



ORIGINAL ARTICLE

Study Relation Between α -fetoprotein with Repeated Abortion in Pregnant Women in the Iraqi Population

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ABSTRACT

Background: Alpha-fetoprotein was even a minor reason for the frequent abortion in the woman.

Objective: The study aimed to know the relationship between Alpha-fetoprotein infection and women who suffer from repeated abortion.

Methods: A sample from 115 women, in age between 20 to 05 years were enrolled in the current studies, and each patient and control blood samples were collected, and appreciation of IgG and IgM rate of Alpha-fetoprotein in serum of woman by enzyme-linked immune sorbent assay (ELISA) technique was done.

Results: By ELISA technique test, 7.8% Alpha-fetoprotein circulating level IgM and IgG antibody increasing showed results in the current study between the in woman's with repeated abortion history from total cases in three Iraqi cities. There is a relation between age and repeated abortion in most abortion cases in younger age between 15 to 45 years old and the abortion in pregnant women in the second period of gestation. The result shows there is no relation between abortion and area of life.

Conclusion: Alpha-fetoprotein is an important reason of repeated abortion in women. Alpha-fetoprotein increasing detecting by technique would be done during pregnancy.

INTRODUCTION

Many definitions of miscarriages are present in the true, but it is mostly used that miscarriages were the loosed before the pregnancy's end period.^{1,2} This viability duration would depend on the resource obtainable; numerous resource pauper settings mostly fetus deliver at pregnancy period 28 weeks or mostly survive. In the better-resourced parts of the world, fetuses weighing 500 g or more or a gestational age above 24 weeks can survive although they may be disabled.³ Sera for alpha-fetoprotein (AFP) maternal determination might have importance in this esteem.

The glycoprotein, membered of the albuminoid gene family, that AFP⁴ produces in the early period of fetal life through the liver and yolks sac and small amounts by the gastrointestinal tract.⁵ AFP has a biological half-life of about 5 to 6 days.⁶ The function of AFP during development and subsequently in the adult is largely unknown.⁷ AFP is known to be present in small quantities in normal adults.⁸ In pregnancy, high sera AFP concentrated happened through 12 to 14 weeks of pregnancy, and the produce of AFP begin reduced in the thirty-second week.⁹

Decreased AFP rate rapidly happened after birth, arrived to undetected rate after birth within many months.¹⁰ Level Sera

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AFP is effective through pregnancy age and maternal features, involving ethnic origin, maternal weighing, and smoke of a cigarette.¹¹ By the yolk sac and fetus liver, AFP developed firstly inside the amniotic fluid by fetus renal excreted, passage placental (possible through diffusion), and maternal circulating system come in.¹² The maternal sera can be detected in, so one of the most important characteristics measurement of HAFP level employed as a pregnancy period–dependent fetus disorder marker demonstrates an interest in screening neural tube defects.^{13,14}

The AFP plays a vital role in fetal erythropoiesis and neural tube development, the presence of a rapport between fetal erythropoiesis and AFP came as no abruptness ago the yolk sac and fetus liver comprise the main embryo/fetal position of together erythropoiesis and AFP synthesis¹⁵ also other studies showed a negative relationship of AFP sera rate or concentration immunoglobulin G (IgG) level of maternal.¹⁶ Pregnancy relation with hematologic disorders (anemias) diagnosis with AFP sera rate also had been utilized as an ancillary helped, placenta defect, fetus death, preterm labor and growing restricted/retardation.¹⁷ As tumor marker AFP is also used and was secretion through many carcinomas, therefore, immunosuppressive activities.¹⁸ Rise of AFP concentration may be observed in multiple pregnancies.¹⁹ While the low level is an indicator for a genetic disorder such as Down syndrome.²⁰

MATERIALS AND METHODS

Specimens Collection

A total of 115 women from three provinces in Iraq attended and blood samples were taken from them '25 samples from Martyr Muhammad Baqeri Al-Hakim hospital, Maternity Department in Baghdad city, 60 samples from Women's Hospital and obstetrics in Karbala city; and 30 samples from AL-Batool Hospital, Department of birth, in Dayle city. The sample between December 2020 and May 2021 were collected. They included 115 pregnant women with a history of repeated abortion and detected by ELISA automatic systems we recommended increasing washed steps from 3 to 5 and the size of washed liquid from 300 to 350 μ L to eschew washed effectiveness. Before commencing the test, the distributed and diagnosis policy to all samples and controls would be carefully determined on the resulting paper provided in the kit. Chosen the wanted number of microtiter wells or strips and introduced them into the handle.

Sample Dilution

All samples would be dilution 1+100 with IgG or IgM sample diluent before testing. Mixed 10 μ L sample with 1mL IgG or IgM sample diluent into tubes to get 1+100 diluted and thoroughly mixed with a vortex.

Procedure

The IgM and IgG antibody detected by ELISA methods and repeated after 14 days to confirm the result as a Biocompare company procedure.

Calculation

Measuring plot absorbance against (CAL) concentrated in a line-line graphed convenient intercalation of plotted measured point results in a calibrated curve. The analytic concentrated in the sample can be determined.

Analytic concentrated select an appropriate for calculated and validate curved fitting option (recommended point to point).

RESULTS AND DISCUSSION

52 samples were taken from woman with repeated abortion history in three Iraqi cities Karbala, Baghdad, Diyala. The samples were transported to Karbala gynecology hospital to make an ELISA test, and the results were as follows. Venous blood five ml were collected from each pregnant woman, and blood was transferred to plain tube and for one hour at room temperature for clot formation left to sample. For 10 minutes tube was centrifuged. The serum was stored at -20°C until used. ELISA for the diagnosis of Alpha-fetoprotein IgG/IgM, the test was done according to the company.

The result is shown in **Table 1** infection 7.8% by Alpha-fetoprotein in three Iraqi cities Karbala, Baghdad, and Diyala in arrangement, also shown 5% in Karbala, 4% in Baghdad, and 16.6 % in Diyala. The test is done by detecting IgG and IgM antibodies in the blood of women with a history of repeated abortion.

The result is shown in **Table 2** infection 7.8% by Alpha-fetoprotein in three Iraqi cities Karbala, Baghdad, and Diyala in arrangement, also shown 5% in Karbala, 4% in Baghdad, and 16.6 % in Diyala. The test was done after 14 days from the first test by detection of IgG and IgM antibodies in the blood of women with a history of repeated abortion.

Table 3 shows that the most age period of women infected with Alpha-fetoprotein from 15 to 50 years old, the patient with age (15–25) have one positive infection with percentage 16.6% and then age between (45-50) with percentage 11.7%

Table 1: Percentage of infection by *Alpha-fetoprotein* in three Iraqi cities.

Cities	No. of samples	P(+ve)		N(-ve)		Per%
		IgG	IgM	IgG	IgM	
Karbala	60	2	1	58	59	5
Baghdad	25	1	0	24	25	4
Diyala	30	3	2	27	28	16.6
Total	115	9		106		7.8

The normal value IgG and IgM reference interval for AFP in serum of pregnant women are dependent on the gestational week and shows regional differences. Typical values for the median is as indicated

Gestational week	IgG Median of AFP	IgM Median of AFP
16	33.4 ng/mL	24.6 ng/mL
17	37.5ng/mL	31.5 ng/mL
18	44.8 ng /mL	40.1 ng/mL
19	50.8 ng/mL	52.6 ng/mL
20	58.1 ng/mL	59.3 ng/mL
21	68.2 ng/mL	67.9 ng/mL

because of the number of patient in age, then age between (25–35) and the last age (35–45) with percent 5.7, 3.5% in the arrangement.

The result in **Table 4** shows the relation between infection with Alpha-fetoprotein and the gestation period, so the most abortion in the second period of gestation with a percentage 15%, less affected in the first period and there is no relation with the last period of gestation of pregnancy.

Table 5 shows there is a relation between Alpha-fetoprotein infection and geographical area through the percentage 36.3% Nahr Ibrahim, and there is no relation Alkhalis area in Diyala. In the Alshuela area in Baghdad, there is no relation with the geographical area. The Kerbala city the infection in two areas easkari district, Al eamil district this appear through result by percentage.

Table 6 shows congenital malformation appears in two Iraqi cities in Diyala city with neural defect tube (anencephaly) and placenta defect in Baghdad city. There is no congenital malformation in Kerbala city. Current research found and

according to the results showed in the tables above there six positive cases in the increasing of AFP, five cases in Diyala and one case in Baghdad, with two different congenital malformations.

In the first case, the miscarried fetus had anencephaly, neural tube defects type (NTD), the AFP rates were raised in mother blood. When a pregnant woman carries a fetal with open NTD, the high fetal concentration of Alpha-fetoprotein in the presence of opened NTD are released by the place medullo-vasculosa and through cerebrospinal fluid infiltrate into the amniotic liquid, thus causing high diffused into mother sera. Defects in the neural tube (NTDs) were between the more widespread and acute problems associated with the highest maternal serum alpha-fetoprotein (MSAFP) rats.²¹ The part of the developing embryo neural tube to development of the brain and spinal cord form. If the neural tube does not close correctly through the fourth week after pregnancy, congenital

Table 2: Percentage of infection by Alpha-fetoprotein in three Iraqi cities After 14 days from the first test.

Cites	No.of samples	P(+ve)		N(-ve)		Per%
		IgG	IgM	IgG	IgM	
Karbala	60	2	1	58	59	5
Baghdad	25	1	0	24	25	4
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19	50.8ng/mL	52.6ng /mL
20	58.1ng	59.3ng/mL
21	68.2ng/mL	67.9ng/mL

Table 3: Relationship between Age and number of infections with Alpha-fetoprotein

Age of patients.	No.of samples	P(+ve)	N(-ve)	Per%
15-25	18	3	15	16.6
25-35	52	3	49	5.7
35-45	28	1	27	3.5
45-50	17	2	15	11.7
Total	115	9	106	7.8

Table 4: Relation of Alpha-fetoprotein infection and the period of gestation.

Gestation period	No. of abortion	Positive	Negative	Percentage%
First gestation period	60	3	60	5
Second gestation period	40	6	40	15
Third gestation period	15	0	15	0
Total	115	9	106	7.8

Table 5: Relation of Alpha-fetoprotein infection and area of life.

Region	City	No. of samples	P(+ve)	N(-ve)	Per%
Al easkari district	Karbala	3	1	2	33.3
Al eamil district	Karbala	6	1	5	16.6
Al antifada district	Karbala	1	0	1	0
Al sumud district	Karbala	1	0	1	0
Imam Ali district	Karbala	1	0	1	0
Al ghadir district	Karbala	1	0	1	0
Al muazafin district	Karbala	1	0	1	0
Al hur district	Karbala	3	1	2	33.3
Al markazia	Karbala	1	0	1	0
Al binaa aljahiz	Karbala	1	0	1	0
Almuemalajiu	Karbala	1	0	1	0
Alnasr district	Karbala	4	0	4	0
Aleabassia	Karbala	1	0	1	0
Alatarat	Karbala	1	0	1	0
Alsalam district	Karbala	1	0	1	0
Majamea aldura	Karbala	1	0	1	0
Al askan	Karbala	1	0	1	0
Al shuela	Baghdad	6	1	5	16.6
Sukuk district	Baghdad	3	0	3	0
Um najim district	Baghdad	2	0	2	0
Nahr abraham	Daily	11	4	7	36.3
Alkalis	Daily	1	1	0	100
Total		115	9	106	7.8

Table 6: Relation of Alpha-fetoprotein infection with presence of congenital malformation.

City	Positive	Presence of congenital malformation	Malformation type	Per%
Karbala	3	0		0
Baghdad	1	1	placenta defect	100
Diyala	5	5	Anencephaly	100
Total	9	6		66.6

disability like anencephaly might result. Approximately 2,500 fetuses are born each year with congenital disabilities.^{22,23}

While the second patient was suffering from the endocrine disorder, activity estrogen-binding of AFP was pivotal important be caused of ability might represent an important regulated mechanism through embryonic growth, Alpha-fetoprotein might be implicated in regulated of concentrations of active, free, the shape of hormones in vivo.²⁴ This may be protected fetus tissues from circulated maternal estrogens and prevention degraded of hormone molecules.²⁵

In the third case, the patient the level of AFP was also found to increase. The mother had a placenta defect. During pregnancy, placental septa are important. Any pathological alterations of the septa will change the transport of substances among the mother and the fetus to cause placental dysfunction. Women's with rising MS-AFP, result to potential placenta septa dysfunction normal utilized cured dose or pollution in environment that caused fetus can endure many caused for the pathogenic intrauterine exposition of the fetus.²⁶⁻²⁷

Bredaki *et al.* proposed that the reasoned 2^{ed} trimester Alpha-fetoprotein might be increased in integration with a normal created fetal could be attributed majorly to modified in the placental which had the possession of responses to a negative effect of the environment through raised surface exchanged.²⁸ The explanted for the relation between increased mother sera alpha-fetoprotein and reversed pregnancy result is not obvious, but is probable a sign of placenta dysfunction, involving partial placenta discontinuity, abnormal implantation and fetomaternal bleeding.^{29,30}

This is consistent with Karolina Barkute, Dalia Balsyte, Josef Wisser, and Juozas Kurmanavicius' research results. [Raised level of the maternal serum AFP occurred in abortion, were no fetal defects] what was found by Markku Seppala and Erkki Ruoslahti in their research, which contradict our results.

REFERENCES

1. Silver RM, Branch DW, Goldenberg R, *et al.* Nomenclature for pregnancy outcomes: time for a change. *Obstet Gynecol* 2011; 118:1402–8.
2. Farquharson RG, Jauniaux E, Exalto N. Updated and revised nomenclature for description of early pregnancy events. *Hum Reprod* 2005; 20:3008–3011.
3. Royal College of Obstetricians and Gynaecologists (RCOG). The management of early pregnancy loss. Green-top guideline no. 25. London: RCOG, 2006.
4. Sturgeon CM, Duffy MJ, Stenman UH, *et al.* National Academy of Clinical Biochemistry laboratory medicine practice guidelines for use of tumor marker in testicular, prostate, colorectal, breast and ovarian cancer. *Clin Chem* 2008 Dec; 54(12): e11-79.
5. Spaggiari E, Ruas M, Dreux S, Valat AS, Czerkiewicz I, Guimiot F, *et al.* Management strategy in pregnancies with elevated second-trimester maternal serum alpha-fetoprotein based on a second assay. *Am J Obstet Gynecol* 2013; 208:303. e1-7.
6. Beta, J.B.F., Rodriguez, J., Akolekar, R. and Nicolaides, K. Maternal serum alpha-fetoprotein at 11 - 13 weeks' gestation in spontaneous early preterm delivery. *Fetal Diagnosis and Therapy*. 2011; 30, 88-93.
7. Yefet E, Kuzmin O, Schwartz N, Basson F, Nachum Z. Predictive value of second-trimester biomarkers and maternal features for adverse pregnancy outcomes. *Fetal Diagn Ther* 2017; 42:85–93.
8. Terentiev AA, Moldogazieva NT. Structural and functional mapping of alpha-fetoprotein. *Biochemistry (Mosc)*, 2006; 71: 120-132
9. Bredaki FE, Wright D, Akolekar R, Cruz G, Nicolaides KH. Maternal serum alpha-fetoprotein in normal pregnancy at 11–13 weeks' gestation. *Fetal Diagn Ther* 2011; 30: 274–279
10. Jarvis, G. J., and Johnson A. published online: Low circulating levels of alpha-fetoprotein and missed abortion, *Journal of Obstetrics and Gynaecology*, July 02 2009; Volume 1 (3): 151-152.
11. Huang T, Hoffman B, Meschino W, Kingdom J, Okun N. Prediction of adverse pregnancy outcomes by combinations of first and second trimester biochemistry markers used in the routine prenatal screening of Down syndrome. *Prenat Diagn* 2010; 30: 471–477
12. Richardson B. E., Hulka B. S., David Peck J. L, Hughes C. L., van den Berg B. J., Christianson Ft. E., and Calvin J. A. . levels of maternal serum alpha-fetoprotein(AFP) in pregnant women and subsequent breast cancer risk, *American Journal of Epidemiology*, 1998; (148): pages 719-727.
13. Mizejewski GJ. Levels of alpha-fetoprotein during pregnancy and early infancy in normal and disease states. *Obstet Gynecol Surv* 2003; 58: 804–826.
14. Rozenberg P, Bussieres L, Chevret S, Bernard JP, Malagrida L, Cuckle H, Chabry C, Durand-Zaleski I, Bidat L, Lacroix I, Moulis M, Roger M, Jacquemot MC, Bault JP, Boukobza P, Boccaro P, Vialard F, Giudicelli Y, Ville Y. Screening for Down syndrome using first trimester combined screening followed by second-trimester ultrasound examination in an unselected population. *Am J Obstet Gynecol* 2006; 195: 1379–1387.
15. Bartha JL, Comino-Delgado R, Arce F, Alba P, Brouillon JR, Barahona M. Relationship between alpha-fetoprotein and fetal, erythropoiesis. *J Reprod Med* 1999; 44:689–697.
16. Layde PM, von Allmen S D, and Oakley G P. Maternal serum alpha-fetoprotein screening: a cost-benefit analysis. *Jr, Published Online October 07, 2011.*
17. Rätty R., Virtanen A., Koskinen P., Anttila L., Forsström J., Laitinen P., Mörsky P., Tiitinen A., Ekblad U. Serum-free β -HCG and alpha-fetoprotein levels in IVF, ICSI and frozen embryo transfer pregnancies in maternal mid-trimester serum screening for Down's syndrome, *Human Reproduction*, , Volume 17, Feb. 2002; (2): 481–484, <https://doi.org/10.1093/humrep/17.2.481>
18. Fettke. F., Schumacher.A., Canellada.A., Toledo.N., Bekeredjian-Ding.I, Bond.A., Wuhler.M., Dan Costa.S.,and Claudia Zenclussen. A. Maternal and Fetal Mechanisms of B Cell Regulation during Pregnancy: Human Chorionic Gonadotropin Stimulates B Cells to Produce IL-10 While Alpha-Fetoprotein Drives Them into Apoptosis. *Frontiers in Immunology*. 2016; 495.1-13
19. Gerald J. M., Physiology of Alpha-Fetoprotein as a Biomarker for Perinatal Distress: Relevance to Adverse Pregnancy Outcome, First Published September 01, 2007; <https://doi.org/10.3181/0612-MR-291>
20. BREAKING F. E., SCIORIO C., WRIGHT A., WRIGHT D. and NICOLAIDES K. H. Serum alpha-fetoprotein in the three trimesters, of pregnancy, Wiley Online Library, May 25 2015; 46: 34–41.
21. Wilson RD; SOGC Genetics Committee, Wilson RD, Audibert F, Brock JA, Campagnolo C, Carroll J, *et al.* Prenatal screening, diagnosis, and pregnancy management of fetal neural tube defects. *J Obstet Gynaecol Can.* 2014; 36:927–39.
22. Yu MY, Xi L, Zhang XJ, Zhang SC. Possible connection between elevated serum alpha-fetoprotein and placental necrosis during pregnancy: a case report and review of literature. *World J Clin Cases* 2018; 6:675–8.9.
23. Bartha JL, Illanes S, González-Bugatto F, Abdel-Fattah SA, Mizejewski GJ, Soothill PW. Maternal serum transformed alpha-fetoprotein levels in women, with intrauterine growth retardation. *Fetal Diagn Ther.* 2007; 22:294–8.
24. Tentievna. alpha-fetoprotein; A renaissance, article in tumor biology, pirogov Russian Research Medical University. June 2013; 34(4): 34:2075-2091.
25. Atemezem A, Mbemba E, Marfaing R, Vaysse J, Pontet M, Saffar, L, *et al.* Human alpha-fetoprotein binds to primary macrophages, Immunosuppressive activity, *Biochem Biophys Res Commun.*, 2002; 296:507.
26. Tian X, Zhu M, Du L, Wang J, Fan Z, Liu J, *et al.* Intrauterine inflammation, increases materno-fetal transfer of gold nanoparticles in a size-dependent manner in murine pregnancy. *Small* 2013; 9:2432e9.

27. Bredaki FE, Sciorio C, Wright A, Wright D, Nicolaides KH. Serum alpha-fetoprotein in the three trimesters of pregnancy: effects of maternal characteristics and medical history. *Ultrasound Obstet Gynecol* 2015; 46:34-41.
28. Miranda J, Triunfo S, Rodriguez-Lopez M, Sairanen M, Kouru H, ParraSaavedra M, et al. Performance of third-trimester combined screening model for prediction of adverse perinatal outcome, 50; 2017. p. 353-60
29. Mc Pherson, E., Thomas, G., Mallick, C., Zaleski, C., Reynolds, K., Rasmussen, K. *et al.* Extreme values of maternal serum analytes in second trimester screening. Looking beyond trisomy and NTD's. *Journal of Genetic Counselling*. 2011; 4: 34-47.
30. Bartkute, Karolina; Balsyte, Dalia; Wisser, Josef; Kurmanavicius, Juozas. Pregnancy outcomes regarding maternal serum AFP value in second trimester screening. *Journal of Perinatal Medicine*. 2017; 45(7):817-820. DOI: <https://doi.org/10.1515/jpm-2016-0101>