

MATERNAL SERUM ALPHA-I-FETOPROTEIN IN CASES OF NORMAL PREGNANCY AND ABORTIONS

by

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Introduction

With increasing awareness of the possibilities of congenital malformations the obstetrician's role in genetic counselling is becoming more and more important.

In the modern era of obstetrics it has been possible to predict a number of congenital malformations by studying deficiencies or preponderances of certain enzymatic and other products of fetal metabolism. One such product is the Alpha-I-Fetoprotein (AFP). It is protein of alpha globulin mobility in electrophoresis and is synthesized in the yolk sac in early pregnancy and subsequently by the fetal liver and gut. With a molecular weight of 70,000 it is easily transferred through the placental barrier and therefore reflected concurrently in the maternal serum.

Assay of AFP was originally applied by Brock and Sutcliffe (1972) for the diagnosis of open neural tube defects. Since

that time the estimation of AFP in maternal serum has become increasingly useful in the detection of complications of early pregnancy.

Following these observations the present work was carried out with the following aims and object—

1. Detection of maternal serum AFP levels in various trimesters of normal pregnancy.
2. Measurement of maternal serum AFP level in cases of abortions with the view to detect congenital abnormalities and to determine the prognostic importance of such an assay.

Material and Methods

The present study was carried out in the Department of Obstetrics and Gynaecology and the Nuclear Medicine Unit of the Department of Medicine, S.N. Medical College, Agra.

The cases were selected from the OPD, labour room and inpatient wards.

Thirty cases of normal pregnancy, in different trimesters, served as control and 110 cases of different types of abortions were included in the study group.

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Distribution of the caases in the control and study groups was as follows—

I. Normal pregnancy (control group)	30 cases
1. First trimester	10 cases
2. Second trimester	10 cases
3. Third trimester	10 cases
II. Cases of abortions (study group)	110 cases
1. Threatened abortion	20 cases
2. Inevitable abortion	20 cases
3. Complete spontaneous abortion	40 cases
(a) Neural tube defects	20 cases
(b) Twins	10 cases
(c) Intrauterine death	10 cases
4. Habitual abortion	10 cases
5. Missed abortion	10 cases
6. Vesicular mole	10 cases

Five ml of venous blood of the patient was drawn and centrifuged to separate the serum, which was collected in dry sterile vials and stored at 20°C till assayed.

The AFP estimation of the samples collected was done by the method of Radio-immunoassay using the Radiochemical Centre AFP RIA Kit.

Observations

Observations of the present study are given in the following Tables—

Table I shows the mean maternal

TABLE I
Mean Maternal Serum AFP Levels in Different Trimesters of Normal Pregnancy

Trimester of pregnancy	Mean AFP level in ng/ml	S.D.
First	80.25	43.74
Second	182.50	20.55
Third	213.00	93.25

serum AFP level in the first, second and third trimesters of normal pregnancy to be 80.25, 182.50 and 213 respectively.

Table II shows the mean maternal

TABLE II
Mean Maternal Serum AFP Levels in Different Types of Abortions

Type of abortion	Mean AFP level in ng/ml	S.D.
Threatened abortion	148.8	92.59
Inevitable abortion	228.4	125.35
Complete spontaneous abortion	477.5	244.12
Habitual abortion	262.6	49.57
Missed abortion	65.3	40.22
Vesicular mole	13.0	4.58

serum AFP levels in the study group. It was seen that the AFP values were significantly raised in cases of complete spontaneous abortions which included cases of neural tube defects, twins and intrauterine death. The levels were moderately raised in cases of inevitable and habitual abortion. AFP levels were slightly raised in cases of threatened abortion while they were below the normal pregnant levels in cases of missed abortion and corresponded to non-pregnant levels in cases of vesicular mole.

Table III shows that in the first trimester of pregnancy the values of maternal serum AFP are significantly raised in cases of inevitable abortion while they are only slightly raised in cases of threatened abortion.

In the second trimester of pregnancy the values of AFP in maternal serum in the different types of abortions are in the following ratio—

Normal pregnancy: threatened abortion: inevitable abortion: complete spon-

TABLE III
Comparison of Mean Maternal Serum AFP Levels in Cases of Abortion With Cases of Normal Pregnancy in Different Periods of Gestation

Period of gestation in weeks	Normal pregnancy	Threatened abortion	Inevitable abortion	Complete spontaneous abortion	Habitual abortion	Missed abortion	Vesicular mole
6 - 12	80.25	87	140.66	—	—	—	13.5
13 - 18	166.00	241.5	360.00	420.00	254	32	12.0
19 - 24	199.00	—	—	482.72	267	82	—

taneous abortion; habitual abortion; missed abortion; vesicular mole = 1:1.5:2:2.5:1.5:0.2:0.07.

Table IV shows that the maternal serum AFP levels were almost 2.5 times or even more than the normal pregnancy levels in cases where the underlying cause of spontaneous abortion was neural tube defect.

Maternal serum AFP levels were almost doubled in cases of twins and intrauterine death.

Table V shows that—

(1) The rise of maternal serum AFP level in cases of threatened abortion was not significant in the first trimester of pregnancy, but, was significant in the second trimester of pregnancy.

(2) Maternal serum AFP levels in cases of inevitable abortion were significantly raised during both first and second trimester of pregnancy.

(3) Maternal serum AFP levels were significantly high in cases of habitual abortion and were significantly low in cases of missed abortion and vesicular mole as compared to the normal pregnant levels.

(4) The rise in maternal serum AFP levels in cases of neural tube defects and twin pregnancy was statistically highly significant and was significant in cases of intrauterine death.

Discussion

The mean maternal serum AFP levels in different trimesters of normal pregnancy in the present study do not differ from those reported by Rouslahti and Seppala (1972).

As the fetal serum AFP concentration is highest during the second trimester of pregnancy, even a very small leak of fetal serum (less than 100 μ l) into the maternal circulation can elevate the maternal serum AFP level considerably. In the present

TABLE IV
Comparison of Maternal Serum AFP Levels in Different Cases of Complete Spontaneous Abortion With Normal Pregnancy in Different Periods of Gestation

Period of gestation in weeks	Normal pregnancy	Neural tube defect	Twins	Intrauterine death
9 - 12	80.25	—	—	—
13 - 18	166.00	—	—	420
19 - 24	190.00	534.4	510	610

TABLE V
Statistical Comparison of Maternal Serum AFP Levels in Different Types of Abortions vs. Normal Pregnancy

AFP	Threatened abortion Vs. Normal pregnancy		Inevitable abortion Vs. Normal pregnancy		Habitual abortion Vs. Normal pregnancy	Missed abortion Vs. Normal pregnancy	Vesicular mole Vs. Normal pregnancy	Complete spontaneous abortion Vs. Normal pregnancy		
	1st trimester	2nd trimester	1st trimester	2nd trimester				Neural tube defect	Intra- uterine death	Twins
S.D.	30.51	61.52	39.21	<.05	49.57	40.22	4.58	277.385	134.35	28.28
T-value	0.44	1.917	1.984	5.986	3.004	5.113	3.138	1.873	5.525	16.635
P-value	>0.5	<.05	<.05	<.05	<.05	<.05	<.05	<.001	<.05	<.001
Level of significance	non-sig- nificant	significant	significant	significant	significant	significant	significant	highly significant	significant	highly significant

study it was observed that the maternal serum AFP levels in second trimester of pregnancy were significantly raised in cases of threatened abortion and were almost double the normal pregnant levels in cases of inevitable abortion whereas they remained near normal pregnant levels during the first trimester in cases of threatened abortion. Our findings are similar to those of Seppala and Rouslahti (1972) and Chowchock (1976, 1978). Hence elevated maternal serum AFP levels in first trimester of pregnancy are more indicative of inevitable abortion while elevated second trimester AFP levels may be indicative of threatened abortion even in the absence of clinical signs and symptoms.

In the present study the maternal serum AFP levels were found to be about 2.5 times the normal pregnant levels in cases of neural tube defects. The findings correspond to those reported by workers such as Leek and Chard (1976), Harris and Seppala (1974), Brock and Sutcliffe (1972) and U.K. Collaborative Study. The origin of increased maternal serum AFP in fetal neural tube defect lies in the leakage of protein from fetal serum and cerebrospinal fluid into the amniotic fluid, thus raising the amniotic fluid AFP which is then reflected in the maternal serum.

In the present study the maternal serum AFP levels were found to be almost doubled as compared to normal pregnant levels in cases of twin pregnancy and intrauterine death. Our findings correspond to the observations by other workers as Garoff and Wald *et al* (1975), U.K. Collaborative Study (1977) and Chowchock (1978).

The rise in AFP levels in cases of twins can be explained by the simultaneous production of AFP by two fetuses as well as the increased placental synthesis

of AFP from the large sized placenta. The possible mechanisms of raised maternal serum AFP levels in intrauterine death could be fetal maceration with resorption of fetal elements or placental abruption causing massive fetomaternal transfusion.

The finding of elevated maternal serum AFP level during the second trimester of pregnancy should suggest the possibility of intrauterine death, congenital anomaly of fetus or multiple gestation. A concurrent screening by ultrasonography or other methods then becomes mandatory to assess the viability of the fetus, to detect gross fetal anomaly or to confirm the presence of a twin pregnancy and thereby eliminate the hazards of an unnecessary amniocentesis.

One patient of habitual abortion with raised maternal serum AFP level had undergone cervical cerclage operation at 14 weeks gestation and delivered a premature anencephalic fetus at 28 weeks of gestation. This suggests that maternal serum AFP estimation has an important role in identifying the fetuses who are doomed to abort or who are suffering from gross fetal abnormality and thus reduce needless surgery, emotional disturbance and hospitalisation of the patient concerned. Cases of habitual abortion with no apparent fetal or maternal complication showed normal AFP values.

In the present series all cases of missed abortion showed AFP levels lower than the normal pregnancy levels for that period of gestation. The levels, however, corresponded to the uterine size rather than the duration of amenorrhoea. Thus, if lower than normal AFP levels are found one should think of the possibility of dealing with a case of missed abortion.

In all cases of vesicular mole studied AFP levels were found to correspond to non pregnant levels (mean AFP value be-

ing 12.75 ng/ml) similar observations have been reported by Seppala and Rouslahti (1972) and Chowchock (1978).

This suggests that levels of AFP within non pregnant range in second trimester of pregnancy indicate the absence of a fetus. Such levels have been reported in the past in cases of molar pregnancy, choriocarcinoma and empty gestational sac pregnancy.

Conclusion

From the above data and discussions we can conclude that AFP estimation in maternal serum has an important role to play in the diagnosis, prognosis and management of various types of abortions. Maternal serum AFP estimation is an important diagnostic tool in the identification and management of high risk obstetric patients and should therefore be extensively used for the detection and prevention of abnormal pregnancies.

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