotropins secreting tumors with signs related to hypergonadotropinemia have been rarely reported [21]. In addition the diagnosis of this type of tumor is more difficult and generally is asymptomatic; levels of FSH are often slightly increased above the normal value in reproductive age women [22].

Also, literature review provided diagnostic criteria used in diagnosing of functional gonadotropin adenomas which are either elevated levels of FSH/LH or elevated gonadal steroid levels in the presence of non- suppressed FSH/LH [23]. In this study, the isolated FSH group has mean ratio of FSH/LH of 2.3 which is a diagnostic of functional gonadotropinoma as described by Ntali G C et al who described the identification of gonadotropin secreting tumors to have increased FSH/LH ratio greater than 2 (>2) [24]. Also low serum LH/FSH ratio of less than one, (<1) [25] have been described in clinically functional gonadotroph adenomas and this further confirmed functional gonadotropin secreting tumors in the FSH isolated group in this study that has a mean ratio of LH/FSH of 0.43 and it accounts for 11.6% of reproductive age women (infertile women) in this study.

Furthermore, increased FSH and normal LH values in the FSH isolated group in this study is consistent with work done by several authors who have described the increased in FSH and normal LH in all cases of functional gonadotrophs adenomas [26-30].

In addition, functional gonadotropins adenomas are more common in postmenopausal women who are relatively insensitive to ovarian hyperstimulation and with high values of gonadotropins which is interpreted as physiologic [22]. There are symptom of gonadotropin excess secretion in premenopausal patients which include altered menstrual cycles or amenorrhea, multiple ovarian cysts with abnormal pain and even ovarian hyperstimulation syndrome [31]. The exact mechanism of multiple follicle cysts is not clear but it may be the prevention of apoptosis of numerous antral follicles which maintain their growth under the influence of follicular growth factors and this is as a result of the continuous unsuppressed FSH secretion by the pituitary. Several growth factors like vacular endothelial growth factor, fibroblast growth factor, epidermal growth factor, growth hormone, IGF-1 and transforming growth factor beta may have an intra-ovarian role in follicle growth [32].

In addition, in patients harboring pituitary adenomas, hormonal excess along the hypothalamic-pituitary-gonadal axis should be considered as a strong indicator. Functional gonadotropin adenoma early detection and surgical intervention has the potential to preempt unnecessary and potentially damaging treatment for comorbidities (eg ovarian cyst) and this will improve or restore sexual and reproductive function [33].

Conclusion

The clinical disorder associated with hypergonadotropic hypogonadism, hypogonadotropic hypogonadism and gonadotropin secreting adenomas contributed 26.1% of gonadotropin disorder in this study and accounts for infertility in our reproductive age women. Furthermore, the discovering of functional gonadotropins secreting tumors (11.6%) among our reproductive age women group, need the attention of the Clinical team for early intervention in our setting.

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ISSN: 2332-3442

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