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Evaluation of prognostic nutritional status and lipid profile in gestational diabetes

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ABSTRACT

Objectives: This study aimed to investigate the relationship between controlling nutritional status index (CONUT) and prognostic nutrition index (PNI) scores that are used to evaluate nutritional status and GDM. Also, lipid abnormalities and albumin levels in pregnant women with normal glucose tolerance and GDM were researched.

Material and methods: This study was conducted as a retrospective study at Ankara Etlik City Hospital, Turkey. The study included 67 pregnant women with singleton pregnancies (32 pregnant diagnosed with GDM and 35 pregnant known to be normoglycemic).

Results: There were no statistical differences between the groups in terms of maternal age, gravidity, parity, history of miscarriage and weight gain during pregnancy. Body mass index (BMI) was higher in the GDM group ($p = 0.001$). There was no difference in the CONUT score between the groups ($p = 0.254$). The PNI score was lower in the GDM group ($p = 0.003$). Of the laboratory data, only fasting blood glucose, triglycerides (TG) and total cholesterol (TC) were statistically significantly higher, and albumin was lower in the GDM group ($p = 0.026$, $p = 0.007$, $p = 0.003$ and $p = 0.003$, respectively).

Conclusions: PNI has the potential to be a useful predictor of GDM, whereas CONUT does not. Low albumin levels and increased TG, and TC in the first trimester seem to be significant in the development of GDM.

Keywords: albumin; gestational diabetes; nutrition index

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INTRODUCTION

Gestational diabetes mellitus (GDM) is the onset of diabetes during the second or third trimester in a woman who did not have diabetes before pregnancy [1]. The prevalence of this disease, which affects 17% of pregnant women worldwide, is expected to continue to rise due to higher consumption of processed foods, sedentary lifestyles, older maternal age and increasing obesity [2]. Gestational diabetes mellitus (GDM) is associated with many problems for pregnant women, such as gestational hypertension, pre-eclampsia, premature rupture of membranes, macrosomia and a higher likelihood of cesarean delivery [3]. Risk factors for GDM include older gestational age, obesity, a history of macrosomia, parity (more than three pregnancies) and a family history of diabetes. Nevertheless, it is recommended that all pregnant women be screened for GDM [4, 5]. Although the United States Preventive Services Task Force has indicated that there is a lack of conclusive evidence on the benefits and harms of screening for gestational diabetes mellitus (GDM) before 24 weeks' gestation in all pregnant women [6], early screening for GDM could lead to timely detection and treatment, which could reduce the incidence of adverse perinatal outcomes [7].

Numerous studies on nutritional status can be found in the literature. The CONUT (Controlling Nutritional Status) score and the PNI (Prognostic Nutritional Index) were developed as screening tools to assess nutritional status and are based on serum albumin concentration, total peripheral lymphocyte counts and total cholesterol concentration [8, 9]. While most studies on nutritional status focus on cancer and survival, studies are also investigating how these indices relate to postmenopausal osteoporosis, chronic schizophrenia and even fetal growth restriction [10–12].

Despite extensive research on lipid levels during pregnancy, there is no consensus on the results. There is considerable disagreement in the literature about the possible differences

in lipid patterns in women with GDM in the early stages of pregnancy and whether these early patterns can serve as indicators of pre-existing insulin resistance [13].

Objectives

In this study, the association between GDM and maternal nutrition (CONUT and PNI score) was investigated, considering the relationship between glucose intolerance and nutritional status. The second aim of this study was to investigate the possible detection of lipid abnormalities associated with GDM during the first trimester.

MATERIAL AND METHODS

Study design

This study was conducted as an observational study in the perinatology clinic of Ankara Etlik City Hospital in Turkey. The study included a retrospective review of the medical records of 66 pregnant women who met the eligibility criteria from November 2022 to October 2023. Ethical approval was obtained from the local ethics committee (approval number: AESH-EK1–2023–672). Patient data were extracted from medical records and the hospital's information management system.

Participants in the study

All pregnancies that were monitored in the hospital between the specified dates and had fasting blood glucose, albumin, and cholesterol tests performed in the first trimester were studied. It was found that the reported tests were performed in a total of 97 pregnant women. In addition to the representative cohort of pregnant women diagnosed with GDM, a control group with no medical problems was used for comparison. Women with pre-existing medical problems, women who had not undergone a GOGTT and women with twin pregnancies were excluded from the study. Between 7 and 14 weeks of gestation, laboratory values were collected randomly. GDM was diagnosed according to the IADSPG criteria [14]. After identifying patients who met the exclusion and inclusion criteria, patients were divided into two groups: a control group of healthy pregnant women without GDM or other known diseases (n = 35) and patients with GDM (n = 32). Demographic data, laboratory data (aspartate transferase (AST), alanine transferase (ALT), thyroid stimulating hormone (TSH), hemogram (Hg), fasting blood glucose (FBG), high density lipoprotein (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL), triglyceride (TG), total cholesterol (TC), albumin) and perinatal outcomes were collected.

Calculation of nutritional scores

CONUT score was calculated using the following formula: Serum albumin value (g/dL) + total lymphocyte value + total cholesterol value. This score is calculated with a score between 0 and 12. The interpretation of the score comprises four categories: normal (0–2), mild (2–4), moderate [5–8] and severe [9–12]. The PNI score was calculated using the following formula: PNI = 10*serum albumin (g/dL) +0.005*serum lymphocytes (mm^3).

Statistical analysis

All statistical analyzes were performed using the RStudio integrated development environment for statistical computing (Affero General Public License v3; released 2011. RStudio for Linux, PBC). The study population's demographic and clinical features were summarized using descriptive statistics. The mean ± standard deviation (SD) was used to express continuous data, whereas percentages were used to express categorical variables. The independent t-test was used to compare data that exhibited a normal distribution between groups, while the Man-Witney U-test was used to evaluate data that did not exhibit a normal distribution. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

A summary of the demographic data, clinical results, and laboratory information about study participants is presented in Table 1. Analysis of the data revealed no statistical differences between the groups in terms of maternal age, gravidity, parity, history of miscarriage, history of macrosomia, and weight gain during pregnancy. Body mass index (BMI) and family history of diabetes mellitus were statistically significantly higher in the GDM group (p = 0.001 and p= 0.004). Among the laboratory data, only FBG, TG, and TC were statistically significantly higher, and albumin was lower in the GDM group. There was no difference in CONUT score between groups (p = 0.254). PNI score was statistically lower in the GDM group (p = 0.003).

The pregnancy results of the patients are displayed in Table 2. The only significant difference detected among the pregnancy outcomes of the patients was a lower week of delivery in the GDM group (p = 0.02). While there was no significant difference between the groups in terms of spontaneous vaginal birth and primary cesarean section, the rate of previous cesarean sections was found to be statistically significantly higher in the GDM group. The weeks of labor of patients in the GDM group were earlier. However, there was no

significant difference between the groups in terms of preterm labor. There was no difference between the groups in terms of admission to the NICU. For NICU indications, the rate of NICU admissions due to RDS was found to be statistically significantly higher in the GDM group. The logistic regression analysis and the ROC analysis of BMI, cholesterol, albumin, FBG, TG and PNI values are shown in Table 3 and Table 4, respectively. While increases in PNI and albumin are protective factors for GDM, increases in BMI, cholesterol, FBG, TG are risk factors for GDM. Additionally, ROC analysis of albumin and triglyceride levels is shown in Figure 1 and Figure 2.

A summary of the demographic data, clinical outcomes and laboratory information of the study participants can be found in Table 1. Analysis of the data revealed no statistical differences between the groups in terms of maternal age, gravidity, parity, history of miscarriage, history of macrosomia and weight gain during pregnancy. Body mass index (BMI) and family history of diabetes mellitus were higher in the GDM group ($p = 0.001$ and $p = 0.004$). Of the laboratory data, only FBG, TG, and TC were higher, and albumin was lower in the GDM group. There was no difference in CONUT score between the groups ($p = 0.254$). PNI was statistically lower in the GDM group ($p = 0.003$).

The pregnancy outcomes of the patients are shown in Table 2. The only significant difference between the patients' pregnancy outcomes was a lower week of delivery in the GDM group ($p = 0.02$). While there was no significant difference between the groups for spontaneous vaginal birth and primary cesarean section, the rate of previous cesarean sections was statistically significantly higher in the GDM group. The labor of the patients in the GDM group started earlier. However, there was no significant difference between the groups in terms of preterm labor. There was no difference between the groups in terms of admission to the neonatal intensive care unit (NICU). For NICU indications, the rate of NICU admissions due to RDS was found to be statistically significantly higher in the GDM group. Logistic regression analysis and ROC analysis of BMI, cholesterol, albumin, FBG, TG, and PNI values are shown in Table 3 and Table 4, respectively. While elevated PNI and albumin levels are protective factors for GDM, elevated BMI, cholesterol, FBG and TG levels are risk factors for GDM. The ROC analysis of albumin and triglyceride levels is shown in Figure 1 and Figure 2, respectively. The optimal cut-off level for albumin was 4.1 g/dL [sensitivity 69%, specificity 77%, area under the curve (AUC) 0.711, 95% confidence interval (CI) 0.587–0.815, $p = 0.002$]. The optimal cut-off level for TG was 123 mg/dL [sensitivity 53%, specificity 89%, AUC 0.690, 95% CI 0.565–0.798, $p = 0.005$].

DISCUSSION

There is no study in the literature on CONUT and PNI scores in gestational diabetes. These scores are mainly used for prognosis and long-term survival of cancer and intensive care patients [8, 9, 15]. Although pre-pregnancy BMI, fasting blood glucose, albumin, cholesterol and PNI score were significantly different between the groups, no significant differences were found between the groups in our study in relation to the CONUT scoring system data.

BMI and family history of diabetes were statistically significant between groups, which is consistent with the literature [4]. There were no significant differences between the groups in terms of age and parity. This can be explained by the fact that the patient population consisted only of pregnant women whose blood lipid levels were measured. An actual increased future risk of insulin resistance, higher BMI, central obesity and exaggerated hyperlipidemia compared to normoglycemic pregnant women proves that GDM is a long-standing metabolic disorder that manifests transiently during pregnancy by visible physiologic changes in insulin and lipid metabolism [16]. From this study it can be concluded that high TG and cholesterol levels and low albumin levels in pregnant women in the first trimester can be a sign of gestational diabetes in the following weeks. Studies investigating the relationship between GDM and lipid levels are controversial. It is not clear whether hyperlipidemia and hypertriglyceridemia in pregnant women only occur after insulin resistance or whether they occur early in pregnancy. There are few studies on the lipid profile of women with GDM, particularly in the first trimester of pregnancy. While studies in the literature generally indicate that TG levels increase in pregnant women with GDM in the first trimester [17, 18], a few studies have claimed that TG levels are unrelated to GDM [19]. In a meta-analysis, it was found that TG levels increase significantly in women with GDM from the first trimester, but it was also emphasized that the limitation of the study is that there are few studies on TG in the first trimester [20]. In the same study, they interpreted the reason for high TG as increased adipose tissue exacerbating insulin resistance through an increase in free fatty acids. In our study, which is consistent with the results of this meta-analysis, both BMI and TG levels were significantly higher in the GDM group. In the meta-analysis by Wang et al, 1st trimester TC levels were higher in the GDM group and there was no difference in HDL-C levels [21]. In agreement with Wang's study, we found in our study that TC levels were higher in the GDM group in the 1st trimester, and we found no significant difference in HDL levels between the groups. In addition, Jiang et al. found that elevated TC or TG levels in pregnant women

increased the risk of premature delivery [22]. In contrast to the results of this study, we could not demonstrate that TC and TG levels are involved in the prediction of preterm birth. In our study, the probability of delivery before 37 weeks was the same in both groups, although the GDM group delivered earlier. However, it was found that the labor activity of pregnant women in the GDM group who delivered earlier was lower than that of pregnant women in the control group who delivered earlier, although this was not statistically significant ($p = 0.06$). This finding could explain the high percentage of hypoglycemia, respiratory distress and admissions to the neonatal intensive care unit.

There are many studies that find an association between low albumin and diabetes mellitus. [23, 24]. Low albumin can be caused by malnutrition, nephrotic glomerulopathy, volume overload, liver failure, enteral or interstitial loss [25]. In gestational diabetes, studies generally show that albumin concentrations are similar to normoglycemic women [26, 27]. However, these studies were conducted in the second or third trimester of pregnancy. We conducted our study with women at 6–12 weeks' gestation, when plasma volume is known to increase by 10-15% [28]. We hypothesize that the albumin levels of these pregnant women are lower at the beginning of pregnancy due to their high-carbohydrate and low-protein diet, which is one of the environmental risk factors for diabetes [29], and that this difference will resolve in the following trimesters due to the complicated physiological adaptation of pregnancy. It is also known that the urinary albumin/creatinine ratio increases in women with a history of GDM in the future [30].

The PNI is a score calculated from serum albumin and lymphocytes [9]. In our study, although there was no significant difference between groups in lymphocyte levels, there was a difference in PNI scores due to albumin differences. However, the prediction rate of PNI for GDM (AUC = 0.709, CI: 0.585–0.814, $p = 0.001$) was not better than albumin (AUC = 0.711, CI = 0.587–0.815, $p = 0.001$). No significant difference was found between the groups in terms of CONUT values. Because we believe that nutritional status is as important to the pathophysiology of gestational diabetes as its genetic basis, we examined nutritional scores in gestational diabetes. However, the use of these scores, which are useful in the study of chronic diseases such as cancer, seems to be useless in the prediction of gestational diabetes.

There are some limitations to this study. It was a retrospective study conducted at a single center. The number of diabetic women included in the study is small because the lipid profile measurements were not performed as part of routine antenatal check-ups. We need a much larger sample to further validate the results and show that the lipid profile can be used as a potential index for GDM. In addition, the cut-off values for CONUT and PNI levels in

pregnant women are not known. The strength of this study is that these malnutrition scores have not previously been studied in pregnant women with GDM.

CONCLUSIONS

The results of the study prove beyond doubt that CONUT score does not help predict GDM. Although it is known that lipid parameters increase in normal pregnancy, how it increases in GDM is controversial. Increased TG and TC and low albumin levels in the first trimester seem to be significant in the development of GDM. Although the PNI score can be used to predict GDM based on albumin differences, its prediction rate is not higher than that of albumin levels alone.

Further research is required to investigate the correlation between lipid profile and GDM during the first trimester.

Article information and declarations

Data availability statement

We may share anonymised research data if necessary.

Ethics statement

Ethical approval was obtained from the Ankara City hospital Ethics Committee (approval number: AESH-EK1–2023- 672).

Author contributions

BTÇ — concept, design, data collection or processing, analysis or interpretation, literature search, writing,critical review; GA — concept, analysis or interpretation, writing; GK — concept, analysis or interpretation, writing; ZŞ — design, analysis or interpretation, writing; STS — design, data collection or processing, literature search, critical review; AC — data collection or processing, literature search; SYE — data collection or processing, writing; HEKY — data collection or processing, writing; YAR — literature search, critical review; CTİ — literature search, critical review.

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None.

Conflict of interest

The authors declare no conflict of interest.

Supplementary material

None.

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Table 1. Pregnancy characteristics of the study population

	Control (n = 35)	GDM (n = 32)	Total (n = 67)	p value
Age, years mean ± SD	31.0 ± 5.7	31.2 ± 5.5	31.1 ± 5.6	0.906[a]
G median (IQR)	2 (1–3)	3 (1–3)	2 (1–3)	0.243[b]
P median (IQR)	1 (0–1)	1 (0–2)	1 (0–2)	0.138[b]
A median (IQR)	0 (0–1)	0 (0–0)	0 (0–1)	0.670[b]
BMI (kg/m^2) median (IQR)	24.2 (22.0–28.5)	29.2 (25.9–32.5)	26.5 (23.4–30.4)	**0.001**[b]
Weight gaining (kg) median (IQR)	10 (8–14.2)	10 (8.2–10)	10 (8–13.5)	0.366[b]
History of macrosomia n (%)	1 (2)	5 (15)	6 (8)	0.090[d]
Family history of Diabetes n (%)	7 (20)	17 (53)	21 (31)	**0.004**[c]
FBG (mg/dL) mean ± SD	83 ± 10	89 ± 9	86 ± 10	**0.026**[a]
ALT (IU/L) median (IQR)	15 (10–18)	15 (14–17)	15 (13–18)	0.692[b]
AST (IU/L) median (IQR)	15 (13–17)	16 (13–17)	15 (13–17)	1[b]
TSH (mU/mL) mean ± SD	1.5 ± 1.12	1.6 ± 0.81	1.5 ± 0.91	0.666[a]

Abbreviations: : GDM — Gestationel Diabetes Mellitus; SD — standard deviation; n — number; kg — kilogram; m^2 — square meter; IQR—Inter Quartile Range; g — gram; Dl — deciliter; mcL — microliter; mg — milligram; G — Gravida; P — Parity; A — Abort; BMI: Body Mass Index; FBG — Fasting Blood Glucose; ALT — Alanine Transaminase; AST — Aspartate Transaminase; TSH — Thyroid Stimulating Hormone; HD — High-density Lipoprotein; LDL — Low-density Lipoprotein; VLDL — Very low-density lipoprotein; TC-Total cholesterol; CONUT — The Controlling Nutritional Status; PNI — Prognostic Nutritional Index; Data expressed as n (%); median (interquartile range) or mean (± standard of deviation); [a] — Student_T Test;[b] — Kruskal Wallis Test; c — Chi Square Test; [d] — Fisher Exact Test

Table 2. Pregnancy outcomes of the study groups

	Control (n: 35)	GDM (n: 32)	Total (n: 67)	p value
Neonatal birth weight grams median (IQR)	3190 (2860–3600)	3200 (2770–3445)	3190 (2860–3500)	0.407[a]
Birth week median (IQR)	39 (37–40)	37 (36–38)	38 (37–39)	**0.002[a]**
Delivery type				
Vaginal delivery n (%)	22 (62.9)	11 (34.4)	33 (49.3)	
Primary cesarean section n (%)	8 (22.9)	8 (25%)	18 (23.9)	**0.030[b]***
previous cesarean section n (%)	5 (14.3)	13 (40.6)	18 (26.9)	

Preterm delivery n (%)	7 (20)	9 (28.1)	16 (23.9)	0,622[b]
GW of preterm births mean (min-max)	35,8 (35–36)	34,8 (33–36)	35,3 (33–36)	0,06[a]
NICU Admission n (%)	4 (11.4)	9 (28.1)	13 (19.4)	0,156[b]
NICU Indication				
Indirect hyperbilirubinemia n (%)	2 (5.7)	0 (0)	2 (3)	0.493[b]
Hypoglycemia n (%)	1 (2.9)	2 (6.3)	3 (4.5)	0.603[b]
Transient tachypnea	0 (0)	1 (3)	1 (1)	0.478[b]
Respiratory distress syndrome (RDS) n (%)	1 (2.9)	6 (18.8)	7 (10.4)	**0.048[b]**
Apgar 1. min median (IQR)	9 (9–9)	9 (8–9)	9 (9–9)	0.687[a]
Apgar 5. min median (IQR)	10 (10–10)	10 (9–10)	10 (10–10)	0.792[a]

IQR — interquartile range; GDM — Gestationel diabetes mellitus; GW — Gestationel Weeks NICU — Neonatal Intensive Care Unıt; [a]Kruskal Wallis Test, [b]Chi Square Test *There is a

statistically significant difference between the groups only in terms of previous cesarean delivery

Table 3. Logistic regression analysis for BMI, blood parameters and PNI score

	OR	CI (%95)	p value
BMI (kg/m^2)	1.227	1.076–1.398	0.002
TC* (mg/dL)	1.032	1.011–1.053	0.003
Albumin *(g/dL)	0.049	0.009–0.280	0.001
FBG*(mg/dL)	1.071	1.007–1.138	0.029
TG *(mg/dL)	1.021	1.003–1.038	0.019
PNI Score	0.778	0.659–0.919	0.003

*BMI, age adjusted values are given, TC — Total cholesterol, BMI: Body Mass Index, FPG — Fasting Blood Glucose; TG — Triglyceride, PNI — Prognostic Nutritional Index

Figure 1. ROC Analysis for Albumin levels

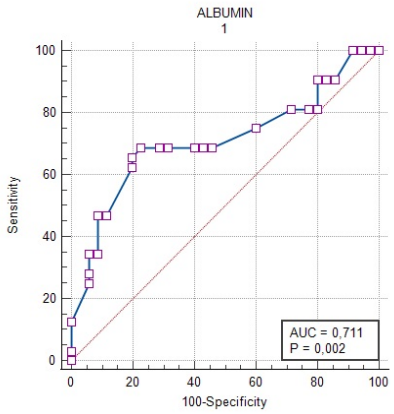

Figure 2. ROC analysis for triglyceride levels

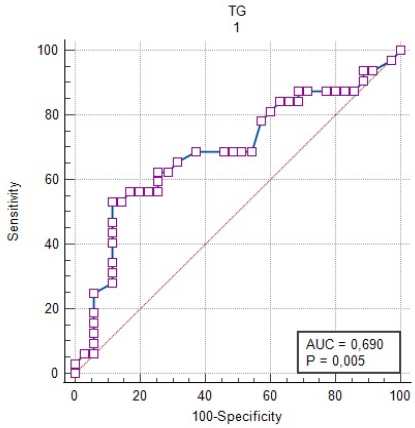

Figure 1: ROC Analysis for Albumin