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Original Research Article

Determinants of plasma protein: A levels first trimester pregnancy

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Abstract

Low maternal serum level of pregnancy associated plasma protein A (PAPP-A) is known to be associated with the development of pregnancy-related complications like small for gestational age infants, intrauterine fetal demise, gestational diabetes and pre-eclampsia. Assessing the level of PAPP-A at 11-13 weeks of gestation can be helpful to predict pregnancy complications and fetal distress at the time of delivery, as well as chromosomal disorders like Down syndrome. This was a prospective study, conducted for a period of one year in the Department of Obstetrics and Gynaecology. 93 females with singleton pregnancies were divided into 2 groups based on their first trimester PAPP-A MoM values as <0.5MoM or >0.5MoM. A significant association was seen between PAPP-A levels and mother's BMI. PAPP-A level in maternal serum in first trimester can indicate fetal distress and other pregnancy complications at the time of delivery, but it has a poor positive predictive value. Hence, further studies are required to confirm its significance to predict pregnancy outcome.

Keywords: PAPP-A, Fetal distress, CTG

Introduction

Prenatal screening for trisomies has become an established part of obstetric practice in many countries, based on the analysis of biochemical markers present in maternal serum. These tests include multiple markers or analytes and are also known as conventional or traditional tests to differentiate them from screening based on cell-free DNA. There are three categories of tests: first-trimester screens, second-trimester screens and combinations of first-and second-trimester screens [1]. Recent prenatal screening for trisomies has focused on the first trimester tests. First trimester screening for aneuploidies represent the most commonly employed test in early pregnancy for the predicting the risk of a later complication of giving birth to an infant with a chromosomal anomaly. The other parameters that are considered include maternal age, fetal nuchal translucency and maternal serum beta human chorionic gonadotropin. Out of theses biochemical markers that are investigated, only maternal serum free b-human chorionic gonadotrophin (free b-hCG) and pregnancy associated plasma protein-A (PAPP-A) has been shown to be of predictive value [2]. Pregnancy associated

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plasma protein A (PAPP-A) is a glycoprotein produced by the placenta and decidua, and it helps in the release of insulin like growth factors. It is one of the parameters that are used at 11-14th weeks of gestation, as a biochemical marker for antenatal screening of aneuploidy as well as fetal anomalies like Down syndrome. PAPP-A is detectable after 28 days of implantation in singleton pregnancies in the maternal blood, following which it increases during the first trimester and then doubles every 3 to 4 days. Until 36 weeks, the increase is gradual and it accelerates thereafter, and attains the maximum serum levels at term [3].
Recent studies that have focused especially on PAPP-A have shown a strong association between its low levels and a number of obstetric complications, mainly intrauterine growth restriction, gestational hypertension, pre-eclampsia, fetal death and preterm delivery. The fact that PAPP-A is produced by the trophoblast explains these findings, and therefore, its abnormal values as early as in the first trimester could suggest abnormal placentation, which usually sustains the afore mentioned pathologic obstetric outcomes. A reduced PAPP-A level also leads to impaired release of insulin like growth factor, thus increasing the tendency for placental insufficiency, in turn resulting in adverse pregnancy outcomes [4].

Methodology

Study design: Cohort study.
Study setting: Department of Obstetrics and gynaecology.
Study population: All singleton pregnancies in their first trimester (11-14 weeks of gestation), visiting the OPD Medical College Hospital, for their antenatal checkup, over a period of 1 year was requested to give an informed consent to be enrolled in the study.

Inclusion criteria

- Singleton pregnancies.
- 11-14th week of gestation.

Exclusion criteria

- Multiple pregnancies.
- Cases with abnormal fetal karyotype.
- Cases with antenatal complications in pregnancy.
- All preterm deliveries.

Sample size

Z1-α/2= 1.96 [at 5% α] Z1-β = 0.84 [at 20% β] P1= 68% and P2 = 42% 7 n= 57 in each group.

Sampling technique: Convenient sampling.

Statistical analysis

All categorical variables were summarized using frequency and percentage. Quantitative variables were summarized using mean and standard deviation if data follows normality, else median and interquartile range.

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Method of collection of data

Every patient visiting the antenatal OPD with a period of gestation of 11-14 weeks was counselled for the testing of first trimester screening to assess fetal well-being. An informed consent was taken from all the participants. In all cases, the mothers were followed up for the duration of their pregnancies.
Eligible mothers had their blood samples taken and the serum levels of PAPP-A were tested and value was adjusted according to the maternal weight, insulin-related diabetes, and smoking habits. Measurement of PAPP-A in maternal serum was done using Enzyme Immunoassay 85. They were divided into 2 groups based on their first trimester PAPP-A MoM values as <0.5MoM (group 1) or >0.5MoM (Group 2). The demographic features, gender, birth weight, mode of delivery and indication for C/S were recorded. 7 These mothers were monitored continuously with CTG while in labour and any abnormality was noted. Fetal distress was diagnosed by the interpretation of CTG traces according to the NICE guidelines. 84 Patients with pathological and suspicious CTG according to NICE guidelines were diagnosed to have fetal distress.

Results

Out of the 93 singleton pregnancies assessed, PAPP-A values were >/= 0.5 MoM (normal) in 47 (50.5%) ladies, whereas it was <0.5 MoM (low) in 46 (49.5%) Ladies.

Table 1: PAPP-A level in study population

Group	Frequency	Percent
Low PAPP-A	46	49.5
Normal PAPP-A	47	50.5
Total	93	100.0

Pearson Chi-Square Test is used to test the association between Age Groups and level of PAPP-A. The frequency distribution of the Age groups across the levels of PAPP-A. The calculated Chi-square value is 1.091 with p value > 0.05. So, there is no significant association between age groups and levels of PAPP-A.

Table 2: Frequency distribution of the Age groups across the levels of PAPP-A

Group	Age Groups				Total	Chi-Square	p value
	19 - 25	26 - 30	31 - 35	36 - 41			
Low PAPP-A	20 (43.5%)	16 (34.8%)	8 (17.4%)	2 (4.3%)	46 (100%)	1.091	0.779
Normal PAPP-A	23 (48.9%)	16 (34.0%)	5 (10.6%)	3 (6.4%)	47 (100%)		
Total	43	32	13	5	93		

Pearson Chi-Square Test.

Pearson Chi-Square Test is used to test the association between BMI and level of PAPP-A. The frequency distribution of the BMI across the levels of PAPP-A. In Low PAPP-A subjects, there are 78.3% are in overweight and only 21.7% are with normal weight. In Normal PAPP-A, 68% subjects are with normal weight and 31.9% are with overweight. So that we can conclude that, Overweight causes Low PAPP-A. The calculated Chi-square value is 20.162 with p value < 0.05. So there is a significant association between BMI and levels of PAPP-A.

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Table 3: Frequency distribution of the BMI across the levels of PAPP-A

Group	BMI		Total	Chi-Square	p value
	Normal Weight	Overweight			
Low PAPP-A	10 (21.7%)	36 (78.3%)	46 (100%)	20.162*	< 0.001
Normal PAPP-A	32 (68.1%)	15 (31.9%)	47 (100%)		
Total	42	51	93		

Pearson Chi-Square Test, *Significant at 0.05 level

PAPP-A was measured at 12 weeks of gestation in 65 patients, out of which 76.6% were normal.

Table 4: Gestational age

PAPP-A	Gestation Age			Total	Chi- Square	p value
	11 week	12 week	13 week			
Low PAPP-A	13 (28.3%)	29 (63%)	4 (8.7%)	46 (100%)	2.543	0.280
Normal PAPP-A	7 (14.9%)	36 (76.6%)	4 (8.5%)	47 (100%)		
Total	20	65	8	93		

Pearson Chi-Square Test

Discussion

Abnormalities in maternal serum analyte levels and fetal measurements obtained during the first trimester screening can be a marker not only for certain chromosomal disorders and anomalies in the fetus but also for specific pregnancy complications [5]. In particular, low maternal serum pregnancy- associated plasma protein-A (PAPP-A), at 11-13 weeks of gestation, is associated with stillbirth, infant death, intrauterine growth restriction (IUGR), preterm birth, and pre-eclampsia in chromosomally normal fetuses, while a raised nuchal translucency is associated with specific structural abnormalities and genetic syndromes [6, 7].
A low PAPP-A is defined as a maternal serum PAPP-A value less than 0.5 MOM at 11-13 weeks of gestation and can result in pregnancy complications and adverse obstetrical outcomes.
Out of the 93 patients studied at 11-13 weeks of gestation, 47 patients had normal and 46 had low PAPP-A values. Majority patients (46.2%) belonged to 19-25 years age group and only 5 (5.4%) patients were of 36-41 years age group, which was found to have no significant association with levels of PAPP-A. This was in contrast to a study by Ajah *et al*., where majority patients belonged to 25-29 years age group [8].

Conclusion

Out of the 93 patients studied at 11-13 weeks of gestation, 47 patients had normal and 46 had low PAPP-A values. Majority patients (46.2%) belonged to 19-25 years age group and only 5 (5.4%) patients were of 36-41 years age group, which was found to have no significant association with levels of PAPP-A.

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