

Interaction between Gonadotropin Hormones and Estradiol Secretion in Menopausal Women of Ijaw Ethnic Group, Niger Delta Region of Nigeria.

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Abstract: The principal Gonadotropin hormones in humans are the Luteinizing hormone (LH) and the Follicle Stimulating hormone (FSH). They are crucial in regulating the function of the ovaries in women. Estradiol (E₂), the primary female sex hormone is responsible for the development and regulation of the female reproductive system. In menopausal women, there is loss of ovarian function, leading to an increased secretion of FSH and LH and decreased secretion of E₂ with aging. This study was designed to determine the relationship between the secretions of these hormones (FSH/LH/E₂) in the Ijaw ethnic group menopausal women of Niger Delta Region of Nigeria with respect to age. A total of six hundred and ninety subjects, divided into four groups of 40-49 (pre menopause), 50-59 (menopause), 60-69 and 70 and above (post menopause) years were used for this study. The enzyme linked immunosorbent assay (ELISA) method was used in the measurement of the hormones. Statistical analysis of the results obtained from the study has shown that the secretion of plasma gonadotropic hormones increases significantly with declining estradiol level with increasing age. The result showed an FSH/LH ratio of 1.2 at menopause, with the ratio increasing with aging. The analysis of the gonadotropin/estradiol secretion showed a negative correlation. **Conclusion:** The study concluded that with the loss of ovarian function, the menopausal women of Ijaw ethnic group in Niger Delta Region of Nigeria have increased secretion of gonadotropin hormone (FSH/LH) and decreased estradiol hormone (E₂) secretion with high FSH/LH ratio that increases with increasing age.

Key Words: Estradiol, Follicle stimulating hormone, Luteinizing hormone, Menopause, Gonadotropin, Ovaries, Menstrual cycle.

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I. Introduction:

Menopause is cessation of the menses. According to World Health Organisation (WHO)⁽¹⁾, Menopause is the term of permanent cessation of menstruation due to loss of ovarian follicular activity. Menopause is a natural biologic process occurring in the body due to changing hormone levels⁽²⁾. It is the point that is defined after 12 months of amenorrhea following the final menstrual period⁽³⁾ and the end of child bearing.

The exact age a woman will experience menopause is not usually known. Some physical characteristics^(4, 5) and health issues⁽⁶⁾ can indicate an earlier or later menopause. Many physiological changes occur during pre-menopause and menopause. The hormonal changes that occur cause physical changes in the body. These hormonal and physical changes cause the symptoms of menopause that includes hot flashes, insomnia, and weight gain and bloating, mood changes, depression, headache, etc⁽⁷⁾. During menopause, a woman experiences a decline in plasma estrogen and progesterone, fluctuation in menstrual cycles begins with stoppage of ovulation because the ovaries do not contain any more eggs. There is an accomplishing loss of ovarian response to gonadotropins. When ovulation stops, the pituitary glands secrete more LH and FSH with no known function⁽⁴⁾. In an attempt to try to force ovulation to occur since no egg is released, plasma estrogen and progesterone cannot be produced. With loss of estrogen, the vaginal epithelium becomes redder as the epithelial layer thins and the small capillaries below the surface become more visible⁽⁸⁾. The menopausal ovary diminishes in size and is no longer palpable during gynaecological examination.

The laboratory markers of menopause include the following:

1. An increase in serum follicle stimulating hormone (FSH) and decreases in Estradiol and inhibin are the major endocrine changes that occur during the transition to menopause⁽⁹⁾
2. FSH levels are higher than Luteinizing hormone (LH) levels, and both rise to even higher values than those seen in the surge during the menstrual cycle⁽¹⁰⁾

3. The FSH rise precedes the LH and the FSH is the diagnostic marker for the ovarian failure, while LH is not necessary to make the diagnosis⁽¹⁰⁾
4. The large cyclical variation of estradiol observed during the menstrual years ceases, and fluctuation in levels is small and inconsequential with the mean value being considerably lower⁽⁹⁾.
5. The progesterone level decline dramatically, as there is no corpus luteum to produce the hormone.

The time spent in menopause, which is estimated to be up to one third of the life cycle now⁽¹⁰⁾ has increased. The average age at which menopause occurs is approximately 50-51 years⁽¹¹⁾ except where there are factors that influence it. Menopause results from the loss of ovarian sensitivity to gonadotropin stimulation, which is directly related to follicular attrition⁽¹²⁾. The most significant hormonal changes in menopause include a decrease in early cycle inhibin B and in anti-mullerian hormone (AMH) levels⁽¹³⁾. The decline in inhibin B results in an increase in FSH, which appears to be an important factor in the maintenance of Estradiol (E₂) concentrations until late in reproductive period^(14, 15). In post menopause, FSH levels are markedly raised; E₂ levels are low, whereas inhibin B and AMH are undetectable. The menopausal transition therefore is a time of marked hormonal instability⁽¹⁶⁾.

The essence of this study in Ijaw ethnic group of the Niger Delta region of Nigeria is to determine the variable pattern of gonadotropin and steroid, estrogen hormone secretion in the menopausal women considering however the estrogen sensitivity, the failure of the Luteinizing hormone surge and permanent amenorrhea in this group of menopausal women.

II. Materials/ Methods:

Study area

The Ijaw ethnic group consists of about 50 loosely affiliated clans situated in the Niger Delta region of Nigeria. Samples for the study were specifically collected from 3 Local government areas of Bayelsa State (Yenagoa, Southern Ijaw and Ekeremor), and 3 Local government areas of Delta State (Ughelli North, Patani and Isoko South). The main occupation of the Ijaw women are mainly fishing and farming.

Study population

A total of six hundred and ninety subjects were used for this study. This comprised of 200 subjects each in the 40-49 (control) and 50-59 years age bracket referred to as pre-menopause and menopause groups. Also included in the study are 180 and 110 subjects in 60-69 and 70 and above year's referred to as post menopause groups. They were randomly selected from the population of pre and post menopausal women from the six Local areas of the States in the Niger Delta region of Nigeria.

Data collection/ethical approval

Verbal consent was obtained from the subjects (respondents and guidance) before samples collection. A written questionnaire was issued to them that has questions about age, local origin (maternal and paternal) last menstrual date and whether on drugs for any illness. Excluded from the study were the women with different category of illness and are on hormone medication. Pregnancy test was conducted for the pre-menopausal groups to confirm their status and last date of menstrual cycle. Ethical clearance was obtained from the committee responsible for human research in the university.

Sample collection and preparation

Blood samples were collected using the standard Venipuncture method. This was discharged into the tube containing lithium heparin anticoagulant. The samples were centrifuged at 3,000 rpm in a centrifuge for about 10 minutes and the Plasma separated from the cell into a plain tube. This was stored in a refrigerator at -20°C prior to the time of sample analysis. Analysis was done within 7 days of sample collection. The study was carried out between May 2012 and June 2017.

Method of hormone assay The Enzyme linked Immunosorbent assay (ELISA) method of hormones estimation was used in this study⁽¹⁷⁾. The Principle is based on the solid phase enzyme linked Immunosorbent assay^(18, 19). The product kit was acquired from Micro Well Laboratories USA. The components of the ELISA kit were specifically designed to analyse the sex hormone, estradiol and the gonadotropic hormones (Follicle stimulating hormone, Luteinizing hormone).

Statistical Analysis:

Data are presented as descriptive statistics, including means, standard errors of the mean/deviation, and percentages. The student's t-test was used to compare the mean (pair two samples for mean) 95% confidence level (P<0.05) were used and considered significant.

III. Results

The result of the study, the blood levels of gonadotropic hormones (Follicle stimulating hormone and Luteinizing hormone) and Estradiol hormone in menopausal women in Niger Delta region of Nigeria is as presented in the tables and the figures below.

Table 1. The plasma levels of gonadotropic hormones (LH/FSH) with age in menopausal women.

AGE GROUPS	NO. OF SUBJECTS	HORMONES			STATISTICAL SIGNIFICANT
		LH (miu/ml)	FSH (miu/ml)	LH/FSH Ratio	
Pre-menopause 40-49years	200	20.0±4.38	24.42 ± 4.29	1:1	
Menopause 50-59years	200	29.64±5.74 ^a	35.91±13.90 ^a	1:2	0.0005
Post-menopause ¹ 60-69years	180	40.46±5.99 ^{ab}	59.30±12.50 ^{ab}	1:5	0.0005
Post-menopause ² Above 70years	110	51.89±8.57 ^{ab}	84.16±15.85 ^{ab}	1:6	0.0005

All value in the table are expressed as mean ± S.D

a or b = P-value <0.05

a = Control (Pre-menopause) Vs menopause, post menopause

b = menopause Vs post menopause^{1,2}

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Table 2. The plasma levels of Estradiol (E₂) hormone in menopausal women with age.

Age groups	No of Subjects	Estradiol(E ₂) (Pg/ml)	Statistical significance
Pre-menopause 40-49years	200	29.30±5.62	
Menopause 50-59years	200	17.68±5.28 ^a	0.0005
Post-menopause ¹ 60-69years	180	11.52±3.28 ^{ab}	0.0005
Post menopause ² Above 70years	110	8.45±4.15 ^{ab}	0.0005

All values in the table are expressed as mean ± S.D

a or b = P-value <0.05

a = control (pre-menopause) Vs menopause, post menopause

b = menopause Vs post menopause^{1,2}.

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Table 3: Correlation between the gonadotropic hormone (FSH/LH) and Estradiol (E₂) secretion in the menopausal women in Niger Delta Region.

Gonadotropic hormone	r-value (-)			
	E ₂	LH	FSH	FSH/LH
LH	0.116*	0.211*	0.271*	0.319*
FSH	0.115*	0.203*	0.277*	0.323*

Pre-menopause subjects (n=200), Post menopause (n=200), post menopause= 290.

*P <0.05, indicate negative correlation (r)

LH = Luteinizing hormone

FSH = Follicle stimulating hormone

E₂ = Estradiol

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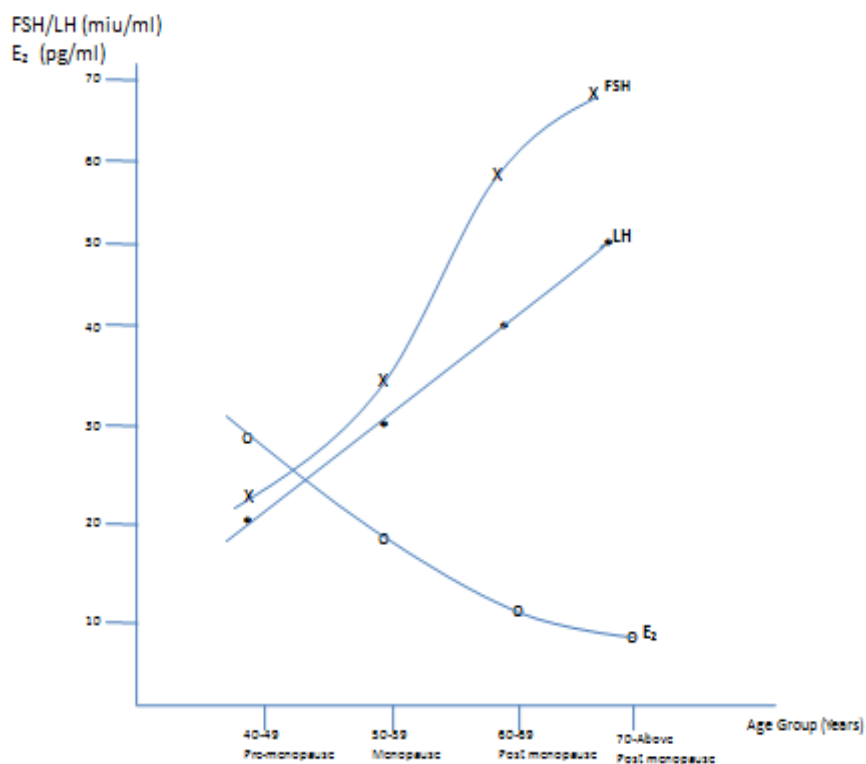


FIGURE 1. Graph showing the secretion pattern of the plasma gonadotropic hormones and estradiol in menopausal women of Ijaw ethnic extraction of Niger Delta Region of Nigeria. The level of E₂ responsible for reproduction decreases, leading to the increase in LH and FSH blood levels with resultant higher FSH/LH ratios and strong negative correlation.

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IV. Discussion

As the ovaries age and release fewer hormones, FSH and LH can no longer perform their usual functions to regulate the estrogens' secretions. The health of women in this state of menopause and post menopause are significantly affected by the inevitable changes in the decline of the estrogens' levels. The relationship in the secretion of these hormones in the women of Ijaw ethnic extraction in Niger Delta Region of Nigeria showed an FSH/LH ratio of 1:2 at menopause and at postmenopausal stages increased up to 1:5 with a strong negative correlation with the estrogens secretion. The result confirms the declining level of ovulation from pre-menopausal state to post menopause. The premenopausal period (climacteric) normally begins in some women as early as 40 years of age with commencement of the regression of ovarian function⁽²⁰⁾. Ovarian follicles deplete resulting in the decline of estradiol levels leading to genital atrophy⁽²¹⁾. This decrease in estradiol diminishes inhibin levels through a negative feedback mechanism that increases the secretion of follicle stimulation hormone^(14, 15). In post menopause, the ovary secretes androgens, but not necessarily estrogens^(22, 23) with the loss of the negative feedback mechanism. At this stage, the estradiol is produced not from the ovaries, but from the Liver, Kidney, Brain and peripheral adipose tissue^(24, 25). Published results^(20, 21) also indicate increased FSH/LH ratio of greater than 1 and this is because gonadotropic hormone levels rise quickly in the absence of ovarian estrogens secretion^(26, 27). Other published results^(28, 29) indicated that women, after the initial elevation of serum gonadotropins that characterizes the menopause, a progressive decline in both follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels occurs with age in the later post-menopausal years. Because of environmental factors⁽³⁰⁾, it's difficult to study the relationship between the estradiol secretion and follicle stimulating hormone concentration with the polymorphisms of various genes of menopause. However at post menopause⁽³¹⁾, women start to feel better because they have adjusted to the lower levels of hormones in their bodies.

V. Conclusion

The sex hormone estrogen and gonadotropins; FSH and LH were measured in menopausal women of Ijaw Ethnic nationality with respect to age groups to determine the variable pattern of gonadotropin and steroid hormone secretion. The Enzyme Linked Immunosorbent assay (ELISA) was used for this measurement. The

result indicated a declining plasma estrogen and increasing gonadotropins (FSH, LH) as the age increases with a FSH/LH ratio greater than 1.0. This ratio increased with increase in the age of the post menopausal women. This result statistically showed a strong negative correlation between the gonadotropins and the estrogen. This is as a result of loss of ovarian function in women that has attained menopause.

Contributions by the authors

The authors worked together in the designing of the topic, data collection; laboratory and statistical analysis, interpretation of results obtained and therefore qualified to co author the work.

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Nil

Conflicts of interest

There are no conflicts of interest

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Study data

The raw data, the plasma Estradiol, Follicle stimulating hormone and Luteinizing hormone values generated from the studied subjects with age used to support the findings of this study are available from the corresponding author upon request. This is because there is no available data base in the institution of the authors at present.

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