Original Article

Serum Gonadotrophin Levels in Breastfeeding Mothers Presenting at Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria

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Abstract

Background: There is paucity of data on serum gonadotrophin levels in breastfeeding mothers in our environment. The study aims at determining the serum level of follicle-stimulating hormone (FSH), luteinizing hormone (LH), and beta human chorionic gonadotrophins (β-hCG) in breastfeeding mothers and comparing with that of the controls. **Subject and Method:** Serum gonadotrophins levels were measured using commercially prepared enzyme-linked immunosorbent assay kit in 100 breastfeeding Nigerian women while 60 nonbreastfeeding ones (30 nonpregnant and 30 pregnant) served as controls. The participants were recruited consecutively from clients attending antenatal care at Usmanu Danfodiyo University Teaching Hospital, Sokoto. **Results:** The mean ± standard error of the mean serum level of FSH, LH, and β-hCG in mIU/ml was 5.97 ± 0.53, 7.15 ± 1.04, and 27.03 ± 3.16, respectively, at puerperium. Serum β-hCG level was significantly higher in breastfeeding group compared to the nonpregnant control ($P < 0.05$), but lower than that of the pregnant control ($P < 0.05$). Serum FSH is significantly lower ($P < 0.05$) in the breastfeeding group (5.97 ± 0.53 mIU/ml) compared to the nonpregnant control (8.99 ± 0.68 mIU/ml), but similar to that of the pregnant control. Serum LH however was significantly lower ($P < 0.05$) in the breastfeeding group (7.15 ± 1.04 mIU/ml) compared to the pregnant control (11.58 ± 0.7 mIU/ml). **Conclusions:** The serum β-hCG level was higher in breastfeeding mothers compared to the nonpregnant control. Thus, there is the need to establish separate reference values for gonadotrophins in mothers during puerperium. These reference values may be beneficial for detection of impaired level, especially of β-hCG in choriocarcinoma and other trophoblastic diseases at puerperium.

Keywords: Gonadotrophin, hormones, puerperium, trophoblastic diseases

Introduction

The developing nations, including Nigeria, have an alarmingly high maternal mortality rate. Maternal death or mortality is defined, in the International Statistical Classification of Diseases and Health-related problems (ICD-10), as a death occurring during pregnancy or within 42 days of childbirth or of an abortion from any cause related to or aggravated by pregnancy or its management but not from accidental or incidental causes.[1] Nigeria loses about 145 women of childbearing age every single day. Similarly, a woman's chance of dying from pregnancy and childbirth in Nigeria is 1 in 13. This makes the country the second largest contributor to the under-five and maternal mortality rates in the world.[2] Some of the causes of death are postpartum hemorrhage (24%); indirect causes such as anemia, malaria, and heart disease (20%); infection (15%); unsafe abortion (13%); eclampsia (12%); and obstructed labor (8%).[3] Postpartum hemorrhage is a major cause of maternal morbidity and mortality worldwide with the highest incidence in developing countries.[4] Choriocarcinoma occurs in 1 in 40,000 pregnancies. It is a highly aggressive malignant tumor of the trophoblasts which could be found in association with any form of gestation.[5] It could also manifest

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as a secondary postpartum hemorrhage. This is associated with markedly elevated human chorionic gonadotrophin (hCG) hormone levels which persists during puerperium. Death resulting from unsafe abortion following unplanned pregnancy also contributes to high rate of maternal mortality. Unsafe abortion is a major contributor to maternal mortality.[6]

Detection of elevated level of beta-hCG s (β-hCG s) in breastfeeding mother could help in early diagnosis and successful management of choriocarcinoma and other gestational trophoblastic diseases that could follow normal pregnancy. In addition, comparing the levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) in nonpregnant and breastfeeding women could serve as a stepping stone to understand more of lactational amenorrhea and how to improve on it to serve as a reliable family planning method. A cheap and reliable family planning method would help in reducing maternal mortality that occurs from unplanned pregnancies and unsafe abortions.

The endocrine system takes part in control of the flow of information between different cells and tissues. The term "endocrine" denotes internal secretion of biologically active substances. The endocrine system releases hormones into circulation to convey information to target cells that contain cognate hormone receptor. It exerts widespread effects on development, growth, and metabolism.[7] Hormone can be defined as a substance that is produced in one part of the body and is carried through blood stream to other organs or tissue where it acts to modify their structure or function. Hormones are secreted by endocrine glands which are also known as ductless gland. They are specialized cells, for example, islets of Langerhans. When the substances secreted by the specialized cells or collections of cells act locally on neighboring cells, it is called paracrine. If they act on the same cells producing them, they are called autocrine. When they are released into the blood stream and their target cells are far away from the site of production, it is called endocrine.[8]

The gonadotrophins control the function and secretion of hormones by the gonads (testes and ovaries), for example, the FSH, the LH, and hCG. The first two examples are commonly referred to as pituitary gonadotrophins.[9] The FSH is a heterodimer glycoprotein made up of α- and β-chains. The α-chain consists of 92 amino acids, while the β-chain consists of 117 amino acids. It stimulates the growth and maturation of ovarian follicle (eggs), stimulates estrogen secretion, and promotes endometrial changes.[10] The combined effect of FSH and LH is necessary, particularly during the follicular phase of the menstrual cycle, to cause ovulation. FSH stimulates spermatogenesis in males.

The LH also referred to as interstitial cell-stimulating hormone is a glycoprotein. Like FSH, it is also a dimer composed of α-subunit and a hormone-specific β-subunit. The α-subunits of the glycoprotein hormones (i. e., TSH, FSH, and LH) are identical and produced from a single gene and have the same amino acid composition although their carbohydrate residues vary. The β-subunits are produced by separate genes and differ in structure, conferring hormonal specificity and the specificity of the biological effects of these hormones. It is made up of 121 amino acids in LH. In males, LH stimulates the interstitial cells of Leydig in the testes to secrete testosterone. The quantity of testosterone secreted increases approximately in direct proportion to the amount of LH available. The testosterone secreted by the testes in response to LH has the reciprocal effect of inhibiting anterior pituitary secretion of LH. Most of this inhibition probably results from a direct effect of testosterone on the hypothalamus to decrease the secretion of GnRH.[11]

The hCG is also a glycoprotein hormone and consists of α and β chains. The alpha chain is similar to that of the aforementioned pituitary gonadotrophins and thyroid-stimulating hormone (TSH). It has intrinsic TSH-like action. The beta chain is made up of about 145 amino acids. hCG is produced by the chorion and the developing placenta during pregnancy. It is similar in structure and action to LH and prevents the involution of the corpus luteum as circulating pituitary gonadotrophins concentrations fall.[9] The hCG molecular structure is in fact remarkably similar to LH, and it binds to the LH receptors. It is generally accepted that hCG is luteotrophic and maintains the activity of the corpus luteum until the fetoplacental unit becomes endocrinologically autonomous, some 9–7 weeks after fertilization.

Pituitary and ovarian functions at the end of pregnancy and during the first 6 weeks after delivery were investigated serially in women who fully breastfed their infants and in women who did not. The levels of FSH in both groups were identical.[12]

The adult pituitary gland weighs approximately 500–600 g and is typically 1.2–1.5 cm in diameter and 0.5 cm thick, occupying approximately 80% of the sellar space. The pituitary gland is connected to the hypothalamus by the infundibulum, or pituitary stalk, and is seated within the sella turcica in the skull base and surrounded by the sphenoid bones on either side.

The pituitary gland consists of anterior and posterior lobes connected by middle, intermediate lobe. The anterior lobe (adenohypophysis) produces and secretes six hormones essential for metabolic function throughout the body. The posterior lobe (neurohypophysis) secretes two hormones: antidiuretic hormone and oxytocin. The neurohypophysis arises from the hypothalamus during fetal development. Both lobes are separated by a section of avascular tissue called the pars intermedius (intermediate lobe). This was originally thought not to function in humans, but some suggested that it plays a role in producing hormone precursors and a small amount of melanocyte-stimulating hormone.[13,14]

Subject and Methods

This was a cross-sectional study designed to determine the serum levels of gonadotrophins: FSH, LH, and hCG in breastfeeding mothers.

This study was conducted in the Chemical Pathology laboratory of Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto. Individuals were recruited from obstetrics and gynecology departments of UDUTH. Consenting individuals who fulfilled the selection criteria were recruited consecutively. The clearance to carry out the research was obtained from Usmanu Danfodiyo University Teaching Hospital ethical committees.

A total of 160 women of reproductive age were recruited for the study. On the average, about 10 individuals were recruited weekly for 16 weeks. This consisted of 100 breastfeeding mothers, 30 pregnant, and 30 nonpregnant women as controls. They were nonhypertensive, nondiabetic, and had no symptoms of any chronic illness or infertility and not on hormonal contraceptives. The 100 breastfeeding mothers were within the first 6-week postpartum. The nonpregnant women were within the first 5 days after menstruation and the pregnant women were at 28–32 weeks of gestational age. Interviewer-administered questionnaires were used to obtain data from them.

Using plain vacutainer sample bottles, venipuncture was done to obtain about three milliliters (3 ml) of blood sample while each patient was comfortably seated. The samples were separated and the sera were stored at −20°C. They were analyzed in batches after bringing them to room temperature. The serum levels of LH, FSH, and β-hCG were determined using commercial Test Kits, based on enzyme-linked immunosorbent assay technique (Accubind).

Statistical analysis

The data obtained from the study were compiled in the form of tables. The International Business Machine, Statistical Package for Social Sciences (SPSS) 20th version (Armonk, New York, United States) was used in analyzing the data. The age, body mass index (BMI), and hormonal level values were analyzed using mean, standard error of mean, and analysis of variance (ANOVA). One-way ANOVA was used to compare the mean levels of each gonadotrophin in the three groups. The level of significance at 95% confidence interval was taken at $P < 0.05$. Bar chart representation of the results was done for easy pictorial comparison of the levels of the hormones in the three groups.

Results

One hundred and sixty women were recruited for the study. These consisted of one hundred breastfeeding mothers and sixty matched nonbreastfeeding controls. The controls were made up of thirty nonpregnant and thirty pregnant women of childbearing age.

Table 1 shows the age range and mean BMI values of the participants.

Table 2 shows comparison of serum FSH, LH, and β-hCG levels between the two controls. The mean serum FSH in pregnant group (4.05 ± 0.57 mIU/ml) was significantly lower compared to that in the nonpregnant group (8.39 ± 0.68 mIU/ml) ($P = 0.001$), whereas the mean levels of LH (11.58 ± 0.7 mIU/ml) and hCG (338.86 ± 7.39 mIU/ml) in the pregnant women were significantly higher compared to those of the nonpregnant group (LH – mean 4.69 ± 0.45 mIU/ml, $P = 0.003$; β-hCG – mean 0.75 ± 0.93 mIU/ml, $P < 0.001$).

Similarly, in Table 3, the mean serum β-hCG level in breastfeeding group (27.03 ± 3.16 mIU/ml) was significantly higher compared to nonpregnant group (0.75 ± 0.93 mIU/ml) ($P = 0.001$).

Table 4 shows the comparison of the gonadotrophins levels between the pregnant and breastfeeding women. The mean values of LH and β-hCG in pregnancy were significantly higher ($P = 0.016$) than the corresponding mean values observed in the breastfeeding group.

Table 5 and Figure 1 show summarized results of evaluations of serum levels of gonadotrophins in the three groups. The mean level of FSH in mIU/ml was 8.99 ± 0.68, 4.05 ± 0.57, and 5.97 ± 0.53, respectively, in the nonpregnant, pregnant, and breastfeeding groups, while LH was 4.69 ± 0.45, 11.58 ± 0.71, and 7.15 ± 1.04, respectively. Furthermore, the mean levels of hCG were 0.75 ± 0.93 mIU/ml, 338.86 ± 7.39 mIU/ml,

Table 1: The age range in years and body mass index (mean±standard error of mean) of the research groups

Study individuals	Age range (years)	BMI (kg/m²)
Nonpregnant (*n*=30)	18-33	23.17±0.80
Pregnant (*n*=30)	17-33	26.77±1.00
Breast feeding (*n*=100)	15-40	25.78±0.54

BMI: Body mass index

Table 2: Serum gonadotrophin levels in the nonpregnant and pregnant groups

	Mean±SEM		
	FSH (mIU/ml)	LH (mIU/ml)	HCG (mIU/ml)
Nonpregnant (*n*=30)	8.99±0.68	4.69±0.45	0.75±0.93
Pregnant (*n*=30)	4.05±0.57	11.58±0.7	338.86±7.39
P	0.001	0.003	0.001

FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, HCG: Human chorionic gonadotrophin, SEM: Standard error of mean

Table 3: Serum gonadotrophin levels in the nonpregnant and breastfeeding groups

	Mean±SEM		
	FSH (mIU/ml)	LH (mIU/ml)	HCG (mIU/ml)
Nonpregnant (*n*=30)	8.99±0.68	4.69±0.45	0.75±0.93
Breast feeding (*n*=100)	5.97±0.53	7.15±1.04	27.03±3.16
P	0.013	0.398	0.001

FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, HCG: Human chorionic gonadotrophin, SEM: Standard error of mean

and 27.03 ± 3.16 mIU/ml for nonpregnant, pregnant, and breastfeeding group, respectively.

Discussions

The serum levels of gonadotrophins in the three groups of women – nonpregnant, pregnant, and breastfeeding mothers were evaluated. The mean level of the FSH was 8.99 ± 0.68 mIU/ml, 4.05 ± 0.57 mIU/ml, and 5.97 ± 0.53 mIU/ml, respectively. As expected, the level of FSH is lower in the pregnant group (4.05 ± 0.57 mIU/ml) than in the nonpregnant group (8.99 ± 0.68 mIU/ml), ($P < 0.05$). This is as a result of the negative feedback by estrogen and progesterone which are in high quantities during pregnancy. After parturition, however, as the serum level of estrogen and progesterone fall, the level of FSH starts rising again (5.97 ± 0.53 mIU/ml). The FSH mean level of 8.99 ± 3.70 mIU/ml in the nonpregnant group is similar to result obtained by Olooto *et al.*, 5.62 ± 2.21 mIU/ml, in south western Nigeria.[15] In Chennai, India, Parijatham and Saikumar obtained FSH serum level of 6.91 ± 3.9 mIU/ml which is also similar to the 8.99 ± 3.7 mIU/ml obtained in the index study.[16] Velasqueez *et al.* also obtained FSH level of 6.9 ± 0.6 mIU/ml.[17] However, Veeresh *et al.* obtained 4.86 ± 1.86 mIU/ml in Mahabubnagar, Telangana, India.[18] The difference could be as a result of using different period of the menstrual cycle. Veeresh *et al*. used samples obtained on 2nd or 3rd day of menstrual cycle. The level of the serum FSH in breastfeeding group was obtained as 5.97 ± 0.53 mIU/ml in this study. However, there is paucity of data on the level of gonadotrophins in breastfeeding mothers. Velasquez *et al.* obtained 8.1 ± 0.6 mIU/ml in breastfeeding mothers.[17] The sample was however taken within 60th and 70th day postpartum. This could explain the difference between Velasquez's value and that obtained in this research.

The LH on the other hand shows mean ± standard deviation levels of 4.69 ± 2.4 mIU/ml, for the nonpregnant group in this research. This is similar to 4.86 ± 1.64 obtained by Olooto *et al.*[15] Velasquez *et al*. also obtained serum LH level of 4.1 ± 1.9 mIU/ml and Parijatham and Saikumar obtained 5.05 ± 2.92 mIU/ml which are similar to the values obtained in this research.[16] However, Veeresh *et al.* obtained a slightly higher (6.9 ± 1.12 mIU/ml). The slight difference could be as a result of difference in period of menstrual cycle when sample collection was done.[18] The serum level of LH in the pregnant group was 11.58 mIU/L. This is higher than the 4.69 ± 0.45 mIU/ml obtained in the nonpregnant group. This is contrary to what is expected. The usual high levels of estrogen and progesterone in pregnancy are expected to send a negative feedback that would suppress the serum level of the LH.

Furthermore, the mean levels of β-hCG were 0.75 ± 0.93 mIU/ml, 338.86 ± 7.39 mIU/ml, and 27.03 ± 3.16 mIU/ml for nonpregnant, pregnant, and breastfeeding group, respectively. It would be expected that the β-hCG level (hormone produced by placenta) should not be detectable in a normal nonpregnant woman. The study however showed that a mean level of 0.75 ± 0.93 mIU/ml of β-hCG was detected in the nonpregnant group. This could

Table 4: Serum gonadotrophin levels in the pregnant and breastfeeding groups

	Mean ± SEM		
	FSH (mIU/ml)	LH (mIU/ml)	HCG (mIU/ml)
Breast feeding (*n*=100)	5.97±0.53	7.15±1.04	27.03±3.16
Pregnant (*n*=30)	4.05±0.57	11.58±0.7	338.86±7.39
P	0.253	0.016	0.001

FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, HCG: Human chorionic gonadotrophin, SEM: Standard error of mean

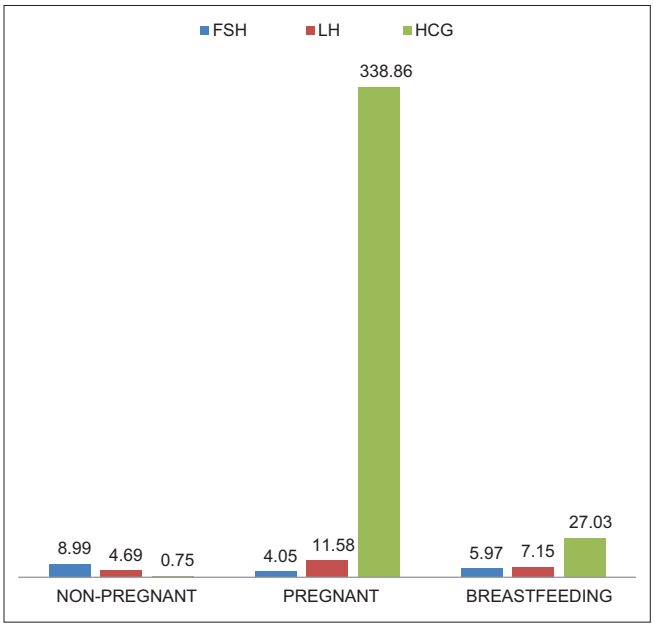

Figure 1: Serum levels of gonadotrophins in all groups (mIU/ml)

Table 5: The serum gonadotrophin levels in all the study groups

Serum parameters	Mean ± SEM		
	Nonpregnant group (*n*=30)	Pregnant group (*n*=30)	Breast feeding group (*n*=100)
FSH (mIU/ml)	8.99±0.68	4.05±0.57[a]	5.97±0.53[b]
LH (mIU/ml)	4.69±0.45	11.58±0.71[a]	7.15±1.04[c]
HCG hormone (mIU/ml)	0.75±0.93	338.86±7.39[a]	27.03±3.16[b,c]

P values: [a]<0.05 pregnant versus nonpregnant group, [b]<0.05 breast feeding versus nonpregnant group, [c]<0.05 breast feeding versus pregnant group. FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, HCG: Human chorionic gonadotrophin, SEM: Standard error of mean

be as a result of a small amount of β-hCG that is normally produced by the pituitary gland.[19]

Conclusions

It could be concluded from this research that hCG hormone was detectable in the serum of breastfeeding mothers and the nonpregnant controls. Thus, there is the need to establish separate reference values for gonadotrophins in mothers during puerperium. These reference values may be beneficial for detection of elevated level, especially of β-hCG in choriocarcinoma and other trophoblastic diseases in breastfeeding mothers. However, further studies should be carried out to gain more understanding of the hormonal basis of lactational amenorrhea and what could be done to improve its reliability as a family planning method.

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Conflicts of interest

There are no conflicts of interest.

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