CORRELATION BETWEEN MATERNAL SERUM ALPHA - FETO PROTEIN AND ULTRASONOGRAPHY IN PREDICTION OF THE OUTCOME OF THREATENED ABORTION

Thesis Submitted

By

MAGED MICHAEL ISKANDER MICHAEL

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SUPERVISED

By

Prof. Dr. EL - SAYED EL - MAHGOUB

Dept. of Gynaecology & Obstetrics

Faculty of Medicine - Ain Shams University

Dr. ALI FARID MOHAMED ALI

Dept. of Gynaecology & Obstetrics

Faculty of Medicine - Ain Shams University

Dr. MONA MOHAMED ABAZA

Dept. of Clinical Pathology

Medical Research Institute - Alexandria University

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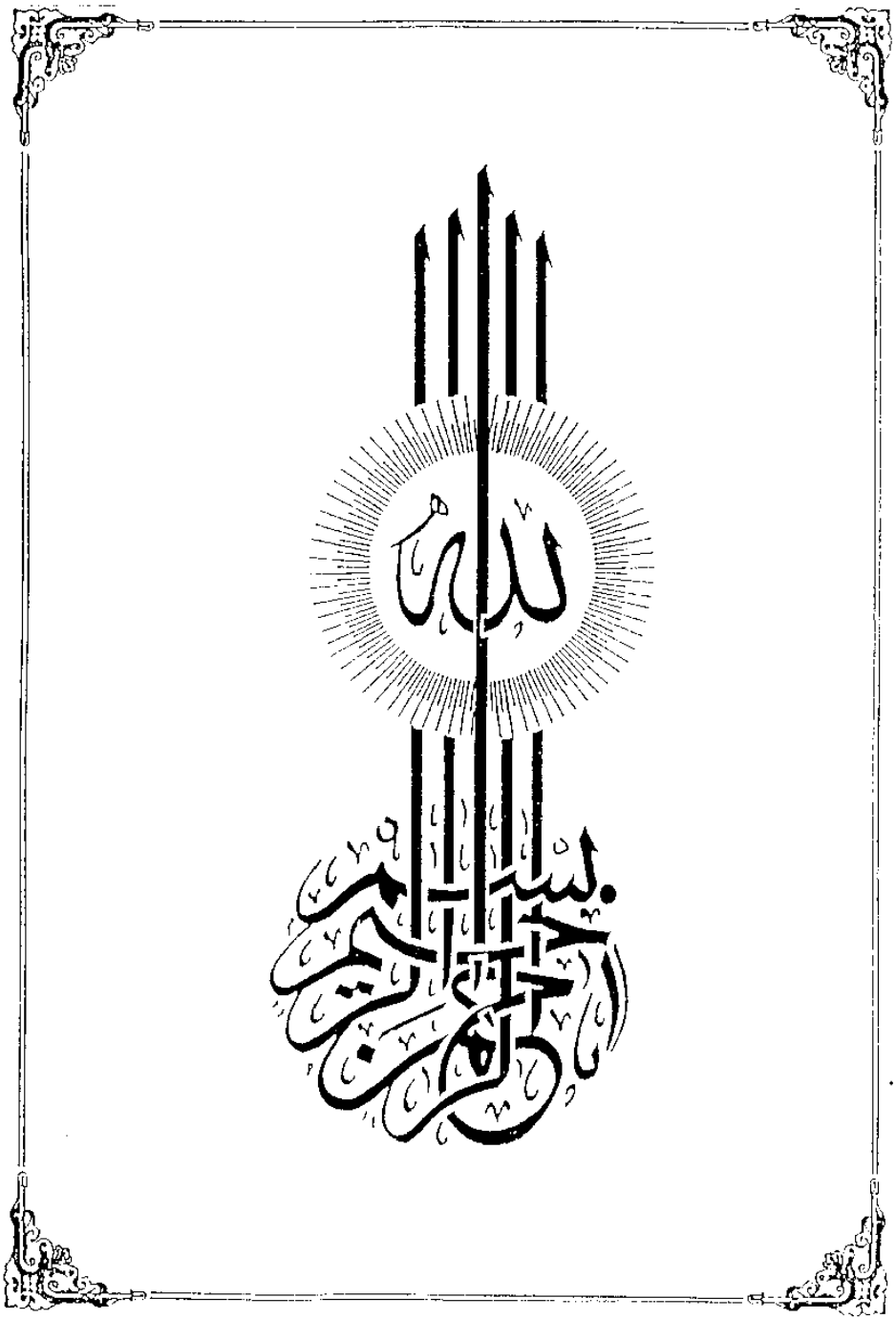

D E D I C A T I O N

TO MY FATHER & TO MY MOTHER ,

FOR THEIR EVERLASTING LOVE AND

ENCOURAGEMENT .

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I THE REVIEW OF ALPHA FETOPROTEIN :

I.1 Introduction & Historical Review :

Alpha - Fetoprotein (AFP) is one of the most througly characterized oncodevelopmental protein. A vast amount of work has been done since this protein was first observed by Bergstrand and Czar (1956) and brought into the lime light by the observation of Abelev and co-workers (Abelev et al., 1963) that AFP was associated with liver cancer.

AFP was first detected by paper electrophoresis of fetal serum (Bergstrand and Czar, 1956), the definition of AFP is still mainly immunochemical. It is detected, quantitated, and even purified using antibodies.

AFP is strongly immunogenic when injected into a foreign species but does not elicit an immune response in the species of origin (Nishi et al., 1972).

In the early work, antibodies to AFP were obtained by immunization with fetal serum followed by absorption of the

resultant antiserum with normal adult serum.

The concentration of AFP in fetal serum is in the range of mg/ml - according to gestation age - and gives rise to production of antibodies, even in an admixture with other fetal serum protein. In most species, AFP is the only fetal serum protein present in appreciable quantities which is not shared by the adult serum. So, elimination of antibodies to adult serum proteins by absorption leaves behind an antiserum which is operationally specific for AFP.

Such antisera react with a single immunodiffusion line against fetal and liver cancer serum and give no reaction against normal adult serum.

The use of purified protein for immunization has become the method of choice.

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I.2 Immunoassay of AFP in biological fluid :

A great variety of methods have been applied (Table I); immunodiffusion was the first method introduced for AFP detection (Abelev et al., 1963).

Since the development of radioimmunoassay for AFP (Ruoslahti and Seppala, 1971), this method has allowed the demonstration and quantitative estimation of AFP in normal human serum at a level of about 0.25 ng/ml and detects any small elevation from the normal level.

Practically, all radioimmunoassays applied to measurement of human AFP (Ruoslahti and Seppala, 1971; Waldmann and Mc Intire, 1972; Purves et al., 1973; Jonsson and Kronwall, 1974; and Leek and Chard, 1974) are based on the principle of competition between labeled antigen for a limited amount of antibody.

Table I

METHODS OF AFP MEASUREMENT

Method	Sensetivity	Reference for AFP estimation
Double diffusion	2.5-5 ug/ml	Abelev et al., I963.
Counter electrophoresis	0.25-0.5 ug/ml.	Smith , I97I .
Rocket immunoelectrophoresis	0.5-I ug/ml	Norgaard-Pedersen and Gaede , I975 .
Latex agglutination inhibition	250 ng/ml	Cahill et al., I974.
Immunoautoradiography	50 ng/ml	Abelev , I97I .
Radioimmunoelectrophoresis	20 ng/ml	Norgaard-Pedersen, I976.
ELISA	3 ng/ml	Belanger et al., I973; Masseyeff et al., I976.
Radioimmunoassay (RIA)	0.5 ng/ml	Ruoslahti and Seppala, I97I .

1.3 Sites of physiological AFP synthesis :

The synthesis of AFP by various fetal organs has been studied by incorporation of radioactivity from labeled amino acids to proteins in tissue culture with subsequent detection of radioactive AFP by antibodies.

The synthesis of AFP has been found to take place in the yolk sac, the fetal liver, and the gastrointestinal tract (Gitlin and Gitlin, 1975). In humans, AFP is first synthesized by the yolk sac and the liver and then predominantly by the liver.

Synthesis in the yolk sac has been demonstrated between the fifth and fourteenth weeks of gestation. It seems to cease as the yolk sac becomes involuted during the first part of the second trimester.

The liver contributes to the AFP synthesis from the fourth week onwards. In the second trimester of human pregnancy, the fetal liver is capable of producing AFP at a rate which reaches 30 mg/day (Kekomaki et al., 1971).

Minor amounts of AFP are being synthesized by other tissues in the gastrointestinal tract (Gitlin et al., 1972).

It is generally agreed that the placenta does not produce AFP to any significant degree, although, in some experiments, small amounts of labeled amino acid precursor were incorporated into AFP by this tissue.

Molar trophoblast (vesicular mole) appears sometimes to be able of producing AFP (Grudzinskas et al., 1977).

A high AFP concentration observed in the molar vesicle fluid obtained by needle aspiration. However, normal AFP levels in molar tissue have also been reported (Seppala et al., 1972).

Immunofluorescence shows that it is the hepatocytes, not the hematopoietic cells, that synthesize AFP in the fetal liver. Up to 80 % of the hepatocytes in fetal liver have been found to synthesize AFP (Abelev, 1979).

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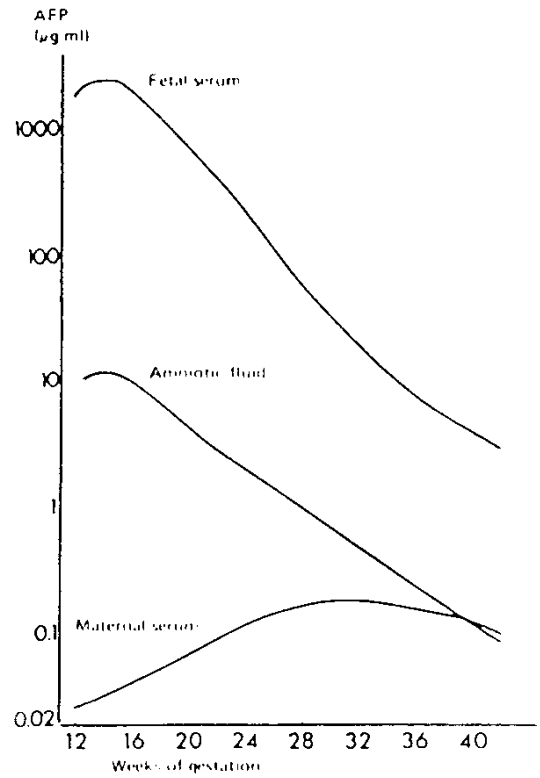
I.4 AFP in body fluids :

The main compartments of interest in terms of AFP concentrations are ; fetal serum , amniotic fluid , maternal serum , cerebrospinal fluid , and urine (Fig. I).



Average AFP levels in fetal serum, maternal serum, and amniotic fluid throughout gestation (Seppala, I977 ; Ruoslahti & Seppala, I979).

Figure I