Original Research Paper

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CORRELATION OF ELEVATED SECOND TRIMESTER MATERNAL SERUM ALFA FETOPROTEIN WITH FETOMATERNAL OUTCOME

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ABSTRACT **Background –** An association was found between increased maternal serum alpha- fetoprotein level with additional structural anomalies. but there may be increased risk of premature rupture of membrane, placenta accreta, placenta increta, placenta previa, preterm birth, fetal growth restriction, low APGAR score and intrauterine fetal death also in non pregnant women and men with liver cancer associated with elevated AFP levels. **Material and method-** This prospective observational study was conducted in Department of Obstetrics & Gynaecology, KGMU, Lucknow (U.P) to study of elevated maternal serum alphafetoprotein in all pregnant female in second trimester after excluding congenital anomaly in fetus through (TIFFA). **Result –** A total of 200 pregnant female enrolled at the gestational age of 15-20 weeks of pregnancy were included in the study who were willing for the study and fulfill all inclusion and exclusion criteria. Subject underwent blood investigation and We observed that increase the MSAFP (MOM) level was significantly positive correlated with Preterm labor (p value <0.019) ,placenta previa (p value<0.028) ,pprom (pvalue<0.019), preterm vaginal delivery (p value>0.002). But MSAFP (MOM) level was not correlated with Abortion, and Placental abruption maternal outcome and also increase the MSAFP (MOM) level was significantly positive correlated with oligohydramios (pvalue<0.017*) and low APGAR score (p value<0.021),neaonatal care fetal outcome(pvalue <0.026). **Conclusion-** our study suggested that elevated maternal alpha fetoprotein in second trimester with excluding congenital anomaly in fetus by using level 2 scan (TIFFA) can cause adverse outcome in pregnancy like placenta previa ,PPROM ,and fetal growth restriction,and NICU admission of neoborn.

KEYWORDS :

INTRODUCTION

BACKGROUND

Alfafeto protein is a tumor associated glycoprotein produced by the embryonic yolk sac and fetal liver involved with both ontogenic and oncogenic growth. Fetal protein is a 69-k Da single polypeptide chain and 3-5% carbohydrate containing triplicate domain structure configured by intramolecular loops dictated by disulfide bridging ,and formed a helical v shaped or u shaped electron dot maps. Alphafetoprotein has been divided into three domain, cystein rich translatedprotein of albuminiod gene family and consist with 4 members albumin, vitaminD- binding protein , AFP and alpha albumin (ALB) AFP level in developing human embryo rises from the end of first trimester and begins to fall after 32 weeks of gestation . 1,2

Measurement of Serum level of alphafetoprotein above the normal range in pregnant women used as Prenatal screening to rule out any congenital malformation of fetus and embryo.other type of birth defect were found to reflect discordant AFP levels , including chromosomal abnormalities (aneuploidies) and various anatomic congenital disorder (3) It was determined that other additional serum analytes together with Maternal serum alfafetoprotein increased prenatal screening detection rates. Maternal blood AFP level often as a part of triple test screening (AFP,ESTRIOL,HCG) or quadruple (AFP, ESTRIOL, HCG, INHIBIN) for birth defects.[4,5].

Maternal serum alfafeto protein level are usually interrupted for age, race, weight and gestation age**.**

An association was found between increased maternal serum alpha-fetoprotein level with additional structural anomalies. but there may be increased risk of premature rupture of membrane, placenta accreta, placenta increta, placenta previa, preterm birth, fetal growth restriction, low APGAR score and intrauterine fetal death also in non pregnant women and men with liver cancer associated with elevated AFP levels.[4,5.)

Subject and Method

This is a prospective observational study done in the Department of Obstetrics and Gynaecology, King George Medical University, Lucknow India. Study period is 1 year, and 200 women were enrolled in the study from May 2019 to April 2020. Ethical committee approval was obtained prior to the study. All samples were collected in OPD basis Department of Obstetrics & Gynaecology, KGMU, Lucknow and followed till delivery to know the fetal and maternal outcome. Patients giving written informed consent will be taken, Age 18-40 years, Singleton pregnancy, gestational age of 15-20 weeks based on reliable last menstrual period (LMP) and / or a dating scan in the first trimester; Spontaneous conception were included in the study. Patients not giving consent, Multiple pregnancies, smoker, women with known case of hypertensive disorders, BMI >30; Any congenital anomaly or birth defect in foetus was could out by obstetrics level 2 scan.Known case of dibaetes mellitus were excluded in the study.

All pregnant women having their antenatal visit within 15-20 weeks of pregnancy and having their delivery at our hospital were included. Women with BMI >30 , multiple pregnancies, hyperemesis gravidarum, with co-existent medical disorders—diabetes, hypertension, epilepsy, bronchial asthma, congenital heart disease, chronic kidney disease, and In-vitro fertilisation, smoker and any congenital anomaly or birth defect rouled out by level 2 scan were excluded. Informed consent was obtained from all the pregnant women after counselled about the importance of maternal serum alphafetoprotein screening. Demographic details and detailed history were collected using a PRISCA prenatal risk calculation software programme. Corrected MoM values were calculated according to the gestational age , socioeconomic status, maternal weight,race, smoking and parity were recorded.

Sample Size

The sample size was calculated based on a previous study that reported that the incidence of adverse pregnancy outcomeswith elevated maternal serum alpha-fetoprotein (MS-AFP) was75.4% ***(Karya et al., 2018)***, 95% level of confidence and Error rate, usually set at 0.05 level is 4. Total 285 patients were included in this study .

Statistical Analysis

The results will be presented in frequencies, percentages and mean±SD. The Descriptive statistics for continues variables were expressed as mean +_ standard deviation or median (interquartile range) , while categorcial variables were expressed in number and percentage.Student t test or mann- witney test was used for continues variables according to the data distribution and chi square or fisher 's exact test for categorical variables according to expected count.The odds ratio (OR) and 95% confidence interval (CI)were calculated to evaluate the relative risk of adverse pregnancy outcomes regarding MSAFP.The receiver operating characterstics (ROC) curves were used to evaluate the predictive efficiency akaplan- meier curve was used to show overall distribution of gestational week at delivery.

RESULTS

- We started our study with 320 patients but 40 patients opted out during the course of study and thus lost to follow up so the final results of our study had 280 patients enrolled and evaluated.
- We will keep as cases of maternal serum alphafetoprotein (MSAFP)>2.5 Mom and as control group MSAFP<2.5Mom .
- Total number of sample size were evaluated =280
- In which the total number of patient with MSAFP >2.5 Mom =162,
- Total number of patient with MSAFP <2.5 Mom =118
- Total patient which was Lost to follow up =40
- Distributions of pregnant women according to second trimester maternal level of serum Alfa MSAFP) are shown in Table 1 .

Table 1: Distribution of cases according to period of gestation (weeks)

POG	MSAFP range ≤2.5 Mom (n=118)		MSAFP range >2.5 Mom (n=162)		Chi sq.	P value
	n	%	N	%		
≤18 Weeks	41	34.75	108	66.66	27.98	<0.001*
>18 weeks	77	65.25	54	32.73		
Mean±SD	21.10±1.59		18.65±2.20		t=8.49	<0.001*

*=Significant (p<0.05)

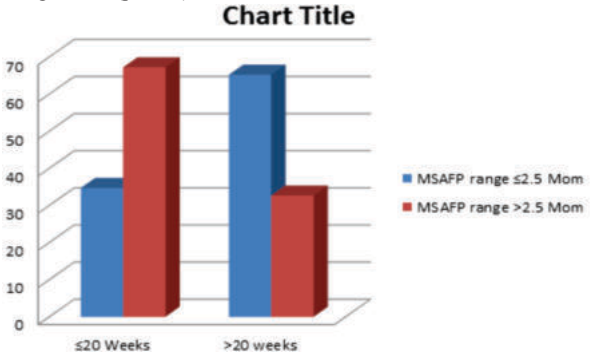

Figure 1. shows the distribution of women according to period of gestation in between MSAFP range ≤2.5 Mom and MSAFP range >2.5 Mom group.

Distribution of women according to period of gestation (POG) in weeks in between MSAFP range ≤2.5 Mom and MSAFP range >2.5 Mom group are shown in Table 1 and Figure 1.

The percentage of ≤18 Weeks, and>18 weeks of 41 (34.75%) and 77 (65.25%) in MSAFP range ≤2.5 Mom group and 108 (66.66%) and 54 (32.73%) in MSAFP range >2.5 Mom, respectively.

The percentage of women with >18 weeks of Period of gestation was significantly lower in MSAFP range >2.5 Mom as compared to MSAFP range ≤2.5mom.

Table 2: Association of Maternal outcome with MSAFP range ≤2.5 Mom and MSAFP range >2.5 Mom groups

Variables	MSAFP range ≤2.5 Mom (n=118)		MSAFP range >2.5 Mom (n=162)		Chi-Sq.	p-value
	N	%	N	%		
Placental abruption	12	10.17	10	10.12	0.102	0.784
PPROM	7	22.86	65	38.18	4.12	0.029*
PROM	20		3	-		
Preterm labor	49	41.53	93	57.36	5.48	0.019*
Abortion	20	16.95	21	25.45	2.43	0.119
2nd trimester (15-18)	18	-	5	-		
2nd trimester (18-20 wk)	2	-	16	-		
Vaginal delivery	56	47	48	29.09	9.21	-0.002*
Term	46		8	-		
Preterm	10		40	-		
Placenta previa	26	22.03	84	51.27	4.75	0.028*
Severe preeclmpsia	20	16.9%	49	30.2%	2.93	0.120

Table no.2 shows the association of maternal outcome in comparison of MSAFP range ≤2.5 Mom and MSAFP range >2.5 Mom group. MSAFP level was significantly positive correlated with Preterm labor,placenta previa ,pprom (p value <0.05) and negative correlated with vaginal delivery. But MSAFP (MOM) level was not correlated with Abortion, and Placental abruption maternal outcome (p value>0.05)

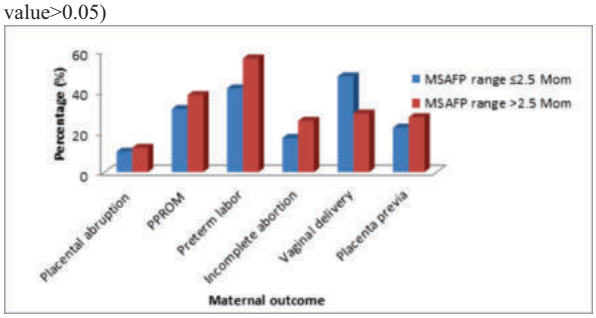

Figure2 : Bar chart shows the association of maternal outcome between groups MSAFP range ≤2.5 Mom and MSAFP range >2.5 Mom group.

The Percentage of Placental abruption,PPROM,Preterm labor, Incomplete abortion,Vaginal delivery and Placenta previa of maternal outcome were comparable between MSAFP range≤2.5 Mom and MSAFP range>2.5 Mom groups.

Table 3: Association Fetal outcome with MSAFP range ≤2.5 Mom and MSAFP range >2.5 Mom groups (n=280)

	MSAFP range ≤2.5 Mom (n=118)		MSAFP range >2.5 Mom (n=162)		Chi-Sq.	p-value
	n	%	n	%		
FGR	41	34.75	64	34.85	2.35	0.11
Oligohydroamnios	26	28.75	82	49.70	5.67	0.017*
Still born	28	23.73	39	24.45	0.04	0.848
Low birth weight baby	47	25.42	65	40.12	1.95	0.162
Low apgar score	22	18.64	92	56.79	3.69	0.021*
Neonatal care admission	30	30.51	78	48.58	3.22	0.026*

*=Significant (p<0.05)

Table no3 shows the association of fetal outcome in comparison of MSAFP range ≤2.5 Mom and MSAFP range >2.5 Mom group. MSAFP level was significantly positive correlated with oligohydramnios,low apgar score, neonatal care admission (p value <0.05). But MSAFP (MOM) level was not correlated with FGR,intrauterine fetal death,low birth weight baby (p value>0.05)

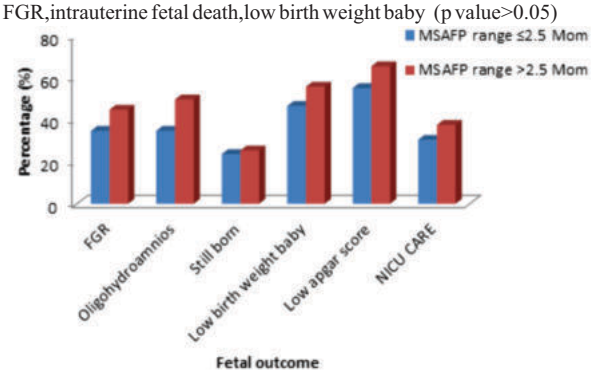

Figure 3: Bar chart shows the association Fetal outcome with MSAFP range ≤2.5 Mom and MSAFP range >2.5 Mom groups

The percentage of oligohydraminos, Low APGAR score,Neonatal CARE ,FGR ,low birth baby and Stillborn were comparable between these groups MSAFP range>2.5 Mom toMSAFPrange≤2.5Mom.

Table 4: Correlation of the MSAFP (MOM) with maternal outcome (n=280)

	Overall	
	Karl-Pearson's correlation coefficient	p-Value
Abortion	0.082	0.169
Placenta previa	0.134	0.037*
PPROM	0.057	0.0341*
Preterm labor	0.137*	0.022*
Vaginal delivery	-0.149*	-0.012*
Placental abruption	-0.019	0.754

*=Significant (p<0.05)

Correlations of the MSAFP (MOM) with maternal outcome are shown in

Table 4.The increase the MSAFP (MOM) level was significantly positive correlated with Preterm labor,placenta previa ,pprom and negative correlated with vaginal delivery. But MSAFP (MOM) level was not correlated with Abortion, and Placental abruption maternal outcome.

Table 5: Correlation of the MSAFP (MOM) with Fetal outcome (n=280)

Fetal outcome	Overall	
	Karl-Pearson's correlation coefficient	p-Value
FGR	0.097	0.102
Oligohydroamnios	0.168	0.0257
Still born	-0.022	0.714
Low birth weight baby	0.0145*	0.14
Low apgar score	0.135*	0.023

*=Significant (p<0.05)

Correlations of the MSAFP (MOM) with fetal outcome are shown in **Table 5**.The increase the MSAFP (MOM) level was significantly positive correlated with oligohydramios and low APGAR score,neaonatal care fetal outcome. Moreover, the increased the MSAFP (MOM) level I increased chances of low apgar score, neonatal care and oligohydramnios ,.

DISCUSSION

This is the prospective observational study done for 1 year from june 2019 to may 2020 included all outdoor and indoor pregnant female.

Maternal serum alpha -fetoprotein (MSAFP) levels,other than for NTD screening , with beta- hcg and uE3 (trisomy) screening tests in second trimester are included in the antenatal care (7) .

several studies have shown that MS-AFP level of >2.5Mom in second trimester, except from cases of multiple gestation or fetal anomalies are associated with an increased risk of preeclampsia , IUGR ,preterm delivery , placental abruption and fetal loss (12,13).

The result of this study showed that coorelation maternal serum AFP levels in second trimester of pregnancy is related with maternal and fetal and neonatal complications.

The study shows the result of maternal outcome with MSAFP >2.5 Mom with p value <0.05 with PPROM, preterm labor, placenta previa, ie. significantly correlated almost comparable to study done by **jilin hu et al .** in their study found that elevated first-trimester MS-AFP is associated with increased risks of preterm birth, preeclampsia and SGA. However, the predictive efficiencies were low.

Further, the result of our study fetal outcomes with MSAFP> 2.5 Mom with p value<0.05 with neonatal care , low APGAR score and oligohydramnios were significantly correlated and FGR, low birth baby and Still born were not significantly correlated. **Ketz et al 1990** found that excluding anomalies evaluated by ultrasound and / or amniocentesis , elevated MS-AFP ,preterm delivery and IUGR were associated with a 2 -4 fold increase risk in risk of giving birth to low birth baby ,meanwhile , unexplained elevated AFP levels (2.0 -3.0 Mom)were associated with 10- fold increase in placental abruption and perinatal mortality .similarily our study are consistent with previous study .

Anthore study , **anufuso et al 2007** . showed that unexplained high MSAFP levels (>2.5 Mom) due to any visible cause and compared them to women with normal MS-AFP levels . they were found to have a 5.8 – fold increased risk of preterm birth , a 15.2 – fold increased risk of PPROM, a 2.6- fold risk increased risk of preeclampsia /HELLP syndrome, a 5.9 – fold increased risk of IUGR ,and a significantly increased risk of intrauterine fetal demise .

Similarly our study , we identified the risk of Preterm labor and PPROM , Placenta previa , neonatal care and low apgar score to be significantly increased almost comparable with this study.

On the other hand Davidson, kang and wald did not find any significant increase in MSAFP levels in preeclamptic women. we also found no singnificant difference in rate of preeclampsia between groups **in** our study .

In our study we found that increased risk of preterm birth (p-value -< 0.05) with raised level of MS-AFP is significantly coorelated . and **smith et al.** conducted a cohort study and found that in women with a high MS-AFP level , a statistically significant increased risk of preterm birth and stillbirth bu our study showed that stiibirth not significantly coorelated with raised MS-AFP .

Bernstein et al .1992.reported that women with elevated levels had an increased incidence of preterm labor and fetal growth restriction and fetal death .In our study ,with high level of MSAFP is coorelated with preterm birth and neonatal care and low apgar score almost comparable with above study our findings are consistent with the study by **Kuo et al 2003 .**investigated the association between elevation of MS-AFP and pregnancy outcomes on 168 singletone pregnancies . they suggested that screening for pregnancies with elevated MS-AFP and pregnancy outcome included preterm labor , preeclampsia , intrauterine fetal demise would help to identify the low risk cases and facilitate cost effective management .Anthore study showed that increases risk of pregnancy induced hypertension , preterm labor , oligohydramnios and placental abruption are associated with elevated MS-AFP levels **huerta-enochian G et al.2001**

CONCLUSION

our study suggested that screening for pregnancies with elevated maternal serum alphafetoprotein in second trimester would help to identify the risk of preterm labor ,prematurity,low birth weight ,PPROM,placenta previa,fetal growth restriction and to prevent the complication during and after the delivery.and improve maternal and fetal outcome .

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