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Alpha-Fetoprotein Values in Maternal Serum and Amniotic Fluid for Prenatal Screening of Genetic Disorders

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Prenatal alpha-fetoprotein screening may serve as an index of suspicion of many congenital anomalies of the fetus including neural tube defect and aneuploid fetus. This study was undertaken to determine the normal ranges of AFP in maternal serum and amniotic fluid at 9 to 41 weeks gestation which thus far had not been established in Korea. Normal ranges of maternal serum and amniotic fluid AFP from 9 to 34 weeks and from 16 to 41 weeks gestation were obtained respectively from 198 uncomplicated pregnant women delivered of normal singleton baby. Maternal serum AFP values showed an increasing trend from 12 weeks gestation reaching a peak level at 29 to 34 weeks gestation and after which there was a gradual decline. Amniotic fluid AFP values was the highest at 17 weeks gestation and declined as pregnancy approached term. The corrrelation of a median value between AF AFP and MS AFP was 100 to 1 in ratio in each week. The authors conclude that this initial experience in Korea with maternal serum AFP values could efficiently detect genetic disorders, perhaps with high sensitivity and provide a proper management scheme of pregnant women with abnormal high and low AFP values during the midtrimester of pregnancy.

Key Words: Alpha-fetoprotein (AFP), maternal serum (MS), amniotic fluid (AF), multiple of median (MOM), genetic disorders.

In modern obstetrics, measurement of alpha-fetoprotein is widely used in prenatal fetal diagnosis, especially in detecting neural tube defect and certain other congenital malformations of fetus and aneuploid fetus (Adams and Windham 1984; Merkatz et al. 1984; Doran *et al.* 1986). Measurement of AFP particularly in the early detection of genetic disorders has advantages of being simple and applicable throughout the whole gestational period especially in 14-22 weeks gestation unlike the techniques applicable only to limited periods of gestation (Leonard 1981).

Current trend in research is in favor of using maternal serum AFP measurement which is simpler than the amniotic fluid AFP measurement which carries additional complications such as infection, hemorrhage, abortion, and preterm labor.

The purpose of this study first conducted in Korea was to establish the standards for both maternal serum and amniotic fluid alpha-fetoprotein values for the prenatal diagnosis of congenital malformation of fetus.

MATERIALS AND METHODS

From January 1 to October 30, 1985, a total of 198 pregnant women between 9 to 41 weeks gestation were screened for AFP levels at the department of Obstetrics and Gynecology, Yonsei University Medical Center. From each of these pregnant women, 5 ml of antecubital vein blood was obtained and stored at −20°C. After ultrasonographically localizing placenta, amniocentesis was performed transabdominally using 22 gauge needle to obtain amniotic fluid, which was also stored at −20°C. For determination of fetal blood contamination of the amniotic fluid, Kleihauer test was not performed in this study, but instead the naked eyes were used to exclude such contamina-

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tion. AFP was assayed using solid phase enzyme immunoassay (ELISA, Behring Enzygnost AFP, 1 IU/ml = 1.5 ng/ml, sensitivity 0.5 IU/ml) employing peroxidase as conjugated antibody.

If AFP was elevated, repeat assay was performed to confirm it and to correct gestational age. If the repeat assay was again elevated, the patient was put into the high-risk category and counselled as to the possible risks and further evaluations including ultrasonogram and amniotic fluid AFP assay and karyotyping by amniotic fluid cell culture were followed. Utilizing above procedures and techniques, AFP levels in maternal serum and amniotic fluid from 198 uncomplicated pregnant women delivered of normal singleton baby were expressed as multiple of median. AFP levels were classified and assigned into the normal group if the values were from 0.25 MOM to 2.0 MOM and into the abnormal group if the values were below 0.25 MOM or above 2.0 MOM and the comparisons of the values between the two groups were made with respect to several obstetrical parameters.

In addition, normal ranges of maternal serum and amniotic fluid by each gestational week were determined and graphically presented. The correlation between the levels of AFP in maternal serum and amniotic fluid were analyzed in conjunction with the results of ultrasonogram, karyotype and pregnancy outcome.

These data were statistically evaluated by means of regression and student's t-test. A difference between groups was considered significant if the P value was <0.05.

RESULTS

A. Diagnostic procedures and screening method

From the present study, of the 198 women screened, maternal serum AFP level was measured in 198 and in 14 serial measurements were carried out. Of the 28 cases that had undergone ultrasonography, twenty-two were normal, two multiple pregnancies, one polyhydramnios, one threatened abortion, one missed abortion, and one was suspected as a meningomyelocele or teratoma, later confirmed as a teratoma of tongue by autopsy.

Using the median value obtained from the study, the standard values were established according to each gestational week, 20 cases (10.1%) had the values above 2.0 MOM, 7 cases (3.5%) were below 0.25 MOM.

Amniocentesis was performed in 18 cases in which AFP levels of amniotic fluid were all within the normal ranges. All 9 cases of amnitoic fluid cell culture were diploid in karyotype; 6 cases (66.7%) were 46, XY and 3 other cases (33.3%) were 46, XX (Table 1).

B. Maternal serum and amniotic fluid AFP level

Normal levels of maternal serum AFP were measured during the periods between 9 and 34 weeks gestation except in two cases of twin pregnancies and one case each of missed abortion, threatened abortion and teratoma of tongue.

Maternal serum AFP level showed an increasing trend from 12 weeks gestation reaching a peak level

Table 1. Diagnostic procedures and screening method

	Number	Percent
Cases with MS AFP screended once	198	
serially	14	
Cases with MS AFP above 2.0 MOM first time	20	10.1
second time	2	
Cases with MS AFP below 0.25 MOM	7	3.5
Cases with AF AFP screened	18	9.1
Ultrasonographic evaluation	28	14.1
Normal	22	
Abnormal	6	
Fetal karyotyping	9	4.5
46 XY	6	
46 XY	3	
Total pregnancy screened	198	100

Table 2. Concentrations of maternal serum AFP during pregnancy

Gestational weeks	N	Median (IU/ml)	2.0 MoM (IU/ml)	2.5 MoM (IU/ml)	0.25 MoM (IU/ml)	Range (IU/ml)
9	1	16.0	32.0	40.0	4.0	16.0
10	4	4.5	9.0	11.3	1.1	4.0- 29.0
11	2	5.0	10.0	12.5	1.3	4.0- 6.0
12	11	10.0	20.5	25.6	2.6	3.0- 27.0
13	10	17.0	34.0	42.5	4.3	3.0- 24.0
14	14	21.5	43.0	53.8	5.4	3.0-115.0
15	16	23.5	47.0	58.8	5.9	10.0- 50.0
16	17	31.0	62.0	77.5	7.8	13.0- 82.0
17	12	37.5	75.0	93.8	9.4	19.0- 72.0
18	17	32.5	64.5	80.6	8.1	10.0-115.0
19	7	60.0	120.0	150.0	15.0	18.0-156.0
20	8	67.5	135.0	168.8	16.9	27.0-185.0
21	8	57.5	115.0	143.8	14.4	21.0-190.0
22	13	88.7	177.5	221.9	22.2	4.0-250.0
23	5	77.0	154.0	192.5	19.3	42.0- 98.0
24	15	115.0	230.0	287.5	28.8	36.0-230.0
25	11	80.0	160.0	200.0	20.0	16.0-230.0
26	3	156.0	312.0	390.0	39.0	113.0-165.0
27	6	185.0	370.0	462.5	46.3	105.0-223.0
28	3	183.0	366.0	457.5	45.8	125.0-198.0
29	1	200.0	400.0	500.0	50.0	200.0
30	1	86.0	172.0	215.0	21.5	86.0
31	1	148.0	296.0	370.0	37.0	148.0
34	1	175.0	350.0	437.5	43.8	175.0
Total	187					

* N: Number, MoM: Reference to Multiple of Median

Table 3. Concentrations of amniotic fluid AFP during pregnancy

Weeks	N	Median (IU/ml)	2.0 MoM (IU/ml)	2.5 MoM (IU/ml)	0.25 MoM (IU/ml)	Range (IU/ml)
16	3	12322.0	24644.0	30805.0	308.1	8980-30300
17	2	21917.0	43834.0	54792.5	547.9	13130-21917
18	3	16614.5	33229.0	41536.3	415.3	16261-23230
19	1	11514.0	23028.0	28785.0	287.8	
22	1	11918.0	23836.0	29795.0	297.9	
24	2	16564.0	33128.0	41410.0	414.1	
27	1	4192.0	8384.0	10480.0	104.8	
28	1	3788.0	7576.0	9470.0	947.0	
31	1	4545.0	9090.0	11362.5	113.6	
33	1	808.0	1616.0	2020.0	202.0	
34	1	657.0	1314.0	1642.5	164.3	
41	1	303.0	606.0	757.5	75.8	
Total	18					

* N: Number, MoM: Reference to Multiple of Median

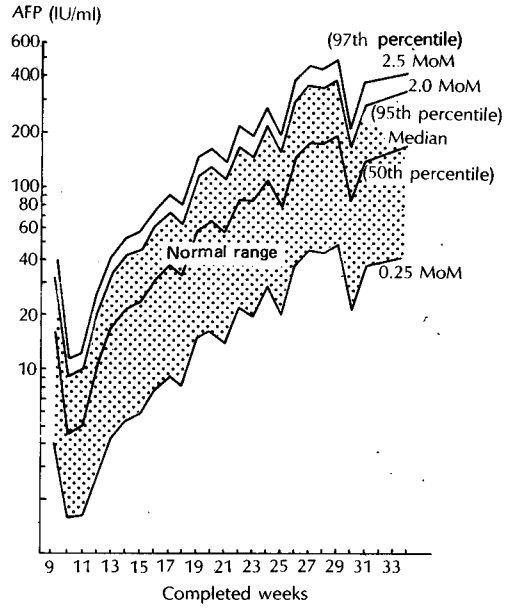

Fig. 1. Normal range for maternal serum AFP (9-34 weeks).

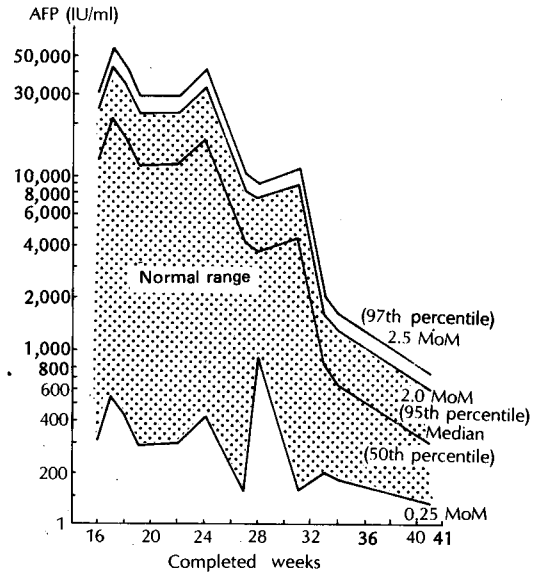

Fig. 2. Normal range for amniotic fluid AFP (16-41 weeks)

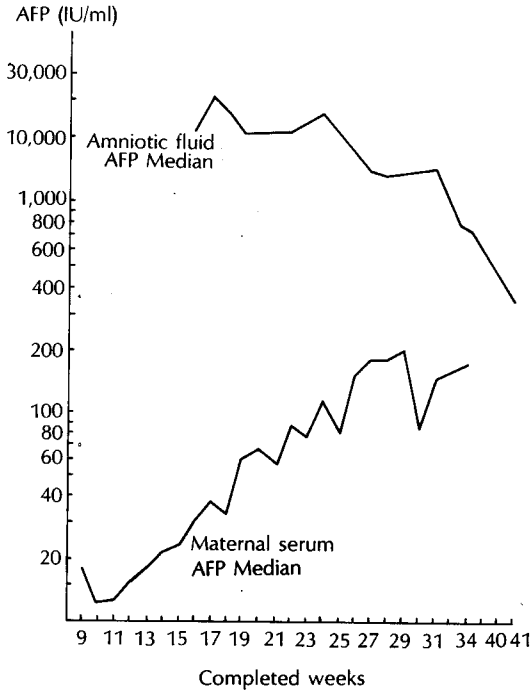

Fig. 3. Correlation between maternal serum AFP and amniotic fluid AFP median level (9-41 weeks)

at 29 to 34 weeks gestation, and after which there was a gradual decline (Table 2, Fig. 1). AFP levels of amniotic fluid were measured between 16 and 41 weeks gestation. The results of this study indicated that the level was the highest at 17 weeks gestation and declined as the pregnancy approached term (Table 3, Fig. 2). The correlation of a median value between amniotic fluid AFP and maternal serum AFP was 100 to 1 in ratio in each week (Fig 3).

Table 4. Levels of AFP in maternal serum & amniotic fluid in relation to obstetric parameter

Parameters	No.	Serum AFP (IU/ml)	No.	Amniotic Fluid AFP (IU/ml)
Parity				
Primiparous	101	64.7±62.6	5	11180.8±12305.8
Multiparous	88	62.6±57.4	13	11586.2±7190.8
Sex of fetus				
Male	28	82.2±66.4	6	13879.2±9769.6
Female	18	125.4±72.5*	3	3013.3±2353.8

Values refer to Mean±S.D.
*P<0.05 compared to male

Table 5. Comparative analysis between screening method & pregnancy outcome

Case	Gestation weeks	Age	Parity	Past history & Clinical finding	Serum AFP (IU/ml)	Amniotic fluid AFP (IU/ml)	Sonogram	Karyo type	Pregnancy outcome
1	16	32	1	1st baby; Down's syndrome	82 >2.5 MoM	8989	WNL	46 XX	Follow up
2	16	39	3	3rd baby; Down's syndrome	60 >2.5 MoM	12322	WNL	46 XY	Follow up
3	16	22	0	Threatened abortion	21	30300	Threatened abortion		Midtrimester termination male, 0.5 Kg
4	17	41	3		19	21917	WNL	46 XY	
5	17	29	2			13130	WNL	46 XY	Follow up
6	18	31	2		24	16261	WNL	46 XY	Follow up
7	18	30	2			23230	WNL	46 XY	Follow up
8	18	29	2	1st baby; Cleft palate 2nd baby; Ptosis of eye	24	16968	WNL	46 XY	Follow up
9	19	31	2	1st baby; Hemophilia 2nd baby; Hemophilia (1st; male, 2nd; male)	156 >2.0 MoM	11514	WNL	46 XY	Follow up
10	22	27	1	Preterm labor	4 <0.25 MoM	11918			Spontaneous vaginal delivery male, 0.4 Kg
11	24	27	0	Preterm labor	195	16564			Spontaneous vaginal delivery male, 0.8 Kg
12	24	25	1	Preterm labor		4444			Breech delivery male, 0.8 Kg
13	27	29	0	Preterm labor	223	4192			Spontaneous vaginal delivery female, 1.0 Kg
14	28	29	0	Intrauterine fetal death	126	3788			Spontaneous vaginal delivery male, 1.4 Kg
15	28	21	0	Congenital anomaly of fetus	2200 >2.5 MoM		R/o Meningomyelocele, teratoma		Cesarean section female, 1.2 Kg Teratoma of tongue
16	31	25	0	Preterm labor	148	4545			Spontaneous vaginal delivery female, 1.8 Kg
17	33	31	0	Rh negative sensitized mother	29 weeks; 200, 33 weeks; 808 34 weeks; 175, 34 weeks; 657		WNL		Cesarean section female, 2.6 Kg
18	41	36	0			303			female, 2.5 Kg

Table 6. Comparative analysis between abnormal serum AFP level and pregnancy outcome

Case	Gestation weeks for Serum AFP (weeks)	Age	Parity	Serum AFP (IU/ml)	Mode of delivery	Pregnancy Outcome
A. Group	(>2.0 MoM)					
1	12	39	0	27	C/S	normal male, 2.6 Kg
2	14	25	0	115	C/S	normal male, 3.3 Kg
3	14	30	1	58	S.V.D.	normal female, 0.7 Kg
4	16	30	0	63	V.E.	normal male, 3.3 Kg
5	17	28	1	65	C/S	normal male, 3.2 Kg
6	18	37	4	18 weeks; 115 19 weeks; 130	Midtrimester termination	
7	22	27	0	250	N.S.V.D.	normal female, 3.6 Kg
8	24	24	0	230	N.S.V.D.	normal female, 3.0 Kg
9	28	21	0	2200	C/S	abnormal female, 1.2 Kg Teratoma of tongue
B. Group	(<0.25 MoM)					
1	22	27	1	4	S.V.D.	normal male, 0.4 Kg
2	25	26	0	16	N.S.V.D.	normal male, 3.0 Kg

C/S = Cesarean section
S.V.D. = Spontaneous vaginal delivery
V.E. = Vaccum extraction
N.S.V.D. = Normal spontaneous vaginal delivery

C. AFP level in relation to obstetric parameters

The mean maternal serum AFP values for primigradiva and multigravida were 64.7 ± 62.6 IU/ml and 62.6 ± 57.4 IU/ml ($p>0.05$), respectively and the mean amniotic fluid AFP values in each group were 11,180.8 ± 12,305.8 IU/ml and 11,586.2 ± 7,190.8 IU/ml ($p>0.05$), respectively; no significant difference between the two groups was observed. The mean maternal serum AFP levels in mothers who had given birth to male and female infants were 82.2 ± 66.4 IU/ml and 125.4 ± 72.5 IU/ml respectively and the difference between the two was statistically significant ($p<0.05$). The mean AFP levels of the amniotic fluid with respect to male and female infants were 13,879.2 ± 9,769.6 IU/ml and 3,013.3 ± 2,353.8 IU/ml each and the difference was not satistically significant ($p>0.05$) (Table 4).

D. Comparative analysis between screening method and pregnancy management.

Of the 18 cases, the cases 1 and 2 each showed a past history of Down syndrome and the maternal serum AFP level was 2.5 times above the normal; however, there was no notable congenital anomalies detected under ultrasonographic examination. In both cases, the results of chromosome study were normal with 46, XX and 46, XY, respectively. In the case 9 with the past history of having 2 offsprings with hemophilia, the maternal serum AFP level was twice above the normal level, no signs of congenital anomaly under ultrasonography were seen, and karyotype was 46, XY. In the case 15, which had no specific past or family history of congenital malformation and in which the patient was primigravid at 28 weeks gestation, the maternal serum AFP level was elevated 4.5 times above normal. Ultrasonography subsequently revealed a congenital anomaly: the baby delivered by a cesarean section was 1.2 kg female with cystic teratoma of tongue and died immediately after birth (Table 5).

E. Pregnancy outcomes of normal and abnormal group

In the normal group which was followed up until delivery the average body weight of the infants was 3.9 kg and the average Apgar Score at 1- and 5-minutes were 8.2, and 9.8 respectively. In the abnormal group, of the 9 cases with high AFP values, one case with teratoma of tongue was delivered, and aneuploid fetus was observed in neither of the 2 cases with low AFP values (Table 6).

DISCUSSION

AFP is a glycoprotein with a molecular weight of 65,000 and is structurally related to serum albumin containing 3 to 4 percent of carbohydrate and half life of 4 to 5 days, and is normally present at a very low concentration up to 7 IU/ml (10ng/ml) in healthy person (Pedersen *et al.* 1975).

After Bergstrand and Czar's (1956) first report on a specific substance in the fetal blood during early pregnancy, Giltin and Boesman (1966) named it "alpha-fetoprotein" and Seppala and Ruoslahti (1972) documented the changes in the levels of AFP in maternal serum with progression of gestation in normal pregnant women. Brock and Sutcliffe (1972) were first to report on the elevated AFP levels in the amniotic fluid in pregnancies associated with anencephaly, spina bifida, and many researchers came up with the similiar findings in meningocele and several other congenital anomalies (UK Collaborative study 1977; Klejer *et al.* 1978).

To date, a number of fetal malformations other than neural tube defect have been identified which were associated with elevated maternal serum and amniotic fluid AFP levels; these include open neural tube defects (anencephaly, meningomyelocele, meningocele, encephalocele, and open spina bifida), congenital nephrosis, bladder neck obstruction, esophageal and duodenal atresia, exomphalos, sacrococcygeal teratoma, pilonidal sinus, Turner syndrome, Potter syndrome (renal agenesis), fetal death, fetomaternal hemorrhage, some low birth-weight fetuses, abdominal pregnancy (Prichard *et al.* 1985).

AFP levels in amniotic fluid, used for prenatal detection of neural tube defect and other geneticall-ly linked diseases, are measured and performed through amniocentesis. Amniocentesis is considered somewhat hazardous to mother and fetus alike, and therefore a simpler and safer means of measuring maternal serum AFP level, known to also increase in neural tube defects, is more commonly being used for screening tests. It is now speculated that the use of ultrasonography in conjunction with maternal serum and amniotic fluid AFP assay in the early detection of congenital anomaly would make a great contribution in the actual clinical settings, mainly because of the limited value of ultrasonography in early detection of congenital malformation of fetus, AFP assay has been accepted and would be more widely so as a more adequate and better applicable method in midtrimester of pregnancy (Milunsky 1980).

The methods of AFP level measurements include immunodiffusion, immunofluorescence, electrophoresis, immunoelectrophoresis, hemagglutin inhibition test, and complement fixation test. A recent quantitative method is solid phase enzyme immunoassay (ELISA) in which antiserum against AFP and peroxidase as conjugate is used in the antigen-antibody reaction between maternal serum and amniotic fluid (Seppala and Ruoslahti 1972).

Of the babies with congenital anomalies who were delivered at our institute between 1979 and 1986, neural tube defects numbered 35 among a total of 16,441 births showing an incidence of 0.21%, similiar to that reported by Macri and Weiss (1982) of 0.20% in U.S.A.

Since prenatal AFP screening of pregnancy populations for the detection of genetic disorders is the first of its kind in Korea, and the value of AFP has not been established in Korea, AFP screening would play a positive role in the detection of fetal anomalies during the pregancy in this country.

AFP is first produced in the embryonal yolk sac during the initial 4 weeks gestation, and is produced almost exclusively in the fetal liver during fetal development after involution of the yolk sac. It is however also produced in small amounts in the gastrointestinal tract and a minute amount is known to be produced in fetal kidney and placenta (Weiss *et al.* 1976). Fetal serum AFP level at 6 weeks gestation reaches approximately 66 μg/ml (44,000 IU/ml), its level peaks to 3,000 μg/ml (2,000,000 IU/ml) at 12-14 weeks gestation, after which it declines to a level of 100 μg/ml (66,667 IU/ml) at full term, and at birth its level is usually at 13-86 μg/ml (8,667-57,333 IU/ml). The total amount of AFP produced in the fetal liver reaches its peak at 20 weeks and is maintained until 32 weeks gestation after which it declined. The lack of proportional increase in fetal serum AFP level with the fetal AFP production is due to a sudden or rapid growth in fetal size and the increase in body fluid in the fetus during the early midtrimester. The reason for the decline in AFP production in the fetal liver with progression of gestation from the mid to late gestational period is not clearly defined, but it is probable that the fetal liver produces AFP only when certain subpopulation of liver cells mature (Adinolfi *et al.* 1978).

AFP is transferred from fetal to maternal circulation across the fetal membranes or via fetal urine to amniotic fluid and then across the placental barrier. Maternal serum AFP level slowly starts to increase over the nonpregnant level when the fetal serum AFP level reaches its maximum after 14 weeks gestation, and it is at its peak with 450 ng/ml (300 IU/ml) at 32 weeks gestation at which time fetal serum AFP level reaches 200,000 ng/ml (133,333 IU/ml) that is a 400

fold increase. After this period as pregnancy advances to its term, the maternal serum AFP level shows a gradual decline. Our study results showed an increasing trend from 12 weeks gestation attaining a peak level at 29 to 34 weeks gestation, and then there was a gradual decline similiar to the other report (Davenport and Macri 1983).

Fetal urine is the most important source of fetal AFP secreted in amniotic fluid. AFP level of amniotic fluid also reaches its peak level of 32 μg/ml (up to 23,000 IU/ml) at 14 weeks gestation at which fetal serum AFP level reaches the peak and gradually declines as pregnancy nears term (Milunsky 1980). Our current study showed the high amniotic fluid AFP level of 21,917 IU/ml at 17 weeks gestation. During 16-18 weeks gestation, the overall levels showed a similarity with the normal values reported by Kleijer *et al.* (1978) in normal pregnant women. The amniotic fluid AFP levels fall exponentially throughout pregnancy in parallel with the fall in fetal serum AFP levels. During the 19-24 weeks gestation, our results showed a gradual decline and at 27 weeks gestation, there was a rapid decline in AFP level in the amniotic fluid, as the pregnancy approached term, which was in agreement with other researchers (Weiss *et al.* 1976; Kleijer *et al.* 1978; Allen *et al.* 1982). The concentration gradient between AFP level of amniotic fluid and maternal serum in pregnant women showed a similiar trend in this study 100 to 1 in ratio as the report by Habib (1977).

Sowers *et al.* (1983) reported that the mean maternal serum AFP level is significantly higher for the male fetus than the female fetus. Our study showed on the contrary that the mean maternal serum AFP level is significantly higher in female fetus than in the male counterpart ($P<0.05$). Apparent cause for these observation, however remains undetermined.

Prenatal detection of neural tube defects, in the cases where the malformation is open or covered by only a thin membrane, is possible by determination of amniotic fluid AFP concentration by means of amniocentesis since it is believed that even in these cases AFP is secreted through the fetal membrane, or meninges as transudate into amniotic fluid. In fetus, neural tube closes properly during the embryonal period at 27 days after fertilization, and however, if it fails to close then either at the cephalic or spinal cord level, anencephaly, spina bifida or meningomyelocele may result (Langman J 1981). According to Macri and Weiss (1982), if there were any congenital anomalies or defects in the fetus during pregnancy, the maternal serum AFP level increased at 16-24 weeks gestation, after which the level might decline, and it was possible to diagnose or detect anencephaly and spina bifida in 88% and 79% of cases respectively during 16-18 weeks gestation.

Because of the difficulties in the diagnosis of neural tube defects by the abdominal X-ray and ultrasonogram before 20 weeks gestation, Campbell (1977) advocated the measurement of AFP level in the amniotic fluid. It has been noted that the maternal serum AFP level significantly increased in multiple pregnancies, congenital nephrosis, and underestimated gestational period (Keilani *et al.* 1978; Macri and Weiss 1982).

Recently, Davis *et al.* (1985) reported that maternal serum AFP level significantly declined in fetal autosomal trisomies such as Down syndrome (trisomy 21), trisomy 13 and trisomy 18. The mechanism responsible for decreased production of AFP by trisomic fetuses is unknown but an explanation could be that of decreased production of AFP due to decreased fetal weight, maturational delay of liver development, and inactivation of the gene(s) for AFP synthesis in trisomic fetuses.

Elevated maternal serum AFP levels are associated with teratoma of ovary, and testis containing extraembryonic vitteline sac structures accounting for the AFP synthesis and a number of fetal teratomas including sacrococcygeal teratoma, pharyngeal teratoma all associated with elevated AFP level have been reported (Anderson *et al.* 1984; Fuhrmann and Weitzel 1985). This report documents a previously unreported fetal lesion, a cystic teratoma of tongue with elevated second trimester maternal serum AFP level.

Milunsky and Alpert (1976) reported that 3% of AFP levels were false positive and in this study, by defining false positive as those with the levels above 2.5 MOM who were delivered normal babies. Congenital anomalies of fetus were not observed in 7 cases (3.5%) with the values above 2.5 MOM and a teratoma of tongue was detected in the group with AFP values above 2.5 MOM. No chromosomal abnormalities were observed in the group with the values below 0.25 MOM. It is suspected that the minute amounts of fetal blood contaminating the sample have resulted in increased AFP levels. However, it was not possible to ascretain definitely the above suspicion because of the omission of the steps to detect such contamination in this study. For detection of such contamination, Kleihauer test is often employed but was not done in the amniotic fluid samples that were considered to have been grossly contaminated by naked eyes.

The risk rises precipitously in the families with a prior history of neural tube defect in either parents or siblings (Janerich and Piper 1978). In this study, one

case which had a history of anencephaly had the subsequent delivery of a normal baby.

Researchers have asserted that the AFP level in the amniotic fluid has the specificity for the diagnosis of neural tube defects, but acetylcholinesterase measurement in amniotic fluid should be used to decrease both the incidences of false positives and negatives by the AFP measurements (Chubb and Springell 1979; Milunsky and Sapirstein 1982). However, acetylcholinesterase measurement in ammiotic fluid had not been performed in this study.

It is concluded that ultrasonogram could be used in the detection of neural tube defects and congenital anomalies during the early periods of pregnancy, but it cannot be applied to all pregnant women. Therefore, the authors suggest that the maternal serum AFP level be first measured and, depending on its results, then the following methods of ultrasonogram, measurement of AFP and acetylcholinesterase in the amniotic fluid and chromosome analysis of amniotic fluid by amniocentesis be performed for better differential diagnosis of congenital malformations of fetus.

The authors consider that the use of the inexpensive and simple technique of maternal serum AFP measurements would help in the early detection of congenital anomalies and with this maiden experience with AFP in Korea, it indeed became plausible that prior to performing ultrasound or amniocentesis, matermal serum AFP assay should be recommended as a routine screening method and a guidline to the management, during the midtrimester of pregnancy especially in 14-22 weeks gestation. The preliminary determination of the median and the normal ranges of maternal serum and amniotic fluid AFP values by each gestational weeks in uncomplicated pregnant Korean women delivered of normal singleton would be valuable for prenatal screening of genetic disorders.

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