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Beta-HCG Levels and Ovarian Ultrasonography Results among Non-Pregnant Women of Reproductive Age in Port Harcourt, Nigeria: A Cross-Sectional Study

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Abstract

Background: Certain ovarian cancers that were previously common in post-menopausal women are now increasingly observed in women of reproductive age. The research on using β-HCG as a diagnostic biomarker for ovarian cancer in women of reproductive age is ongoing. **Aim:** This study assessed the level of serum β-HCG in non-pregnant women of reproductive age and determined its potential association with suspicious ovarian ultrasonography results. **Methods:** The study was conducted in Port Harcourt, Nigeria. This study adopted a cross-sectional design on a quota sample of 224 case notes of women aged 18 - 40 years obtained from eight diagnostic centres. A data extraction form was used for data collection. Data analysis employed descriptive statistics, Chi-square, Fisher's exact test, and Odds Ratio at 95% confidence and 5% significance levels. **Results**: About 5.8% of the participants exhibited detectable levels of serum β-HCG above 5 IU/L (World Health Organization reference) at a mean concentration of 5.87 (±1.75) IU/L. About 4.0% of the participants had suspicious ovarian lesions identified through ultrasonography. Participants with elevated serum β-HCG levels above the WHO reference were 59 times more likely to have suspicious ovarian lesions (Odds ratio: 59.4, 95%CI: 12.3 - 287.8, $p < 0.001$). There was a significant association between serum β-HCG level and age ($p = 0.041$) as well as parity ($p < 0.001$). **Conclusion:** Serum β-HCG levels above the WHO reference in non-pregnant women were associated with suspicious ovarian lesions. More rigorous primary research, systematic reviews, and meta-analyses are needed to confirm the findings of

this study.

Keywords

Biomarkers, Ovarian Cancer, Pregnancy, Ultrasonography

1. Introduction

Ovarian neoplasm is one of the most common cancers and a leading cause of mortality among women [1]. It is often diagnosed at an advanced stage, resulting in poor health outcomes. Previous studies have suggested that elevated serum levels of gonadotropins, including β-HCG, may be associated with ovarian cancer [2] [3] [4]. However, the use of β-HCG as a diagnostic biomarker in women of reproductive age remains controversial due to various concerns and limitations [5].

The β-HCG is a glycoprotein known to be synthesized by the foetal trophoblast and released into maternal blood. Nonetheless, recent research reports that some cancers produce β-HCG [2] [6]. Clinical laboratory protocols enable the measurement of β-HCG in blood or serum specimens [7]. Initially used for diagnosing and monitoring pregnancy, some studies support its potential as a biomarker for certain cancers, including ovarian cancer [8] [9].

The concerns surrounding β-HCG as a diagnostic biomarker for ovarian cancer are palpable. Firstly, previous studies have observed elevated β-HCG levels in a small percentage of healthy non-pregnant women of reproductive age without detectable ovarian cancer [10]. Secondly, serum β-HCG levels increase with age and parity status, making it challenging to establish standardized cut-off values [11]. Moreover, there is a lack of consensus among laboratories regarding the cut-off values, leading to significant variation in reporting quantitative results [7]. Additionally, the reference limits suggested by manufacturers of commercial HCG assay kits may not align with actual clinical practice [12]. Despite these limitations, some studies support the use of β-HCG as a biomarker for ovarian cancer, particularly in advanced stages [8] [9].

Non-pregnant women of reproductive age (specifically those aged 18 - 40 years) have scarcely been examined by previous studies regarding the prevalence of anomalous ovarian lesions and their association with elevated serum levels of β-HCG. The dearth of literature highlights the need for further research on the subject matter. Understanding the potential of β-HCG as a diagnostic biomarker for ovarian disease in non-pregnant women of reproductive age is crucial for the early detection of ovarian neoplasm. This study aims to investigate the serum β-HCG levels and prevalence of suspicious ovarian lesions among non-pregnant women of reproductive age in Port Harcourt, Nigeria. The findings of this study may contribute to the ongoing discourse surrounding the use of β-HCG as a biomarker for ovarian cancer.

2. Materials and Methods

2.1. Study Design and Sampling

This study utilized a cross-sectional design to investigate a specific research question. The target population for this study consisted of approximately 301,562 women who are residents of Port Harcourt and fall within the age range of 18 to 40 years old.

The sample size for this study, consisting of women of reproductive age, was determined using Cochran's formula [13]. The formula, mathematically represented as $n = [(Z)^2 \times P(1 - P) \div d^2]$, took into account various factors. These included the critical value constant at a power of 80% ($Z = 1.96$), the estimated prevalence based on literature ($P = 84\%$) [14], and the tolerable error level ($d = 5\%$). The computed minimum sample size was 206. This study addressed potential non-response by increasing the minimum sample size by 10% using the non-response formula [15], expressed as $n^* = [n \div (1 - 0.1)]$. It resulted in a final sample size of 224 participants. The selection of case notes from the participating diagnostic centres involved the application of a quota sampling technique. A total of 28 diagnostic case notes were chosen from each of the eight centres ($n = 224$).

The inclusion criteria involved case notes of women who were aged 18 - 40 years and confirmed not pregnant by an attending physician. On the other hand, the exclusion criteria involved women who were pregnant, aged less than 18 years, and residing outside the Port Harcourt Metropolis area.

This study examined case notes in private diagnostic centres in Port Harcourt, Rivers State, Nigeria. Located in the oil-rich Niger Delta, Port Harcourt is the capital of Rivers State. At least 2.4 million persons are residents in the city and engage in various occupations such as construction, trading, and white and blue-collar jobs. However, Port Harcourt has environmental challenges, including the heavy burning of fossil fuels and the resulting soot pollution from clandestine illegal crude oil processing in neighbouring communities. Port Harcourt has many private diagnostic centres, but only eight demonstrated sufficient technology to test and quantify Human Chorionic Gonadotropin. The centres include De-Integrated Medical Diagnostic and Research Laboratory, Asi Ukpo Medical Imaging and Phlebotomy Centre, Bio-systems Medical Diagnostics, Dorek Medical Diagnostics, Pyramids Diagnostics, Index Medical and Diagnostics, Trans-view Diagnostics, and Oasis Diagnostic Centre.

2.2. Instrument and Data Collection

The research team utilized a semi-structured data extraction form consisting of six items to collect relevant data. The form was divided into three sections, namely A, B, and C. Section A gathered background demographic information of the participants, such as age, marital status, parity status, and employment status, using five instrument items. Section B focused on extracting the laboratory results for serum HCG concentration. Section C extracted the results of ovarian

ultrasonography.

2.3. Data Analysis

Data were extracted from the selected case notes. Demographic data of the participants were analysed using descriptive statistical methods, including frequency and percentage. The interval data related to age were summarised using measures such as mean, standard deviation, frequency, and percentages. The association between variables was examined using statistical tests such as the Chi-square test, Fisher exact test, and Odds ratio. These inferential statistics were conducted at a 95% confidence level and a significance level of 5%. The Statistical Products and Service Solutions software version 25 (IBM, Chicago, IL, USA) was used for all the statistical analyses.

2.4. Ethical Consideration

The University of Port Harcourt Institutional Review Board approved this study, with the approval number UPH/CEREMAD/REC/MM87/068. The study followed the guidelines outlined in the Helsinki Declaration of 1975, revised in 2013. Written consent was not obtained as the study reviewed anonymous (de-identified) diagnostic case notes. The study was conducted between November 2022 and May 2023. Recruitment of participant case notes was done in February 2023.

3. Results

All 224 observations were eligible for data analysis. Table 1 summarises the demographic characteristics of the participants and shows that many (52.7%) of the participants in the study fell within the age range of 30 - 35 years. Most of the participants were married (98.7%), had given birth to two or more children (multiparous, 78.6%), and were employed (83.9%).

Table 1. Socio-demographic profile of the respondents, (n = 224).

Variable	Category	f	%
Age	18 -23	12	5.4
	24 - 29	73	32.6
	30 - 35	118	52.7
	36 - 40	21	9.4
Marital Status	Single	3	1.3
	Married	221	98.7
Parity Status	Nullipara	21	9.3
	Primipara	27	12.1
	Multipara	176	78.6
Employment Status	Unemployed	36	16.1
	Employed	188	83.9

f = frequency, % = percentage, n = sample size.

Table 2 summarizes serum β-HCG levels among the participants and indicates that a small proportion (5.8%) of the study participants had a detectable level of serum β-HCG above 5 IU/L, which is the reference value according to the World Health Organization (WHO).

Figure 1 reveals that a few (4.0%) of the study participants were observed to have suspicious ovarian lesions identified during the ultrasonography.

Table 3 summarizes the association between Serum β-HCG concentration and ovarian ultrasonography findings and demonstrates that participants who had elevated serum HCG (>5 IU/L) were 59 times more likely to have a suspicious ovarian lesion ($p < 0.001$).

Table 4 summarizes the association between age and parity with Serum β-HCG concentration and demonstrates a significant association between serum β-HCG level and age ($p = 0.041$) as well as parity ($p < 0.001$).

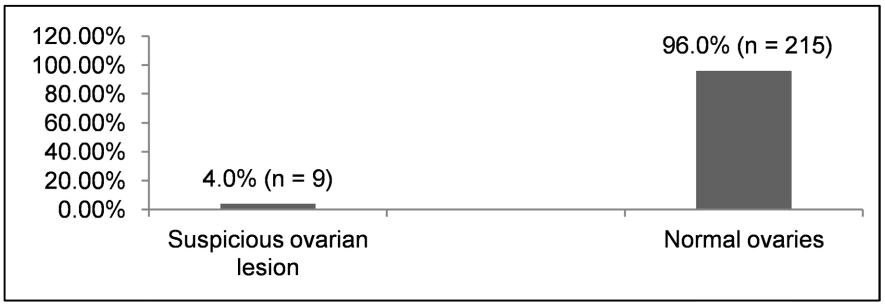

Figure 1. Prevalence of suspicious ovarian lesion among the non-pregnant women, (n =224).

Table 2. Serum concentration of serum β-HCG among non-pregnant women, (n = 224).

Concentration Category	f (%)	Range	*Mean* (*SD*)
<1.0 IU/L	4 (1.8)	-	-
1.0 - 5.0 IU/L	207 (92.4)	1.1 - 4.6	2.95 (0.78)
>5.0 IU/L	13 (5.8)	5.3 - 7.1	5.87 (1.75)
Grand Mean		1.1 - 7.1	2.96 (1.32)

f = frequency, % = percentage, n = sample size, SD = standard deviation.

Table 3. Fisher's exact test of association between serum HCG and Ovarian ultrasound findings, (n = 224).

Variables	Ovarian Ultrasonography findings		df	Fisher	OR (95%CI)	p value
Serum β-HCG	*Normal*	*Suspicious*	1	52.47	59.4 (12.3 - 287.8)	<0.001*
>5 IU/L (Elevated)	7	6				
<5 IU/L (Normal)	208	3				

df = degree of freedom, Fisher = Fisher's exact test, OR = Odds Ratio, p = p value, * = highlights significant p value.

Table 4. Chi square test of association between age/parity with HCG concentration, (n = 224).

Variables	Serum β-HCG concentration		df	χ^2	p value
Age	<5 *IU/L* (*Normal*)	>5 *IU/L* (*Elevated*)	3	8.24	0.041
18 - 23	12	0			
24 - 29	71	2			
30 - 35	111	7			
36 - 40	17	4			
Parity			2	62.96	<0.001*
Nullipara	12	9			
Primipara	24	3			
Multipara	175	1			

df = degree of freedom, χ^2 = Chi square, p = p value, * = highlights significant p value

4. Discussion

This study found that about one in 20 of the study participants (5.8%) had a detectable level of serum β-HCG above the WHO limit (5 IU/L). This finding contrasts a study conducted in the USA that found that 1.7% of women had HCG levels above 5 IU/L [12]. The disparity in findings can be attributed to the different populations studied. This study focused on women of black African origin, while the USA study examined women of Caucasian and Hispanic origin. The genetic differences between these populations likely contribute to variations in serum β-HCG levels. This finding contrasts with another study that reported a higher prevalence (8%) of women with levels above the WHO limits [7]. The difference in sample sizes may contribute to this discrepancy. This study's findings also exceeded the range of serum β-HCG levels reported in a Norwegian study that found a range of 0.1 - 0.2 IU/L among 732 women below 45 years old [6]. The low levels in the Norwegian study can be explained by variations in menstrual cycle phases, as they examined women during the secretory phase, whereas this study did not consider the menstrual cycle.

In this study, about one in 25 of the study participants (4.0%) had suspicious ovarian lesions. The prevalence of ovarian lesions in this study was higher than the reports by a study in the USA that reported a prevalence of 0.04% among 20 - 39 year old women [16]. The dissimilarity in findings can be attributed to variations in sample size. This study utilized a smaller sample of 224 participants compared to the larger census samples used in the USA study. Furthermore, two other studies in the USA reported higher prevalence rates of 9.2% and 5% respectively [17] [18]. The dissimilarity in findings could be due to the retrospective designs and census sampling methods differing from the cross-sectional and quota sampling approach used in this study, potentially introducing selection bias.

This study found that participants who had elevated serum HCG (>5 IU/L)

were 59 times more likely to have a suspicious ovarian lesion. This finding corroborates a Germany that found significantly higher serum beta-HCG concentrations among women with malignant ovarian tumours compared to those with benign tumours [19]. The similarity in findings was expected since collected data were analysed at a 5% level of significance and 95% confidence interval.

This study found a significant association between serum β-HCG level and age as well as parity. This finding suggests that age is marginally associated with serum HCG concentration. Thus, if an individual is older, the possibility of having an ovarian lesion is perhaps more. This finding corroborates a study that noted that Age was significantly associated with serum HCG levels [7]. Given that both studies were non-experimental, the similarity in findings was quite expected. This finding corroborates the findings of a pivotal study that found a significant association between parity and serum HCG such that maternal serum β-HCG decreased with increasing parity ($p < 0.050$) among 20,009 women aged 18 - 40 years [20]. This finding implies that increasing parity reduces serum HCG and hence protective to the ovaries.

The key limitations of this study are as follows. This study utilized a relatively small quota sample of 224 women, which may not fully represent the larger population of women of reproductive age in Port Harcourt, Nigeria. The findings may not be generalizable to a broader population, limiting the external validity of the study. The study employed a quota sampling method, which introduces the potential for selection bias. Quota sampling may not provide an equal chance of selection to all members of the target population, leading to a non-representative sample but it was the most feasible method.

5. Conclusion

Non-pregnant women with elevated levels of serum β-HCG were likely to have suspicious ovarian lesions. The association between serum β-HCG levels and increasing age and parity further emphasizes the importance of monitoring β-HCG levels in the different demographic groups. More rigorous primary research, systematic reviews, and meta-analyses are needed to confirm the findings of this study.

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Informed Consent

The authors obtained verbal and written informed consent from each respondent before data collection.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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