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Relationship between Serum Asprosin and Diabetic Nephropathy in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background: Diabetic kidney disease (DKD) is a major cause of end-stage renal disease (ESRD) in type 2 diabetes mellitus (T2DM). Traditional markers such as albuminuria and eGFR often indicate renal injury only after irreversible damage. Asprosin, a fasting-induced adipokine linked to insulin resistance, hyperglycemia, and inflammation, may serve as an early biomarker for diabetic kidney injury.

Aim: This study aimed to assess serum asprosin levels in T2DM cases with and without diabetic nephropathy (DN) and to explore their relationship with, urine albumin-to creatinine ratio (UACR) and eGFR.

Methods: In this cross-sectional analysis, 80 subjects were equally distributed into four groups: healthy control (Group I), T2DM cases without nephropathy (Group II), those with microalbuminuria (Group III) and those with macroalbuminuria (Group IV). Clinical, biochemical, and ultrasonographic assessments were conducted and serum asprosin concentration was measured by ELISA. **Results:** Mean serum asprosin levels were significantly higher in group IV (131.48 ng/ml) than in groups I (26.04 ng/ml), II (30.87 ng/ml), and III (42.55 ng/ml) ($P<0.001$). Asprosin discriminated nephropathy (micro- and macroalbuminuria) from normoalbuminuria with an AUC of 0.955, sensitivity 95.0% and specificity 87.5% at a cut-off > 32.26 ng/ml. Asprosin showed substantial positive correlations with waist circumference (WC), BMI, serum urea, creatinine, UACR, HbA1c, FBS, HOMA-IR, and TGs, and a marked negative correlation with eGFR (all $P < 0.05$). Multivariate analysis identified serum urea, creatinine, UACR, and HbA1c as independent predictors of asprosin. **Conclusions:** Higher serum asprosin levels observed in T2DM cases with nephropathy were significantly linked to parameters of renal dysfunction and altered metabolic status, underscoring its value as a potential early indicator of DKD.

Keywords: Diabetic nephropathy, Asprosin, Insulin resistance, Type 2 diabetes mellitus.

INTRODUCTION

Diabetic kidney disease (DKD), a common complication of type 2 diabetes mellitus (T2DM), remains the leading cause of end-stage renal disease (ESRD) worldwide. Despite notable improvements in diabetes care, a substantial proportion of T2DM cases still progress to ESRD, necessitating dialysis or renal transplantation and resulting in considerable health and economic burdens [1].

One of key challenges in preventing ESRD in T2DM is lack of effective early diagnostic tools to identify and monitor diabetic kidney injury before irreversible damage occurs. Therefore, early detection and control of risk factors are essential to halt or slow disease progression. Identifying novel biomarkers associated with glucose metabolism and renal function could provide critical insights for timely intervention [2].

Asprosin, a newly discovered adipokine secreted by white adipose tissue during fasting, promotes a rapid hepatic release of glucose into bloodstream [3]. Since its discovery, several studies have demonstrated elevated circulating asprosin levels in T2DM and its association with insulin resistance (IR), suggesting its potential role in metabolic dysregulation [4, 5]. This investigation aimed to determine serum asprosin levels in T2DM cases, with and without DKD, and to investigate their correlation with eGFR and UACR, exploring potential of asprosin as a biomarker for early identification and monitoring of DKD.

PATIENTS AND METHODS

Design and population: This cross-sectional investigation included a total of 80 participants, consisting of 60 cases diagnosed with T2DM and 20 sex- and age-matched healthy as control group. Participants were recruited from Outpatient Clinic and Nephrology Unit of Internal Medicine Department, Tanta University Hospital. The study was conducted between October 2022 and January 2024.

Eligibility criteria: The study enrolled cases diagnosed with T2DM, including those with and without DN.

Exclusion criteria: Cases with T1DM or secondary forms of diabetes, those presenting with acute metabolic complications such as hyperosmolar hyperglycemic state, diabetic ketoacidosis, or lactic acidosis, as well as subjects with advanced hepatic or renal dysfunction, major cardiovascular or cerebrovascular disease, malignancy, urinary tract infection and pregnancy.

Participants were classified into four groups of 20 each: **Group I** (healthy control), **Group II** (diabetic cases without nephropathy), **Group III** (diabetic cases with microalbuminuria, ACR 30–300 mg/g) and **Group IV** (diabetic cases with macroalbuminuria, ACR >300 mg/g).

All cases were subjected to clinical and laboratory assessment: All participants underwent comprehensive evaluation including detailed history taking and routine laboratory investigations. HOMA-IR was calculated for cases not on insulin therapy. Serum asprosin was

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quantified by ELISA, and comprehensive pelvi-abdominal ultrasonography was conducted for each participant.

Sample collection and asprosin measurement: From each subject, 7.5 mL of venous blood were obtained under aseptic conditions and transferred into sterile tubes containing EDTA and clot activator. EDTA samples were used for HbA1c measurement and for storage at -20 °C for subsequent asprosin analysis. Serum was separated by centrifugation at 1000 × g for 15 minutes for immediate routine assays, while frozen samples were thawed only once prior to analysis to avoid degradation. Hemolyzed samples were excluded. Serum asprosin levels were determined by double-antibody sandwich ELISA: samples were incubated in wells precoated with asprosin monoclonal antibody, followed by biotin-labelled antibodies and streptavidin-HRP, with subsequent colorimetric detection at 450 nm. Optical densities were measured, and asprosin concentrations were calculated based on a standard curve generated from calibrators.

Ethical considerations: The study was done after being accepted by the Research Ethics Committee, Tanta University. All patients provided written informed consents prior to their enrolment. The consent form explicitly outlined their agreement to participate in the study and for the publication of data, ensuring protection of their confidentiality and privacy. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical methods

IBM SPSS Statistics version 20.0 (Armonk, NY, USA) was used for all statistical analyses. Qualitative data were summarized as counts and percentages, whereas quantitative data were tested for normality via Shapiro–Wilk test and described as range (minimum–maximum), mean ± SD, median, and IQR. Chi-square test was utilized for categorical comparisons and applying Monte Carlo correction when >20% of expected cell frequencies were below five. Parametric data were analyzed by one-way ANOVA with Tukey's post hoc test. Non-parametric data were assessed using Mann–Whitney U test for two groups or Kruskal–Wallis test with Dunn's post hoc analysis for more than two groups. Statistical significance was set at $p \leq 0.05$.

RESULTS

Among the four groups, gender distribution was comparable with no substantial variation (P=0.939). Age increased markedly across groups (P<0.001), with group I having youngest mean age (42.80 ± 6.21 years) compared to groups II (51.30 ± 6.55), III (53.40 ± 6.48) and IV (57.65 ± 10.58). BMI differed notably (P=0.010), with group III showing a lower BMI (23.55 ± 3.97 kg/m²) than groups I and II. WC also varied markedly (P=0.017), with group III demonstrating lowest mean value (77.17 ± 13.14 cm). Diabetes duration increased progressively from group II (7.45 ± 0.83 years) to groups III (9.95 ± 2.16) and IV (10.35 ± 2.54), showing notable variations (P<0.001). Regarding treatment, OHD use differed substantially (P<0.001), with all cases in groups II–IV receiving oral hypoglycemic drugs (OHD), unlike group I. Insulin therapy was significantly more frequent in group III (45%) and group IV (100%) relative to none in groups I and II (P<0.001) (Table 1).

Table (1): Baseline demographic and clinical characteristics of the studied groups

	Group I (n=20)	Group II (n=20)	Group III (n=20)	Group IV (n=20)	P-value
Gender					
Male	8 (40.0%)	10 (50.0%)	9 (45.0%)	9 (45.0%)	0.939
Female	12 (60.0%)	10 (50.0%)	11 (55.0%)	11 (55.0%)	
Age (years)	42.80 ± 6.21	51.30 ± 6.55	53.40 ± 6.48	57.65 ± 10.58	**<0.001***
p_0		**0.004***	**<0.001***	**<0.001***	
Sig. bet. groups		p_1=0.822, p_2=0.051, p_3=0.305			
BMI (kg/m²)	27.40 ± 4.19	27.36 ± 3.38	23.55 ± 3.97	25.95 ± 4.43	**0.010***
p_0		1.000	**0.017***	0.664	
Sig. between groups		**P_1=0.018***, P_2=0.683, P_3=0.240			
WC (cm)	89.42 ± 15.15	89.52 ± 10.45	77.17 ± 13.14	85.07 ± 15.23	**0.017***
p_0		1.000	**0.029***	0.745	
Sig. between groups		**P_1=0.027***, P_2=0.730, P_3=0.267			
Diabetes duration (years)	-	7.45 ± 0.83	9.95 ± 2.16	10.35 ± 2.54	**<0.001***
Sig. between groups		**P_1=0.001***, **P_2<0.001***, P_3=0.800			
OHD, n (%)	0 (0.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)	**<0.001***
Insulin, n (%)	0 (0.0%)	0 (0.0%)	9 (45.0%)	20 (100.0%)	**<0.001***

n: number, OHD: Oral Hypoglycemic Drugs, BMI: Body Mass Index, WC: Waist Circumference, *: Significant P-value.

Serum urea, creatinine, eGFR, UACR, HbA1c, FBS, 2HPP, and asprosin levels showed substantial variations among all groups (all P<0.001). Serum urea and creatinine levels progressively increased from groups I to IV, with notable pairwise differences observed between groups I and III, I and IV, and II and III for both parameters. eGFR notably decreased across groups, with group IV having lowest mean (31.37 ± 5.56 ml/min/1.73m²), showing notable pairwise differences in all comparisons.

UACR increased markedly from normoalbuminuria in group I (median 10.8 mg/g) to macroalbuminuria in group IV (median 435.1 mg/g), with all pairwise comparisons notable.

HbA1c rose notably across groups, from 5.03 ± 0.32% in group I to 8.10 ± 0.40% in group IV. FBS and 2HPP values also increased substantially, with group IV displaying highest levels. FBS pairwise comparisons showed marked variations except between groups III and IV (P3=0.981), while 2HPP variations were significant except between groups II and III (P1=0.948).

Relative to group I, both groups II and III demonstrated substantially higher HOMA-IR values (P < 0.001). However, no meaningful variation was noted between groups II and III themselves (P_1 = 0.858).

A marked intergroup variation in cholesterol levels was also detected (P = 0.010), with group III showing a substantial reduction compared to group IV (P_3 = 0.027). Asprosin levels increased substantially across groups, from a median of 26.04 ng/ml in group I to 131.48 ng/ml in group IV, with notable pairwise differences between groups I and III (P1=0.016), I and IV (P2<0.001) and II and IV (P3=0.001). In contrast, TGs, HDL, and LDL did not differ substantially among groups (Table 2 & Figure 1).

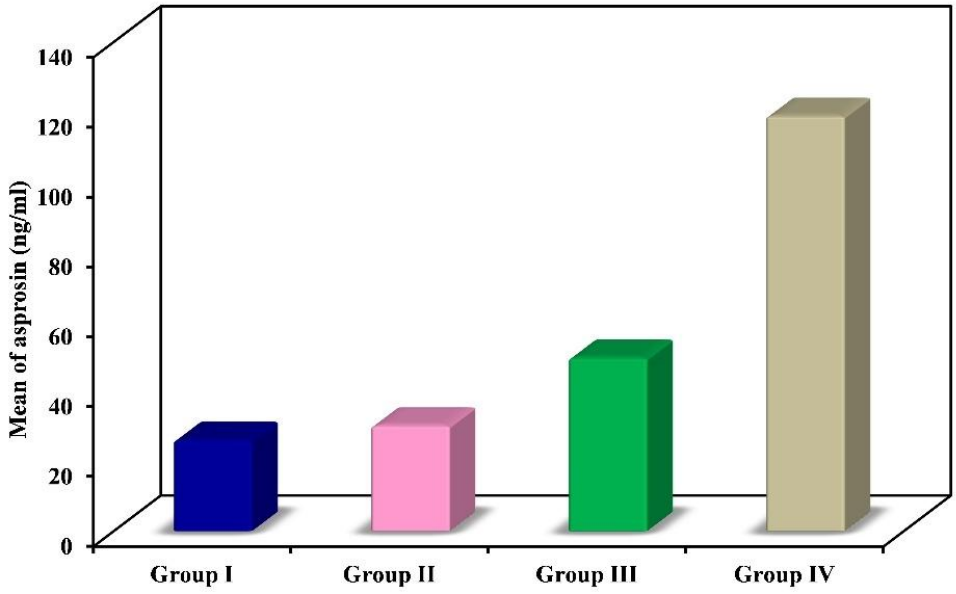

Figure (1): Comparison between the four studied groups according to asprosin.

Table (2): Laboratory data comparison across studied groups

	Group I (n=20)	Group II (n=20)	Group III (n=20)	Group IV (n=20)	P-value
Serum Urea (mg/dL)	17.38 ± 1.72	28.65 ± 3.09	103.4 ± 22.68	118.2 ± 28.73	**<0.001***
p0		0.221	**<0.001***	**<0.001***	
Sig. between groups			**P1<0.001***, **P2<0.001***, P3=0.061		
Creatinine (mg/dL)	0.83 ± 0.09	0.90 ± 0.14	2.20 ± 0.29	3.40 ± 0.83	**<0.001***
p0		0.954	**<0.001***	**<0.001***	
Sig. between groups			**P1<0.001***, **P2<0.001***, **P3<0.001***		
eGFR (ml/min/1.73m²)	90.70 ± 9.59	79.83 ± 9.90	70.05 ± 5.09	31.37 ± 5.56	**<0.001***
p0		**<0.001***	**<0.001***	**<0.001***	
Sig. between groups			**P1<0.001***, **P2=0.001***, **P3<0.001***		
UACR (mg/g)	10.80 (10.58 – 11.85)	25.0 (18.75 – 27.0)	147.9 (82.10 – 158.45)	435.1 (336.4 – 515.0)	**<0.001***
p0		**0.006***	**<0.001***	**<0.001***	
Sig. between groups			**P_1=0.006***, **P_2<0.001***, **P_3=0.006***		
HbA1C (%)	5.03 ± 0.32	7.03 ± 0.42	7.59 ± 0.60	8.10 ± 0.40	**<0.001***
p0		**<0.001***	**<0.001***	**<0.001***	
Sig. between groups			**P1=0.001***, **P2<0.001***, **P3=0.003***		
FBS (mg/dL)	95.0 (87.0 – 97.50)	130.0 (97.50 – 146.50)	160.0 (145.0 - 168.0)	160.0 (129.0 –172.0)	**<0.001***
p0		**0.003***	**<0.001***	**<0.001***	
Sig. between groups			**P1=0.008***, **P2=0.007***, P3=0.981		
2HPP (mg/dL)	140.5 (137.0 – 148.0)	225.0 (185.0 – 250.0)	225.0 (200.0 – 241.50)	300.8 (242.52 – 323.36)	**<0.001***
p0		**<0.001***	**<0.001***	**<0.001***	
Sig. between groups			P1=0.948, **P2=0.003***, **P3=0.004***		
HOMA-IR	1.09 ± 0.36	4.08 ± 0.25	4.14 ± 0.25	–	**<0.001***
p0		**<0.001***	**<0.001***	**–**	
Sig. between groups			P1=0.858, P2=–, P3=–		
Cholesterol (mg/dL)	195.2 ± 17.64	191.7 ± 17.33	178.0 ± 15.61	195.2 ± 17.64	**0.010***
p0		0.927	**0.016***	0.998	
Sig. between groups			P1=0.079, P2=0.974, **P3=0.027***		
TG (mg/dL)	141.4 ± 13.41	141.3 ± 12.19	141.8 ± 11.82	151.9 ± 18.44	0.052
HDL (mg/dL)	47.95 ± 5.97	48.79 ± 5.14	50.89 ± 6.10	50.90 ± 7.11	0.316
LDL (mg/dL)	122.2 ± 11.11	124.3 ± 13.84	121.4 ± 16.53	128.6 ± 12.21	0.349
Asprosin(ng/ml)	26.04 (22.60 – 29.50)	30.87 (26.23 – 32.10)	42.55 (33.29 – 72.26)	131.48 (88.82 – 159.30)	<0.001*
p0		0.094	**<0.001***	**<0.001***	
Sig. between groups			**P_1=0.016***, **P_2<0.001***, **P_3=0.001***		

eGFR: estimated Glomerular Filtration Rate, HbA1C: Hemoglobin A1C, FBS: Fasting Blood Sugar, 2HPP: 2-Hour Postprandial Glucose, TGs: Triglycerides, HDL: High-Density Lipoprotein, LDL: Low-Density Lipoprotein, *: Significant P-value.

Ultrasonographic findings: A substantial variation was observed between studied groups regarding U/S findings ($P < 0.001$). In group I, all participants (100%) showed normal U/S patterns, while in group II, 70% had normal findings and 30% exhibited grade I changes. In group III, none of participants had normal U/S findings, instead 15% had grade I and 85% had grade II changes. In group IV, no cases had normal or grade I/II patterns; 90% showed grade III changes, and 10% demonstrated grade IV changes.

Correlation between asprosin and different parameters in groups II, III and III: Asprosin revealed significant positive correlations with BMI, WC, serum urea, creatinine, UACR, HbA1c, FBS, HOMA-IR, and TG. In contrast, it showed a substantial negative correlation with eGFR. No marked correlations were detected between asprosin and 2HPP, cholesterol, HDL, or LDL. In group II, asprosin showed notable positive correlations with BMI, WC, serum urea, creatinine, eGFR (negative correlation), UACR, FBS, HOMA-IR, and TG. No substantial correlations were found with HbA1c, 2HPP, cholesterol, HDL, or LDL. In group III, asprosin exhibited significant positive correlations with BMI, WC, serum urea, creatinine, UACR, and TG, while showing a significant negative correlation with eGFR. No substantial correlations were observed with HbA1c, FBS, 2HPP, cholesterol, HDL, or LDL (Table 3).

Table (3): Correlation between asprosin and different parameters in Group II, III and III

	Group II		Group III		Group IV	
	r	**P-value**	**r**	**P-value**	**r**	**P-value**
BMI (kg/m²)	0.682	**0.002***	0.627	**0.007***	0.629	**0.003***
WC (cm)	0.605	**0.005***	0.688	**0.001***	0.579	**0.007***
Serum Urea (mg/dl)	0.58	**0.007***	0.597	**0.005***	0.988	**<0.001***
Creatinine (mg/dl)	0.69	**0.001***	0.561	**0.010***	0.988	**<0.001***
e-GFR (ml/min/1.73 m²)	-0.501	**0.025***	-0.689	**0.001***	-0.983	**<0.001***
UACR (mg/g)	0.579	**0.007***	0.529	**0.017***	0.96	**<0.001***
HbA1C (%)	0.513	**0.021***	0.369	0.109	0.153	0.52
FBS (mg/dl)	0.498	**0.025***	0.513	**0.021***	0.149	0.53
2HPP (mg/dl)	0.278	0.236	0.386	0.093	0.149	0.53
HOMA-IR	0.616	**0.004***	0.654	**0.029***		
Cholesterol (mg/dl)	0.026	0.915	0.144	0.544	0.229	0.332
TG (mg/dl)	0.659	**0.002***	0.495	**0.027***	0.495	**0.027***
HDL (mg/dl)	-0.035	0.884	-0.19	0.422	-0.343	0.139
LDL (mg/dl)	0.412	0.071	0.421	0.064	0.28	0.232

BMI: Body Mass Index, WC: Waist Circumference, eGFR: estimated Glomerular Filtration Rate, LDL: Low-Density Lipoprotein, HbA1C: Hemoglobin A1C, FBS: Fasting Blood Sugar, 2HPP: 2-Hour Postprandial Glucose, TGs: Triglycerides, HDL: High-Density Lipoprotein, *: Significant P-value.

Relation between asprosin and US grading in total cases: A highly significant correlation was identified between serum asprosin levels and U/S grading across entire study cohort ($P < 0.001$). Cases with normal U/S findings had lowest asprosin levels, with a mean of 30.53 ± 7.10 ng/mL. Asprosin levels increased progressively with worsening U/S grades: Cases with grade I and II changes showed elevated means of 44.11 ± 23.49 ng/mL and 45.46 ± 18.05 ng/mL respectively. Notably, grade III cases exhibited a marked rise in asprosin levels with a mean of 113.05 ± 45.42 ng/mL and highest levels were recorded in grade IV cases (mean 171.05 ± 0.87 ng/mL). These findings indicated a clear trend of rising serum asprosin concentrations correlating with increasing severity of renal ultrasonographic abnormalities (Figure 2).

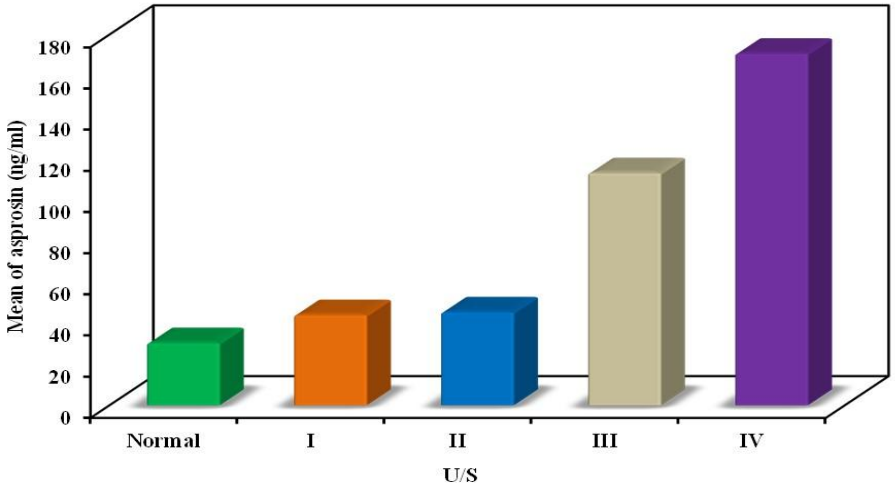

Figure (2): Relation between asprosin and US grading in total cases (n = 60).

Asprosin demonstrated excellent diagnostic performance in differentiating albuminuria categories. For distinguishing albuminuria (microalbuminuria and macroalbuminuria) from normoalbuminuria, asprosin showed an AUC of 0.955 (95% CI: 0.914–0.996, P<0.001) at a cutoff > 32.26 ng/ml, with a 95.0% sensitivity and 87.5% specificity. In discriminating between microalbuminuria and macroalbuminuria, AUC was 0.920 (95% CI: 0.837–1.0, P<0.001) with a cutoff > 65.01 ng/ml, sensitivity of 80.0% and specificity of 75.0%. For distinguishing microalbuminuria from normoalbuminuria, asprosin achieved an AUC of 0.870 (95% CI: 0.759–0.981, P<0.001) at a cutoff >32.34 ng/ml, 85.0% sensitivity and 80.0% specificity **Figure 3.**

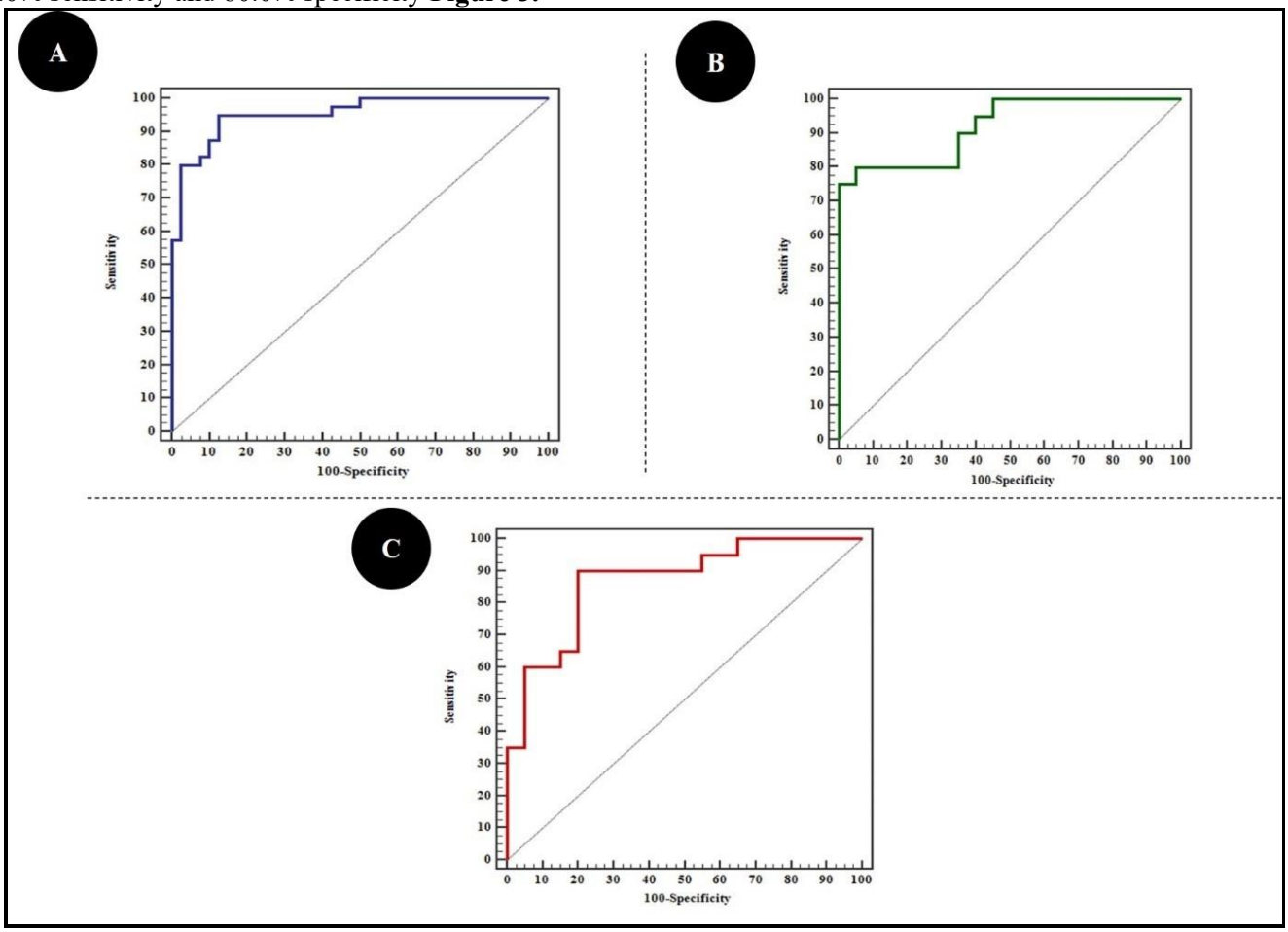

Figure (3): ROC curve for asprosin in differentiating: A) macroalbuminuria and microalbuminuria from normoalbuminuria, B) macroalbuminuria from microalbuminuria, C) microalbuminuria from normoalbuminuria.

In multivariate regression, only creatinine (P=0.003), UACR (P<0.001), HbA1c (P=0.022), and U/S (P<0.001) remained significant predictors (Table 4).

Table (4): Linear regression analysis for the parameters affecting asprosin in total patients

	Univariate		Multivariate	
	B (95%CI)	**P-value**	**B (95%CI)**	**P-value**
Age (years)	0.724(-0.769 - 2.217)	0.336		
Gender	-7.848(-32.880 - 17.184)	0.533		
BMI (kg/m²)	3.303(0.417 - 6.189)	**0.026***	-0.020 (-1.558 - 1.518)	0.979
WC (cm)	0.948(0.071 - 1.825)	0.035*	0.204 (-0.247 - 0.655)	0.368
DM duration (years)	2.764(-.2.586 - 8.113)	0.305		
Serum Urea (mg/dl)	0.839(0.662 - 1.016)	**<0.001***	0.137 (-0.094 - 0.367)	0.239
Creatinine (mg/dl)	38.575(34.166 - 42.984)	**<0.001***	21.788 (7.547 - 36.029)	**0.003***
e-GFR (ml/min/1.73 m²)	-1.834(-2.134 - -1.534)	**<0.001***	-0.308 (-0.884 - 0.268)	0.288
UACR (mg /g)	0.242(0.214 - 0.269)	**<0.001***	0.163 (0.077 - 0.249)	**<0.001***
HbA1C (%)	39.592(22.996 - 56.188)	**<0.001***	8.929 (16.503 - 1.355)	**0.022***
FBS (mg/dl)	0.630(0.176 - 1.085)	**0.007***	0.030 (-0.130 - 0.190)	0.706
Cholesterol(mg/dl)	0.484(-0.172 - 1.140)	0.145		
TG (mg/dl)	1.675(0.960 - 2.389)	**<0.001***	0.287 (-0.032 - 0.606)	0.077
HDL (mg/dl)	1.543(-0.474 - 3.559)	0.131		
LDL (mg/dl)	0.295(-0.581 - 1.171)	0.503		
Ultrasound	28.204(20.923 - 35.485)	**<0.001***	17.926 (26.571 - 9.281)	**<0.001***

BMI: Body Mass Index, UACR: Urinary Albumin-to-Creatinine Ratio, HbA1C: Hemoglobin A1C, FBS: Fasting Blood Sugar, TGs: Triglycerides, HDL: High-Density Lipoprotein, *: Significant P-value.

DISCUSSION

T2DM has become a significant global health concern, with its prevalence expected to affect 10.4% of adults worldwide by 2040. DN, a key complication of T2DM characterized by proteinuria and renal insufficiency, is leading cause of chronic kidney disease and ESRD, accounting for approximately 50% of ESRD cases requiring dialysis or transplantation [6]. Asprosin, a newly identified hormone that stimulates hepatic glucose release, has been linked to DKD risk factors such as hyperglycemia, IR and inflammation, with elevated asprosin levels observed in experimental models of T2DM and IR [7]. This cross-sectional observational investigation aimed to evaluate serum asprosin levels in T2DM cases with and without DKD, including 60 T2DM cases divided into three groups—diabetics without nephropathy (Group II), with microalbuminuria (Group III), and with macroalbuminuria (Group IV)—alongside with 20 healthy controls (Group I).

Our findings demonstrated that mean serum asprosin levels were substantially elevated in group IV relative to groups I, II & III and were also markedly elevated in group III relative to groups I and II. No marked difference was detected between groups I and II. ROC analysis demonstrated that asprosin could accurately distinguish diabetic cases with nephropathy (micro- and macroalbuminuria) from normoalbuminuric individuals at a threshold of > 32.26 ng/ml, achieving 95.0% sensitivity, 87.5% specificity, 88.4% PPV and 94.6% NPV.

Significant positive correlations were found between asprosin and BMI, WC, serum urea, creatinine, UACR, HbA1c, FBS, HOMA-IR and TGs across diabetic groups, while eGFR showed a substantial negative correlation with asprosin in all groups. Univariate regression identified BMI, WC, serum urea, creatinine, TGs and ultrasonographic findings as significant predictors of asprosin with multivariate analysis confirming serum urea and creatinine as independent predictors. The observed positive correlation between asprosin and BMI is consistent with asprosin's role as a fasting-induced adipokine that promotes hepatic glucose release and appetite stimulation, processes that can exacerbate obesity, IR and impaired glucose homeostasis.

Several clinical studies have highlighted asprosin role in metabolic disorders. **Ulloque-Badaracco *et al.*** [8] reported substantially elevated asprosin levels in T2DM cases, metabolic syndrome and obesity. **Diao *et al.*** [9] proposed that asprosin may play a role in pathogenesis of diabetes by modulating glucose homeostasis, insulin secretion, appetite regulation and insulin sensitivity. Similarly, **Zhang *et al.*** [10] found elevated asprosin levels in individuals and animal models with IR, T2DM or obesity. The association between asprosin and obesity has yielded inconsistent findings. **Wang *et al.*** [11] and **Ugur *et al.***

[12] reported notably higher asprosin levels in obese adults, with **Wang *et al.*** [11] also linking elevated asprosin to IR in obese children, while **Long *et al.*** [13] found lower asprosin levels in obese children relative to normal-weight peers, with notable gender differences. **Duerrschmid *et al.*** [14] demonstrated that circulating asprosin crosses blood-brain barrier to activate orexigenic AgRP neurons, stimulating appetite and fat accumulation. Corroborating our findings, **Kim *et al.*** [15] and **Lv *et al.*** [16] reported positive correlations between asprosin and TGs, BMI, WC, fasting blood glucose (FBG) and HbA1c, while **Mirr *et al.*** [17] observed positive correlations with BMI, WC, and HOMA-IR. **Corica *et al.*** [18] noted a decrease in fasting asprosin with increasing BMI.

Wang *et al.* [19] found elevated asprosin in individuals with impaired glucose regulation and T2DM, which is aligning with our results and other studies reported positive correlations between asprosin, FBG & HOMA-IR and negative correlations with HOMA-β, underscoring asprosin's role in glucose metabolism. Elevated asprosin promotes hepatic gluconeogenesis and glucose release, exacerbating hyperglycemia and IR, thereby contributing to a cycle of impaired insulin action and metabolic dysregulation.

Animal studies by **Duerrschmid *et al.*** [14] and **Romere *et al.*** [20] reported increased asprosin in insulin-resistant models with Olfr734 identified as its hepatic receptor mediating glucose production. Olfr734 deficiency improved insulin sensitivity and reduced glucose output. Asprosin also promotes inflammation, where Li ***et al.*** [21] showed that it induced TLR4 expression and β-cell dysfunction, while **Jung *et al.*** [22] found that it impaired insulin sensitivity via inflammatory pathways.

Clinically, multiple studies reported elevated asprosin in T2DM cases with nephropathy, including **Liu *et al.*** [23], **Mahat *et al.*** [24], **Liang *et al.*** [25], **Li *et al.*** [26], **Ma *et al.*** [27] and **Abd-Alwahid *et al.*** [28], all associating high asprosin with DKD severity. Studies by **Zhou *et al.*** [29], **Xu *et al.*** [30], **Wang *et al.*** [31], **Oruc *et al.*** [32], **Deng *et al.*** [33] and **Zhang *et al.*** [10] consistently confirmed increased asprosin correlates with progression or early detection of DKD. Elevated asprosin likely exacerbates renal injury by upregulating pro-inflammatory cytokines (TNFα, IL1β, IL-8 & IL-12) and promoting fibrosis.

Positive correlations between asprosin and serum urea or creatinine may reflect increased protein catabolism, impaired renal clearance, or both, which is supported by **Shabir *et al.*** [34], **Goodarzi *et al.*** [35], **Wang *et al.*** [31] and **Deng *et al.*** [33], who consistently found that asprosin positively associated with BMI, HbA1c, IR markers, serum creatinine & uACR and negatively with eGFR, highlighting its potential role in DKD pathogenesis.

LIMITATIONS

Certain limitations must be considered when interpreting present findings. The single-center design may constrain their applicability to broader populations. The relatively limited sample size may have reduced statistical robustness and increased susceptibility to sampling bias. Moreover, the study did not include serial assessments of serum asprosin during different treatment phases, precluding evaluation of its longitudinal behavior and its prospective value in reflecting treatment efficacy or disease progression.

CONCLUSIONS

Serum asprosin levels were notably higher in T2DM cases with nephropathy, correlated with renal and metabolic parameters and effectively distinguished nephropathy stages. These results support asprosin as a promising biomarker for early detection and monitoring of DKD in T2DM.

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