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Assessment of the Fibrinogen-to-Albumin Ratio in Patients with Type 2 Diabetes Mellitus: A Comparative Analysis with a Control Group

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Abstract

Objective: Previous studies have reported an association between the fibrinogen-to-albumin ratio and diabetic complications; however, its role prior to the development of overt complications remains unclear. This study aimed to evaluate fibrinogen-to-albumin ratio levels in patients with type 2 diabetes mellitus without complications and to compare them with those in patients with established microvascular complications and healthy controls. In addition, the association between the fibrinogen-to-albumin ratio and glycemic parameters was examined.

Methods: This retrospective study consisted of 305 patients (244 with type 2 diabetes mellitus and 61 controls), aged 27–77 years, followed at the Internal Medicine Outpatient Clinic of a tertiary hospital between October 1, 2023, and March 31, 2024. Patients with diabetes were categorized into four subgroups with equal sample sizes: those without diabetic complications, those with isolated diabetic neuropathy, those with isolated microalbuminuria, and those with at least two diabetic complications. Fasting blood glucose, HbA1c, fibrinogen, fibrinogen-to-albumin ratio, albumin, and microalbumin levels were compared between the groups. To identify the independent predictors of the burden of complications, a multinomial logistic regression analysis was applied.

Results: The fibrinogen-to-albumin ratio did not differ significantly between the controls and patients without complications ($p>0.05$); however, it was significantly elevated in patients with complications ($p<0.001$). The ratio increased progressively across complication groups and exhibited a moderate positive correlation with fasting blood glucose and glycated hemoglobin levels ($p<0.001$). In multivariable analysis, the fibrinogen-to-albumin ratio was independently associated with increasing complication burden, while age, sex, and glycated hemoglobin were not.

Conclusion: In patients with type 2 diabetes mellitus, a higher Fibrinogen-to-albumin ratio is associated with an increased risk of diabetic microvascular complications. This association is independent and progressive. Higher levels are linked to both isolated and multiple complications, suggesting its potential role as a simple marker for identifying patients at increased risk of complication development.

Keywords: type 2 diabetes mellitus, fibrinogen, diabetic neuropathy, diabetic microalbuminuria

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Tip 2 Diyabetes Mellituslu Hastalarda Fibrinojen-Albümin Oranının Değerlendirilmesi: Kontrol Grubu ile Karşılaştırmalı Bir Analiz

Öz

Amaç: Daha önceki çalışmalar fibrinojen-albümin oranı ile diyabetik komplikasyonlar arasında bir ilişki olduğunu bildirmiş olsa da, belirgin komplikasyonlar gelişmeden önceki rolü henüz net değildir. Bu çalışma, komplikasyonu olmayan tip 2 diyabetes mellitus hastalarında fibrinojen-albümin oranı düzeylerini değerlendirmeyi ve bu düzeyleri yerleşmiş mikrovasküler komplikasyonları olan hastalar ile sağlıklı kontrollerle karşılaştırmayı amaçlamıştır. Ayrıca, fibrinojen-albümin oranı ile glisemik parametreler arasındaki ilişki de araştırılmıştır.

Yöntemler: Bu retrospektif çalışmada, 1 Ekim 2023 ile 31 Mart 2024 tarihleri arasında bir üçüncü basamak hastanenin Dahiliye Polikliniği'nde izlenen, yaşları 27 ile 77 arasında değişen 305 hasta (244 tip 2 diyabet mellitusu olan ve 61 kontrol) yer aldı. Diyabetik hastalar, eşit örneklem büyüklüğüne sahip dört alt grupta sınıflandırıldı: diyabetik komplikasyonu olmayan hastalar, izole diyabetik nöropatisi olan hastalar, izole mikroalbüminürisi olan hastalar ve en az iki diyabetik komplikasyona sahip olan hastalar. Tüm gruplar açlık kan şekeri, HbA1c, fibrinojen, fibrinojen/albumin oranı, albümin ve mikroalbümin düzeyleri açısından karşılaştırıldı. Komplikasyon yükünün bağımsız belirleyicilerini saptamak amacıyla multinomiyal lojistik regresyon analizi yapıldı.

Bulgular: Kontrol grubu ile Grup 1 arasında fibrinojen/albumin oranı açısından istatistiksel olarak anlamlı bir fark gözlenmedi ($p>0,05$). Ancak, kontrol grubu ile diğer gruplar arasında anlamlı bir fark bulundu ($p<0,001$). Korelasyon analizinde, fibrinojen/albumin oranı ile hem açlık kan şekeri hem de HbA1c düzeyleri arasında orta düzeyde pozitif bir korelasyon saptandı ($p<0,001$). Çok değişkenli analizde, fibrinojen-albümin oranının artan komplikasyon yükü ile bağımsız olarak ilişkili olduğu, buna karşın yaş, cinsiyet ve glikozile hemoglobin düzeylerinin anlamlı bulunmadığı saptandı.

Sonuç: Tip 2 diyabetes mellitus hastalarında, fibrinojen-albümin oranı diyabetik mikrovasküler komplikasyon yükü ile bağımsız ve kademeli olarak ilişkilidir. Daha yüksek düzeyler hem izole hem de çoklu komplikasyonlarla bağlantılı olup, bu durum fibrinojen-albümin oranının komplikasyon gelişimi açısından artmış risk taşıyan hastaları belirlemede basit bir belirteç olarak potansiyel rolünü düşündürmektedir.

Anahtar kelimeler: tip 2 diyabetes mellitus, fibrinojen-albümin oranı, diyabetik nöropati, diyabetik mikroalbüminüri.

INTRODUCTION

Type 2 diabetes mellitus (DM) represents a prevalent global health concern, with its complications contributing to elevated rates of morbidity and mortality, and subsequently increasing healthcare expenditure[1]. Diabetic neuropathy and diabetic nephropathy are two of the most common complications associated with diabetes mellitus. Diabetic peripheral neuropathy is characterized by a discernible reduction or loss of sensory and/or motor nerve function[2]. One study demonstrated that pain associated with diabetic peripheral neuropathy is linked to an enhanced risk of vascular events and mortality[3]. Diabetic nephropathy is a severe complication that develops over several years following a diabetes diagnosis. Early detection of this condition is paramount, as it influences treatment viability and the potential to halt progression to more advanced stages[4,5].

Fibrinogen, a protein involved in blood coagulation, demonstrates increased concentrations in the presence of inflammation, thereby increasing blood viscosity[6]. It also plays a role in the development of many diseases by influencing inflammation, blood viscosity changes, endothelial damage, and thrombus formation[7,8]. Several studies have linked elevated fibrinogen levels to the development of diabetes-related complications[9,10]. Albumin is involved in inflammation suppression and platelet activation pathways[11]. Albumin indicates the nutritional status of the body, and studies have shown that it decreases in diabetic complications[12]. The fibrinogen-to-albumin ratio (FAR) is a recently identified biomarker of

inflammatory and hemodynamic changes. The FAR is the ratio of these two parameters, which is indicative of inflammatory and hemodynamic changes. Its utility has been investigated in various cardiovascular diseases and malignancies[13-16]. The extant literature on diabetic nephropathy and diabetic neuropathy is scant[17,18]. The current literature lacks research assessing FAR levels in the context of diabetic complications and their absence.

Although previous studies have reported an association between FAR and diabetic complications, its role prior to the development of overt complications remains unclear. This study aimed to evaluate FAR levels in patients with type 2 DM without complications and compare these levels with those of patients with established microvascular complications and healthy controls. Furthermore, this study investigated the relationship between FAR and glycemic parameters to provide further insight into its potential utility as an early biomarker.

METHODS

Study Population

The researchers conducted a retrospective analysis of 305 individuals, comprising 244 patients with type 2 DM and 61 healthy controls aged 27–77 years. Data were collected from patients at the Internal Medicine Outpatient Clinic of Mersin City Training and Research Hospital between October 1, 2023, and March 31, 2024. Blood and urine test results, as well as electromyography findings, were extracted from the hospital 's electronic information system. A sample size of 305 was determined using G-Power 3.1, with a 95% confidence interval and medium effect size (N = 5, N1/2 = 1).

Sixty-one patients comprised the control group (Group 1). DM was ruled out in all participants within this control group via a 75-g oral glucose tolerance test. Furthermore, all patients in the control group exhibited normal arterial blood pressures. This group consisted of individuals adhering to the Mediterranean diet and demonstrating low physical activity levels. Participants were excluded from the control group and, consequently, from the study if they aligned with the following criteria: 1. Individuals with any chronic disease, 2. Use of herbal supplements intended to lower blood glucose levels or blood thinners; 3. Use of oral anticoagulants, anti-aggregants, non-steroidal anti-inflammatory drugs, or corticosteroids affecting blood viscosity; 4. Pregnant women, 5. Autoinflammatory rheumatologic diseases; or 6. Individuals with a history of surgery for any reason in the previous 1 year.

The 244 patients in the diabetic group were divided into four equal subgroups of 61 patients each: patients with no diabetic complications (Group 2); patients with diabetic neuropathy without microalbuminuria/overt proteinuria or retinopathy (Group 3); patients with isolated microalbuminuria without diabetic neuropathy or retinopathy (Group 4); and patients with microalbuminuria/overt proteinuria, diabetic retinopathy, and diabetic macrovascular complications (Group 5). All patients in the diabetic group were on a Mediterranean diet and exhibited a low level of physical activity. All patients included in the diabetic group were normotensive. The exclusion criteria for all patients in the diabetic group were as follows: 1. Patients with any chronic disease other than DM. 2. Being pregnant, 3. Use of herbal supplements or blood thinners that lower blood sugar; 4. Use of oral anticoagulants, anti-aggregants, non-steroidal anti-inflammatory drugs, or corticosteroids that affect blood viscosity; and 5. individuals with a history of surgery within the previous 1 year.

Proteinuria screening was conducted in patients with diabetes and a control group, involving the calculation of the albumin-to-creatinine ratio from spot urine samples. Microalbuminuria is defined as a urinary

albumin excretion of 30–300 mg/day or an albumin-to-creatinine ratio of 30–300 mg/g, and its persistence (≥2 out of 3 samples within 3–6 months) is considered an early marker of diabetic nephropathy[19]. Proteinuria is defined as a total urinary protein excretion ≥150 mg/day, while overt proteinuria is typically considered at levels ≥300 mg/day or an albumin-to-creatinine ratio of >300 mg/g[19]. Electromyography results for patients with DM were evaluated for evidence of diabetic neuropathy.

Data on antidiabetic medication use, including insulin, oral antidiabetic agents, SGLT-2 inhibitors, and GLP-1 receptor agonists, were obtained from medical records and recorded for all patients.

Laboratory assays

Fasting blood glucose, albumin, total cholesterol, HbA1c, high-density lipoprotein cholesterol, fibrinogen, triglycerides, low-density lipoprotein cholesterol, hemogram, creatinine, spot urine albumin, and spot urine creatinine levels were evaluated using an levels were measured using chemiluminescent immunoassay (Siemens Advia 2120i, Siemens Healthcare Diagnostics Inc. Erlangen, Germany). Proteinuria screening was administered to both the patient and control groups using the albumin-to-creatinine ratio in spot urine. Patients who were screened for diabetic retinopathy using fundoscopy were enrolled in the study. Patients whose EMG results were evaluated by a neurologist for diabetic neuropathy were included in the study.

Statistical Analysis

All statistical analyses were conducted using SPSS version 24 (IBM Corp., Chicago, IL, USA). The normality of continuous variables was assessed visually using probability plots and histograms and analytically, via the Shapiro-Wilk test. As the data did not follow a normal distribution, continuous variables are expressed as medians and interquartile ranges (IQR). For categorical variables, the data are displayed as counts (n) and percentages (%), and the suitability of the chi-square test or Fisher's exact test is evaluated to determine which test is used to compare differences between groups.

Comparisons across the five study groups were performed using the Kruskal–Wallis test. Post hoc pairwise comparisons using the Mann–Whitney U test were conducted when overall differences were significant, with Bonferroni correction applied to adjust for multiple comparisons. Since ten pairwise comparisons were made, the adjusted significance level was set at $p < 0.005$ (0.05/10) for all analyses.

A multinomial logistic regression analysis was implemented to ascertain the independent predictors of the burden of diabetic complications. Odds ratios (ORs) and their respective 95% confidence intervals (CIs) were calculated for each outcome. The model fit was evaluated using two methods: the likelihood ratio chi-square test and pseudo R-squared indices. A two-tailed p value of less than 0.05 was recognized as statistically significant. The Declaration of Helsinki's ethical guidelines were the basis for the study's conduct. Prior to the inception of the study, ethical approval was obtained from the Clinical Research Ethics Committee of Mersin University on May 8, 2024 (protocol number: 2024/418).

RESULTS

The average age of diabetic patients was 55 (27-77), while the average age of the control group was 53 (31-68). In the diabetes group, there were 147 female participants (60.2%) and 158 male participants (39.8%); in the control group, there were 38 female participants (62.3%) and 23 male participants (37.7%). No statistically significant differences were found between the groups in terms of sex distribution (p=0.696), age (p=0.145), BMI (p=0.099), or serum

albumin levels (p=0.571). However, statistically significant differences were found between the groups in terms of HbA1c, fasting blood glucose, diabetes duration, fibrinogen levels, FAR, and spot urine albumin/creatinine ratio (p<0.001). In the pairwise (post-hoc) comparisons, no significant difference was observed between the control (Group 1) and uncomplicated diabetes (Group 2) groups in terms of FAR levels (p>0.005). However, a marked increase in FAR levels was detected with the progression of diabetic complications. In particular, the FAR levels of Group 5, which had multiple complications, were significantly higher than those of the control group and all other diabetic subgroups (p<0.005). The demographic characteristics of the control and diabetic groups, treatments received, and blood and urine parameter results are presented in Table 1. The subgroup analysis results showing the differences between the groups are presented in Table 2.

Table I: Control and diabetic groups demographic characteristics and blood and urine parameter results

Parameters	**Groups**					**P Value**
	Group 1 (n=61)	Group 2 (n=61)	Group 3 (n=61)	Group 4 (n=61)	Group 5 (n=61)	
Gender*[n (%)]*						
Female	38(62.3)	36(59)	37(60.6)	35(57.4)	39(63.9)	0.696**
Male [n (%)]	23(37.7)	25(41)	24(39.4)	26(42.6)	22(36.1)	
Age *(year) mean (min-max)*	53 (31-68)	54 (29-70)	56 (33-77)	55 (27-68)	56 (32-70)	0.145
BMI *(kg/m2) Mean (min-max)*	28.7(18.7-40)	28.2(17.8-40.8)	29.3(20.8-43.2)	31(20.5-43)	29.3(19.7-43.3)	0.099
T2DM duration(years) Mean (min-max)		6 (1-20)	10 (1-20)	6 (1-20)	12 (2-25)	<0.001*
Medication *n (%)*						
Insulin therapy	0	4(6.5)	28(45.9)	12 (19.9)	42 (54.3)	
Metformin use	0	30 (49.4)	16 (26.5)	28 (45.9)	9 (14.7)	
SGLT-2 inhibitors	0	10 (16.4)	5 (8.1)	9 (14.7)	11 (18)	0.550**
DPP-4 inhibitors	0	9 (14.7)	4 (6.5)	7 (11.4)	6 (9.8)	
Sulfonylureas	0	3 (4,9)	5 (8.1)	2 (3.2)	1 (1.6)	
Pioglitazone	0	5 (8.1)	3 (4.9)	3 (4.9)	1 (1.6)	
GLP-1 Receptor Agonists	0	0	0	0	0	
Laboratory blood and urine parameters **[**Median (IQR)]						
HbA1c %	5.7 (5.4-6)	7.7(6.7-8)	7.2(6.7-9.2)	7.8(6.9-9.1)	8.6(7.3-10)	<0.001*
Fasting Blood Glucose (mg/dl)	90(75-99)	138(126-159)	156(133-205)	153(133-205)	191(139-258)	<0.001*
Albumin(g/dL)	4,5(4.4-4.7)	4.5(4.3-4.7)	4.5(4.3-4.7)	4.5(4.3-4.7)	4.5(4.3-4.6)	0.571
Fibrinogen (mg/dl)	270(210-307)	283(230-318)	377(323-402)	377(342-421)	428(401-460)	<0.001*
Fibrinogen-to-albumin ratio	6(4.4-6.8)	6.2(5.1-7.1)	8.2(7.4-9.1)	8.2(7.4-9.5)	9.5(8.7-10.8)	<0.001*
Albumin-to-creatinine ratio in spot urine	<0.02	<0.02	<0.02	0.26(0.058-1,2)	0.42(0.078-2)	<0.001*

**p<0.05, Kruskal-Wallis test; ** p<0.05, Chi-square test*

BMI, Body mass index; T2DM, Type 2 diabetes mellitus; GLP-1, Glucagon-Like Peptide-1 ; SGLT-2, Sodium–Glucose Cotransporter-2; DDP-4, Dipeptidyl Peptidase-4.

Group 1: Control

Group 2: Type 2 diabetes mellitus (no complications)

Group 3: Type 2 diabetes mellitus + neuropathy (no proteinuria, no retinopathy)

Group 4: Type 2 diabetes mellitus + microalbuminuria (no retinopathy, no neuropathy)

Group 5: Type 2 diabetes mellitus + neuropathy + retinopathy +proteinuria

Table II: Statistical results of the data for the diabetic and control groups

Parameters	Groups					P Value
	Group 1 (n=61)	Group2 (n=61)	Group3 (n=61)	Group4 (n=61)	Group5 (n=61)	
HbA1c %	5.7 (5.4-6)	7.7(6.7-8)[a]	7.2(6,7-9.2)[b]	7.8(6.9-9.1)[c]	8.6(7.3-10)[gij]	<0.001*
Fasting blood sugar	90(75-99)	138(126-159)[a]	156(133-205)[b]	153(133-205)[c]	191(139-258)[gij]	<0.001*
Albumin	4.5(4.4-4.7)	4.5(4,3-4.7)	4.5(4.3-4.7)	4.5(4.3-4.7)	4.5(4.3-4.6)	0.571
Fibrinogen	270(210-307)	283(230-318)	377(323-402)[b]	377(342-421)[c]	428(401-460)[dgij]	<0.001*
Fibrinogen-to-Albumin Ratio	6(4.4-6.8)	6.2(5.1-7.1)	8.2(7.4-9.1)[b]	8.2(7.4-9.5)[c]	9.5(8.7-10.8)[dgij]	<0.001*
Albumin-to-creatinine ratio in spot urine	<0.02	<0.02	<0.02	0.257(0.058-1.2)[cfh]	0.42(0.078-2) [dgij]	<0.001*

Data are presented as median values with interquartile ranges (IQR). Differences among the groups were analyzed using the Kruskal–Wallis test. Post hoc pairwise comparisons were performed using the Mann–Whitney U test with Bonferroni correction for multiple comparisons (adjusted significance level p < 0.005). A two-tailed p-value < 0.05 was considered statistically significant.

aGroup 1 vs. Group 2 bGroup 1 vs. Group 3 cGroup 1 vs. Group 4 dGroup 1 vs. Group 5 eGroup 2 vs. Group 3 fGroup 2 vs. Group 4 gGroup 2 vs. Group 5 hGroup 3 vs. Group 4 ıGroup 3 vs. Group 5 jGroup 4 vs. Group 5

Correlation analysis results between the FAR and fasting blood glucose and spot urine albumin-to-creatinine ratio showed a moderate positive correlation (p<0.001). The findings of the correlation analyses between the FAR and other parameters are shown in Table 3.

Table III: Correlation analysis results between fibrinogen-to-albumin ratio and other parameters

Variables	r (Spearman's correlation coefficient)	p value
HbA1c	0.459	<0.001*
Fasting plasma glucose	0.435	<0.001*
Urinary albumin-to-creatinine ratio	0.492	<0.001*

Spearman's rank correlation analysis was used to analyze the data collected. Statistical significance was set at p < 0.05.

A multinomial logistic regression analysis was carried out to determine independent predictors of complication burden, with patients without complications (Group 1) designated as the reference group. The overall model was statistically significant ($\chi^2 = 125.189$, p<0.001). The pseudo R-squared values were 0.401 (Cox and Snell), 0.428 (Nagelkerke), and 0.185 (McFadden). The analysis demonstrated that the FAR was an independent predictor of an increased complication burden. Compared with patients without complications, the odds of being in Groups 2, 3, and 4 increased progressively with higher FAR levels (OR 2.31, 2.73, and 3.86, respectively; p <0.001 for all). Age, sex, and HbA1c levels were not significantly associated with the complication burden (p > 0.05). The multinomial logistic regression results are presented in Table 4.

Table IV: Multinomial logistic regression analysis of independent predictors of complication burden in patients with type 2 diabetes mellitus

Variable	Comparison Group	Odds Ratio (OR)	95%CI	p value
Fibrinogen-to-albumin ratio	Group 3 vs Group 2	2.309	1.721–3.097	<0.001
Fibrinogen-to-albumin ratio	Group 4 vs Group 2	2.727	2.002–3.714	<0.001
Fibrinogen-to-albumin ratio	Group 5 vs Group 2	3.857	2.749–5.410	<0.001
Age	All comparisons	Not significant	–	>0.05
HbA1c	All comparisons	Not significant	–	>0.05
Sex	All comparisons	Not significant	–	>0.05

Reference category: Group 2 (diabetic patients without complications)

Group 3: Type 2 diabetes mellitus + neuropathy (no microalbuminuria/proteinuria, no retinopathy)

Group 4: Type 2 diabetes mellitus + microalbuminuria (no retinopathy, no neuropathy)

Group 5: Type 2 diabetes mellitus + neuropathy + retinopathy + proteinuria

Notes: OR = Odds Ratio; CI = Confidence Interval

DISCUSSION

This study aimed to assess the FAR in patients with DM, both with and without diabetic complications, and to compare the results with those of a control group. The findings indicated

no significant difference in the FAR between the control group and patients without diabetic complications. However, FAR was significantly higher in patients with diabetic nephropathy and neuropathy than in those without diabetic complications.

Fibrinogen is a critical component of the coagulation process in the human body[7,8]. Numerous studies have demonstrated a correlation between diabetic nephropathy, retinopathy, HbA1c, and plasma fibrinogen levels[20-22]. A separate study that compared fibrinogen levels in patients with type 1 or type 2 DM and healthy individuals observed higher levels in the diabetic group[23]. Contrary to the evidence reported in the literature, our study showed no statistically significant difference in fibrinogen levels between the non-complicated diabetic and non-diabetic groups. However, the results observed in patients with DM and diabetic complications were consistent with those reported in the literature. We hypothesize that the inconsistency between our findings and those reported in the extant literature may be attributable to the absence of screening for diabetic complications in patients included in previous studies.

From a mechanistic perspective, several biological pathways may explain the association between elevated fibrinogen and FAR levels and the development of diabetic complications. Chronic hyperglycemia promotes oxidative stress and systemic low-grade inflammation, both of which are central to endothelial dysfunction in diabetes[24]. Hyperglycemia-induced reactive oxygen species reduce nitric oxide bioavailability and activate inflammatory signaling pathways, resulting in endothelial activation and increased expression of adhesion molecules. This contributes to leukocyte recruitment, vascular inflammation, and microvascular damage[25].

Inflammatory cytokines, including interleukin-6 and tumor necrosis factor-α, stimulate the upregulation of fibrinogen, an acute-phase reactant. Elevated fibrinogen levels increase blood viscosity, enhance platelet aggregation, and promote a prothrombotic state, thereby impairing the microcirculatory flow. In diabetic nephropathy, these processes may contribute to glomerular endothelial injury and progressive albuminuria, whereas in diabetic neuropathy, impaired microvascular perfusion may lead to chronic nerve ischemia and axonal degeneration[26].

The FAR is indicative of inflammatory and hemodynamic changes 11. Several studies have examined the relationship between FAR and diabetes mellitus. A literature review suggested that FAR is an established predictor of diabetic retinopathy in patients with type 2 DM[27]. Further investigation into the relationship between diabetes and nephropathy revealed that FAR functioned as an independent predictor in patients diagnosed with diabetic kidney disease, in contrast to those with non-diabetic kidney disease[18]. A subsequent cohort study showed a correlation between FAR and coronary artery disease and an unfavorable prognosis when FAR was higher in individuals with DM than in those without DM[28]. Another study demonstrated that FAR is an independent risk factor for diabetic cardiac autonomic neuropathy[29]. Furthermore, higher far levels in individuals with diabetes than in those without diabetes were associated with a poorer prognosis for coronary artery disease[30]. Elevated FAR levels have also been associated with the presence of nerve damage in diabetic neuropathy[17,31], highlighting its potential as a biomarker of microvascular and macrovascular complications.

Importantly, most prior studies have focused on patients who already presented with complications. In contrast, our study evaluated the FAR in patients before the onset of diabetic complications. We observed moderate positive correlations between the FAR and fasting blood

glucose, HbA1c, and spot urine albumin-to-creatinine ratio. These findings suggest that an elevated FAR may indicate suboptimal glycemic control and could predict early microalbuminuria, thereby providing a valuable tool for the early identification of patients at risk for nephropathy.

Multinomial logistic regression analysis demonstrated that FAR was an independent predictor of the diabetic complication burden. Higher FAR levels were associated with progressively increased odds of having established complications, whereas age, sex, and HbA1c levels were not independently predictive. This supports the potential utility of FAR as a biomarker for risk stratification, emphasizing its clinical relevance in identifying high-risk patients for closer monitoring and early intervention.

Our study has several important limitations. First, this study employed a retrospective design. Second, the sample size was comparatively diminutive. Third, due to its retrospective nature, a comprehensive evaluation of individual diabetic microvascular and macrovascular complications was not possible. Fourth, although sodium–glucose cotransporter-2 inhibitor use was present in all diabetic groups, the sample size was limited, and the potential impact on microvascular outcomes cannot be entirely ruled out. Finally, the impact of blood glucose regulation on the FAR could not be assessed retrospectively.

CONCLUSION

In patients with type 2 DM, FAR is independently and progressively associated with the burden of microvascular complications. Elevated levels were observed in patients with isolated and multiple complications, whereas age, sex, and HbA1c levels were not independent predictors. These findings suggest that FAR may serve as a simple and accessible marker for the early identification of patients at an increased risk of developing diabetic microvascular complications. However, larger prospective studies are warranted to confirm these findings and to further establish the clinical utility of this marker in predicting complication development.

Author Contributions: Idea/Concept: A1, Design: A1,A2, Data Collection/Processing: A1, A2, Analysis/Interpretation: A1, Literature Review: A1, A2 Drafting/Writing: A1, Critical Review: A1, A2.

Ethical Approval: This study was approved by the Mersin University Ethical Committee (protocol number 2024/418) on May 8, 2024.

Conflict of Interest: The author(s) declare that there is no financial conflict of interest related to this article.

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