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Association Between Ultrasonographically Detected Fatty Liver and Maternal Lipid Levels and Adverse Obstetric Outcomes

Ultrasonograf ile Saptanan Yağlı Karaciğerin Maternal Lipid Düzeyleri ve Olumsuz Obstetrik Sonuçlarla İlişkisi

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Abstract

Objective: Fatty liver, which is increasingly common in pregnancy, is associated with maternal health risks. This study aimed to explore the association between ultrasound-detected fatty liver, maternal lipid levels, and adverse obstetric outcomes

Method: This prospective cohort study included pregnant women who attended the Gynecology Department of University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital between 24 and 42 weeks of gestation for their antenatal visit. The study period was from February 1, 2020, to December 31, 2020.

Results: The 232 participants were divided into two groups based on ultrasound findings: Group 1 (n=121) with grade 0-1 fatty liver, and Group 2 (n=111) with grade 2-3 fatty liver. Statistically significant increases in maternal age, pregestational body mass index (BMI), and fetal weight were observed among women diagnosed with fatty liver on ultrasound. Regarding BMI, a cut-off value of ≥27.2 kg/m2 exhibited a sensitivity of 58.6%, specificity of 66.12%, positive predictive value (PPV) of 61.30%, negative predictive value (NPV) of 63.50%, and LR(+) of 1.73%. Similarly, for triglycerides, a cut-off value of ≥240 mg/dL showed sensitivity of 62.16%, specificity of 87.60%, PPV of 82.10%, NPV of 71.60%, and LR(+) of 5.01%. Multivariate logistic regression analysis revealed a decreased risk of small for gestational age [0.98 (0.96-1.00) odds ratio (OR) 95%

Öz

Amaç: Gebelikte giderek yaygınlaşan yağlı karaciğer, maternal sağlık riskleriyle ilişkilidir. Bu çalışma, ultrasonografi ile tespit edilen yağlı karaciğerin, maternal lipid düzeyleri ve olumsuz obstetrik sonuçlarla olan bağlantısını araştırmayı amaçlamaktadır.

Yöntem: Bu prospektif kohort çalışması, 1 Şubat 2020-31 Aralık 2020 tarihleri arasında Sağlık Bilimleri Üniversitesi, Prof. Dr. Cemil Taşçıoğlu Şehir Hastanesi, Kadın Hastalıkları ve Doğum Kliniği'ne 24-42 haftalık gebelik döneminde antenatal ziyaret için başvuran hamile kadınları içermektedir.

Bulgular: Ultrasonografi bulgularına dayanarak 232 katılımcı iki gruba ayrılmıştır: Grup 1 (n=121) derece 0-1 yağlı karaciğer, ve Grup 2 (n=111) derece 2-3 yağlı karaciğer olanlar. Ultrasonografi ile yağlı karaciğer tanısı konulan kadınlarda maternal yaş, gebelik öncesi vücut kitle indeksi (VKİ) ve fetal ağırlıkta istatistiksel olarak anlamlı artışlar gözlenmiştir. VKİ için, ≥27,2 kg/m² eşik değeri %58,6 duyarlılık, %66,12 özgüllük, %61,30 pozitif öngörü değeri (PPV), %63,50 negatif öngörü değeri (NPV) ve 1,73 pozitif olasılık oranı LR(+) bulunmuştur. Benzer şekilde, trigliseritler için, ≥240 mg/dL eşik değeri %62,16 duyarlılık, %87,60 özgüllük, %82,10 PPV, %71,60 NPV ve 5,01 LR(+) göstermiştir. Çok değişkenli lojistik regresyon analizi, gestasyonel diyabet riskinde artış [0,98 (0,96-0,99) olasılık oranı (OO) %95 güven aralığı (GA); p=0,045)] ve gestasyonel yaşa göre düşük

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Abstract

confidence interval (CI); p=0.016)] and an increased risk of gestational diabetes mellitus [0.98 (0.96-0.99) OR 95% CI; p=0.045)].

Conclusion: Fatty liver in pregnancy is associated with an increased risk of gestational diabetes mellitus (GDM), but not with other adverse obstetric outcomes.

Keywords: Adverse obstetric outcome, fatty liver, pregnancy, maternal lipid levels

Öz

doğum ağırlığı riskinde azalma [0,98 (0,96-1,00) OO %95 GA; p=0,016)] ortaya koymuştur.

Sonuç: Gebelikte yağlı karaciğer, gestasyonel diyabet riskinde artış ile ilişkilidir, ancak diğer olumsuz obstetrik sonuçlarla ilişkili değildir.

Anahtar kelimeler: Gebelik, maternal lipid düzeyleri, olumsuz obstetrik sonuçlar, yağlı karaciğer

Introduction

Pregnancy is associated with certain physiological changes that aim to provide adequate energy stores for both the mother and the fetus. These adaptations affect maternal blood lipid concentrations, and the levels of high-density lipoprotein (HDL), total cholesterol (TC), low-density lipoprotein (LDL), and triglycerides (TG) increase significantly as the pregnancy progresses (1). In later weeks of pregnancy, insulin resistance increases ketogenesis, gluconeogenesis, and lipolysis in fasting pregnant women. Placental lipoprotein lipase hydrolyzes TG to reach the fetus. TG must be hydrolyzed to free fatty acids and transported across the placenta (2). HDL-C has vasodilatory, antioxidant, antithrombotic, and anti-inflammatory effects, and its levels increase after 12 weeks of pregnancy as a result of elevated blood estrogen concentrations, whereas TC and LDL-C levels increase in the second and third trimesters (3,4).Non-alcoholic fatty liver disease (NAFLD) encompasses a significant number of diffuse liver diseases. NAFLD is defined as the presence of hepatic steatosis, either by radiological methods or histological analysis, in the absence of alcohol consumption and other secondary causes of fatty liver. Obesity, diabetes, and metabolic syndrome are the risk factors for NAFLD. Maternal NAFLD has been found to be associated with abnormal fetal growth and obstetric complications (5,6). B-mode ultrasound allows the assessment of the grades of fatty liver. The total area of steatotic hepatocytes exceeding 20% exhibited higher sensitivity and specificity for the diagnosis of fatty liver. Although ultrasound testing has a higher diagnostic specificity in lower grades of fatty liver, its diagnostic sensitivity decreases because of high rates of false negative results (7,8).Preeclampsia, gestational diabetes mellitus (GDM), preterm birth, and macrosomia have been reported in women with dyslipidemia and high cholesterol, low-density lipoprotein, TG, and low HDL levels (9,10). Fat infiltration in the liver parenchyma affects blood lipid levels. A limited number of studies on fatty liver during pregnancy have also found a relationship between NAFLD and adverse obstetric outcomes (11,12).The aim of this study was to examine the association between fatty liver detected on ultrasound and maternal lipid levelsmitigate and to investigate its relationship with adverse obstetric outcomes.

Materials and Methods

This prospective cohort study included pregnant women who attended the Gynecology Department of Universirt of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital between 24 and 42 weeks of gestation for their antenatal visits. The study period was from February 1, 2020, to December 31, 2020. Gestational age was calculated according to the date of the last menstrual period or ultrasound findings at <20 weeks of gestation. The exclusion criteria were as follows: multiple pregnancies, smoking, alcohol use, maternal age of <18 years, chromosomal anomalies, maternal chronic liver, kidney, thyroid, or heart disease, asthma, chronic hypertension, autoimmune disorders, pregestational diabetes, metabolic storage disease, inflammatory bowel disease, polycystic ovary syndrome, chronic drug use, positive hepatic markers, and previously diagnosed dyslipidemia. Participation in the study was voluntary. Written informed consent was obtained from all participants. Fasting blood samples were obtained from all mothers at ≥24 weeks of gestation. Lipid profile tests, including low-density lipoprotein (LDL-C), high-density lipoprotein (HDL-C), TG, and TC, were performed as part of the routine pregnancy follow-up during the antenatal visits. Obstetric ultrasound was performed to monitor fetal development, and hepatic ultrasound was used to determine the grade of fatty liver infiltration. All obstetric examinations were conducted by a single obstetrician (S.G), while hepatic assessments were performed by a lone radiologist (S.O), using the Esaote My Lab Seven machine equipped with a 1-8-MHz convex-array abdominal probe. The intraclass correlation coefficient

(ICC) was used to evaluate the consistency of the results. Specifically regarding ultrasound assessments for fatty liver disease, the level of agreement between observers was determined by conducting two separate examinations, spaced 1 h apart, involving a cohort of 20 pregnant women. The resulting ICC was 0.83 [with a 95% confidence interval (CI) of 0.68-0.90].

The US grading criteria for fatty infiltration of the liver were follows (13): Grade 0 (Normal) - normal liver echotexture; Grade 1 (Mild) - diffuse and slight increase in fine echoes in the hepatic parenchyma, with normal visualization of the portal vein borders and diaphragm; Grade 2 (Moderate), moderate and diffuse increase in fine echoes, with slightly impaired visualization of the portal vein borders and diaphragm; and Grade 3 (Severe), marked increase in fine echoes, with poor or no visualization of the diaphragm, portal vein borders, and posterior portion of the right lobe.

The patients were followed up until delivery. Out of the 244 pregnant women initially selected, 232 were included in the study because the birth records of 12 patients were not available. Fetal weight, gestational age at delivery, mode of delivery, indications for cesarean delivery, neonatal gender, and maternal and obstetric outcomes were recorded. The following reference ranges were established: serum TG <150 mg/dL, TC <200 mg/dL, LDL <130 mg/dL, and HDL >50 mg/dL.

The diagnosis of GDM was made in 1 step, as recommended by the International Association of Diabetes and Pregnancy Study Groups (14). The diagnosis of preeclampsia was made according to the criteria of the International Society for the Study of Hypertension in Pregnancy (15).

Ethical Approval

This study was conducted in accordance with the Declaration of Helsinki. The Ethics Committee of University of Health Sciences Turkey, Prof. Dr. Cemil Taşçıoğlu City Hospital, approved the study (date: 27/01/2020../no: 48670771-514.10./15).

Statistical Analysis

Statistical analyses were performed using number cruncher statistical system 2007 Statistical Software (Utah, USA).

Apart from descriptive methods (mean, standard deviation, median, interquartile range), the Shapiro-Wilk normality test was used to check whether the variables followed a normal distribution, the independent t-test was used for pairwise comparisons of groups with normally distributed variables, and the Mann-Whitney U test was used for variables with non-normal distribution. Chi-square and Fisher's Exact tests were used to compare qualitative data. The areas under the receiver operating characteristic curve were calculated for differential diagnosis in the presence of grade 2-3 fatty liver, sensitivity, specificity, positive and negative predictive values, LR (+) and the cut-off values of the variables were determined. A p-value of <0.05 was considered statistically significant.

Results

The 232 participants were subdivided into Group 1 (n=121), consisting of pregnant women with ultrasound findings of steatosis grade 0-1, and Group 2 (n=111), consisting of pregnant women with ultrasound findings of steatosis grade 2-3. It should be noted that patients with grade 0-1 steatosis according to ultrasound findings were not diagnosed with NAFLD.

Maternal demographic characteristics and lipid levels are presented in Table 1. Maternal age and body mass index (BMI) were significantly higher in Group 2 than in Group 1 (p=0.011, and p=0.0001, respectively). There were no significant differences between the groups with respect to gravidity, parity, miscarriage rate, mode of delivery, and indications for cesarean delivery.

Mean fetal weight was significantly higher in Group 2 (3336.94±435.01 g) than in Group 1 (3196.98±438.4 g) (p=0.016). Patients in group 2 had significantly higher TG levels and lower HDL-C levels (p=0.0001 and p=0.008 respectively) compared with those in group 1. However, there were no statistically significant differences in TC and LDL-C levels between the two groups.

The pregnancy outcomes are presented in Table 2. There were no significant differences between the groups with respect to the development of adverse outcomes, including large for gestational age (LGA) infants, preeclampsia, abruptio placentae, fetal demise, GDM, oligohydramnios, polyhydramnios, preterm premature rupture of membrane (PPROM), low birth weight (LBW), premature rupture of membrane (PROM), macrosomia, preterm birth, and postterm birth. However, the incidence of small for gestational age (SGA) was significantly lower in Group 2 than in Group 1 (p=0.024).

Receiver operator characteristic curves were created and in predicting the presence of fatty liver, the area under the curves (AUCs) for HDL, LDL, and cholesterol were as follows: HDL: 0.604 (95% CI: 0.538-0.668); LDL: 0.529 (95% CI: 0.463-0.595), and cholesterol: 0.532 (95% CI: 0.466-0.598).

Table 1. Demographic characteristics and maternal lipid levels

		Group1 n=121 (Grade 0-1)		Group 2 n=111 (Grade 2-3)		p
Age	**Mean (SD)**	28.47±6.07		30.45±5.68		**0.011**[a]
Delivery	**Vaginal**	51	42.15%	52	46.85%	0.472[b]
	Cesarean	70	57.85%	59	53.15%	
Indications for cesarean sections	**Previous cesarean**	42	58.34%	31	52.54%	0.471[b]
Fetal distress		12	16.67%	11	18.64%	
Progress failure		5	6.94%	10	16.95%	
Cephalopelvic disproportion		7	9.72%	2	3.39%	
Macrosomia		2	2.78%	2	3.39%	
Malpresantation		3	4.17%	2	3.39%	
Placenta previa		1	1.39%	1	1.69%	
Gravida	**Mean (SD)**	2.44±1.34		2.72±1.54		0.163[c]
	Median (IQR)	2 (1-3)		2 (2-4)		
Parity	**Mean (SD)**	1.09±1.09		1.34±1.16		0.085[c]
	Median (IQR)	1 (0-2)		1 (1-2)		
Abortus	**Mean (SD)**	0.36±0.72		0.38±0.83		0.804[c]
	Median (IQR)	0 (0-1)		0 (0-0)		
Test weeks	**Mean (SD)**	31.43±4.1		34.01±3.08		**0.0001**[a]
Maternal weight	**Mean (SD)**	65.69±11.22		71.18±12.65		**0.001**[a]
Maternal height	**Mean (SD)**	160.56±5.5		159.75±4.93		0.238[a]
BMI	**Mean (SD)**	25.43±4.31		27.87±5.01		**0.0001**[a]
HDL-C	**Mean (SD)**	69.07±14.06		64.23±13.31		**0.008**[a]
LDL-C	**Mean (SD)**	140.93±40.11		140.05±57.28		0.893[a]
Cholesterol	**Mean (SD)**	245.75±49.44		251.12±53.45		0.428[a]
Trygliseride	**Mean (SD)**	180.36±47.36		264.55±79.57		**0.0001**[a]
Fetal weight	**Mean (SD)**	3196.98±438.4		3336.94±435.01		**0.016**[a]
Gestational age	**Mean (SD)**	38.64±1.59		38.76±1.69		0.582[a]
Gender	**Female**	52	42.98%	55	49.55%	0.337[b]
	Male	69	57.02%	56	50.45%	
Assisted reproductive technology		1	0.83%	0	0.00%	0.316[d]

[a]: Independent t-test, [b]: Chi-square test, [c]: Mann-Whitney U test, [d]: Fisher's Exact test, BMI: Body mass index (kg/m^2), SD: Standard deviation, IQR: Interquartile range, HDL-C: High-density lipoprotein, LDL-C: Low-density lipoprotein

The AUC values for BMI (0.645, 95% CI: 0.579-0.706) and TG (0.828, 95% CI: 0.773-0.874) exceeded the threshold values, indicating significant predictive capability. Subsequently, cut-off values were calculated, as illustrated in Figure 1.

BMI, at a cut-off value of ≥27.2 kg/m^2, had a sensitivity of 58.6%, specificity of 66.12%, positive predictive value (PPV) of 61.30%, negative predictive value (NPV) of 63.50%, and LR (+) of 1.73% in predicting grade 2-3 fatty liver. Meanwhile, TG at a cut-off value of ≥240 mg/dL had a sensitivity of 62.16%, specificity of 87.60%, PPV of 82.10%, NPV of 71.60%, and LR(+) of 5.01% in predicting grade 2-3 fatty liver.

Regarding the distribution of adverse obstetric outcomes, no statistically significant differences were observed between the <240 mg/dL TG and ≥240 mg/dL TG groups or between the <27 kg/m^2 BMI and ≥27 kg/m^2 BMI groups (Table 3).

Multivariate logistic regression analysis for fatty liver in predicting obstetric outcomes was performed after adjusting for maternal age and BMI (Table 4). NAFLD was found to be an independent predictor of lower risk for SGA [0.98 (0.96-1.00) odds ratio (OR) 95% CI; p=0.016)], and elevated risk for GDM [0.98 (0.96-0.99) OR 95% CI; p=0.045)].

Table 2. Obstetric outcomes

	Group1 n=121 (Grade 0-1)		Group 2 n=111 (Grade 2-3)		p
LGA	11	9.09%	17	15.32%	0.143[a]
Preeclampsia	7	5.79%	9	8.11%	0.485[a]
Abruptio placentae	1	0.83%	2	1.80%	0.511[b]
SGA	8	6.61%	1	0.90%	**0.024[b]**
Fetal demise	1	0.83%	0	0.00%	0.337[b]
GDM	6	4.96%	8	7.21%	0.472[a]
Oligohydramnios	7	5.79%	3	2,70%	0.248[a]
Polyhidramnios	2	1.65%	0	0.00%	0.174[b]
PROM	7	5.79%	4	360%	0.435[a]
PPROM	1	0.83%	1	0.90%	0.951[b]
LBW	9	7.44%	3	2.70%	0.104[a]
Macrosomia	5	4.13%	6	5.41%	0.649[a]
Preterm birth	14	11.57%	10	9.01%	0.522[a]
Postterm birth	1	0.83%	2	1.80%	0.511[b]

[a]: Chi-square test, [b]: Fisher's Exact test, LGA: Large for gestational age, SGA: Small for gestational age, GDM: Gestational diabetes mellitus, PROM: Premature rupture of membrane, PPROM: Preterm premature rupture of membrane, LBW: Low birth weight

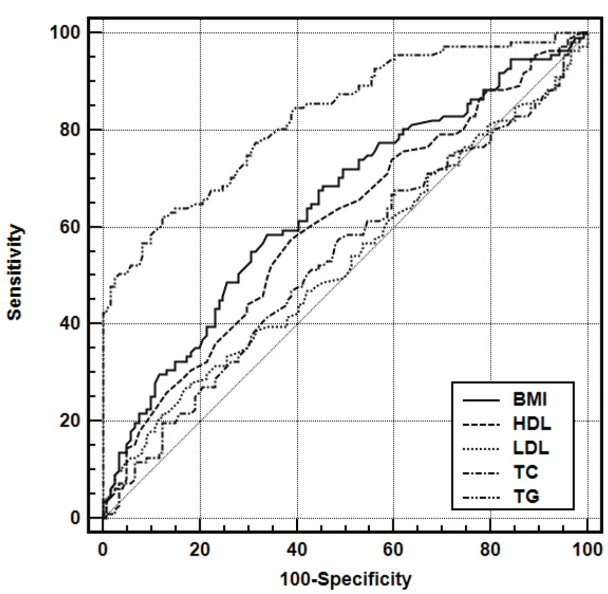

Figure 1. Receiver operating characteristic curve of maternal serum triglycerid (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol (TC) and body mass index (BMI) in the prediction of Grade 2-3 fatty liver in pregnancy

Discussion

Fatty liver during pregnancy, particularly in the context of NAFLD, has been correlated with a high incidence of adverse obstetric outcomes. Patients with NAFLD during gestation exhibit a notable increase in the incidence of several complications compared with those without the condition. Specifically, they are more frequently diagnosed with gestational diabetes (7-8% vs. 23%), hypertensive complications (4% vs. 16%), postpartum hemorrhage (3-5% vs. 6%), and preterm birth (5-7% vs. 9%). These findings underscore the importance of recognizing and managing NAFLD during pregnancy to mitigate maternal and fetal health risks.In this study, maternal age, pregestational BMI, and fetal weight were significantly higher in women with fatty liver on ultrasound. In addition, higher maternal serum TG and lower HDL levels were observed in that group. Lower risk for SGA but elevated risk of GDM were observed after adjusting for maternal age and BMI.

In a meta-analysis, liver ultrasound was found to be a reliable tool, with 84.8% sensitivity and 93.6% specificity, for detecting moderate to severe fatty liver (16). The prevalence of NAFLD in pregnant women was found to be 18.4% in Korean and 17.6% in Canadian populations (17,18). In our study, the rate of fatty liver in pregnancy detected on ultrasound was 47.8%, which is extremely high as compared with other studies. The difference might have resulted from the fact that our study population was >24 gestational weeks, whereas other studies were conducted in the first trimester, and maternal lipid levels are known to increase in late pregnancy. In one study, an increase in serum TG levels and a decrease in HDL-C levels were found in patients with moderate and severe steatosis (19). In our study, TG levels were found to be significantly higher and HDL levels were lower in the fatty liver group, which is consistent with the literature. When the cut-off value of

Table 3. Adverse obstetric outcomes of the triglyceride and BMI groups

	<240 mg/dLTG		≥240 mg/dLTG		p	<27 kg/m² BMI		≥27 kg/m² BMI		p
LGA	14	9.52%	14	16.47%	0.118[a]	13	10.57%	15	13.76%	0.456[a]
Preeclampsia	8	5.44%	8	9.41%	0.250[a]	7	5.69%	9	8.26%	0.441[a]
Abruptio placentae	2	1.36%	1	1.18%	0.905[b]	1	0.81%	2	1.83%	0.492[b]
SGA	7	4.76%	2	2.35%	0.360[a]	7	5.69%	2	1.83%	0.129[a]
Fetal demise	1	0.68%	0	0.00%	0.446[b]	1	0.81%	0	0.00%	0.345[b]
GDM	9	6.12%	5	5.88%	0.941[a]	7	5.69%	7	6.42%	0.815[a]
Oligohydramnios	8	5.44%	2	2.35%	0.264[a]	4	3.25%	6	5.50%	0.399[a]
Polyhydramnios	2	1.36%	0	0.00%	0.280[b]	1	0.81%	1	0.92%	0.932[b]
PROM	9	6.12%	2	2.35%	0.193[a]	8	6.50%		2.75%	0.180[a]
PPROM	1	0.68%	1	1.18%	0.694[b]	1	0.81%	1	0.92%	0.932[b]
LBW	10	6.80%	2	2.35%	0.140[a]	7	5.69%	5	4.59%	0.705[a]
Macrosomia	7	4.76%	4	4.71%	0.985[a]	5	4.07%	6	5.50%	0.607[a]
Preterm birth	13	8.84%	11	12.94%	0.323[a]	13	10.57%	11	10.09%	0.905[a]
Postterm birth	2	1.36%	1	1.18%	0.905[b]	2	1.63%	1	0.92%	0.634[b]

[a]: Chi-square test, [b]: Fisher's Exact test, LGA: Large for gestational age, SGA: Small for gestational age, GDM: Gestational diabetes mellitus, PROM: Premature rupture of membrane, PPROM: Preterm premature rupture of membrane, LBW: Low birth weight

TG was set as ≥240 mg/dL, no increase in adverse obstetric outcomes was detected.

Weight gain and obesity are important risk factors for developing fatty liver, and 80% of NAFLD cases are associated with obesity and BMI >30 kg/m² (20,21). Insulin resistance plays an important role in hepatic steatosis. Higher maternal BMI was found to be associated with higher TC levels in early pregnancy and elevated TG levels in both early and late pregnancy (22). In another study, elevated levels of total cholesterol, LDL-C, and TG but decreased levels of HDL-C were observed in patients with high BMI (22,23). In our study, the cut-off value for BMI was ≥27.2 kg/m², and BMI was found to be significantly higher in patients with grade 2-3 steatosis, which is consistent with other reports. Interestingly, no increase in poor obstetric outcome rate was observed in the high-BMI group versus the low-BMI group.

Maternal TG levels are important predictors of fetal size in late pregnancy. Low HDL-C levels and hypertriglyceridemia are predictive of macrosomia (24). In one study, fasting TG levels in the 95th centile were found to be associated with LGA (25). However, in our study, no increase in the risk of LGA and fetal macrosomia was detected in patients with hypertriglyceridemia.

Unlike other trials, our study was conducted in patients in late pregnancy. Although there was no increase in LGA and macrosomia rates, fetal birth weight was significantly higher and the rate of SGA infants was significantly lower in the group with Grade 2-3 steatosis. However, some studies were not able to find a relationship between NAFLD and SGA infants (12), although Hagström et al. (26) found an increased risk of LBW in mothers with fatty liver in their study, and an elevated risk of gestational diabetes in pregnant women with NAFLD was reported. De Souza et al. (18) stated that fatty liver detected on ultrasound between 11-14 weeks of gestation was a reliable predictor of mid-pregnancy dysglycemia. In a multicenter study, a higher risk for GDM in NAFLD and its correlation with the severity of steatosis were reported (17). Herath et al. (12) found a relationship between NAFLD and hyperglycemia, but the correlation was not significant after adjusting for BMI and age. In our study, a higher risk for GDM in women with Grade 2-3 fatty liver was confirmed after adjusting for maternal age and BMI.

Numerous studies have investigated the relationships between variations in maternal lipid levels and poor obstetric outcomes, without resorting to ultrasound testing in pregnant women with fatty liver. A higher risk of GDM was found to be correlated with elevated TG levels (27). In a meta-analysis comparing groups with and without GDM, TC and LDL-C levels remained unchanged, whereas HDL-C levels significantly decreased in the GDM group in the second and third trimesters of pregnancy. In addition, TG levels in GDM were found to be higher in the third trimesters (28).

Dyslipidemia detected during pregnancy may cause preeclampsia and endothelial dysfunction. In the Chinese population, increased maternal serum TG levels in late pregnancy were independently associated with an elevated risk of preeclampsia, GDM, macrosomia, and LGA but a decreased risk of SGA. A statistically significant relationship was found between decreased HDL-C levels and elevated risk of GDM and fetal macrosomia (29).Hagström et al. (26) observed an increased risk for PE in women with NAFLD, but the statistical significance disappeared after adjusting for maternal BMI. In our study, no increased risk for developing preeclampsia was found in women with fatty liver.

Apart from studies that linked decreased TG levels and preterm birth, the literature offers reports about the relationship between high maternal lipid levels and elevated risk for preterm birth (1,30). Some studies among pregnant women with NAFLD found a higher risk for preterm birth in the fatty liver group (26). While others detected no such relationship (12). In our study, an increased risk of preterm birth was not detected, either in women with high-grade fatty liver or those with elevated TG levels.

Regarding the mode of delivery, in addition to publications confirming higher rates of cesarean section in women with NAFLD, some reports found that delivery mode was not affected (12,26). In our study, no differences were found between the groups in terms of cesarean section rates or indications for cesarean delivery.

Study Limitations

The study has several limitations. Data on socio-economic status, race, nutritional status, and maternal education were not analyzed. In addition, it is possible for the NAFLD grading to change during pregnancy due to differences in dietary habits, emesis gravidarum, and weight gain. The main limitation of this study was that longitudinal follow-ups for fatty liver in the first trimester and postpartum period could not be performed.

Conclusion

Fatty liver in pregnancy is associated with increased rates of adverse obstetric outcomes. It is necessary to distinguish between hyperlipidemia detected during pregnancy and physiological processes. However, there is no consensus on determining the cut-off values of lipid levels. In our study, Grade 2-3 steatosis was associated with more advanced maternal age, significantly higher BMI, and higher fetal weight. Increased maternal TG levels and decreased HDL levels were detected in that group. Although we found no relationship between obstetric outcomes such as preeclampsia, abruptio placenta, fetal loss, LBW, LGA, preterm birth, PROM, PPROM, and fatty liver, multivariate logistic regression analysis revealed an elevated risk for GDM and a decreased risk for SGA. It may be necessary to classify these pregnant women as “high-risk” patients and examine their long-term health outcomes because they may face cardiovascular risks later in life. Ultrasound testing is an important imaging modality in the diagnosis of fatty liver during pregnancy, especially because of its low cost and lack of exposure to radiation.

Ethics

Ethics Committee Approval: This study was conducted in accordance with the Declaration of Helsinki. The Ethics Committee of University of Health Sciences Turkey, Prof. Dr. Cemil Taşçıoğlu City Hospital, approved the study (date: 27/01/2020../no: 48670771-514.10./15).

Informed Consent: Informed consent was obtained from all participants.

Authorship Contributions

Concept: S.G., M.İ.T., V.M., Design: S.G., M.İ.T., V.M., Data Collection or Processing: Ç.N.E., Y.Ö., S.Ö., S.G., Analysis or Interpretation: M.Ç., M.İ.T., Drafting Manuscript: S.G., Ç.N.E., Y.Ö., S.Ö., Critical Revision of Manuscript: V.M., M.Ö., M.İ.T., Technical or Material Support: S.Ö., M.İ.T., S.G., Supervision: V.M., S.G., M.Ö., Final Approval and Accountability: S.G., Ç.N.E., Y.Ö., Writing: S.G., Ç.N.E., Y.Ö.

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