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PREVALENCE AND PROPERTIES OF PREGNANT WOMEN WITH LOW PREGNANCY ASSOCIATED PLASMA PROTEIN A (PAPP-A) IN THE FIRST TRIMESTER SCREENING

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ABSTRACT

Background and Aims*:* Pregnancy associated plasma protein A *(*PAPP-A*)* is a large glycoprotein which is produced by the placenta and deciduas. It is supposed that PAPP-A serves to prevent the recognition of the fetus by the maternal immune system**.** The aims of the present study were to evaluate the prevalence of low PAPP-A in the first trimester among screened population of pregnant women as well as their properties. **Materials and Methods:** This retrospective medical record reviews study was performed on the 137 singleton pregnant women with PAPP-A<0.4 MOM in Imam Khomeini Hospital (a tertiary, general and teaching hospital, Ahvaz, Iran between Sep 2011 to Sep 2013. At this time period, of 8703 women who underwent the first trimester screening, 137 had low PAPP-A (less than 0.4 MoM). Anonymous and confidentiality were guaranteed. Characteristics and clinical information were collected by one trained abstractor. **Results**: 137from 8703 (1.57%) were mothers with PAPP-A <0.4. The mean scores for maternal age and weight were 29.84 ± 5.5 years and 68.97 ± 12.41 kg, respectively. 44% were n*ullipara*. Adjusted risk for trisomy 13 and 18 was significantly higher than background risk in mothers with PAPP-A<0.4, while this difference for trisomy 21 was not significant**. Conclusion:** The goal of our study was not to assess

relationship between low PAPP-A and SGA which has been previously proven. Becuase in our region, mothers with low PAPP-A are not considered properly and missed undiagnosed; therefore our goal was to report and describe properties of this group of pregnant women. We should more attention to pregant women to prevent and decrease adverse subsequnets which are resulted from low PAPP-A (<0.4 MoM).

KEY WORDS: Pregnancy associated plasma protein A *(*PAPP-A*),* first trimester screening.

INTRODUCTION

Pregnancy associated plasma protein A *(*PAPP-A*) is* a large glycoprotein produced by the placenta and decidua thought to have several function, including prevention of the fetus by the maternal immune system, matrix mineralization and angiogenesis. This plasma protein is a major risk factor for SGA (small for gestational age). Mothers with an unexplained low PAPP-A *(*< 0.4 MoM*)* need to undergo assessments such as fetal size and umbilical artery Doppler between 26 – 28 weeks of gestation. Therefore, low PAPP-A should be considered as a descriptive of poor early placentation, which results in complications including fetal growth restriction, fetal demise, preterm birth, and preeclampsia in the third trimester [1]. Abnormal results of first trimester screening is associated with adverse pregnancy outcomes such as pregnancy loss, fetus infection, fetal heart abnormality, and other structural disorders. PAPP-A <0.4 MoM is a valuable predictive value for subsequent fetal growth restriction. Low PAPP-A is associated with the higher risk of fetal loss before 24 weeks, low birth weight, preeclampsia, gestational hypertension, preterm birth and still birth, premature rupture of membranes *(*PROM), and placental abruption [2]. The smaller Crown-Rump Length *(*CRL) and low PAPP-A are predictors of birth weight less than 10th percentile for gestational age [3]. In the first trimester screening, low PAPP-A (<0.4 MoM) is associated with a Down syndrome fetus [4]. In present study we evaluated the prevalence of low PAPP-A in the first trimester among screened population as well as their properties.

MATERIAL AND METHODS

This retrospective medical record reviews study was performed on 137 singleton pregnant women with PAPP-A<0.4 MOM in Imam Khomeini Hospital (a tertiary, general and teaching hospital), Ahvaz, Iran, between Sep 2011 to Sep 2013. At this time period, of 8703 women who underwent the first trimester screening, 137 had low PAPP-A (less than 0.4 MoM). Anonymous and confidentiality were guaranteed. Characteristics and clinical information were collected by one trained abstractor. The study was approved by the Ethics

Committee of Department of Obstetrics and Gynecology (Ahvaz Jundishapur University of Medical Sciences (AJUMS)). Characteristics data included maternal age, weight, and parity. Clinical infomormation such as gestational age, placental location, βhcG, FHR (fetal heart rate), CRL (crown-rump length) NT (nuchal translucency) were abstracted from medical charts. The background (B) and adjusted (A) risk for trisomies 13, 18, and 21 were calculated using FMF (Fetal Medicine Foundation) software. Women were eligible to include in the study if they have singleton pregnancy with PAPP-A <0.4 MoM which had been measured and reported in the first trimester screening. The analysis was carried out with SPSS software program version 17. Continuous variables were described with mean ± standard deviation, and qualitative variables were expressed as percentage value.

RESULTS

Overall, 137 from 8703 (1.57%) had PAPP-A <0.4 MoM. The mean scores for maternal age and weight were 29.84 ± 5.5 years and 68.97 ± 12.41 kg, respectively. Table 1 shows our observations. 44% of these mothers were n*ullipara*. Adjusted risk (A risk) for trisomy 13 and 18 was significantly higher than background risk in mothers with PAPP-A<0.4 MoM, while this difference for trisomy 21 was not significant. The placental site in 57% of these cases was high. The mean CRL was 62.1 ± 9.7 mm and 5.8% of the cases had CRL more than 95 percentile. The mean scores of FHR and NT were 162.75 ± 9.5 and 1.7 ± 0.45, respectively. Besides, 1.45% of the study population had NT more than 3 MoM. The mean score of serum *beta-hCG* was 0.890 MoM.

Table 1. Characteristics and clinical information of 137 singleton women with PAPP-A < 0.4 MoM in the first trimester

Characteristics	Value†#	Missing data
Weight (kg)	68.97 ± 12.41	0
Age(years)	29.84 ± 5.5	0
parity		0
0	61 (44.5 %)	
1	56 (40.9 %)	
multi	20 (14.5%)	
GA	12.59 ± 0.7	0
Placenta location		48
High	51 (37.2%)	
Low	38 (27.7%)	
Missing data	48 (35.0%)	
FHR	162.75 ± 9.5	3
CRL (mm)	62.1 ± 9.7	0

NT (mm)	1.7 ± 0.45	0
GA: gestational age, CRL: crown-rump length, FHR: fetal heart rate, NT: Nuchal Translucency, †: mean ± SD, #: number (%).		

Table 2. Trisomies information of 137 singleton women with PAPP-A < 0.4 MoM in the first trimester

βhcG	0.89 ± 1.25	0
B risk Trisomy 13	1.45 ± 0.24	33
B risk Trisomy 18	1.36 ± 0.25	1
B risk Trisomy 21	1.45 ± 0.2	0
A risk Trisomy 13	1.36 ± 0.24	33
A risk Trisomy 18	1.41 ± 0.27	33
A risk Trisomy 21	1.42 ± 0.24	34
Trisomy 13		0
More	116 (84.7%)	
less	21 (15.3%)	
Trisomy 18		0
More	103 (75.2%)	
less	34 (24.8%)	
Trisomy 21		0
More	61 (44.5%)	
less	76 (55.5%)	
CRL percent		0
Yes	8 (5.8%)	
No	129 (94.2%)	
B risk: Background risk, A risk: Adjusted risk , †: mean ± SD, #: number (%).		

DISCUSSION

Present medical chart reviews study was designed to describe the prevalence and properties pregnant women with low PAPP-A (<0.4 MoM) in the first trimester. In our region (Khuzestan, Ahvaz, Iran), we not paying attention to low PAPP-A results. We found that its prevalence is 1.57% (137 out of 8703) which shows high frequency. Pregnant women with low PAPP-A were younger than 35 years (mean score was 29.84 ± 5.5 years), so this marker was not only seen in mothers older than 35-year. Only 1.45% of mothers with PAPP-A < 0.4 MoM had NT greater than 3 mm, so this chemical marker itself may be used for prediction in cases with SGA. Placental site had no significant difference, and low placental site has no predictive effect in PAPP-A < 0.4 in our study.

Recent evidence has shown that low levels of PAPP-A at the first trimester screening can be an independent risk factor for certain adverse pregnancy outcomes such as intrauterine fetal death after 24 weeks, spontaneous fetal loss before 24 weeks, preterm birth , gestational hypertension, preeclampsia and low birth weight [5]. Another study has shown that first trimester maternal serum PAPP-A level less than 5^{th} percentile is independently associated with spontaneous fetal and neonatal loss, IUGR, PPROM, gestational hypertension, preeclampsia, abruption, preterm labor and preterm birth [6]. Abnormal first trimester analysts predict only a fraction of later IUGR cases, but PAPP-A< 0.29 identifies a subset of patients with a more than 5-fold increased risk of IUGR. These patients should receive sonography evaluation of growth after 28 weeks [7].

CONCLUSION

The goal of our study was not to assess relationship between low PAPP-A and SGA which has been previously proven. Becuase in our region, mothers with low PAPP-A are not considered properly and missed undiagnosed; therefore our goal was to report and describe properties of this group of pregnant women. We should more attention to pregant women to prevent and decrease adverse subsequnets which are resulted from low PAPP-A (<0.4 MoM).

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Conflict of interest: The authors declare that there is no conflict of interests.

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