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Evaluation of AST/Platelet Ratio Index, AST/Creatinine Ratio Index, and AST/ALT Ratio (De Ritis) in Type 2 Diabetes Mellitus: A Tertiary Center Case–Control Study

Tip 2 Diabetus Mellitus Tanılı Gebe Hastaların AST/Platelet Ratio İndex ve AST/Kreatinin Ratio İndeks, AST/ALT Ratio İndekslerinin Değerlendirilmesi. Bir Tersiyer Merkez Vaka -Kontrol Çalışması

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ABSTRACT

Aim: The aim of this study was to compare the aspartate aminotransferase/platelet ratio index (APRI), aspartate aminotransferase/creatinine ratio index (ACRI), and AST/ALT ratio (De Ritis) between pregnant women diagnosed with tip 2 diabetes mellitus (DM) and healthy controls.

Materials and Methods: This retrospective, single-center study was conducted in a tertiary referral hospital between January 2023 and January 2025. A total of 190 pregnant women were included: 95 with tip 2 DM(group 1) and 95 without(group 2). The APRI and ACRI indices, as well as the maternal and fetal outcomes, were compared between the groups.

Results: In the study group, first-trimester(tr) creatinine ($p<0.001$) and leukocyte (WBC) counts ($p=0.003$), as well as third-tr AST ($p<0.001$) and creatinine ($p<0.001$), were significantly higher. In the study group, first-tr ACRI ($p=0.006$) and De Ritis ratio ($p=0.008$) were significantly lower, whereas third-tr APRI ($p<0.001$), ACRI ($p=0.040$), and De Ritis ratio ($p=0.002$) were significantly higher.

Conclusions: In this study, first-tr ACRI and De Ritis ratios were significantly lower, while third-tr APRI, ACRI, and De Ritis ratios were significantly higher in patients with tip 2 DM compared to controls. Although first- and third-tr APRI, ACRI, and De Ritis indices differed significantly from those of the control group, they did not demonstrate predictive value for NICU admission. These indices may reflect metabolic and hepatic changes in tip 2 DM but lack independent predictive value, though they could support multivariate models.

Keywords: Pregnancy, Diabetes Mellitus,Type 2, Aspartate Aminotransferases, Creatinine, Intensive Care Units, Neonatal

ÖZ

Amaç: Bu çalışmanın amacı tip 2 diabetus mellituus(DM) tanılı hastaların AST/platelet ratio indeks (APRİ) ve AST/kreatinin ratio indeks (ACRİ), AST/ALT ratio (De Ritis)' larının sonuçlarını sağlıklı gebelerle karşılaştırmak ve bu indekslerin yeni doğan yoğun bakıma yatış(NICU)'ları öngörücü etkinliğini araştırmaktır.

Gereç ve Yöntemler: Bu çalışma tek merkezli, üçüncü basamak bir merkezde retrospektif olarak tasarlandı. Çalışmaya ocak 2023 ile ocak 2025 tarihleri arasında tip 2 DM tanılı 95 ve tip 2 DM tanılı olmayan 95 toplamda 190 gebe hasta dahil edildi. Çalışmaya dahil edilen hastalar tip 2 DM (grup 1) ve kontrol (grup 2) olacak şekilde 2 grup oluşturuldu. Grupların maternal laboratuvar sonuçları sonrası oluşturulan APRİ ve ACRİ indeksleri ve maternal, fetal sonuçları karşılaştırıldı.

Bulgular: Çalışma grubunda 1.trimester(tr) kreatinin ($p<0.001$), lökosit (wbc) ($p=0.003$), 3.tr AST($p<0.001$), kreatinin ($p<0.001$) anlamlı ve yüksek izlendi. Çalışma grubunda 1.tr ACRİ($p=0.006$), De Ritis ($p=0.008$) anlamlı, düşük izlenirken, 3.tr APRİ($p<0.001$), ACRİ($p=0.040$), De Ritis ($p=0.002$) anlamlı, yüksek izlenmiştir.

Sonuç: Bu çalışmada tip 2 DM'li hastalarda 1.tr ACRİ, De Ritis anlamlı ve düşük 3.tr APRİ, ACRİ, De Ritis ise kontrol gruplarına göre anlamlı ve yüksek izlenmiştir. 1.tr ve 3.tr APRİ, ACRİ, De Ritis sonuçları kontrol grubuna göre anlamlı çıkmasına rağmen NICU'yu öngörü etkinliğinin olmadığı sonucuna vardık. Tip 2 DM'de bu indekslerin etkili olabileceği yerler olabilir ancak öngörücü olarak kullanımı uygun görülmemektedir. Bununla birlikte daha anlamlı kılabilecek çok parametreli modellere dahil edilebilirler.

Anahtar Kelimeler: Gebelik, Tip 2 diyabetes mellitus, Aspartat Aminotransferaz, Kreatinin, yeni doğan yoğun bakım

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INTRODUCTION

Pregestational diabetes mellitus (PreGDM) refers to type 1 diabetes mellitus (DM) or type 2 DM diagnosed before pregnancy and is associated with significant risks for both maternal and fetal outcomes. In type 2 DM, processes such as insulin resistance, inflammation, and oxidative stress induced by hyperglycemia affect not only glucose metabolism but also liver and renal functions, thereby predisposing patients to systemic complications (1–3). In recent years, there has been increasing interest in simple and noninvasive biochemical indices that may reflect these systemic effects. In this context, the aspartate aminotransferase (AST) -to-platelet ratio index (APRI), AST-to-creatinine ratio index (ACRI), and the De Ritis ratio (AST / alanine aminotransferase (ALT) have emerged as promising indicators.

The aspartate APRI was originally developed to assess liver fibrosis in patients with chronic hepatitis C and is calculated based on the ratio between AST and platelet count. This index can noninvasively reflect the degree of fibrosis by its association with increased AST and decreased platelet counts (4). The ACRI is a relatively novel parameter calculated by dividing AST by creatinine and is considered to be helpful particularly in the diagnosis of nonalcoholic steatohepatitis (NASH). Since creatinine may be influenced by metabolic factors such as muscle mass, renal function, and insulin resistance, ACRI has the potential to reflect both hepatic and renal metabolic dysfunction simultaneously (5).

The De Ritis ratio was first described in 1957 and has been widely used in the differential diagnosis of liver diseases. Higher ALT compared with AST are typically observed in conditions such as acute hepatitis, whereas an AST to ALT ratio greater than 1 suggests alcoholic hepatitis or fibrotic processes (6). Moreover, several studies have shown that this ratio may also be associated with type 2 DM and metabolic syndrome (7). These findings suggest that liver enzyme patterns may serve not only as indicators of hepatic disease but also as markers of systemic metabolic burden.

During pregnancy, serum creatinine levels physiologically decrease, while AST and ALT enzymes generally remain within normal ranges. Therefore, in the presence of additional stressors such as type 2 DM, deviations in these parameters may indicate underlying metabolic disturbances. Recent evidence suggests that these ratios may reflect not only hepatic involvement but also have an impact on neonatal prognosis (8,9). In this context, we aimed to compare APRI, ACRI, and De Ritis ratios in pregnant women with type 2 DM and healthy pregnant controls, and to evaluate their potential role in predicting adverse outcomes.

MATERIALS AND METHODS

Study Population

This study was designed as a single center retrospective case control study. Pregnant women aged 18 to 45 years with a diagnosis of type 2 DM who were followed and treated at the Department of Obstetrics and Gynecology of Gazi Yaşargil Training and Research Hospital between January 2023 and January 2025 were included. The diagnosis of type 2 DM was established before pregnancy based on at least one of the following criteria: hemoglobin A1c level of 6.5 percent or higher, fasting plasma glucose level of 126 mg/dL or higher, 2 hour plasma glucose level of 200 mg/dL or higher during an oral glucose tolerance test, or random plasma glucose level of 200 mg/dL or higher (3).

The exclusion criteria were the presence of major fetal anomalies, multiple pregnancies, pregnant women with additional chronic diseases, cases with preterm premature rupture of membranes(PPROM), and patients who smoked or consumed alcohol. Participants were matched into a study (group 1) and a control (group 2). The study group consisted of pregnant women with type 2 DM, while the control group included low risk pregnant women without systemic diseases such as neurological, cardiovascular, respiratory, gastrointestinal, genitourinary, endocrine, or gastrointestinal disorders, and without obstetric complications including preeclampsia, gestational diabetes mellitus (GDM), or PPROM.

Homogeneity was ensured between the study and control groups with respect to blood parameters obtained during the first trimester(tr), defined as 0 to 14 weeks of gestation, and the third tr, defined as 28 to 36 weeks of gestation. Clinical and demographic data of the participants were recorded, including age, body mass index (BMI), gravidity, parity, gestational age at delivery, birth weight, mode of delivery, umbilical cord pH, 1 minute and 5 minute Apgar scores, neonatal intensive care unit (NICU) admission and indications, hemoglobin(hgb), platelet (PLT), creatinine, white blood cell (WBC), ALT, AST, APRI, ACRI, and De Ritis ratio. Hgb, WBC, PLT levels were measured using the Mindray BC-6000 device (China); ALT, AST, creatinine level was analyzed using the Architect C8000 system (Abbott, USA).

APRI was calculated by accepting the upper limit of AST as 35 U/L and dividing AST by the platelet count. ACRI was calculated by accepting the upper limit of AST as 35 U/L and dividing AST by the creatinine level. The De Ritis ratio was calculated as the ratio of AST to ALT. All statistical analyses were performed using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). The study was conducted in accordance with the principles of the Declaration of Helsinki, and ethical approval was obtained from the Ethics Committee of the

Gazi Yaşargil Training and Research Hospital on July 25, 2025, with decision number 575.

Statistical Analysis

Statistical analyses were performed using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). The normality of data distribution was assessed using the Kolmogorov Smirnov test and the Shapiro Wilk test. The Mann Whitney U test was used to compare variables that did not show a normal distribution. Descriptive statistics for non normally distributed variables were presented as median and interquartile range. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive value of type 2 DM for NICU admission. The chi square test was used to compare categorical variables. A $p<0.05$ was considered statistically significant.

RESULTS

A total of 190 patients were included in this study, with 95 patients in the type 2 DM group and 95 patients in the control group. There were no significant differences between the groups in terms of age, gravidity, parity, BMI, mode of delivery, or fetal birth weight ($p>0.05$). However, significant differences were observed between the groups with respect to gestational age at delivery, 1st and 5th minute Apgar scores, and cord pH ($p<0.001$) (Table 1). The gestational weeks at which laboratory parameters were obtained in the first and third tr were similar between the groups (Table 1). NICU admission was significantly more frequent in the type 2 DM group ($p<0.001$) (Table 1). The NICU indications of the type 2 DM and control groups are presented in Table 1.The median hemoglobin A1c in the study group was 7.0 (Table 1).

No significant differences were observed between the groups regarding first tr hemoglobin, PLT, ALT and AST ($p > 0.05$). In contrast, first tr creatinine ($p < 0.001$) and WBC ($p = 0.003$) differed significantly between the groups (Table 2). In the third tr, no significant differences were found in hemoglobin ($p = 0.093$), WBC ($p = 0.809$), PLT ($p = 0.941$), or ALT levels ($p = 0.003$), whereas AST ($p < 0.001$) and creatinine ($p < 0.001$) showed significant differences between the groups (Table 2).

Regarding inflammatory indices, no significant difference was observed in first tr APRI values between the groups ($p = 0.088$). However, significant differences were detected in first tr ACRI ($p<0.006$) and De Ritis ratio ($p = 0.008$), as well as in third tr APRI ($p< 0.001$), ACRI ($p = 0.040$), and De Ritis ratio ($p = 0.002$) (Table 2).

Table 1. Evaluation of the clinicodemographic characteristics of the type 2 DM and control groups.

		Group1 (Type 2 DM) (n:95)	Group 2 control (n:95)	p value
Age(years), Median (IQR)		32.0(7.0)	30.0(4.0)	0.089
Gravidy, Median (IQR)		2.0(3.0)	2.0(1.0)	0.247
Parity, Median (IQR)		1.0(2.0)	1.0(1.0)	0.848
BMI (kg/m²), Median (IQR)		27.2(4.55)	26.7(2.86)	0.169
hbA1c, Median (IQR)		7.0(2.3)		
Week of blood sampling, Median (IQR)	1st tr	10.4(2.95)	10.1(3.05)	0.501
	3rd tr	32.0(3.50)	31.5(3.75)	0.827
Weeks of bırth, Median (IQR)		37.0(2.0)	39.0(2.0)	**<**0.001
Weigth of bırth(gr), Median (IQR)		3270.0(680.0)	3190.0(600.0)	0.184
Apgar 1st minute, Median (IQR)		7.0(1.0)	8.0(1.0)	<0.001
Apgar 5th minute, Median (IQR)		9.0(1.0)	9.0(0.0)	<0.001
Cord pH, Median (IQR)		7.4(0.01)	7.4(0.0)	<0.001
NICU indications (n/%)	Respiratory problems	6.0 (%40)	2.0(%100)	<0.001
	Hypoglycemia	4.0 (%26)	0.0 (%0)	
	Hyperbilirubinemia	3.0 (%20)	0.0 (%0)	
	Prematurity	2.0 (%14)	0.0 (%0)	
NICU, (n/%)		15.0(15.8%)	2.0(2.1%)	<0.001
Mode of delivery(n/%)	Nvd	41.0(43.2%)	53.0(55.8%)	0.082
	C/S	54.0(56.8%)	42.0(44.2%)	

NICU: Neonatal intensive care unit, IQR: İnterquartıle range, 1st: first, 3rd: third , Nvd: vajinal delivery c/s: sezaryen sectıo, BMI: Body mass index, Statistical Test: Mann-whitney U, Signıficant value p<0.05

Table 2. Evaluation of maternal laboratory parameters, APRI, ACRI, and De Ritis ratios in the type 2 DM and control groups.

	Group1 (type 2 DM) (n:95) Median(IQR)	Group 2(control) (n:95) Median (IQR)	p value
1st tr Hgb (g/dL)	12.3(1.9)	12.5(1.3)	0.493
1st tr wbc (10^9/L)	8.9(2.5)	8.3(2.46)	0.003
1st tr plt (10^9/L)	265.0(88.0)	256.0(80.0)	0.823
1st tr creatinine (mg/dl)	0.56(0.14)	0.5(0.1)	<0.001
1st tr ALT (U/L)	15.5(13.5)	15.0(5.0)	0.629
1st tr AST (U/L)	12.0(9.0)	14.0(5.0)	0.152
3rd tr Hgb (g/dL)	11.7(1.6)	11.9(2.0)	0.093
3rd tr wbc (10^9/L)	9.8(4.4)	9.98(2.98)	0.809
3rd tr plt (10^9/L)	245.0(133.0)	235.0(88.0)	0.941
3rd tr creatinine (mg/dl)	0.57(0.18)	0.49(0.13)	<0.001
3rd tr ALT (U/L)	14.5(9.8)	15.0(6.0)	0.664
3rd tr AST (U/L)	21.0(10.0)	13.0(7.0)	<0.001
1st tr APRI	0.42(0.03)	0.52(0.03)	0.190
1st tr ACRI	21.8(9.99)	26.3(10.5)	0.006
1st tr DE Ritis	0.80(0.41)	0.93(0.31)	0.008
3rd tr APRI	0.10(0.09)	0.05(0.04)	<0.001
3rd tr ACRI	39.3(10.3)	26.8(18.5)	0.040
3rd tr De Ritis	1.2(1.43)	0.87(0.75)	0.002

APRİ: AST/ PLT ratio, ACRİ: AST/ creatinine ratio, wbc: whıte blood cell, plt: Platellet , Hgb: hemoglobin, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase De Ritis : AST/ALT ratio, Statistical test: Mann- whitney U, Significant value p<0.05, tr: trimester, 1st: first, 3rd: third

Table 3. ROC curve results of significant laboratory parameters and indices for predicting NICU admission in the type 2 DM group

		Area	Standard deviation	p value	AUC %95 lower	AUC %95 upper	Cut off-value	sensitiviy (%)	specificity (%)
NICU	3rd tr AST	0.546	0.088	0.597	0.374	718	15.5	58.3	56.7
	3rd tr ALT	0.489	0.094	0.900	0.304	0.674	14.5	58.3	55.4
	1st tr creatinine	0.528	0.094	0.750	0.328	728	0.53	58.2	41.8
	3rd tr creatinine	0.627	0.102	0.144	0.443	811	0.54	66.7	63.4
	3rd tr APRI	0.530	0.084	0.732	0.366	0.694	0.063	50.0	49,6
	1st tr ACRI	0.418	0.085	0.346	0.254	0.582	24.09	50.0	49.6
	3rd tr ACRI	0.494	0.084	0.946	0.329	0.659	30.80	50.1	46.7
	1st tr De Ritis	0.534	0.097	0.699	0.343	0.724	0.87	50.0	49.6
	3rd tr De Ritis	0.564	0.092	0.462	0.384	0.744	0.97	58.3	51.1

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, APRI: AST/ PLT ratıo, ACRI: AST/kreatinin ratıo, NICU: neonatal intensive care unit, De Ritis : AST/ALT Ratıo significant value p<0.05, tr: trimester, 1st:first, 3rd:third

ROC curve analyses performed to evaluate the predictive value of first and third tr APRI, ACRI, and De Ritis ratios, as well as third tr ALT and AST, for NICU admission in the type 2 DM group did not yield statistically significant results ($p > 0.05$). The results are presented in Table 3, and the ROC curve is shown in Figure 1.

DISCUSSION

The aim of this study was to compare APRI, ACRI, and De Ritis indices in patients with type 2 DM and healthy pregnant women, and to evaluate their predictive value for NICU admission.

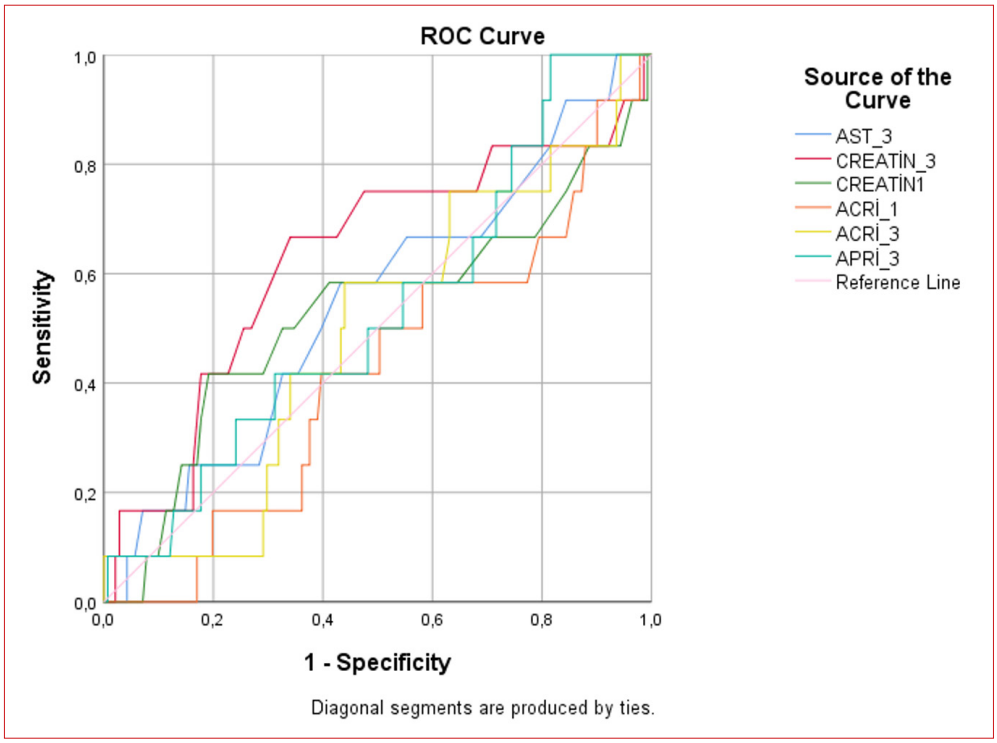

Figure 1. ROC curves of laboratory parameters and indices for predicting NICU admission in the type 2 DM group

In our study, gestational age at delivery, 1st and 5th minute Apgar scores, and cord pH were significantly lower in the type 2 DM group, while NICU admission was more frequent in this group. In the study group, first tr ACRI and De Ritis ratios were significantly lower, whereas third tr APRI, ACRI, and De Ritis ratios were significantly higher.

APRI is a simple index that was initially defined in patients with chronic hepatitis C to noninvasively assess liver fibrosis (10). As AST levels increase and PLT counts decrease with higher degrees of fibrosis, APRI reflects these opposing changes and has been shown to be effective in identifying significant fibrosis, with reported area under the curve values of approximately 0.80 for fibrosis and 0.89 for cirrhosis in hepatitis C patients (10). Although data on the use of APRI in obstetrics are limited, recent studies, particularly those focusing on intrahepatic cholestasis of pregnancy, are noteworthy. For example, Saadi et al. reported that third trimester APRI scores were significantly higher in pregnant women with intrahepatic cholestasis compared with healthy controls, with a cutoff value of approximately 0.42, sensitivity of 65%, and specificity of 73% (11). Similarly, Eyisoy et al. demonstrated that APRI scores were associated with disease severity in intrahepatic cholestasis of pregnancy, with significantly higher values observed in severe cases compared with mild cases. They also reported that elevated APRI levels were associated with meconium stained amniotic fluid, NICU and preterm birth, with a cutoff value of approximately 1.06 (12). These findings suggest that APRI may reflect the severity of pregnancy related liver involvement.

In our study, no significant difference was observed between the groups in first tr APRI values. However, third tr APRI values were significantly higher in diabetic pregnancies compared with controls. This finding may indicate mild hepatic stress or enzyme elevation in the later stages of pregnancy. Nevertheless, ROC curve analysis showed that APRI did not demonstrate significant predictive performance for NICU with an area under the curve of approximately 0.53 and a $p>0.05$. Overall, APRI may reflect metabolic stress in diabetic pregnancies, but it appears to have limited predictive value for neonatal outcomes.

ACRI is not a widely established biochemical index in the literature, and data regarding its use during pregnancy are scarce. This ratio combines AST, a marker of hepatic function, with creatinine, a marker of renal function, and aims to reflect potential hepatorenal alterations. In normal pregnancy, serum creatinine decrease significantly due to increased glomerular filtration rate, which represents a physiological adaptation. The reference range for creatinine in pregnancy is generally accepted as approximately 0.4 to 0.8 mg/dL, which is lower than that in the nonpregnant population (13). In diabetic pregnancies, serum creatinine may remain above this physiological range due to long standing diabetes related renal involvement.

One of the few studies evaluating ACRI was conducted by Mohamed et al. in patients with cirrhosis, where the index was used to predict the presence of esophageal varices. In that study, an ACRI cutoff value greater than 40 demonstrated good diagnostic accuracy,

with sensitivity of 80%, specificity of 82.5%, and an area under the curve of approximately 0.85 (14). The authors also emphasized that ACRI had not been previously used for this purpose (14). Additionally, several studies have indirectly reported associations between AST and creatinine and metabolic disturbances in diabetic individuals (15). In this context, our study represents one of the first investigations to evaluate the ACRI index during pregnancy, particularly in a diabetic population.

According to our findings, first trimester ACRI values were significantly lower in the type 2 DM group compared with controls. This difference may be explained by the physiologically lower creatinine levels observed in healthy pregnancies. In the third tr, however, ACRI values were significantly higher in the diabetic group. This increase may be attributed to elevated AST combined with relatively higher creatinine in diabetic pregnancies, possibly reflecting mild hepatic enzyme elevation and early diabetic nephropathy. Despite these biochemical differences, ACRI showed weak clinical predictive performance, as neither first nor third tr ACRI values significantly predicted NICU with area under the curve values ranging from approximately 0.42 to 0.49 and $p>0.05$. Therefore, although ACRI reflects biochemical alterations, it does not appear to be a useful practical predictor of NICU admission.

The De Ritis ratio, also known as the AST to ALT ratio, has long been used in hepatology. First described by Fernando De Ritis in 1957, this ratio is particularly useful in differentiating various types of liver injury (7). In acute viral hepatitis, ALT are typically higher than AST, resulting in a De Ritis ratio below 1, whereas in alcoholic hepatitis or advanced fibrosis, AST exceed ALT, leading to a ratio greater than 1 (16).

In recent years, the De Ritis ratio has also been associated with conditions beyond liver disease. Elevated De Ritis ratios have been linked to metabolic syndrome, insulin resistance, type 2 DM, and cardiovascular diseases (17). For instance, Li et al. demonstrated increased De Ritis ratios in the presence of preGDM and metabolic syndrome (18). In pregnancy related research, Dinçgez et al. reported that pregnant women with lower De Ritis ratios had a higher risk of developing gestational diabetes mellitus (19). These findings suggest that liver enzyme patterns may provide insights into metabolic risk even in early pregnancy.

In our study, the course of the De Ritis ratio in type 2 diabetic pregnancies was evaluated. While the ratio remained below 1 in all groups during the first tr, it increased significantly in the third tr in the diabetic group, exceeding 1. This increase may be explained by a greater rise in AST compared with ALT and may be associated with hepatic stress or nonalcoholic steatohepatitis (16). Our findings indicate altered liver enzyme dynamics in diabetic pregnancies and are consistent with data related to metabolic syndrome (9). However, the De Ritis ratio did not show significant predictive value for NICU admission, with an area under the curve of approximately 0.56 and a p value greater than 0.4. Thus, the De Ritis ratio may be better interpreted as a marker of maternal metabolic status rather than a predictor of neonatal outcomes.

This study is among the first to simultaneously evaluate changes in APRI, ACRI, and De Ritis indices during both the first and third tr in type 2 DM and to assess their role in predicting NICU admission. The main strengths of the study include the comparative analysis between distinct groups and a relatively larger sample size compared with similar studies. The limitations of the study include its single center and retrospective design.

In conclusion, our study demonstrates that indices based on hepatic function tests show systematic differences in diabetic pregnancies compared with healthy controls. In the third trimester, increases in AST levels were accompanied by significant changes in APRI, ACRI, and De Ritis scores, highlighting the importance of monitoring liver enzymes in diabetic pregnancies. However, these indices were not sufficient predictors of NICU admission. Therefore, these parameters should be interpreted with caution in clinical decision making. Our findings provide a foundation for future large scale prospective studies.

Author Contributions: H.K: Oversaw the overall coordination of the study, contributed to the conception and study design, supervised data collection processes, ensured the accuracy and integrity of the data, and guided the statistical and methodological workflow. Reviewed all stages of manuscript development, provided critical intellectual input, ensured compliance with ethical and publication standards, and approved the final version of the manuscript for submission. S.A: Led the conception and design of the study, contributed to data acquisition, performed statistical analyses, and drafted the original manuscript.

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Conflict of Interest: The authors declare that there is no conflict of interest.

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