To Evaluate the Correlation of Second Trimester Maternal Serum Alphaprotein in 14-22 Weeks and Adverse Pregnancy Outcome

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ABSTRAT
Aim: To evaluate the correlation of Second Trimester Maternal Serum AlphaproteinIn 14-22 Weeks and Adverse Pregnancy Outcome.
Materials and methods: This prospective observational study was carried out in the Department of Obstetrics and Gynaecology,180 pregnancies women were reviewed by the maternal serum alpha-fetoprotein screening program. The age and weight of all pregnant women were 20-30 years old at conceptions and 55-70kg respectively. Participants are ideally screened between 14-22 weeks' gestation.
Results: 180 pregnant women between the 14th and 22th weeks of gestation were evaluated. The mean age of the participants was 24.7±3.01 years. The mean of the birth weight was 3057±510 gram (1700-4340gram). The mean maternal serum Alpha- fetoprotein was 44.57±39.2 ng/cc (2.3-250 ng/cc). The median MSAFP was 34 ng/cc. Of 180 pregnant women, 150 had without preterm labor and 30 had preterm labor .The frequency of pregnant outcomes were as following: 5 (1.01%) stillbirths, 30(16.677%) preterm labor, 9(5%) PROM, 14(7.78%) pre-eclampsia, 25(13.89%) oligohydramnious, 2(1.11%) miscarriage. There was a correlation between preterm labor and higher MSAFP. The mean was 53.14 ng/cc in preterm labor and 35.13 ng/cc in term labor (P- value~0.021). The mean MSAFP was 75.16 ng/cc in pre-eclamptic women while it was 40.75 ng/cc in pregnant women without pre-eclampsia. Therefore, second trimester MSAFP levels were significantly higher in women with pre-eclampsia (P <0.001). Also, an association was found between level of MSAFP and oligohydramnious. It was higher in pregnancy women with oligohydramnious compared with normal women (76.39 ng/cc vs. 39.61 ng/cc) (P <0.001). The association between low birth weight and the levels of MSAFP was significant. With increasing MSAFP between 14-22 weeks' gestation, birth weight decreased (P <0.001).
Conclusion: We concluded that the elevated MS-AFP is associated with increased risks of APOs. ONTDs complicate merely a small proportion of pregnancies with elevated MS-AFP, and the rest of them have high risks of obstetric complications.
Keywords: oligohydramnious, pre-eclampsia, Serum Alphaprotein.

Introduction

Adverse pregnancy outcomes (APOs), such as structural fetal abnormalities, spontaneous abortion, preterm birth, stillbirth and preeclampsia, are the major causes of death and complications for fetuses and neonates, and even the mothers, especially in many low-resource settings.[1,2]The combined multi-marker screening for preeclampsia has achieved great progress in recent years. For women at high-risk of preeclampsia, low-dose aspirin started from 11 to 14 weeks of gestation can achieve remarkable preventive effect, which has been recommended for preeclampsia prevention by the American College of Obstetricians and Gynecologists.[3,4] But until now, except for preeclampsia, other APOs lack effective methods for prediction. Maternal serum biomarkers have been used in prenatal screening for decades. Based on the extensive experience, abnormal values of many serum markers have been linked to a variety of APOs. Alpha-fetoprotein (AFP) is the marker for fetal open neural tube defects (ONTDs) and a frequently-used marker for fetal chromosomal aneuploidy. AFP

is a 69 kDa fetal-derived glycopro- tein which is mainly produced by yolk sac and fetal liver.[5]Elevated maternal serum alpha-fetoprotein (MS-AFP) suggests high risk of fetal ONTDs, and requires a fetal ultrasonography and sometimes amniotic fluid AFP and acetylcholinesterase test for prenatal diagnosis, as well as maternal tumor screenings.[6]However, after excluding fetal ONTDs and maternal tumors, these women with elevated MS-AFP, also described as "unexplained elevated MS-AFP" due to the unknown cause, have higher risks of APOs in their later gestations.[7,8] Therefore, it is possible that MS-AFP helps to identify these women at high risk of APOs and can be a biomarker for APOs predictions. As already known, MS-AFP concentrations are varied with several factors, including the racial origin.[9]

Materials and methods

This prospective observational study was carried out in the Department of Obstetrics and Gynaecology, after taking the approval of the protocol review committee and institutional ethics committee. 180 pregnancies women were reviewed by the maternal serum alpha-fetoprotein screening program. In this study, the age and weight of all pregnant women were 20-30 years old at conceptions and 55-70kg respectively. Participants are ideally screened between 14-22 weeks' gestation (Table1). All screened women gave informed consent to data acquisition and review as part of their participation in the MSAFP program. Gestational age of patients is ascertained by last menstrual period (LMP) or early ultrasound dating when dating is uncertain. The MSAFP levels are reported in ng/cc by a single central reference laboratory and an experienced person. Demographic characteristics of these women were maternal age, birth weight, and gestational age at the time of MSAFP draw. Weight of the fetus was estimated by the Honarvar 2 equation and compared with real weight.[10]

SPSS software was used for statistical analysis of data. The appropriate statistical tests including student's T Test, chi- square, ANOVA and exact test were used to compare the results. The differences were considered statistically significant if P value was less than 0.05.

Results

In this study, 180 pregnant women between the 14th and 22th weeks of gestation were evaluated. The mean age of the participants was 24.7±3.01 years .The mean of the birth weight was 3057±510 gram (1700-4340gram). The mean maternal serum Alpha- fetoprotein was 44.57±39.2 ng/cc (2.3-250 ng/cc). The median MSAFP was 34 ng/cc. Of 180 pregnant women, 150 had without preterm labor and 30 had preterm labor .The frequency of pregnant outcomes were as following: 5 (1.01%) stillbirths, 30(16.677%) preterm labor, 9(5%) PROM, 14(7.78%) pre-eclampsia, 25(13.89%) oligohydramnious, 2(1.11%) miscarriage. There was a correlation between preterm labor and higher MSAFP. The mean was 53.14 ng/cc in preterm labor and 35.13 ng/cc in term labor (P- value~0.021). With respect to compare these mean, the mean of MSAFP in preterm labor was significantly associated with higher level of MSAFP than term labor.

Table 1: Age and Gestation period

Age	20-30 yrs
Gestation period	14-22 weeks

Table 2: Risk of pre-eclampsia, preterm labor, PROM, oligohydramnious, stillbirth and miscarriage by mean level of maternal serum alpha-fetoprotein.

Parameter	Number	MSAFP (n/cc)	P-value	Parameter	Number	MSAFP (ng/cc)	P
Pre-eclmpasia	14	75.16±69.5	0.001	Oligohydramnious	25	76.39±59.3	0.000
Without pre-eclampsia	166	40.75±35.01		Without oligohydramnios Stillbirth	155	39.61±34.3	
Preterm labor	30	53.14±31.5	0.020		5	35.13±9.5	0.73
Without preterm labor	150	40.17±38.9		Without Stillbirth	175	42.62±38.26	
PROM	9	41.3±14.12	0.90	miscarriage	2	39.2±10.11	1.000
Without PROM	171	42.6±38.67		Without miscarriage	178	42.5±27.41	

The mean MSAFP was 75.16 ng/cc in pre-eclamptic women while it was 40.75 ng/cc in pregnant women without pre-eclampsia. Therefore, second trimester MSAFP levels were significantly higher in women with pre-eclampsia (P <0.001). Also, an association was found between level of MSAFP and oligohydramnious. It was higher in pregnancy women with oligohydramnious compared with normal women (76.39 ng/cc vs. 39.61 ng/cc) (P <0.001). The association between low birth weight and the levels of MSAFP was significant. With increasing MSAFP between 14-22 weeks' gestation, birth weight decreased (P <0.001). There was no relation between preterm rupture of membranous (PROM), stillbirth and miscarriage with the level of MSAFP (P =0.90, P =0.73, P =1 respectively) (Table 2). However, the number of patients with stillbirth and miscarriage was not enough for decision.

Discussion

The results of this study confirmed the association of elevated MS-AFP with increased risks of APOs in Chinese population, and demonstrated that elevated MS-AFP could be a predictor of a series of APOs, which was consistent with previous western reports. Although these are not novel findings, it is still meaningful in our population that we can also use MS-AFP to identify the women at high risk of APOs in early second-trimester. Moreover, ONTDs complicate merely a small proportion of pregnancies with elevated MS-AFP, and the rest of them have high risk of obstetric complications. Besides structural fetal abnormalities, other APOs like pre- eclampsia, preterm birth, spontaneous abortion, stillbirth, low birth weight, oligohydramnios, placental abruption and fetal growth restriction accounted for a large proportion in elevated MS-AFP group, 33.80% vs. 6.04% in normal MS-AFP group in this study. However, these APOs may be preventable if intervened in the earlier stage of gestation.[11]Although knowing the high risk of APOs among these women, we do not have any intervention at present time. Intensifying routine antenatal care does not improve their pregnancy outcomes.[12]

In our study, unexplained high levels of MSAFP have been associated with pre-eclampsia, preterm labor, oligohydramnios and LBW. Bernstein et al (1992) reported that women with elevated MSAFP level had an increases incidence of preterm labor, fetal growth retardation and fetal death.[13] In our research, high level of MSAFP was in correlation with increasing

preterm labor too. Neggers et al (2000) evaluated the relationship of MSAFP to preterm labor. They stated that MSAFP levels greater than the 90th percentile significantly increased the risk of preterm labor.[14] Our findings are the same with them. Kuo et al (2003) investigated the association between elevation of MSAFP and pregnancy outcomes on 168 singleton pregnancies. They suggested that screening for pregnancies with elevated MSAFP and pregnancy outcomes included preterm labor, preeclampsia, intrauterine fetal death would help to identify the low-risk cases and facilitate cost-effective management.[15] Another study showed that increases risk of pregnancy-induced hypertension, preterm labor, oligohydramnious and abruption placenta are associated with elevated MSAFP levels.[16]
Our findings are consistent with the study by Tikkanen et al (2007), Waller et al (1996) and Williams et al (1992) about the correlation of preeclampsia and MSAFP.[17-18-19]while Khoo's study (1978) showed, in preeclamptic women; significantly lower man AFP values were obtained. [20] Wald et al (2006) identified in the pregnancies that went on to develop pre-eclampsia, early second trimester inhibin-A and hCG values were significantly raised and uE3 values were significantly lowered, while AFP values were not significantly altered.[21]Kiran et al (2005), Brock et al (1982), Haddaw et al (1987), Mariona et al (1984) and Morssink et al (1997) revealed an association between low birth weights with abnormal unexplained high levels of second trimester MSAFP levels.[22-26] Their finding was paralled our result. In our study, the significant associations were not found between levels of MSAFP and miscarriage and stillbirth because the number of cases with miscarriage and stillbirth was not enough to evaluate the relationship between MSAFP level and them; whereas another study has found significant associations between elevated MSAFP and stillbirth and miscarriage.[27] On the other hand, Burton (1988) and Baschat et al (2002) reported patients with unexplained low levels of MSAFP had a significantly greater risk of fetal loss.[28, 29] Also, Simpson et al (1991) suggested that women with PROM showed elevated second trimester MSAFP.[30] while there was no association between MSAFP and PROM in our study. In conclusion, however, in pregnancies with an unexplained elevated second- trimester MSAFP, the rate of adverse pregnancy outcomes such as Oligohydramnious, Preterm labor, Pre-eclmpasia and low birth weight increased but screening for MSAFP in the second trimester seems to be of no value in predicting PROM.

Conclusion

We concluded that the elevated MS-AFP is associated with increased risks of APOs. ONTDs complicate merely a small proportion of pregnancies with elevated MS-AFP, and the rest of them have high risks of obstetric complications. MS-AFP can help to identify these women at high risk of APOs in earlier second-trimester.

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