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Amniotic Fluid and Maternal Lipid Profiles and Pregnancy Outcomes: Is There any Relationship?

Sedigheh Borna[1], Nasim Khorami[1], Azin Ghamari[2], Fahimeh Ghotbizadeh Vahdani[1]*

1. *Maternal-Fetal and Neonatal Research Center, Tehran University of Medical Sciences, Tehran, Iran*
2. *Growth and Development Research Center, Children Medical Center of Excellence, Tehran University of Medical Sciences, Tehran, Iran*

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Corresponding Information:
Fahimeh Ghotbizadeh Vahdani, Maternal-Fetal and Neonatal Research Center, Tehran University of Medical Sciences, Tehran, Iran
Email: Fghotbi@yahoo.com
Tel: 09123973373

ABSTRACT

Background & Objective: This prospective study aimed to determine the relationship between maternal and amniotic fluid (AF) lipid profiles in the second trimester with pregnancy outcomes.

Materials & Methods: One hundred-eighty singleton pregnant women, with a gestational age of 16-22 weeks, were enrolled in this study. All women underwent amniocentesis, and 2 mL of AF was investigated for AF lipid profile. Furthermore, the serum maternal lipid profile was evaluated simultaneously. All participants were followed up until the delivery, and postnatal outcomes were recorded.

Results: Mean maternal age and body mass index (BMI) of all participants were 5.8±33 years and 25.6±2.8 kg/m^2, respectively. Mean maternal estriol, cholesterol, and triglyceride levels, as well as mean cholesterol and triglyceride levels of AF, were significantly different between term and preterm; intrauterine growth retardation (IUGR) and non-intrauterine growth retardation (non-IUGR); and low birth weight and normal weight neonates (P<0.001). The AF cholesterol level was an independent predictor of term or preterm delivery, while the maternal estriol level was an independent predictor of IUGR or normal growth.

Conclusion: Maternal and amniotic fluid lipid profiles could be good indicatives of fetus growth.

Keywords: Amniotic fluid, Lipid profile, Pregnancy outcome

Introduction

As an essential component in all human cells, cholesterol is crucial for cell membrane fluidity, construction of the oxysterols, neurosteroids, glucocorticoids, mineralocorticoids, and sex hormones such as estrogen and testosterone **(1,2)**. Cholesterol plays an important role in the activation of Hedgehog proteins. These proteins activate and repress genes by transcription factors, and consequently they are essential for developing different organs in the fetus **(2,3)**. Therefore, a sufficient cholesterol level is vital for fetus development **(4)**.

Previous studies have indicated that there is a significant association between the maternal cholesterol level and fetal cholesterol collection **(5,6)**. Vuorio *et al.* found that plant sterol levels in cord blood samples were equal to 40-50% of those of maternal blood sample levels, which reflects active maternal-fetal sterol transport **(7)**. It is well established that there are low-density lipoprotein receptors in the amniotic fluid (AF) and lipoprotein lipase on the apical surface of the amniotic membrane **(8)**. By evaluating AF of one healthy fetus from the second trimester, Baardman *et al.* reported a lower level of cholesterol biosynthesis markers until the 19th week of gestation and rapid increase of cholesterol level after the 19th week **(2)**. They concluded that maternal lipid concentration, as an exogenous supply, has a crucial role in early fetal development. In this regard, all previous studies were cross-sectional studies, and postnatal outcomes were not investigated. The goal of this prospective study was to determine the relationship between maternal lipid profile and AF lipid profile in the second trimester with pregnancy outcomes.

Materials and Methods

This study was conducted as a prospective study in Imam Khomeini hospital complex, Tehran, Iran. One hundred-eighty singleton pregnant women, with a gestational age of 16-22 weeks, were enrolled in this study. Thirty-eight subjects were excluded from the study due to the loss of follow-up.

All women underwent amniocentesis due to the increased risk for aneuploidy or the increased maternal age in the second trimester. Abortion or rupture of membranes,

following the amniocentesis, presence of fetal syndromes, and loss to follow-up, were considered as the exclusion criteria.

During amniocentesis, 2 mL of AF samples were obtained and centrifuged for 10 min at 2000 rpm to remove cell materials and then stored at−20◦C. At the time of performing amniocentesis, venous samples of fasting mothers were collected for lipid profile analysis, and if the fasting interval was not enough, the lipid profile analysis was performed after 2-3 days following the enough fasting. All participants were followed-up until the delivery.

Data were recorded for all subjects regarding maternal age, body mass index (BMI), gestational hypertension (HTN), positive history of preeclamsia, gestational diabetes mellitus (GDM), mode of delivery, intrauterine growth retardation (IUGR), and low birth weight. IUGR was considered positive if it was confirmed by sequential ultra-sonographies. Birth weight below the 2,500 grams was considered as positive low birth weight.

Ethical Consideration

Informed consent was obtained from all participants. The study was approved by the institutional board review of Tehran University of Medical Sciences.

Statistical Analysis

All data were analyzed by using SPSS 22 (SPSS Inc., Chicago, Illinois, USA). All quantitative variables were expressed by mean ± standard deviation. The Student's t-test and chi-square test were applied for continuous and categorical variables assessment. The correlation coefficient calculated for continuous variables. By considering preterm birth, low birth weight, and IUGR as the dependent variables, logistic regression analysis was performed. P-value<0.05 was considered statistically significant.

Results

Mean maternal age and BMI of all participants were 33±5.8 years and 25.6±2.8 kg/m^2, respectively (Table 1). Twenty cases were positive for preterm labor, which was due to premature rupture of membranes (PROM) for eight subjects, spontaneous preterm labor for seven subjects, abnormal heart rate for two subjects, and severe preeclampsia for three subjects.

The mean cholesterol and triglyceride level of AF did not differ between different gestational ages (P=0.9). Term and preterm neonatal groups were significantly different, regarding the mean maternal estriol, cholesterol, and triglyceride levels, as well as mean cholesterol and triglyceride levels of AF(P<0.001) (Table 2) similar to low birth weight and normal weight group (P<0.001) (Table 2).

IUGR and normal neonatal group were significantly different, regarding the mean maternal estriol (P<0.001), cholesterol (P=0.003), and triglyceride levels (P<0.001), as well as mean cholesterol and triglyceride levels (P<0.001) of AF (Table 2). By considering term or preterm labor as a dependent variable, we found that the AF cholesterol level was an independent predictor of term or preterm delivery (Table 3). By considering IUGR or normal growth as dependent variables, we found that maternal the estriol level was an independent predictor of IUGR or normal growth (Table 3). By considering low birth weight or normal weight as dependent variables, we found that the maternal estriol level was an independent predictor of IUGR or normal growth (Table 3).

Table 1. Demographic characteristics of all patients

Variable	Results
Age	5.8± 33
Parity	0.7 ± 0.7
Maternal estriol	0.75 ± 0.4
BMI	25.6 ± 2.8
Gestational HTN	
Yes	(%5.6)8
No	(%94.4)134
Preeclampsia	
Yes	(%6.3)9
No	(%93.7)133
Mode of delivery	
C/S	(%61.3)87
NVD	(%38.7)55
GDM	
Yes	(%14.1)20
No	(%85.9)122

Variable	Results
IUGR	
Yes	(%19.7)28
No	(%80.3)114
Low birth weight	
Yes	(%16.2)23
No	(%83.8)119
Preterm birth	
Yes	20(14%)
No	122(86%)

GDM: gestational diabetes mellitus; IUGR: intrauterine growth retardation

Table 2. Different variables among term and preterm group; IUGR and normal group; and normal birth weight and low birth weight group

	Maternal estriol	Amniotic fluid triglyceride	Amniotic fluid cholesterol	Maternal cholesterol	Maternal triglyceride
Preterm group (N=20)	0.53 ± 0.11	18.8 ± 6.6	18 ± 4.1	150.5 ± 8.7	81.5 ± 6.2
Term group (N=122)	0.79 ± 0.42	49.1 ± 17.5	50.7 ± 19	161.1 ± 9.9	97.6 ± 11.6
P-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
IUGR group	0.54 ± 0.12	28.8 ± 15.2	29.5 ± 17.2	154.4 ± 10.9	86.8 ± 10
Normal group	0.8 ± 0.42	48.7 ± 18.4	50.2 ± 19.9	160.9 ± 9.9	97.4 ± 12
p-value	< 0.001	< 0.001	< 0.001	0.003	< 0.001
Normal birth weight	0.78 ± 0.42	49.3 ± 17.6	51.1 ± 19	161.4 ± 9.7	97.6 ± 11.8
Low birth weight	0.55 ± 0.1	21.7 ± 9.9	20.3 ± 7.4	150.4 ± 8.9	83.4 ± 7.6
P-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

IUGR: intrauterine growth retardation

Table 3. Logistic regression tests by considering term or preterm labor; IUGR or normal growth; and low birth weight or normal birth weight as the dependent variables

	Maternal estriol		Amniotic fluid triglyceride		Amniotic fluid cholesterol		Maternal cholesterol		Maternal triglyceride	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Term or preterm labor as dependent variables	2	0.01-287	1	0.8-1.1	1.3	1.03-1.7	1	0.9-1.1	0.9	0.8-1.1
P-value	0.7		0.9		0.05		0.3		0.7	
IUGR or normal growth as dependent variables	17.7	0.01-287	1	0.8-1.1	1	1.03-1.7	1	0.9-1.1	0.9	0.8-1.1
P-value	0.03		0.2		0.5		0.2		0.4	
Low birth weight or normal weight as dependent variables	22.8	1.41-354	1	0.9-1.1	1	0.9-1	0.9	0.8-1	1	0.9-1.1
P-value	0.02		0.1		0.7		0.2		0.4	

IUGR: intrauterine growth retardation

Discussion

The results of the current study showed that mean cholesterol and triglyceride levels of AF were significantly lower in low birth weight, IUGR, and preterm neonates. On the other hand, we found that mean maternal estriol, cholesterol, and triglyceride levels were significantly lower in low birth weight, IUGR, and preterm neonates. The current study also found that the AF cholesterol level was an independent predictor of term or preterm delivery, while the maternal estriol level was an independent predictor of IUGR or normal growth.

Cholesterol biosynthesis takes place in two pathways: Bloch and Kandutsch-Russell pathways **(9)**. Previous studies have indicated that the Bloch pathway is activated in brain tissue between 10 and 20 weeks of gestation, and the Kandutsch-Russell pathway is activated after 19 weeks of gestation **(2)**. There are three types of AF cells: epithelioid type (E-type) cells, amniotic fluid-specific type (AF-type) cells, and fibroblastic type (F-type) cells. The origin of E-type cells are the fetal skin and urine; the origin of AF-type cells are the fetal membranes and placental trophoblasts; and the origin of F-type cells are the connective and mesenchymal tissues and dermal fibroblasts. All three type cells contribute significantly to cholesterol synthesis **(10)**. Therefore, sufficient cholesterol is essential for fetal development. AF belongs to the fetal compartment, and lipid concentration belongs to the fetal pool that can be considered as the representative of maternal-fetal cholesterol transfer.

Similar to the findings of the current study, Edison *et al.* reported that the total maternal serum cholesterol level, less than the 10th population percentile, is associated with preterm labor among low-risk white mothers. They also indicated that the infants of mothers, with lower cholesterol levels, have a lower birth weight among all races **(11)**.

Although in the current study all maternal cholesterol levels were within the normal ranges, pregnancy outcome was not satisfactory for all subjects. This could indicate that maternal lipid profile alone could not predict the outcome of pregnancy. Moreover, it could be concluded that other variables, including fetus adrenal, placental barrier, and amniotic membranes, are important to determine the outcome of the pregnancy. On the contrary, Catov *et al.* demonstrated that a high level of cholesterol and triglyceride before the 15 weeks of gestation is associated with an increased risk of preterm labor. The rate of preterm labor before 34 weeks of gestation is higher in overweight women, which have higher levels of LDL at the beginning of pregnancy. Putting all together, they indicated the presence of dyslipidemia among women with spontaneous preterm labor **(12)**.

Amaral *et al.* found that as gestational age increases, levels of the total cholesterol and its precursors increase **(1)**. Vuorio *et al.* found that the cholesterol concentration of the blood cord was 40%–50% of that of maternal levels, which indicates the maternal-fetal sterol transport **(7)**. In the present study, the cholesterol level of AF increased after 20 weeks of gestation, while in the study of Baardman *et al.* the mean cholesterol level increased after 19 weeks of gestation **(2)**. These findings are in favor of the maternal origin of the lipids during the early pregnancy period and mostly the fetus origin of them after 19-20 weeks of gestation.

Conclusion

The results of this study indicated that the maternal estriol level is a predictor for IUGR and low birth weight. As a matter of fact, the maternal estriol level is an indicator of the maternal and fetal health status, indicating the normal function and structure of the fetus's adrenal, placenta, amniotic membranes, and liver. The maternal estriol level has become an alternative to the 24th-hour urine estrogen, recently. Putting all these together, maternal estriol could be considered as an important indicator of fetus growth and development; this finding calls for appropriate intervention for mothers with disturbed maternal estriol level.

The current study was conducted in a single tertiary center among women with 16-22 weeks of gestation. A multicentric study with larger sample size is recommended to achieve more reliable results.

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Conflict of Interest

Authors declared no conflict of interests.

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