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The Relationship between Second Trimester Maternal Serum BhCG Levels and Adverse Pregnancy Outcome in a Tertiary Care Centre

Boysungni E. Zaro[1*], Constance E. Shehu[1], Panti A. Abubakar[2], Muhammad B. AbdulRahman[2], Jamila Garba[1], Abdullahi A. Habib[3]

[1]*Usman Danfodiyo University Teaching Hospital, Sokoto, Nigeria*

[2]*Usman Danfodiyo University, Sokoto, Nigeria*

[3]*Rasheed Shekoni Federal University Dutse, Jigawa State, Nigeria*

*Correspondence should be addressed to Boysungni E. Zaro: freecaremulticlinics@gmail.com

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ABSTRACT

Background: The first trimester serves as a crucial screening period for identifying patients at risk for Down syndrome. Elevated second-trimester maternal serum β-human Chorionic Gonadotropin (βhCG) levels were initially introduced to detect trisomy 21 and various complications such as neural tube defects, ectopic pregnancy, and preeclampsia. This study aimed to explore the relationship between elevated βhCG levels and adverse maternal and neonatal outcomes among women receiving antenatal care at Usmanu Danfodiyo University Teaching Hospital, Sokoto.

Methods: It was a prospective study involving three hundred and fourteen (314) pregnant women attending antenatal care, who completed a structured questionnaire. A Nuchal Translucency (NT). A scan was performed between 11 and 13^{+6} weeks, followed by βhCG level assessments at 16-18 weeks. Patients were monitored until delivery, and any adverse outcomes were documented. Data were analysed using SPSS Version 29.0, applying the Chi-square and Fisher's Exact tests for statistical significance, with a p-value of less than 0.05 deemed significant.

Results: Results indicated that 311 (99.0%) of participants had normal ultrasound findings, while 3 (1.0%) showed fetal congenital anomalies, primarily hydrocephalus. The mean βhCG level recorded was 1.11 MoM. Most patients experienced spontaneous vaginal deliveries (270, 86.0%), while 44 (14.0%) underwent cesarean sections. Elevated maternal βhCG levels were significantly associated with adverse pregnancy outcomes, including increased rates of intrauterine growth restriction (IUGR), preeclampsia, abruptio placentae, and congenital anomalies. Women with elevated βhCG had a higher likelihood of both maternal and fetal complications and a markedly lower proportion of uneventful pregnancies compared to those with normal βhCG levels ($p < 0.001$).

Conclusion: The study demonstrated a significant association between elevated maternal βhCG levels and adverse pregnancy outcomes. These findings support the use of βhCG as a valuable early screening marker for identifying pregnancies at increased risk of maternal and fetal complications, thereby aiding timely intervention and improved prenatal care.

1.0 INTRODUCTION

First- and Second-Trimester Serum Screening is a well-established technique adopted several years ago to detect pregnancies at high risk of open neural tube defects and chromosomal aberrations, especially trisomy 21 and trisomy 18. Alpha-fetoprotein, human chorionic gonadotropin, unconjugated estriol, inhibin-A, and pregnancy-associated plasma protein-A constitute the commonly used first- and second-trimester serum screening markers [1].

Human chorionic gonadotropin (hCG) belongs to the family of glycoprotein hormones (hCG, follicle-stimulating hormone [FSH], luteinizing hormone [LH], and thyroid-stimulating hormone [TSH]) [2]. Each is a dimeric molecule composed of a common alpha subunit and a hormone-specific beta subunit that associates non-covalently [2–4]. The α-subunit consists of 92 amino acids, while the β-chain of hCG (β-hCG; 145 amino acids) is encoded by six highly homologous genes located on chromosome 19q. The biological activity of hCG is determined by the distinct combination of these two subunits [2]. In clinical practice, pregnancy is commonly identified by detecting hCG [3]. Nevertheless, β-hCG may also be produced in non-germinomatous germ cell tumours and gestational trophoblastic disease [4]. During pregnancy, hCG is mainly synthesised by the placental syncytiotrophoblast [5], although minor production has been reported in the fetal kidney and fetal liver [6]. Circulating hCG is metabolised primarily by the liver [7].

The primary role of hCG in early pregnancy is the maintenance of the corpus luteum. It replaces LH to stimulate progesterone production by ovarian luteal cells, thereby preventing menstruation and sustaining implantation [6]. Progesterone production is particularly crucial within the first 3–4 weeks following implantation [4]. The hCG receptor gene is expressed in the uterine spiral arteries, where hCG promotes angiogenesis and increased uterine blood supply to support fetal growth. Additional functions of hCG include cytotrophoblast differentiation, modulation of the maternal immune response, and regulation of trophoblastic invasion [7]. In Sokoto State [8] and many parts of Nigeria [9], serum β-hCG estimation is not routinely included in antenatal care for identifying women at risk of fetal anomalies, high-risk pregnancies, or pregnancy-related medical disorders. Although serum β-hCG testing is non-invasive compared with procedures such as chorionic villus sampling, amniocentesis, and cordocentesis, a standardised protocol for fetal chromosomal and congenital anomaly screening has not yet been established in our Department of Obstetrics and Gynaecology. Hence, this study aims to provide baseline data to facilitate the design and implementation of a screening protocol within the fetomaternal unit, particularly given the limited local studies available.

Moreover, abnormal levels of serum b-hCG in the maternal body have not only been linked to the appearance of chromosomal aberration issues but also to unfavourable obstetric results, including pre-eclampsia, intrauterine growth retardation, preterm births, and placental dysfunctions [10, 11]. High levels can indicate abnormal placentation and invasion of the uterine wall by trophoblastic cells, whereas low levels may indicate a retarded placental development or a pregnancy failure [12, 13]. Thus, b-hCG can also serve as a convenient biochemical predictor of placental health and pregnancy viability, in addition to its diagnostic role in aneuploidy screening.

In several well-developed health systems, first-trimester combined screening of pregnancies based on maternal age, ultrasound reduction (e.g., nuchal translucency), and biochemical reduction (e.g., b-hCG and PAPP-A) has improved early risk stratification of pregnancy [14]. Nevertheless, in resource-constrained locations, such as some parts of Nigeria, coverage of standardised prenatal screening programs remains poor due to high costs, inadequate laboratory facilities, and limited awareness among health care providers [15, 16]. As a result, numerous fetal anomalies are observed at late pregnancy stages or during post-delivery life, which limits the possibility of early counselling and proper obstetric care and management [17, 18].

It is thus crucial to develop locally applicable reference values for maternal serum b-hCG because population differences in ethnicity, nutrition, and environmental factors, as well as gestational dating, can affect the interpretation of biochemical markers [19, 20]. The results of this study will lead to the development of population-specific reference ranges and enhance prenatal screening practices. This can eventually increase the detection of high-risk pregnancies at their onset, improve antenatal surveillance, and support evidence-based clinical decision-making in maternal and fetal care in the study setting.

The study aims to determine the relationship between elevated second-trimester maternal serum βhCG levels and adverse maternal and neonatal outcomes among women attending antenatal care at Usmanu Danfodiyo University Teaching Hospital, Sokoto.

2.0 METHODOLOGY

2.1 Study Area and Research Design

This prospective study was conducted at the Usmanu Danfodiyo University Teaching Hospital.

2.2 Population, Inclusion and Exclusion Criteria of the Study

Pregnant women with a singleton pregnancy of 11-13^{+6} weeks of gestation were included in the study. Confirmation of gestational proximity was established with respect to the last menstrual period or early ultrasound (<14 weeks).

2.2.1 Inclusion criteria

Women with a known gestational age of 11-13^{+6} weeks, pregnant with only one fetus, who volunteered to take part were recruited.

2.2.2 Exclusion criteria

Women were excluded from the study if they presented with biodemographic or clinical characteristics that could influence maternal serum β-hCG levels or pregnancy outcomes. These included women with multiple pregnancies, known fetal congenital anomalies detected during antenatal screening, pre-existing maternal medical conditions such as diabetes mellitus, chronic hypertension, renal disease, or thyroid disorders. In addition, women who were unable to provide complete clinical or obstetric information, those who declined consent, or those who did not attend follow-up were excluded from the study.

2.3 Sample Size and Sampling Method

The study population was calculated using the Cochran formula, with a 95 per cent confidence level, a 5 per cent margin of error, and a prevalence of 50 per cent, indicating that a sample size of 384 is required. However, in a bid to cushion against the expected 10 per cent attrition rate, 402 patients were recruited for the study.

Only 314 (78.1%) participants had complete data, as some lacked complete records due to missing folders, had lost their referrals, or had unmonitored home deliveries. On average, 20 women were signed in each week at both the booking clinic and the gynaecology emergency clinic.

2.4 Procedure of the Study

A self-administered structured questionnaire was also used in gathering biodata and other pertinent obstetric information. Weight and height were measured, and BMI was calculated. A complete history, physical, and obstetric examination was conducted. Maternal venous blood samples (5 mL) were collected between 16 and 18 weeks of gestation and centrifuged to obtain serum. Serum β-hCG levels were measured using a chemiluminescent immunoassay with a commercially available kit (Monobind Inc., California, USA; ISO13485). The assays were performed according to the manufacturer's instructions. Calibration of the analyser was conducted using standard calibrators provided with the kit. Internal quality control was ensured by running low- and high-control sera with each batch of samples. The intra-assay and inter-assay coefficients of variation were maintained within the acceptable range recommended by the manufacturer. The mean βhCG value was 1.11 MoM in pregnancy, and values higher than 1.20 MoM were considered elevated, as recommended by Hematian *et al.* [21]. All the participants were followed up to their delivery, and the outcome of the fetus was noted as live birth, stillbirth, neonatal death, birth weight, Apgar score, fetal anomaly, and the way the child was delivered.

2.5 Ethical Clearance

All the participants signed informed consent. The research activity was conducted in compliance with ethical norms and was authorised by the Usman Danfodiyo Teaching Hospital Ethical Committee under approval number ID: DUTH/HREC/2016/No.503. All women were allowed to withdraw at any time, and confidentiality was maintained.

2.6 Analysis of Data

SPSS version 29.0 and Microsoft Excel were used to analyze data. The chi-square test was used to compare categorical variables, and $p < 0.05$ was considered statistically significant. The correlation between maternal and neonatal βhCG levels and pregnancy outcomes was calculated to determine whether there was a meaningful relationship between the two βhCG measures and pregnancy outcome. Where applicable, descriptive statistics were used.

3.0 RESULTS

Table 1 summarizes the socio-demographic and clinical characteristics of 314 respondents in the study, showing that the majority were within the 20¨C29 years age group (54.8%), with few participants below 20 years (6.4%). Most respondents were of Hausa/Fulani ethnicity (66.6%), while Igbo (12.1%), Yoruba (10.2%), and other ethnic groups (11.1%) made up smaller proportions. A

Table 1. Socio-demographic Characteristics of the Participants

Socio-demographic characteristics	Frequency	Per cent (%)
Age in years		
< 20 years	20	6.4
20 – 29	172	54.8
30 – 39	117	37.3
40 – 49	5	1.6
Total	314	100
Tribe		
Hausa/Fulani	209	66.6
Igbo	38	12.1
Yoruba	32	10.2
Others	35	11.1
Total	314	100
Educational status		
No formal education	21	6.7
Primary	31	9.9
Secondary	77	24.5
Tertiary	185	58.9
Total	314	100
Social history		
Smoking	2	0.6
Alcohol	9	2.9
Non-Alcoholic/Smoker	303	96.5
Total	314	100
Past medical history		
Diabetes	6	1.9
Hypertension	12	3.8
Sickle cell disease	5	1.6
Asthma	5	1.6
No past medical history	286	91.1
Total	314	100

high level of education was observed, with 58.9% having tertiary education and 6.7% no formal education. Social history revealed very low prevalence of smoking (0.6%) and alcohol consumption (2.9%), with the majority (96.5%) reporting neither behavior. Additionally, most participants (91.1%) had no past medical history, while hypertension (3.8%), diabetes (1.9%), and both sickle cell disease and asthma (1.6% each) were reported in small proportions, indicating generally low levels of comorbidities among the study population.

Figure 1 shows that the majority of participants had vaginal delivery (86%), while a smaller proportion underwent caesarean section (14%), indicating that vaginal delivery was the predominant mode of delivery among the study population.

The prevalence of elevated βhCG was 48 (11.9%). Table 2 presents the association between maternal β-hCG levels

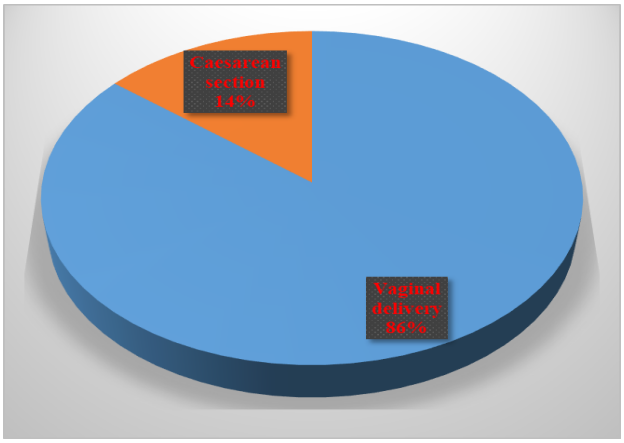

Figure 1. Mode of delivery

Table 3. Maternal β-hCG Levels and Rare Outcomes

Outcome	Normal β-hCG n (%)	Elevated β-hCG n (%)	P-value*
Prematurity	8 (80.0)	2 (20.0)	1.000
Birth asphyxia	6 (85.7)	1 (14.3)	1.000
IUFD	3 (75.0)	1 (25.0)	1.000
Congenital anomaly	2 (50.0)	2 (50.0)	1.000
Chorioamnionitis	1 (100.0)	0 (0.0)	1.000
Postpartum haemorrhage (PPH)	2 (100.0)	0 (0.0)	1.000
Anaemia	4 (100.0)	0 (0.0)	0.548
Abruptio placenta	0 (0.0)	2 (100.0)	0.133
Preterm labour	1 (50.0)	1 (50.0)	1.000
Placenta previa	5 (100.0)	0 (0.0)	0.306
PROM	8 (100.0)	0 (0.0)	0.109
Oligohydramnios	3 (75.0)	1 (25.0)	1.000
Perinatal morbidity	1 (100.0)	0 (0.0)	1.000
Postdatism	14 (93.3)	1 (6.7)	0.667

Notes: Percentages are calculated **within each outcome category**, not of the total sample. P-values were calculated using Fisher's Exact test

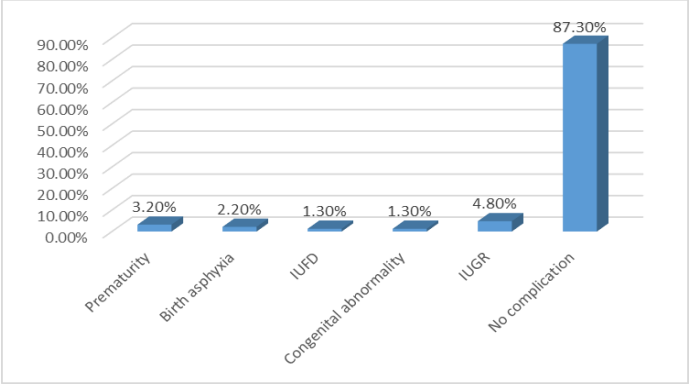

Figure 2. Foetal outcome

and selected fetal and maternal outcomes. For fetal outcomes, intrauterine growth restriction (IUGR) occurred in 7 women with normal β-hCG (46.7%) and 8 women

Table 2. Association Between Maternal β-hCG Levels and Selected Pregnancy Outcomes

Outcome	Normal β-hCG n (%)	Elevated β-hCG n	Adjusted OR (95% CI)*	P value
Fetal Outcomes				
Intrauterine Growth Restriction (IUGR)	7 (46.7)	8 (53.3)	6.84 (2.05–22.81)	0.002
Maternal Outcomes				
Preeclampsia	25 (65.8)	13 (34.2)	3.48 (1.52–7.95)	0.003

Note: Adjusted odds ratios (AORs) were obtained using multivariate logistic regression models controlling for maternal age, parity, body mass index (BMI), socioeconomic status, and pre-existing medical conditions in pregnancy. Each outcome variable was analysed as a bina-

with elevated β-hCG (53.3%), with an adjusted odds ratio (AOR) of 6.84 (95% CI: 2.05–22.81, p = 0.002). Among maternal outcomes, preeclampsia was observed in 25 women with normal β-hCG (65.8%) and 13 with elevated β-hCG (34.2%), with an AOR of 3.48 (95% CI: 1.52–7.95, p = 0.003). The majority of participants experienced uneventful pregnancies (207 with normal β-hCG, 90.4%; 22 with elevated β-hCG, 9.6%), which served as the reference category. After adjusting for maternal age, parity, BMI, socioeconomic status, and pre-existing medical conditions, elevated maternal β-hCG levels remained significantly associated with increased odds of intrauterine growth restriction (AOR = 6.84, p = 0.002) and preeclampsia (AOR = 3.48, p = 0.003).

Table 3 presents the distribution of selected maternal and fetal outcomes by maternal BhCG levels. Most outcomes occurred more frequently among women with normal β-hCG levels; however, a few conditions, such as abruptio placentae, occurred more frequently in the elevated β-hCG group. Overall, no statistically significant associations were observed between β-hCG levels and the listed outcomes.

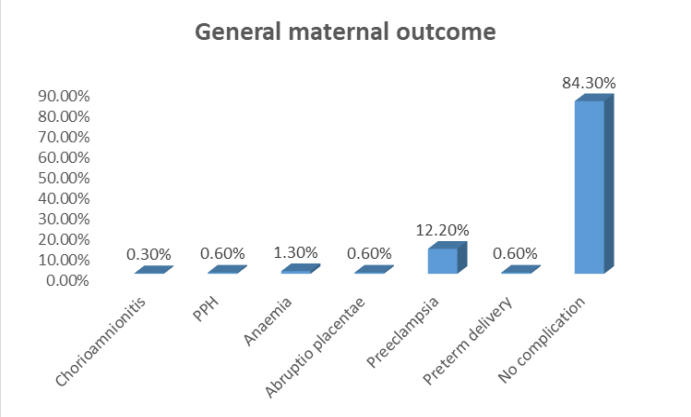

Figure 3. Maternal outcome

The majority of foetal outcomes showed no complications (87.3%), while adverse outcomes were relatively low, with intrauterine growth restriction (4.8%) being the most common (Figure 2: Foetal outcome), followed by prematurity (3.2%), birth asphyxia (2.2%), and smaller proportions of intrauterine foetal death and congenital abnormalities (1.3% each).

Most mothers experienced no complications (84.3%), while preeclampsia was the most common adverse outcome (12.2%); other complications such as anaemia (1.3%), postpartum haemorrhage (0.6%), abruptio placentae (0.6%), preterm delivery (0.6%), and chorioamnionitis (0.3%) occurred at much lower rates (Figure 3: Maternal outcome)

4.0 DISCUSSION

Transfusion In this prospective study of 314 pregnant women attending antenatal care at Usmanu Danfodiyo University Teaching Hospital, Sokoto, elevated second-trimester maternal serum β-hCG levels were observed in 48 participants (11.9%) and were significantly associated with specific adverse pregnancy outcomes. The mean BhCG level recorded in the study was 1.11 MoM. Most participants had normal ultrasound findings (99.0%) and experienced spontaneous vaginal delivery (86.0%), indicating that the study population was generally low risk. These characteristics provide an important backdrop for interpreting the significance of elevated BhCG values.

After adjusting for potential confounders, including maternal age, parity, body mass index, socioeconomic status, and pre-existing medical conditions, elevated BhCG was independently associated with intrauterine growth restriction (IUGR) and preeclampsia. Specifically, women with elevated BhCG had a 6.84-fold increase in odds of IUGR (95% CI: 2.05-22.81, p = 0.002) compared with women with normal BhCG, and a 3.48-fold increase in odds of preeclampsia (95% CI: 1.52-7.95, p = 0.003). These findings suggest that elevated BhCG may reflect underlying placental dysfunction, a finding supported by the existing literature [22]. Abnormal trophoblastic signalling and impaired placental vascular development can lead to decreased nutrient and oxygen delivery to the fetus, contributing to growth restriction and hypertensive disorders of pregnancy [22].

While the abstract also mentioned associations with abruptio placentae and congenital anomalies, these outcomes were too rare in the present cohort to support reliable statistical inference; frequencies of these events were reported descriptively. For example, congenital anomalies occurred in only four participants overall, and abruptio placentae occurred in two women with elevated BhCG. Given the very low counts, statistical modelling, such as logistic regression, was not appropriate for these outcomes, and descriptive reporting avoids misleading statistical interpretations.

Elevated serum BhCG levels in the second trimester are associated with an increased risk of developing preeclampsia, particularly when measured between 13 and 20 weeks of gestation. Studies indicate that a MoM (Multiple of Median) value <2 can act as an early marker

for predicting the subsequent development of hypertensive disorders of pregnancy [23].

Research conducted by Kokori [24] on Prevalence and materno-fetal outcomes of preeclampsia/eclampsia among pregnant women in Nigeria: a systematic review and meta-analysis, highlights that hypertensive disorders of pregnancy (HDP) remain a major public health concern, with preeclampsia and eclampsia contributing substantially to maternal morbidity, mortality, and adverse perinatal outcomes. Reported prevalence rates of HDP in tertiary care settings vary widely, from 4.42% to 31.0%, with meta-analytic estimates indicating pooled prevalence rates of 4.51% for preeclampsia and 1.39% for eclampsia in Nigeria.

HDP is a leading cause of maternal mortality in the country, accounting for approximately 15% to 29% of all maternal deaths in public hospitals. In some northern regions, eclampsia alone has been reported to contribute to over 40% of maternal deaths. Among the spectrum of hypertensive disorders, preeclampsia is often the most prevalent. It is strongly associated with adverse maternal and fetal outcomes, including high rates of emergency cesarean deliveries, which in many studies exceed 60% of HDP cases.

Perinatal complications are also significant. Preeclampsia and eclampsia are linked to elevated perinatal mortality rates, reported in some tertiary hospital reviews as high as 195-236 per 1,000 births [25]. These disorders are strongly associated with preterm delivery, affecting up to 48.7% of cases, as well as low birth weight and birth asphyxia. A key determinant of adverse outcomes is antenatal booking status. The majority of maternal deaths and severe complications occur among unbooked patients, emphasising that late presentation and delayed referral remain critical contributors to the high burden of HDP in Nigerian tertiary care facilities. Although these studies did not use BhCG levels specifically as predictors, they contextualise the importance of identifying risk factors for preeclampsia in this population.

In conclusion, this study demonstrates that elevated second-trimester maternal serum BhCG MoM levels are associated with increased risks of IUGR and preeclampsia in this tertiary care setting. The findings align with the biological understanding of placental dysfunction and support further investigation of BhCG as part of multifactorial risk assessment. However, claims regarding its utility as an early screening marker should be tempered until future research explicitly evaluates its predictive performance.

We recommended as follows: Women with elevated second-trimester BhCG MoM levels should be considered at higher risk for adverse outcomes such as intrauterine growth restriction (IUGR) and preeclampsia. Clinicians should implement closer fetal growth monitoring, more frequent blood pressure assessments, and timely interventions to reduce maternal and perinatal complications.

While BhCG elevations are associated with adverse outcomes, they should be used in combination with other maternal and fetal risk factors, including maternal age, parity, body mass index, and comorbidities. Future antenatal protocols in Nigerian tertiary care centres could consider multifactorial risk assessment models incorporating BhCG to improve identification of pregnancies at risk for placental-related complications.

Conflicts of Interest

The authors declare that there is no conflict of interests.

Authors' Contributions

BEZ conceived and designed the study, contributed to data collection, and manuscript writing. **CEH** supervised the study. **PAA** contributed to the study design and co-supervised the study. **MBA** contributed to data collection and analysis of data. **JG** contributed to data analysis tools. **AAH** contributed to data collection. All authors approved the final copy of the manuscript.

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