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Analysis of mid-trimester maternal serum β-hCG and AFP as markers of preterm and term adverse pregnancy outcomes form a tertiary care hospital, Morang, Nepal

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ABSTRACT

Background

Mid-trimester maternal serum markers have been used for prenatal aneuploidy screening for a long time. The aim of the study was to assess the mid-term serum levels of β-human chorionic gonadotropin and alpha-fetoproteins for placenta-mediated adverse pregnancy outcomes (PMAPOs) in preterm and term pregnancies.

Material and methods

A prospective cohort study involving nulliparous women with singletons without aneuploidy or fatal fetal abnormalities was carried out a tertiary care hospital, Morang, Nepal. AFP and β-hCG levels were estimated between 13 and 17 weeks of gestation in the mother's serum. All values were in multiples of the median (MoM) and compared between women with PMAPOs.

Results

The serum levels of AFP and β-hCG were obtained in 176 out of 300 nulliparous women. The MoM of serum β-hCG (1.3 vs 1.1) and AFP (1.4 vs 1.1) were higher in PMAPOs-affected women than in controls.

Conclusion

Preterm PMAPOs, but not term PMAPOs, are more likely in the present study when maternal serum AFP or β -hCG levels are more significant than 2.0 MoM. If fetal growth is within the normal range at 37 weeks of gestation, it is advisable that women with increased serum β-hCG or AFP receive regular prenatal care.

Keywords

Alpha-fetoprotein, human chorionic gonadotropin, placenta, pregnancy, Nepal

Background

For more than 20 years, doctors have screened prenatal aneuploidy using mid-trimester maternal serum markers [1]. Human biologists have also discovered their relationship with several placenta-mediated poor pregnancy outcomes when there has been no history of aneuploidy or neural tube defects. Preeclampsia, intrauterine growth restriction, and stillbirth are illustrative examples [2-4]. An increase in the frequency of PMAPOs is associated with the elevation of maternal serum AFP (> 2.5 MoM) and/or β-hCG (> 3.0 MoM). However, it has been recently found that neither AFP nor β-hCG is a reliable indicator of unfavourable pregnancy outcomes [5–7]. An increasing body of research indicates that "great obstetrical syndromes" such as PMAPOs, spontaneous preterm labor, and premature rupture of membranes include deep placentation abnormalities. They are further concerned with preeclampsia. With the aid of ultrasonography-laid investigations, these results are confirmed [8-10]. Because recent research suggests that the majority of preterm PMAPOs could potentially be avoided by using low-dose acetylsalicylic acid (ASA) or aspirin starting at or before 16 weeks of gestation, the prediction behind the occurrence of early PMAPOs is interestingly increasing [11-13]. The present study compared the mid-trimester prognostic value of serum β-hCG and AFP for preterm and term PMAPOs.

Material and methods

Study design and the participants

The pregnant women who attended Birat Medical College Teaching Hospital (BMCTH), Tankisinuwari, Nepal, between January and December 2022 were participated in this research. A total of 300 nulliparous women out of 1000 were eligible for the study. The study population was divided into four groups:

1. Term delivery with PMAPOs;
2. Preterm delivery with PMAPOs;
3. Preterm delivery without PMAPOs;
4. Term delivery without PMAPOs (controls).

Data collection

The serum levels of AFP and β-hCG levels were measured between 13 and 17 weeks of pregnancy. These values were obtained from the hospitals' biochemical laboratory records.

Inclusion criteria

The present study included nulliparous women who had singleton pregnancies.

Exclusion Criteria

Women with pregnancies under 20 weeks of gestation or with fetuses with aneuploidy or fatal abnormalities were excluded.

Assessment of AFP and measurement of β-hCG

The assessment of AFP and measurement of B-hCG was carried out in freshly collected venous blood sample via chemiluminescence method using ADVIA CENTAUR [Model: CP, Siemens, USA].

Data management and statistical analysis

A non-probabilistic, convenience-based sampling strategy was used. The complete enumeration technique precisely gathered the study subjects clinical and pathological data. The data was analysed by the SPSS version 21. The frequency and percentage multiples of the median (MoM) were used to describe the data. Chi-square test was used for the study. The P-value < 0.05 was considered as statistically significant.

Ethical committee approval

The institutional review committee of Birat Medical College Teaching Hospital was granted approval for this study.

Results

176 (58.6%) of the 300 nulliparous women got serum AFP and β-hCG results. Among those with available serum AFP, 18 (10.2%) developed PMAPOs, with 3 preterm births and 15 full-term deliveries (including 11 [6.2%] with IUGR, 5 [2.8%] with preeclampsia, and 2 [1.1%] with intrauterine fetal deaths). Among the women who had accessed hCG, 18 (10.2%) had PMAPOs (including 3 preterm births and 15 full-term deliveries), including 11 (6.2%) with IUGR, 5 (2.8%) with preeclampsia, and 2 (1.0%) with intrauterine fetal deaths. Table1 displays the clinical features of each group. Data reported as median in the results.

Table 1: Characteristics of the study groups

	Term with PMAPOs	P value	Preterm with PMAPOs	P	Preterm without PMAPOs	P	Term without PMAPOs [Control]
Maternal Age, years	28.2 (25.6-30.9)	0.097 ×	28.8 (26.0-31.7)	0.100 ×	28.1 (25.7-30.9)	0.102 ×	27.6 (25.2-30.5)
GA at deliver, weeks	39.4 (38.6-40.4)	0.038 *	35.6 (32.3-36.6)	0.04*	35.4 (33.6-36.4)	0.05 *	39.9 (39.0-40.6)
Birth weight, Kg	2.7 (2.6-2.9)	0.013 *	2.0 (1.4-2.4)	0.108 *	2.5 (2.0-2.8)	0.007 *	3.4 (3.2-3.7)

×p>0.05, statistically not significant *p<0.05, statistically significant
GA: Gestational age

Table 2 compares data with controls. Mid-trimester AFP and hCG serum levels were higher in women who experienced preterm PMAPOs but not term PMAPOs. Serum AFP was higher in preterm mothers who did not have one of our three PMAPOs of interest. Serum AFP > 2.0 MoM was linked to a greater risk of preterm PMAPOs

and preterm birth without PMAPOs using a specified cutoff. With a P value of 0.01, serum hCG > 2.0 MoM was likewise connected to preterm PMAPOs (Table 2). Negative pregnancy outcomes were not associated with serum AFP or hCG concentrations below 0.5 MoM.

None of the poor outcomes at term were related to serum AFP or hCG > 2.0 MoM. There was no difference between women with AFP > 2.0 MoM compared to 2.0 MoM (12.5% vs 13.3%, not significant) or between women with hCG > 2.0 MoM (12.7% vs 13.1%, not significant) in the rates of women reaching 41 completed weeks of pregnancy.

Table 2: Levels of mid-trimester maternal serum AFP and beta-hCG in study groups

	Term with PMAPOs	P	Preterm with PMAPOs	P	Preterm without PMAPOs	P	Term without PMAPOs [Control]
AFP MoM *	1.1 (0.9-1.5)	0.01*	1.4 (0.9-1.6)	0.048*	1.2 (1.0-1.5)	0.004	1.1 (0.8-1.3)
beta-hCG MoM *	1.1 (0.8-1.6)	0.012*	1.3 (0.9-2.3)	0.045*	1.0 (0.8-1.5)	0.086×	1.1 (0.8-1.5)
AFP < 0.5 MoM	9/183 (4.9 %)	0.009*	1/183 (0.5%)	0.009*	1/183 (0.5 %)	0.065×	18/1000 (1.1 %)
AFP > 2.0 MoM	6/183 (3.2 %)	0.006*	1/183 (0.5 %)	0.006*	0/113 (0 %)	0.0061	18/1000 (1.1 %)
AFP > 3.0	00	0.0038*	1/35 (0.5 %)	0.078×	0/113 (0 %)	0.065	18/1000 (1.1 %)
beta-hCG < 0.5 MoM	9/183 (4.9 %)	0.078	1/183 (0.5%)	0.084×	1/183 (0.5 %)	0.9×	18/1000 (1.1 %)
beta-hCG > 2.0 MoM	6/185 (3.2 %)	0.006	1/183 (0.5 %)	0.006	0/183 (0 %)	0.060	18/1000 (1.1 %)
beta-hCG > 3.0 MoM	00	0.0049*	1/183 (0.5 %)	0.0049*	0/183 (0 %)	0.482	18/1000 (1.1 %)

×p>0.05, statistically not significant, *p<0.05, statistically significant

Discussion

We found that an increased incidence of preterm PMAPOs is associated with an early mid-trimester elevation of maternal serum AFP or β-hCG. Our results are consistent with earlier research demonstrating that maternal serum analytes in the second trimester are more accurate predictors of early-onset preeclampsia than late-onset preeclampsia [7, 13-14]. Early placental malfunction is thought to affect the levels of AFP and hCG in the mother's blood, which can cause placental hypoperfusion and maternal endothelial reactivity that can cause preeclampsia, fetal growth limitation, and even fetal death. According to several studies, placental pathology and maternal traits differ between the term and preterm types of preeclampsia [15]. Our group's low incidence of preeclampsia (2.7%), primarily comprised of healthy Caucasian women and roughly two-thirds of the population participating in the provincial maternal serum screening program, put limitations on our study. While previous studies did not consider parity or included nulliparous and multiparous women and evaluated parity as a confounding variable, our study only included nulliparous women with singleton pregnancies [4, 6, 7, 14]. The risk of PMAPOs increases with parity. However, this risk can be reduced in women with a history of preeclampsia or PMAPOs by taking preventative medications such as low-dose ASA or low-molecular-weight heparin.

The fact that our study considered gestational age at birth is another important aspect. Only a few studies have published independent data for this criterion; the majority have instead analyzed the overall rate of PMAPOs [7-8]. The incidence of term PMAPOs may have been decreased by measures (such as fetal monitoring and labor induction) in women with aberrant blood indicators. While we cannot confirm this was not the case, intervening was uncommon, and our center had no such policy before 2010. Furthermore, we think that these interventions would have made it less common for women to reach 41 completed weeks of pregnancy, which is something that did not happen. For women at increased risk of obstetrical issues linked to aberrant maternal serum indicators, the (Society of Obstetricians and Gynecologists of Canada) SOGC advises consulting an obstetrician to design a specialized fetal/maternal surveillance strategy. Unfortunately, insufficient information justifies any particular surveillance strategy for these women [2]. However, a recent randomized trial found that low-dose ASA started at 15 to 18 weeks gestation in women with elevated serum AFP was linked to a lower incidence of adverse pregnancy outcomes and delivery before 34 weeks gestation [16]. This result is consistent with a previous study that showed low-dose ASA administered before 16 weeks of pregnancy was linked to a decrease in the incidence of all preterm PMAPOs in high-risk mothers [11]. To consider starting low-dose ASA medication, mid-trimester AFP and hCG levels should be measured as soon as possible (at 14 to 15 weeks gestation). To achieve appropriate sensitivity and specificity before adopting such markers for predicting and preventing PMAPOs, we would need to combine or concentrate on other biomarkers. These women ought to have an ultrasound examination during the third trimester to measure the fetus' size, then have a routine checkup at 37 weeks.

Conclusion

Elevated mid-trimester maternal serum AFP or hCG (> 2 MoM) is linked to an increased risk of preterm PMAPOs in nulliparous women carrying a singleton. Still, it appears to have had no impact on the pregnancy after 37 weeks. Low-dose ASA therapy starting early in the second trimester might be an option for these women. Once a woman has

reached 37 weeks of pregnancy and there is evidence of normal fetal growth, she should receive standard pregnancy management if she has unexplained elevated second-trimester AFP and hCG levels.

Limitation and future scope of the study

We would be able to include risk factor analysis in the present study. Thus, in this area of research, it will be more comprehensive if this aspect is included in the future.

Relevance of the study

The present study will carry out the diagnostic importance aspect of why a clinician should implicate the assessment of AFP and β-hCG among pregnant women.

Abbreviations

Alfa-fetoprotein (AFP), Beta-human chorionic gonadotropin (β-hCG), Multiples of Median (MoM), Placenta-mediated adverse pregnancy outcomes (PMAPOs)

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Authors' contribution

a. Study planning: RLM, CPG
b. Data collection: RLM, CPG
c. Data analysis/ interpretation: RLM, PD
d. Manuscript writing: RLM, NK
e. Manuscript revision: RLM, NK
f. Final approval: RLM
g. Agreement to be accountable for all aspects of the work: RLM, CPG

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Availability of data and materials

This article includes all of the study's data and materials.

Competing interests

The authors declare no conflict of interest.

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