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Evaluating Urinary Thrombospondin 2 (TSP-2) Levels in Patients with Diabetic Nephropathy: A Cross-Sectional Study

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KEYWORDS

Urinary Thrombospondin 2, Diabetic nephropathy, Microalbuminuria, Macroalbuminuria

ABSTRACT:

Background: In diabetic nephropathy, changes in the renal microenvironment can lead to increased fibrosis and inflammation, processes in which thrombospondin-2 (TSP-2) may be implicated.

Objective: To determine urinary thrombospondin-2 levels in patients with diabetic nephropathy.

Methods: This was a hospital-based cross-sectional study conducted in the Department of Biochemistry, Vinayaka Mission's Kirupananda Variyar Medical College and Hospital, Tamil Nadu, India between January 2024 and June 2024. The study included 40 healthy individuals as controls (Group A) and 120 diabetic patients diagnosed with nephropathy, up to stage 3 classification based on urinary albumin levels [Group B, patients with normoalbuminuria (UACR <30mg/g); Group C, microalbuminuria (UACR between 30 and 300mg/g); and Group D, macroalbuminuria (UACR >300mg/g)].

Results: The study found significant differences in alcoholism prevalence, BMI, and diabetes duration among the groups. Group D had the highest prevalence of alcoholism (37.5%, $p = 0.010$). BMI progressively increased from Group A (23.8 ± 2.5 kg/m²) to Group D (28.4 ± 3.9 kg/m², $p = 0.004$). Diabetes duration was longest in Group D (10.1 ± 3.1 years) and shortest in Group B (6.5 ± 2.3 years, $p < 0.001$). No significant differences were noted in smoking, blood pressure, or hypertension. Blood glucose and HbA1c levels were significantly higher in diabetic groups ($p < 0.001$), with Group A having the lowest mean glucose level (98.5 ± 12.4 mg/dL) and Group C the highest (280.2 ± 105.6 mg/dL). Insulin levels did not differ significantly among groups ($p = 0.987$). Lipid profile variations were not statistically significant, including cholesterol ($p = 0.231$), triglycerides ($p = 0.180$), HDL ($p = 0.975$), LDL ($p = 0.328$), and VLDL ($p = 0.865$). Urinary TSP-2 levels showed no significant differences across groups ($p = 0.702$). Correlation analysis indicated no significant associations between TSP-2 and clinical parameters, including UACR, glucose, HbA1c, and creatinine. ROC analysis for TSP-2 as a diagnostic marker for diabetes and macroalbuminuria yielded poor discriminatory performance (AUC = 0.504 and 0.528, respectively).

Conclusion: The study found that urinary thrombospondin-2 levels do not significantly differ among diabetic patients with varying degrees of nephropathy and do not serve as a reliable biomarker for diabetes or renal impairment.

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Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both.(1) It is one of the leading causes of morbidity and mortality globally, affecting millions of individuals.(2) Diabetic nephropathy (DN), a severe complication of diabetes, is marked by progressive renal impairment and is a significant contributor to end-stage renal disease (ESRD).(3) Early detection and intervention are crucial for preventing the progression of diabetic nephropathy, which can manifest as increased urinary albumin excretion.(4)

Thrombospondin-2 (TSP-2) is a matricellular protein that plays a multifaceted role in tissue remodelling, inflammation, and fibrosis.(5) It is primarily produced by various cell types, including fibroblasts and endothelial cells, and is involved in the regulation of extracellular matrix (ECM) turnover.(6) Studies have suggested that TSP-2 may have a role in the pathogenesis of diabetic complications, including nephropathy, by influencing fibrotic processes in the kidney.(7, 8) Elevated levels of TSP-2 in tissue and plasma have been associated with various chronic diseases, including cardiovascular disease and renal disorders.(9) In diabetic nephropathy, changes in the renal microenvironment can lead to increased fibrosis and inflammation, processes in which TSP-2 may be implicated.(10) However, while some studies have indicated a relationship between TSP-2 and renal fibrosis, the specific role of urinary TSP-2 as a biomarker for diabetic nephropathy remains unclear. Previous research has focused on other biomarkers such as urinary albumin and various inflammatory markers, but the utility of urinary TSP-2 in this context has not been studied. Against this background, the aim of the present study was to determine urinary thrombospondin-2 levels in patients with diabetic nephropathy.

Materials and Methods

This was a hospital-based cross-sectional study conducted in the Department of Biochemistry, Vinayaka Mission's Kirupananda Variyar Medical College and Hospital, a tertiary teaching healthcare facility in Salem, Tamil Nadu, India between January 2024 and June 2024. The study was approved by the Institutional Human Ethics Committee (IHEC). The participants were given the Participant Information Sheet (PIS) in their native language, and its contents were verbally explained to ensure their understanding and satisfaction. Enrolment into the study proceeded upon receipt of written informed consent.

The total sample size was 160 – divided into four groups based on urinary albumin creatinine ratio (UACR).(11) The study included 40 healthy individuals (caregivers of patients, friends, staff members, and family) as controls (considered Group A). Also, the study included 120 diabetic patients diagnosed with nephropathy, up to stage 3 classification based on urinary albumin levels – Group B, 40 diabetic patients with normoalbuminuria (UACR <30mg/g); Group C, 40 diabetic patients with microalbuminuria (UACR between 30 and 300mg/g); and Group D, 40 diabetic patients with macroalbuminuria (UACR >300mg/g).(12) However, patients with acute/chronic infection, hepatic dysfunction, severe heart failure, hypo or hyperthyroidism, pregnancy and malignancy were excluded. The blood and urine samples of each study participant were analysed for fasting blood glucose, postprandial blood glucose levels, serum urea, serum creatinine, lipid profile including total cholesterol, serum triglycerides, high density lipoprotein (HDL), low density lipoprotein (LDL), and very low-density lipoprotein (VLDL) using a fully automated analyser (Erba EM-200). The glycated haemoglobin levels (HbA1c) were measured using nephelometry. TSP-2 was analysed using quantitative sandwich enzyme-linked immunosorbent assay (ELISA; Thermo Fisher Scientific).(13)

The data obtained was manually entered into Microsoft Excel and analysed using Statistical Package for Social Sciences (SPSS) v23. All the categorical variables were summarised using frequencies and percentages. Continuous variables were summarized using mean (standard deviation) and/or median (interquartile range) (based on the results of data normality, tested using Kolmogorov–Smirnov test and the Shapiro–Wilk test). To test for statistical significance, Chi square test or Fisher exact test (for categorical variables) and independent “t” test or Mann Whitney U test (for continuous variables) was used. Pearson’s correlation coefficient was estimated to assess the correlation between two continuous variables. We used receiver

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operating characteristic (ROC) analysis to determine the area under the curve (AUC) for TSP-2 to predict diabetes and diabetic nephropathy. Statistical significance was considered at p value less than 0.05.

Results

The mean age of the study participants was 54.0 ± 7.2 years. The prevalence of alcoholism was significantly different among the groups, with the highest percentage in Group D (37.5%) and the lowest in Group A (7.5%), showing a significant p-value of 0.010. The mean BMI progressively increased from Group A (23.8 ± 2.5 kg/m²) to Group D (28.4 ± 3.9 kg/m²), with a statistically significant difference (p = 0.004). The duration of diabetes mellitus was also significantly different among the diabetic groups, with Group D having the longest duration (10.1 ± 3.1 years) and Group B the shortest (6.5 ± 2.3 years), with a highly significant p-value (<0.001). However, no significant differences were observed for smoking (p = 0.178), systolic blood pressure (p = 0.062), diastolic blood pressure (p = 0.095), or hypertension (p = 0.072) among the groups.

Blood glucose levels were significantly elevated in diabetic groups compared to the healthy control group (Group A). The mean blood glucose level in Group A was 98.5 ± 12.4 mg/dL, whereas diabetic groups exhibited higher levels: Group B at 210.7 ± 65.3 mg/dL, Group C at 280.2 ± 105.6 mg/dL, and Group D at 260.1 ± 120.4 mg/dL (p < 0.001). Similarly, HbA1c levels were significantly increased in diabetic patients. Group A had an HbA1c level of 5.8 ± 1.1%, while Groups B, C, and D showed 7.1 ± 1.5%, 7.9 ± 2.1%, and 8.8 ± 3.0%, respectively (p < 0.001). Insulin levels did not show significant differences among the groups, with Group A at 52.3 ± 58.4 µIU/mL, and comparable values observed in the diabetic groups (p = 0.987). Serum urea levels varied from 21.1 ± 5.8 mg/dL in Group A to 27.3 ± 13.2 mg/dL in Group C, but these differences were not statistically significant (p = 0.362). Likewise, serum creatinine levels remained comparable across the groups, ranging from 0.7 ± 0.2 mg/dL in Group A to 1.0 ± 0.4 mg/dL in Group D (p = 0.472).

Lipid profile parameters showed minor variations. Total cholesterol was slightly higher in Group B (190.1 ± 38.6 mg/dL) compared to Group A (168.2 ± 32.7 mg/dL), but the difference was not statistically significant (p = 0.231). Triglyceride levels were elevated in diabetic groups, with Group B showing the highest level at 200.5 ± 150.1 mg/dL, though the differences were not statistically significant (p = 0.180). HDL, LDL, and VLDL levels were similar across groups, with no significant differences (p = 0.975, p = 0.328, and p = 0.865, respectively). Microalbumin levels were significantly elevated in diabetic patients, Group B (20.8 ± 9.0 mg/dL), Group C (179.4 ± 55.2 mg/dL), and Group D (367.1 ± 58.6 mg/dL), in comparison with Group A (12.6 ± 24.5 mg/dL).

Comparison of urinary TSP-2 between the study groups: In the study, TSP-2 levels were measured across the four groups, but no statistically significant differences were found between them. Group A, the control group, had a mean TSP-2 level of 5.3 ng/mL (± 2.8), which was similar to the TSP-2 levels observed in Group B (7.1 ng/mL ± 2.6), representing diabetic patients with normoalbuminuria. Group C, comprising diabetic patients with microalbuminuria, showed a slightly higher mean TSP-2 level of 8.3 ng/mL (± 5.8). Group D, consisting of diabetic patients with macroalbuminuria, had a mean TSP-2 level of 9.0 ng/mL (± 5.1). Despite these variations, the differences in TSP-2 levels across the groups were not statistically significant (p = 0.702).

Pearson's correlation coefficient analysis between urinary TSP-2 levels and various clinical parameters: Pearson's correlation analysis was conducted to evaluate the relationship between TSP-2 and various clinical parameters. The correlation between TSP-2 and UACR was weakly positive (r = 0.095) but not statistically significant (p = 0.373). Similarly, TSP-2 showed a weak negative correlation with blood glucose (r = -0.066, p = 0.476) and HbA1c (r = -0.162), though the latter approached statistical significance (p = 0.076). Additionally, the correlation between TSP-2 and serum urea was negligible (r = -0.024, p = 0.792), as was the correlation with serum creatinine (r = -0.076, p = 0.408). A weak negative correlation was also observed between TSP-2 and uric acid levels (r = -0.122), but this was not statistically significant (p = 0.186).

ROC analysis of urinary TSP-2 levels: ROC analysis was performed to assess the predictive ability of urinary TSP-2 levels for diabetes and diabetic patients with macroalbuminuria (UACR >300 mg/g). For predicting diabetes, TSP-2 had an AUC of 0.504, with a 95% CI

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ranging from 0.387 to 0.621. A cutoff value of >5.3 ng/mL for TSP-2 resulted in a sensitivity of 62.2% and a specificity of 43.3%, indicating a poor discriminatory ability (p = 0.942). For diabetic patients with macroalbuminuria (UACR >300 mg/g), the AUC was slightly higher at 0.528, with a 95% CI of 0.409 to 0.647. Using a cutoff value of >6.1 ng/mL, TSP-2 demonstrated a sensitivity of 63.3% and a specificity of 57.8%, suggesting only marginally better diagnostic performance, though still not statistically significant (p = 0.643).

Discussion

Aging is a well-documented risk factor for metabolic disorders, including T2DM, as it is associated with increased insulin resistance, pancreatic beta-cell dysfunction, and an overall decline in glucose metabolism.(14) Older adults with diabetes are also at higher risk for cardiovascular complications, neuropathy, and nephropathy due to prolonged exposure to hyperglycaemia and associated metabolic stress.(15)

Alcohol consumption was significantly different among the groups, with the highest prevalence in Group D (37.5%) and the lowest in Group A (7.5%) (p = 0.010). Chronic alcohol consumption is associated with increased risks of insulin resistance, obesity, and liver dysfunction, all of which contribute to diabetes progression and complications.(16) Studies suggest that excessive alcohol intake exacerbates metabolic syndrome by influencing hepatic glucose production, lipid metabolism, and inflammatory pathways.(17) The mean BMI progressively increased from Group A (23.8 ± 2.5 kg/m²) to Group D (28.4 ± 3.9 kg/m²), demonstrating a statistically significant trend (p = 0.004). Obesity is a well-established risk factor for diabetes development and progression, with excess adiposity contributing to insulin resistance, chronic inflammation, and dyslipidaemia.(18) Higher BMI has been linked to poor glycaemic control and an increased risk of diabetic complications, including cardiovascular disease and kidney dysfunction.(19)

The duration of diabetes significantly differed among the diabetic groups, with Group D having the longest duration (10.1 ± 3.1 years) and Group B the shortest (6.5 ± 2.3 years) (p < 0.001). Longer disease duration is associated with a higher risk of complications, including retinopathy, neuropathy, nephropathy, and cardiovascular diseases due to cumulative hyperglycaemic damage.(20) Chronic exposure to elevated blood glucose levels contributes to endothelial dysfunction, oxidative stress, and chronic inflammation, further exacerbating disease progression and comorbid conditions.(21)

The finding that diabetic groups (Groups B, C, and D) had significantly higher blood glucose levels compared to the healthy control group (Group A) is consistent with the progression of diabetes and its complications. Group B, representing diabetic patients with normoalbuminuria, had blood glucose levels (210.7 mg/dL) that were already markedly higher than the control group (98.5 mg/dL), with even higher levels observed in Groups C (280.2 mg/dL) and D (260.1 mg/dL), reflecting worsening nephropathy. Hyperglycaemia is known to contribute to kidney damage through mechanisms such as advanced glycation end-products (AGEs) formation, increased oxidative stress, and pro-inflammatory pathways.(22-24) Elevated HbA1c levels in diabetic patients further corroborate this, with a progressive increase from Group B (7.1%) to Group D (8.8%). HbA1c reflects long-term glycaemic control, and its elevation in diabetic nephropathy patients underscores poor glycaemic management, which is closely associated with renal impairment.(25) Interestingly, insulin levels did not show significant differences across the groups. Furthermore, no significant variation in serum urea (p = 0.362) and serum creatinine (p = 0.472) was found, which may be explained by the fact that the study only included patients with diabetic nephropathy up to stage 3, where kidney function may still be relatively preserved. Early stages of diabetic nephropathy typically involve microalbuminuria without significant impairment in GFR or overt signs of renal failure.(26)

Although total cholesterol, triglycerides, and LDL levels were higher in the diabetic groups compared to controls, the differences were not statistically significant. Dyslipidaemia is common in diabetes and has been implicated in the progression of diabetic nephropathy.(27) The absence of significant differences could be attributed to the relatively small sample size or the possibility that lipid-lowering treatments, such as statins, were being used by the diabetic participants, masking potential differences. However, the slightly

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elevated triglyceride levels in Group B (200.5 mg/dL) are in line with the known association between hypertriglyceridemia and insulin resistance in diabetic patients.(28)

Although differences in TSP-2 values were observed between groups, there were no statistically significant differences between the control group (Group A) and the diabetic groups (Groups B, C, and D) suggests that urinary TSP-2 may not serve as a robust biomarker for differentiating between stages of diabetic nephropathy, at least in the early stages included in this study. The lack of significant variation between these groups contrasts with studies where TSP-2 has been implicated in other renal conditions, suggesting that its role in diabetic nephropathy may be limited or context-dependent.(29, 30) Thrombospondins, particularly TSP-1 and TSP-2, are known to be involved in tissue remodelling, inflammation, and fibrosis, processes that are central to the progression of diabetic nephropathy.(6) However, the specific role of TSP-2 in the pathophysiology of diabetic kidney disease remains less clear than that of TSP-1, which has been more consistently associated with renal fibrosis and the progression of chronic kidney disease.(31) This could explain why urinary TSP-2 levels did not correlate significantly with the severity of nephropathy. The study's focus on patients with up to stage 3 nephropathy may further explain the absence of significant differences, as TSP-2 might be more relevant in advanced stages of the disease where fibrosis is more pronounced.

The weak and statistically non-significant correlations between TSP-2 and various clinical parameters, such as UACR, blood glucose, HbA1c, and renal function markers, suggest that urinary TSP-2 is not strongly associated with glycaemic control or kidney function in the early stages of diabetic nephropathy. This finding is consistent with earlier studies where serum TSP-2 did not show strong diagnostic potential for diabetic nephropathy, despite its established role in extracellular matrix formation and tissue repair.(32) The weak positive correlation between TSP-2 and UACR ($r = 0.095$, $p = 0.373$) indicates that higher levels of urinary albumin excretion are not strongly related to TSP-2 concentrations. This suggests that urinary TSP-2 may not reflect early glomerular damage as well as other markers like albumin. Albuminuria is one of the earliest indicators of diabetic nephropathy, and its relationship with other proteins, such as TSP-1 and TSP-2, might become more pronounced in later disease stages.(33) Given that the patients in this study had nephropathy up to stage 3, the weak correlation could reflect the fact that TSP-2 is not yet playing a major role in kidney damage at this point in disease progression. The weak negative correlations between TSP-2 and both blood glucose ($r = -0.066$, $p = 0.476$) and HbA1c ($r = -0.162$, $p = 0.076$) are unexpected, as one might assume that poorer glycaemic control would be associated with higher levels of tissue remodelling proteins like TSP-2 due to increased kidney damage. However, the lack of statistical significance suggests that TSP-2 levels may not fluctuate in direct response to short- or long-term glycaemic control, at least in the stages of nephropathy studied. HbA1c, a measure of long-term glycaemic control, approached statistical significance ($p = 0.076$), which may hint at a potential link between hyperglycaemia and TSP-2 production that could become more apparent with a larger sample size or in more advanced stages of nephropathy.(34) The negligible correlations between TSP-2 and markers of renal function, such as serum urea ($r = -0.024$, $p = 0.792$) and serum creatinine ($r = -0.076$, $p = 0.408$), further suggest that urinary TSP-2 is not a reliable indicator of renal function in diabetic patients with early nephropathy. Serum creatinine is typically a late marker of kidney damage, and its correlation with other markers like TSP-2 may only emerge in more advanced stages of renal impairment.(35) The weak negative correlation between TSP-2 and uric acid levels ($r = -0.122$, $p = 0.186$), though not statistically significant, is an interesting finding. Uric acid has been implicated in the development of kidney disease through mechanisms involving endothelial dysfunction, oxidative stress, and inflammation.(36) While this correlation is not significant, the relationship between TSP-2 and uric acid may warrant further investigation in larger cohorts or in more advanced stages of nephropathy, as both factors are linked to inflammation and fibrosis in renal disease.

The ROC analysis for predicting diabetes using urinary TSP-2 levels yielded an AUC of 0.504, indicating a very poor discriminatory capacity. The AUC value, which reflects the ability of a test to distinguish between disease and non-disease states, suggests that TSP-2 levels are no better than random chance at predicting the presence of diabetes.(37) The confidence interval (95% CI: 0.387–

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0.621) further supports the conclusion that TSP-2 lacks diagnostic precision for diabetes. A cutoff value of >5.3 ng/mL for TSP-2 provided a sensitivity of 62.2% and a specificity of 43.3%, indicating a limited ability to accurately classify individuals as diabetic based on TSP-2 levels alone ($p = 0.942$). This poor performance is in line with prior studies showing that while TSP-2 plays a role in tissue remodelling and inflammation, it may not be directly involved in the metabolic pathways that drive hyperglycaemia or insulin resistance, the hallmarks of diabetes.(32) In fact, biomarkers that are more closely linked to metabolic control, such as HbA1c or fasting blood glucose, are much better suited for diagnosing diabetes.(38) Therefore, TSP-2's low predictive power for diabetes could be attributed to its more peripheral role in the pathological processes directly related to blood sugar regulation. The ROC analysis for diabetic patients with macroalbuminuria (UACR >300 mg/g) yielded slightly better results than for diabetes, but the AUC of 0.528 still indicates poor diagnostic performance ($p = 0.643$). A cutoff value of >6.1 ng/mL for TSP-2 yielded a sensitivity of 63.3% and a specificity of 57.8%, demonstrating marginal improvement over its performance for diabetes but still lacking the statistical significance necessary for clinical utility. Previous studies have identified markers such as albuminuria, serum creatinine, and eGFR as more reliable indicators of renal dysfunction in diabetic patients.(26) The limited ability of urinary TSP-2 to predict macroalbuminuria is in line with these findings and suggests that while TSP-2 may be implicated in the fibrotic processes characteristic of advanced diabetic nephropathy, it does not exhibit the sensitivity or specificity required to serve as a standalone biomarker for diagnosing or staging the disease.

Limitations

The present study has limitations. This was a cross-sectional study with limited sample size which restricts the ability to draw conclusions about causal relationships between urinary TSP-2 levels and diabetic nephropathy.

Conclusion

This study highlights significant metabolic and clinical differences among diabetic and non-diabetic individuals, particularly in blood glucose, HbA1c, BMI, alcohol use and diabetes duration. Even though serum TSP-2 levels in patients with T2DM have shown conflicting results, the present study did not show a significant elevation in urinary TSP-2 levels in patients with diabetic nephropathy.

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Table 1: Comparison of study groups, by demographic and clinical characteristics

	Group A N = 40	**Group B N = 40**	**Group C N = 40**	**Group D N = 40**	**P value**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	
Age (in years)	54.2 (7.5)	53.8 (7.1)	53.3 (6.8)	54.6 (7.2)	0.761
Smoking, n (%)	5 (12.5)	8 (20.0)	10 (25.0)	12 (30.0)	0.178
Alcoholism, n (%)	3 (7.5)	10 (25.0)	12 (30.0)	15 (37.5)	0.010*
SBP (in mmHg)	118.5 (8.2)	126.2 (9.1)	132.8 (10.4)	138.6 (11.2)	0.062
DBP (in mmHg)	76.1 (5.4)	78.9 (6.2)	80.5 (6.8)	82.2 (7.1)	0.095
Hypertension, n (%)	6 (15.0)	12 (30.0)	18 (45.0)	22 (55.0)	0.072
BMI (in kg/m2)	23.8 (2.5)	25.6 (3.1)	27.1 (3.6)	28.4 (3.9)	0.004*
Duration of DM (in years)	–	6.5 (2.3)	8.2 (2.6)	10.1 (3.1)	<0.001*
*Statistically significant at p<0.05 SBP, Systolic blood pressure; DBP, Diastolic blood pressure; BMI, Body mass index; DM, Diabetes Mellitus					

Table 2: Comparison of study groups, by blood glucose, insulin, renal parameters, lipid parameters, and electrolytes

	Group A N = 40	**Group B N = 40**	**Group C N = 40**	**Group D N = 40**	**P value**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	

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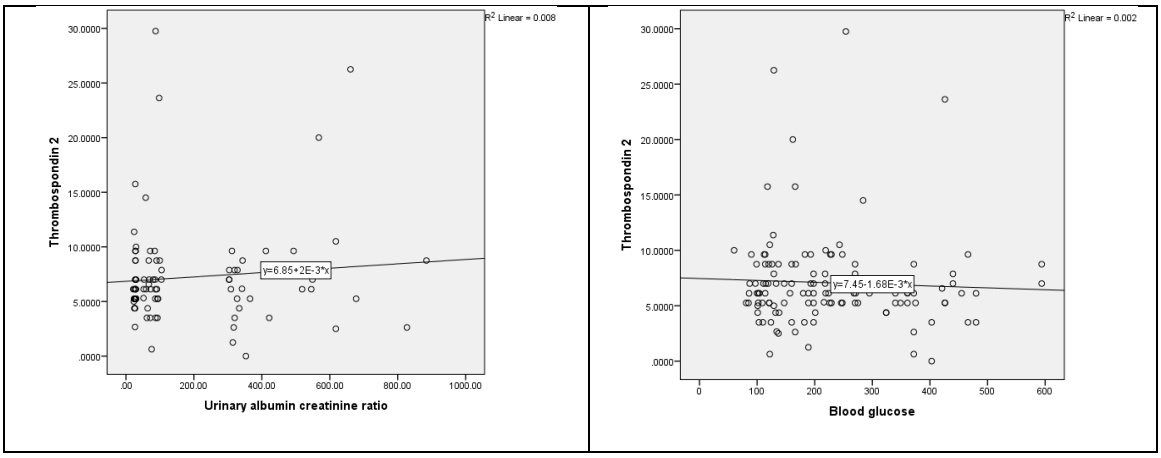
Blood glucose (mg/dl)	98.5 (12.4)	210.7 (65.3)	280.2 (105.6)	260.1 (120.4)	<0.001*
HbA1c (%)	5.8 (1.1)	7.1 (1.5)	7.9 (2.1)	8.8 (3.0)	<0.001*
Insulin (μ/ml)	52.3 (58.4)	50.6 (49.5)	53.9 (72.1)	49.2 (51.8)	0.987
Serum Urea (mg/dl)	21.1 (5.8)	24.8 (8.9)	27.3 (13.2)	25.5 (7.1)	0.362
Serum creatinine (mg/dl)	0.7 (0.2)	0.9 (0.3)	0.9 (0.3)	1.0 (0.4)	0.472
Total cholesterol (mg/dl)	168.2 (32.7)	190.1 (38.6)	182.9 (35.4)	175.6 (41.2)	0.231
Triglycerides (mg/dl)	140.3 (70.2)	200.5 (150.1)	176.8 (95.6)	192.9 (82.3)	0.180
HDL (mg/dl)	45.1 (6.9)	44.5 (8.7)	43.9 (9.5)	42.8 (9.2)	0.975
LDL (mg/dl)	98.6 (28.5)	110.2 (27.8)	104.5 (30.1)	101.8 (31.4)	0.328
VLDL (mg/dl)	35.4 (18.9)	38.2 (15.7)	39.7 (20.3)	36.9 (28.1)	0.865
Microalbumin (mg/dl)	12.6 (24.5)	20.8 (9.0)	179.4 (55.2)	367.1 (58.6)	<0.001*
*Statistically significant at p<0.05 HbA1c, Glycated haemoglobin; HDL, High density lipoprotein; LDL, Low density lipoprotein; VLDL, Very low-density lipoprotein					

Table 3: Comparison of study groups, by urinary TSP-2

	Group A N = 40	**Group B N = 40**	**Group C N = 40**	**Group D N = 40**	**P value**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	
TSP2	5.3 (2.8)	7.1 (2.6)	8.3 (5.8)	9.0 (5.1)	0.318
*Statistically significant at p<0.05 TSP2, Thrombospondin 2					



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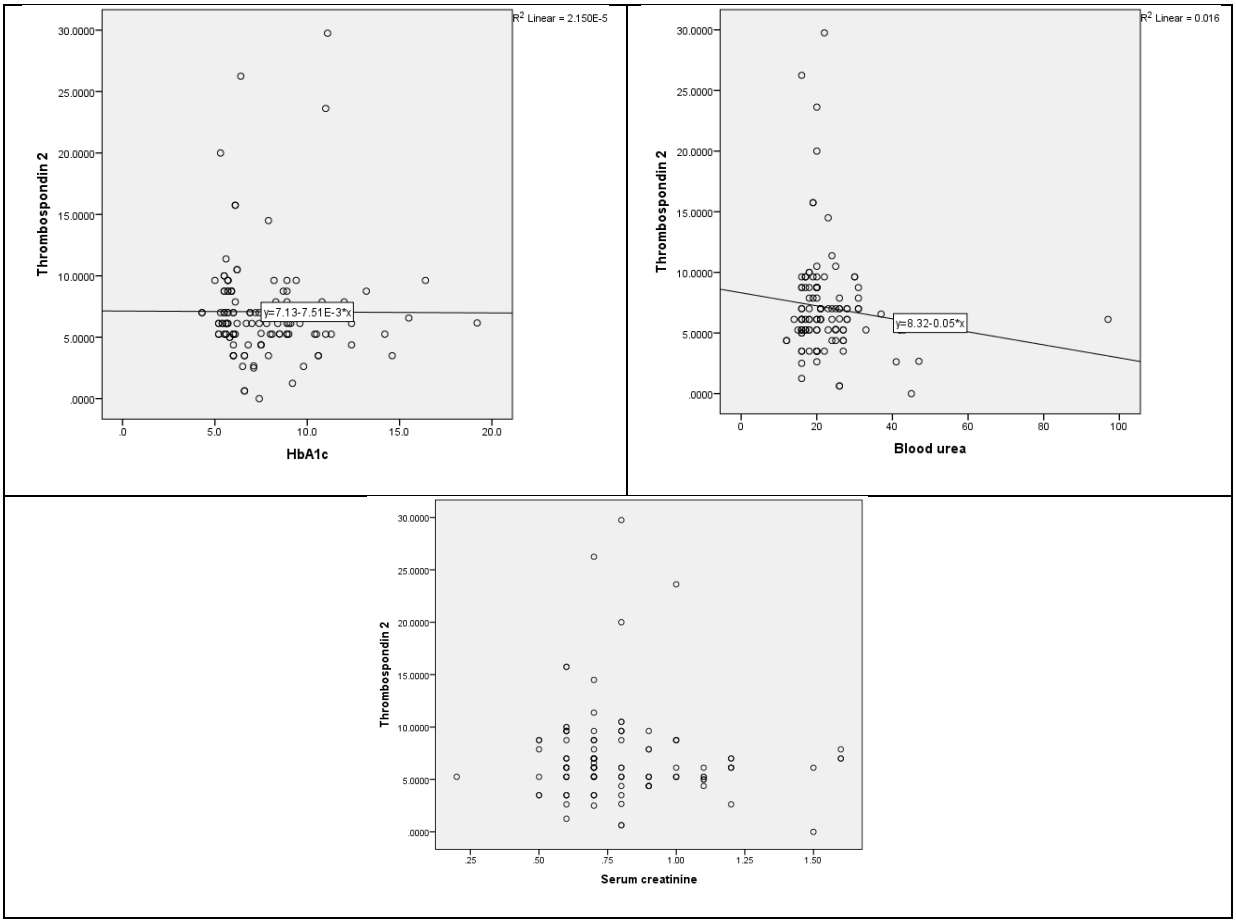

Figure 1: Pearson's correlation coefficient analysis between urinary TSP-2 levels and various clinical parameters

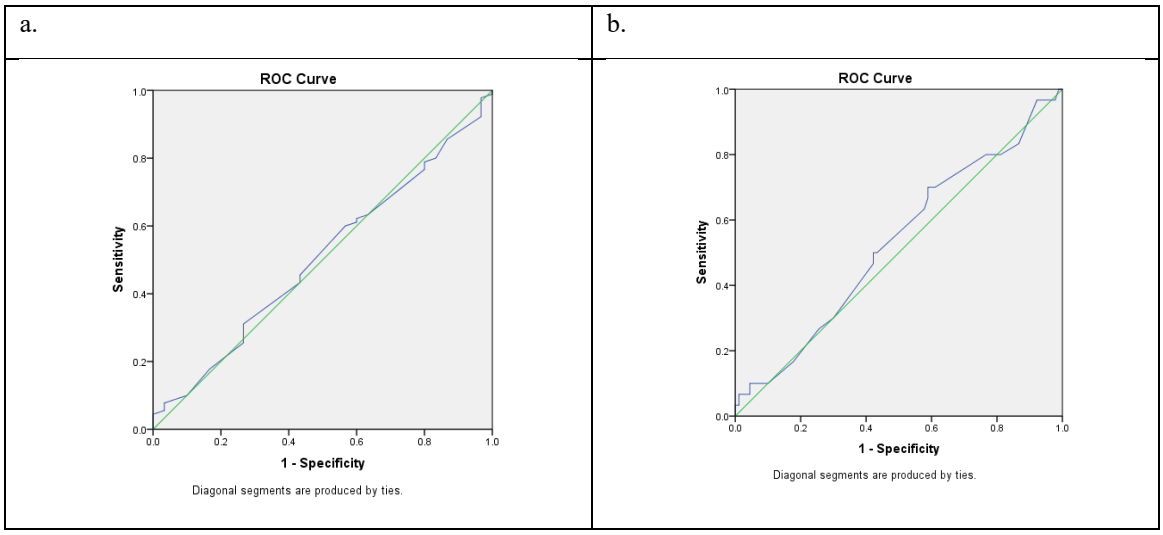

Figure 2: ROC analysis of urinary TSP-2 levels

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Table 3: ROC analysis of urinary TSP-2 levels

TSP2	AUC	95% CI	Cutoff	Sensitivity	Specificity	P value
Diabetes	0.504	0.387 to 0.621	>5.3	62.2	43.3	0.942
DM with macroalbuminuria (UACR >300mg/g)	0.528	0.409 to 0.647	>6.1	63.3	57.8	0.643