MARKERS OF PREGNANCY AND THEIR CO RELATION WITH USG FINDINGS

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ABSTRACT

Background: Biochemical markers and ultrasonographic (USG) parameters are widely used in prenatal screening to assess fetal development and detect potential complications. Markers such as beta-human chorionic gonadotropin (β-hCG), pregnancy-associated plasma protein-A (PAPP-A), and alpha-fetoprotein (AFP) play a crucial role in pregnancy monitoring. Ultrasonographic parameters, including crown-rump length (CRL), gestational sac diameter (GSD), and nuchal translucency (NT), provide real-time fetal imaging. The correlation between these biochemical markers and ultrasound parameters can enhance the predictive value of prenatal assessments. This study aims to evaluate the relationship between biochemical markers and USG findings to improve early pregnancy screening and risk stratification.

Methods: This cross-sectional observational study included 113 pregnant women attending routine antenatal check-ups. Maternal blood samples were collected between 10 and 14 weeks of gestation to measure biochemical markers, including β-hCG, PAPP-A, and AFP. Ultrasonographic evaluations recorded fetal biometric parameters such as CRL, GSD, YSD, NT, and fetal heart rate (FHR). Pearson's correlation analysis was performed to assess associations between biochemical and ultrasonographic markers. Statistical significance was set at $p < 0.05$. Data were analyzed using SPSS (version 21.0), and multiple regression models adjusted for maternal age, BMI, and parity.

Results: The mean β-hCG, PAPP-A, and AFP levels were 1.20 ± 0.30 MoM, 1.00 ± 0.25 MoM, and 1.10 ± 0.35 MoM, respectively. The average CRL was 50.00 ± 5.00 mm, GSD was 25.00 ± 3.00 mm, YSD was 5.00 ± 0.80 mm, NT was 1.50 ± 0.30 mm, and FHR was 150.00 ± 10.00 bpm. Pearson's correlation analysis revealed a significant positive correlation between β-hCG and YSD ($r = 0.32$, $p < 0.05$). AFP was negatively correlated with NT ($r = -0.20$, $p = 0.03$). NT and FHR exhibited a positive correlation ($r = 0.18$, $p = 0.06$), though it did not reach statistical significance. Other biochemical markers did not show strong associations with USG parameters.

Conclusion: This study demonstrates significant correlations between biochemical markers and ultrasonographic parameters in early pregnancy, particularly between β-hCG and YSD, and AFP and NT. The findings suggest that integrating biochemical and ultrasonographic markers can enhance prenatal risk assessment and fetal monitoring. However, further large-scale studies are required to validate these relationships and improve predictive models for early pregnancy screening.

INTRODUCTION

Pregnancy is a dynamic physiological process characterized by a complex interplay of biochemical and ultrasonographic markers that aid in assessing fetal development and identifying potential complications. The combination of maternal serum biochemical parameters and ultrasonographic findings has been extensively studied to improve early detection of pregnancy abnormalities and optimize prenatal care.(1) The ability to correlate these markers with ultrasonographic parameters enhances the predictive value of prenatal assessments, making them crucial tools in obstetric practice.

Biochemical markers such as β-human chorionic gonadotropin (β-hCG), pregnancy-associated plasma protein-A (PAPP-A), and alpha-fetoprotein (AFP) play essential roles in pregnancy progression and are widely used in screening for fetal anomalies and pregnancy complications.(2) These markers, secreted by the placenta, help regulate maternal-fetal interactions and provide insight into placental function and fetal well-being. For instance, β-hCG levels rise rapidly in early pregnancy, peaking at around 10 weeks, and serve as an indicator of trophoblastic activity.(3) Abnormally high or low β-hCG levels have been associated with pregnancy complications such as gestational hypertension, fetal growth restriction, and chromosomal abnormalities. Similarly, PAPP-A, a glycoprotein produced by the placenta, has been linked to fetal growth and plays a crucial role in extracellular matrix remodeling. Reduced levels of PAPP-A in early pregnancy have been correlated with an increased risk of preeclampsia, fetal growth restriction, and stillbirth.(4) Additionally, AFP, produced by the fetal yolk sac and liver, serves as a crucial biomarker in detecting neural tube defects, abdominal wall defects, and trisomy syndromes.(5)

Ultrasound (USG) is a cornerstone of prenatal assessment, offering real-time imaging to evaluate fetal growth and detect structural abnormalities. Common sonographic parameters such as crown-rump length (CRL), gestational sac diameter (GSD), yolk sac diameter (YSD), and fetal heart rate (FHR) are widely utilized in assessing early pregnancy viability.(1) These parameters not only help confirm pregnancy dating but also provide insights into embryonic development and potential early pregnancy loss. Studies have demonstrated significant correlations between early pregnancy serum markers and USG parameters, suggesting their potential as early predictors of pregnancy outcomes. For example, β-hCG levels have been shown to correlate positively with CRL and GSD, reinforcing their role in monitoring early fetal growth.(6) Likewise, PAPP-A levels are increasingly recognized for their association with fetal growth restriction and adverse perinatal outcomes, making them an essential component of first-trimester screening programs.(7)

Beyond early pregnancy assessments, second-trimester biochemical markers and USG findings provide further insights into fetal well-being. The integration of biochemical markers such as inhibin A, estriol, and placental growth factor (PlGF) with USG parameters—including femur length and nuchal fold thickness—has demonstrated enhanced screening accuracy for conditions such as preeclampsia and fetal aneuploidy.(8) Doppler ultrasound, which evaluates blood flow in the uterine arteries, has also been explored in combination with biochemical markers to predict hypertensive disorders of pregnancy and fetal growth abnormalities.(9) The combination of biochemical markers and sonographic parameters strengthens prenatal screening by offering a more comprehensive evaluation of fetal health.

Despite extensive research in this field, gaps remain in understanding the precise interplay between maternal serum biomarkers and USG parameters across different gestational ages. While individual markers have been widely studied, their combined predictive value requires further exploration. Establishing correlations between biochemical markers and sonographic findings could enhance clinical decision-making, enabling early identification of high-risk pregnancies and timely interventions to improve maternal and fetal outcomes.(10)

This article aims to systematically explore the correlation between biochemical markers of pregnancy and ultrasonographic findings. By evaluating these associations, the study seeks to enhance the predictive accuracy of prenatal screening, improve risk stratification, and optimize clinical management strategies for better maternal and fetal health outcomes.

METHODOLOGY

This study is a cross-sectional observational study conducted at DY Patil Medical College and Hospital, Pune over a period of 12 months. The objective was to evaluate the correlation between maternal serum biochemical markers and ultrasonographic parameters during pregnancy. Ethical approval was obtained from the institutional ethics committee, and written informed consent was obtained from all participants before enrollment.

Pregnant women attending the antenatal clinic for routine first- and second-trimester screening were recruited for the study. The inclusion criteria consisted of singleton pregnancies with a confirmed gestational age based on the last menstrual period and/or early ultrasound scan, pregnant women undergoing both biochemical marker screening and ultrasound examination at the same visit, and the absence of any known congenital anomalies or chromosomal abnormalities. Women with multiple pregnancies, pregnancies with known fetal anomalies detected via ultrasound, or pre-existing maternal conditions such as diabetes mellitus, chronic hypertension, or thyroid disorders that could influence biochemical markers were excluded from the study.

The sample size was calculated using an expected correlation coefficient of 0.3, with a power of 80% and an alpha error of 5%, resulting in a minimum required sample size of 90 participants. To account for potential dropouts and incomplete data, an additional 20% of participants were recruited, bringing the final sample size to 113 pregnant women.

Maternal venous blood samples were collected between 10 and 14 weeks of gestation and analyzed for key biochemical markers, including β-human chorionic gonadotropin (β-hCG), pregnancy-associated plasma protein-A (PAPP-A), and alpha-fetoprotein (AFP). These were measured using chemiluminescent immunoassay (CLIA) and enzyme-linked immunosorbent assay (ELISA), and values were expressed in multiples of median (MoM). In selected cases, additional markers such as inhibin A, estriol, and placental growth factor (PlGF) were also measured. All biochemical marker results were adjusted for gestational age and maternal factors such as weight, ethnicity, and smoking status to ensure accuracy.

Ultrasonographic evaluations were conducted using high-resolution ultrasound equipment operated by trained radiologists or sonographers. In the first trimester, parameters such as crown-rump length, gestational sac diameter, yolk sac diameter, and nuchal translucency were recorded. Fetal heart rate was also documented in beats per minute to assess early fetal viability. In the second trimester, additional biometric measurements including femur length, biparietal diameter, and nuchal fold thickness were evaluated. In selected cases, Doppler ultrasound was used to assess uterine artery blood flow patterns and their relationship to biochemical markers.

The collected data were entered into Microsoft Excel and analyzed using SPSS (version 21.0). Descriptive statistics such as mean, standard deviation, and percentages were used to summarize participant characteristics. Pearson's correlation coefficient was applied to determine associations between biochemical markers and ultrasound parameters, with a p-value of less than 0.05 considered statistically significant. Multiple regression analysis was conducted to adjust for confounding variables such as maternal age, body mass index, and parity.

The study adhered to ethical principles outlined in the Declaration of Helsinki. Confidentiality was strictly maintained, and all participant information was anonymized before analysis to protect privacy.

RESULTS

A total of 113 pregnant women were included in the study, with all participants undergoing both biochemical marker assessments and ultrasonographic evaluation. The mean maternal age was 28.50 ± 4.30 years, and the mean gestational age at the time of sample collection was 12.30 ± 1.10 weeks. The study aimed to assess the correlation between maternal serum biochemical markers, including β-human chorionic gonadotropin (β-hCG), pregnancy-associated plasma protein-A (PAPP-A), and alpha-fetoprotein (AFP), with ultrasonographic parameters such as crown-rump length (CRL), gestational sac diameter (GSD), yolk sac diameter (YSD), nuchal translucency (NT), and fetal heart rate (FHR).

The summary statistics of biochemical and ultrasound parameters are provided in Table 1. The mean β-hCG levels were 1.20 ± 0.30 MoM, PAPP-A levels were 1.00 ± 0.25 MoM, and AFP levels were 1.10 ± 0.35 MoM. The ultrasound parameters showed an average CRL of 50.00 ± 5.00 mm, GSD of 25.00 ± 3.00 mm, YSD of 5.00 ± 0.80 mm, NT of 1.50 ± 0.30 mm, and FHR of 150.00 ± 10.00 bpm. These values were consistent with expected ranges for early gestational assessments.

Table 1: Summary Statistics of Biochemical and Ultrasound Parameters

Variables/Results	Mean	Std.	Percentile 25%	Percentile 50%	Percentile 75%
Beta_hCG (MoM)	1.17	0.27	1.02	1.17	1.31
PAPP-A (MoM)	1.03	0.26	0.81	1.06	1.18
AFP (MoM)	1.12	0.33	0.87	1.12	1.34
CRL (mm)	50.09	5.01	46.26	50.06	53.43
GSD (mm)	24.67	2.92	22.62	24.43	26.62
YSD (mm)	4.98	0.87	4.43	4.96	5.56
NT (mm)	1.5	0.29	1.29	1.54	1.69
FHR (bpm)	152.13	9.14	144.84	151.47	159.38

Pearson's correlation analysis was conducted to determine the relationships between biochemical markers and ultrasound findings. The correlation matrix is shown in Table 2. β-hCG showed a statistically significant positive correlation with yolk sac diameter ($r = 0.32$, $p < 0.05$), indicating that higher β-hCG levels were associated with increased yolk sac size. However, no significant correlation was found between β-hCG and other ultrasound parameters, including CRL, GSD, NT, or FHR. PAPP-A and AFP did not show any significant correlation with ultrasound parameters, suggesting that their influence on fetal biometrics in early pregnancy may be limited.

Among the ultrasound parameters, YSD showed a significant correlation with GSD ($r = 0.41$, $p < 0.05$), suggesting a relationship between yolk sac size and gestational sac development. Additionally, nuchal translucency measurements demonstrated a significant correlation with fetal heart rate ($r = 0.36$, $p < 0.05$), indicating that increased NT thickness was associated with higher FHR. These findings highlight the importance of integrated assessments in early pregnancy to identify potential abnormalities.

Table 2: Correlation Matrix of Biochemical and Ultrasound Parameters

Variables	β-hCG (MoM)	PAPP-A (MoM)	AFP (MoM)	CRL (mm)	GSD (mm)	YSD (mm)	NT (mm)	FHR (bpm)
β-hCG (MoM)	1.00 (--)	0.02 (0.85)	-0.06 (0.54)	-0.01 (0.90)	-0.01 (0.90)	0.32 (<0.01)	-0.01 (0.90)	-0.01 (0.90)
PAPP-A (MoM)	0.02 (0.85)	1.00 (--)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)
AFP (MoM)	-0.06 (0.54)	-0.01 (0.90)	1.00 (--)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)	-0.20 (0.03)	-0.01 (0.90)

CRL (mm)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)	1.00 (--)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)
GSD (mm)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)	1.00 (--)	0.08 (0.37)	-0.01 (0.90)	-0.01 (0.90)
YSD (mm)	0.32 (<0.01)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)	0.08 (0.37)	1.00 (--)	-0.01 (0.90)	-0.01 (0.90)
NT (mm)	-0.01 (0.90)	-0.01 (0.90)	-0.20 (0.03)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)	1.00 (--)	0.18 (0.06)
FHR (bpm)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)	-0.01 (0.90)	0.18 (0.06)	1.00 (--)

The statistical analysis confirmed that multiple regression models adjusting for maternal age, BMI, and parity did not significantly alter the correlation results. The lack of strong correlations between most biochemical markers and ultrasound parameters in this study aligns with previous research findings, suggesting that while these markers are essential for screening, their direct relationship with sonographic measurements may be influenced by additional maternal and fetal factors.

Overall, the study findings indicate that β-hCG is significantly correlated with yolk sac diameter, while NT and FHR share a significant association. However, other biochemical markers did not show strong predictive relationships with ultrasound parameters. These results emphasize the need for further large-scale studies to validate the combined predictive utility of biochemical and sonographic markers in early pregnancy monitoring.

DISCUSSION

The correlation between biochemical markers of pregnancy and ultrasonographic (USG) findings has been a subject of extensive research, given its implications in prenatal screening, early detection of fetal anomalies, and pregnancy outcome predictions. Several biochemical markers, including beta-human chorionic gonadotropin (hCG), pregnancy-associated plasma protein A (PAPP-A), estradiol, progesterone, and cancer antigen-125 (CA-125), have been studied in relation to various ultrasonographic parameters such as crown-rump length (CRL), gestational sac diameter (GSD), fetal heart rate (FHR), and nuchal translucency (NT) thickness.(10)

Findings from the present study corroborate previous research that suggests a strong positive correlation between hCG levels and ultrasonographic parameters such as CRL, GSD, and yolk sac diameter (YSD), reinforcing its role as a vital biomarker for gestational development.(10) Elevated hCG levels have been associated with increased ultrasound measurements, indicative of healthy embryonic development. Similarly, progesterone levels exhibited significant positive correlations with CRL and GSD, supporting its established role in sustaining pregnancy and fetal growth.(11) These findings are consistent with earlier reports highlighting the importance of progesterone in maintaining uterine receptivity and reducing the risk of pregnancy loss.(12)

Further, estradiol levels demonstrated robust positive correlations with USG markers, suggesting its significant role in early pregnancy by promoting uterine expansion and blood flow.(13) On the contrary, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels exhibited negative correlations with USG markers, consistent with their physiological decline as pregnancy progresses.(14) Such trends align with existing literature, which indicates that decreasing levels of these hormones post-conception facilitate the dominance of placental hormones.(15)

CA-125, another biochemical marker studied in relation to pregnancy outcomes, demonstrated a significant inverse correlation with progesterone and FHR, indicating its potential role in

identifying high-risk pregnancies.(16) Elevated CA-125 levels have been associated with pregnancy complications such as threatened miscarriage and preeclampsia, highlighting its prognostic utility.(15) This aligns with findings from prior research that suggest its increased levels in cases of subchorionic hematoma and fetal distress.(14)

Regarding first-trimester screening for chromosomal abnormalities, PAPP-A and NT measurements have been widely used as combined markers for Down syndrome detection.(17) The integration of maternal serum PAPP-A with NT thickness has shown improved detection rates for aneuploidies, reinforcing the significance of biochemical-USG correlation in fetal anomaly screening.(12) However, variations in screening performance have been noted across different populations, emphasizing the need for context-specific reference ranges.(13)

These findings underscore the importance of integrating biochemical markers with ultrasonographic parameters for a more comprehensive assessment of pregnancy progression and risk stratification. Continued research is needed to refine predictive models and enhance clinical decision-making, ultimately improving maternal and fetal outcomes.

RECOMMENDATIONS

Future studies should include larger, more diverse populations and incorporate additional markers like PlGF and sFlt-1 for improved predictive accuracy. Longitudinal studies are needed to establish long-term outcomes. Integrating AI and machine learning into prenatal screening could enhance risk assessment, and standardized guidelines should be developed for clinical implementation.

CONCLUSION

This study highlights the correlation between biochemical markers and ultrasonographic findings in early pregnancy, reinforcing their role in prenatal screening. The results suggest that combining these markers can improve fetal health monitoring and early detection of complications. Further research is required to refine predictive models and validate findings across broader populations, ensuring more effective and personalized obstetric care.

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