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ORIGINAL RESEARCH

Association between second trimester maternal serum alpha-fetoprotein in 14-22 weeks and adverse pregnancy outcome

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ABSTRACT

Background:Many screening tests are available for predicting adverse pregnancy outcome and these range from non- invasive to invasive and serum alpha-fetoprotein level estimation is one of them. The present study was conducted to assess association between second trimester maternal serum alpha-fetoprotein in 14-22 weeks and adverse pregnancy outcome.

Materials & Methods: 250 patients of gestational age between 14-22 weeks were included. Maternal serum alpha-fetoprotein was measured in human serum by microplateimmuno-enzymometric assay by EIA-AFP kit. Maternal serum alpha-feto protein level was expressed in IU/ml.

Results: 23 (9.2%) participants out of 250 developed preterm labor. 21 out of 23 had raised value of maternal serum alpha-fetoprotein. 20 (8%) patients out of 250 patients developed oligohydramnios. 13 out of 20 had raised value of maternal serum alpha-fetoprotein. 14 (5.6%) patients out of 250 developed pre-eclampsia, 11 out of 14 had raised values of maternal serum alpha-fetoprotein. 7 (2.8%) patients out of 250 developed premature rupture of membrane (PROM). 4 out of 7 had raised values of maternal serum alpha-fetoprotein.

Conclusion: There is an increased risk of pre-eclampsia, preterm delivery, oligohydramnios and premature rupture of membrane with elevated maternal serum alpha-fetoprotein levels.

Key words: pre-eclampsia, preterm delivery, oligohydramnios

INTRODUCTION

In today's era, antenatal care is not only about treating a pregnant lady but also predicting adverse pregnancy outcome and trying to prevent them.[1]Many screening tests are now available for predicting adverse pregnancy outcome and these range from non- invasive to invasive and serum alpha-fetoprotein level estimation is one of them. Initially, maternal serum alpha-fetoprotein measurement has been used as an antenatal screening test for open neural tube defects and Down's syndrome.[2]

The presence of Alpha-fetoprotein in maternal serum was recognized by Seppala and Ruoslahte in 1972. It consists of a single polypeptide chain with a molecular weight of approximately 70,000 Daltons, slightly larger than albumin. Unlike albumin, alpha-fetoprotein is a glycoprotein containing approximately 4 percent carbohydrate and is after

albumin the major protein in fetal circulation.[3] Alpha-fetoprotein is normally produced during fetal and neonatal development by the liver, yolk sac and in small concentrations by gastrointestinal tract. In human beings, at 4-8 weeks of gestation, the yolk sac rivals the fetal liver in alpha-fetoprotein production. As the yolk sac degenerates at 11.5 weeks, the liver overtakes the function of yolk sac to produce Alpha-fetoprotein.[4]

Measurable concentrations appear in the maternal serum beginning at the end of the first trimester reaching a maximum level during the second trimester. Maternal serum alpha-fetoprotein levels normally rise during pregnancy from a normal non pregnant level of 0-20ngm/ml to a mean level of 250ngm/ml at 32 weeks. Normal level of maternal serum alpha-fetoprotein is dependent on many factors like race, weight and gestational age.[5]The present study was conducted to assess association between second trimester maternal serum alpha-fetoprotein in 14-22 weeks and adverse pregnancy outcome.

MATERIALS & METHODS

The present prospective study was conducted on 250 patients of gestational age between 14-22 weeks in the Postgraduate Department of Gynaecology and Obstetrics, LallaDed Hospital, Government Medical College Srinagar.

Detailed history, general physical examination and local examination were done at each antenatal visit. Relevant investigations were done according to the patients complaint and they were managed according to hospital protocol. Ultrasonography was done at gestational age 28 weeks, 32 weeks and 36 weeks to see gestational age, amount of liquor, fetal weight and placental localization. At delivery timing, mode of delivery, fetal status and baby weight were recorded.

A fasting morning serum sample was obtained. The blood was collected in plain red top venipuncture tube without additives and gel barrier. Serum was separated as soon possible to avoid any hemolysis. Samples with expressed hemolysis, hyperlipidemia and which were preserved by sodium azide were discarded. Maternal serum alpha-fetoprotein was measured in human serum by microplateimmuno-enzymometric assay by EIA-AFP kit. Maternal serum alpha-feto protein level was expressed in IU/ml. The sensitivity of enzyme immunoassay alpha feto-protein kit being 1IU/ml. Results were assessed statistically. P value less than 0.05 was considered significant.

RESULTS

Table I Assessment of second trimester maternal serum alpha-fetoprotein

Variable	No.	Mean	SD	P value
MSAFP (Overall)	250	65.32	33.95	0.02
MSAFP (Normal Outcome)	175	53.47	25.65	
MSAFP (Adverse Outcome)	75	92.96	34.99	

Table I shows that the mean of the maternal serum alphafeto protein (overall) was 65.32±33.95. The mean of the maternal serum alphafeto protein in pregnancies with normal outcome was 53.47±25.65. The mean of the maternal serum alphafeto protein in pregnancies with adverse outcome was 92.96±34.99.

Table II Preterm labour in the studied subjects

Alpha-fetoprotein	Yes		No		Total	
	Count	%age	Count	%age	Count	%age
Normal	2	8.7	181	79.7	183	73.2
Raised	21	91.3	46	20.3	67	26.8
Total	23	100%	227	100%	250	100%
$P-\text{value} < 0.001\ (Sig.)$						

Table II shows that 23 (9.2%) participants out of 250 developed preterm labor. 21 out of 23 had raised value of maternal serum alpha-fetoprotein.

Table III Oligohydramnios in the studied patients

Alpha-fetoprotein	Oligohydramnios					
	Yes		No		Total	
	Count	%age	Count	%age	Count	%age
Normal	7	35.0	176	76.5	183	73.2
Raised	13	65.0	54	23.5	67	26.8
Total	20	100%	230	100%	250	100%
$\mathbf{P-value} < 0.001\ (Sig.)$						

Table III shows that 20 (8%) patients out of 250 patients developed oligohydramnios. 13 out of 20 had raised value of maternal serum alpha-fetoprotein.

Table IV Pre-eclampsia in the studied patients

Alpha-fetoprotein	Pre-eclampsia					
	Yes		No		Total	
	Count	%age	Count	%age	Count	%age
Normal	3	21.4	180	76.3	183	73.2
Raised	11	78.6	56	23.7	67	26.8
Total	14	100%	236	100%	250	100%
$\boldsymbol{P-value} < 0.001\ (Sig.)$						

Table IV shows that 14 (5.6%) patients out of 250 developed pre-eclampsia, 11 out of 14 had raised values of maternal serum alpha-fetoprotein.

Table V Premature rupture of membrane (PROM) in the studied patients

Alpha-fetoprotein	PROM					
	Yes		No		Total	
	Count	%age	Count	%age	Count	%age
Normal	3	42.9	180	74.1	183	73.2
Raised	4	57.1	63	25.9	67	26.8
Total	7	100%	243	100%	250	100%
$\boldsymbol{P-value = 0.159}\ (\boldsymbol{Not\ Sig.})$						

Table V shows that 7 (2.8%) patients out of 250 developed premature rupture of membrane (PROM). 4 out of 7 had raised values of maternal serum alpha-fetoprotein.

DISCUSSION

During gestation, Alpha-fetoprotein is present in the amniotic fluid as a result of fetalmicturation. The fetal to maternal transfer of alpha-fetoprotein occurs by a transplacental and transamniotic route.[6] The transfer of alpha-fetoprotein across the placenta once thought to be accomplished only by paracellular diffusion, involves additional and more complicated mechanisms.[7] Four anatomical barriers which must be traversed between the maternal and fetal circulation are syncytiotrophoblast bathed by maternal blood in the intervillous space, the trophoblast basement membrane, the capillary basement membrane and the fetal capillary endothelium.[8] The transplacental passage of alpha-fetoprotein was found to be asymmetrical and unidirectional displaying a faster transfer rate of alpha-fetoprotein from the fetal to maternal circulation than vice-versa. Fetal alpha-fetoprotein was found to enter the maternal circulation via two possible pathways.[9]The first pathway involved alpha-fetoprotein exiting fetal vessels and passing through the placental villous core. Alpha-fetoprotein can also traverse fibrinoid deposits and cross at sites of discontinuity of the syncytiotrophoblast cells. Thus, alpha-fetoprotein can enter the maternal circulation with or without passage through the cytoplasm of these cells. The second pathway involves alpha-fetoprotein gaining entrance in to the decidua basalis with passage in to the maternal circulation by entering vessels that traverse the basal plate of the decidua.[10]

We found that the mean of the maternal serum alphafeto protein (overall) was 65.32+33.95. The mean of the maternal serum alphafeto protein in pregnancies with normal outcome was 53.47+25.65. The mean of the maternal serum alphafeto protein in pregnancies with adverse outcome was 92.96+34.99. Krause TG et al[11] found that pregnant women with extreme maternal serum alpha-fetoprotein values in the second trimester have an increased risk of fetal and infant deaths.

We found that 23 (9.2%) participants out of 250 developed preterm labor. 21 out of 23 had raised value of maternal serum alpha-fetoprotein. C. M. Buckland et al[12] studied the relationship between MSAFP and low birth weight infants with respect to both prematurity and retarded fetal growth.

We found that 20 (8%) patients out of 250 patients developed oligohydramnios. 13 out of 20 had raised value of maternal serum alpha-fetoprotein. Kiran TS, Bethel J, Bhal PS[13] revealed an association between low birth weight, prematurity and antepartum haemorrhage with abnormal unexplained high levels of second trimester MSAFP levels.

We found that 14 (5.6%) patients out of 250 developed pre-eclampsia, 11 out of 14 had raised values of maternal serum alpha-fetoprotein. MeghanaToalet al[14] found that an elevated serum AFP was associated with higher rates of low birth weight babies.

We found that 7 (2.8%) patients out of 250 developed premature rupture of membrane (PROM). 4 out of 7 had raised values of maternal serum alpha-fetoprotein. EnisOzkaya et al[15] concluded that AFP levels of the second trimester screening test higher than 1.55 MoM is significantly associated with IUGR in hyperemesis gravidarum.

The overall transplacental passage of alpha-fetoprotein is accomplished by the bulk flow of alpha-fetoprotein containing fluids driven by fetal to maternal hydrostatic gradient across the placental villous surface. Fetal arterial perfusion pressures are higher than those in the maternal intervillous spaces. Umbilical venous pressure is also significantly higher than the intervillous space pressure, providing support for the hydrostatic pressure gradient mechanism.[16] Areas of discontinuity in the syncytiotrophoblast layer would provide even more surface area to facilitate such routes. Fibrinoid deposits are thought to further enhance

passage by providing an additional matrix surface area for temporary alpha-fetoprotein adhesion.

CONCLUSION

Authors found thatthere is an increased risk of pre-eclampsia, preterm delivery, oligohydramnios and premature rupture of membrane with elevated maternal serum alpha-fetoprotein levels.

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