



Original Research Article

SERUM THROMBOSPONDIN 1(TSP- 1) LEVEL AND ITS ASSOCIATION WITH CARDIOVASCULAR RISK FACTORS IN TYPE 2 DM

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ABSTRACT

Background: Type 2 DM, which accounts for around 90% of all cases of DM, is now a global health challenge. TSP-1, a multifunctional glycoprotein is released from macrophages, platelets, and adipocytes. Hyperglycaemia promotes up regulation of TSP-1, which is an important mediator of obesity induced inflammation and resistance. It activates various inflammatory markers including Toll-like receptor 4 (TLR-4), Transforming growth factor-beta (TGF- β), and Plasminogen activator inhibitor-1 (PAI-1) & inhibits Nitric Oxide (NO) signalling pathway. Chronic hyperglycaemia, hypertension and dyslipidemia are major contributor of morbidity and mortality in T2DM. TSP-1 also serves as a pro-thrombotic and pro-inflammatory mediator in cardiovascular diseases. **Aim and Objective:** To estimate the level of serum TSP-1 in Type 2 diabetic patients & to find its association with cardiovascular risk factors.

Materials and Methods: The present Cross Sectional Analytical Study was conducted among 40 diabetic patients and 40 healthy subjects within age group 35-60 years, attending the OPD of general medicine VIMSAR, Burla between November 2025 to January 2026. Serum TSP-1 was measured in ELISA and FBS, lipid profile were measured in fully automated analyzer. HbA1C & hsCRP were calculated using turbidimetric assay. Statistical analysis was performed with SPSS software version 21.0 and the p value <0.05 was taken for statistical significant.

Results: The mean value of serum TSP-1, TG, hsCRP was (37142 \pm 3640), (170 \pm 11.8), (2.8 \pm 0.3) respectively in diabetic patients. Serum HDL (32 \pm 4.6) was found to be lower in Diabetic patients as compared to control. Serum TSP-1 showed strong positive correlation with cardiovascular risk factors like hsCRP, TG, BMI, SBP but correlated negatively with HDL.

Conclusion: As the present study revealed positive correlation of TSP-1with cardiovascular risk factors, so it may serve as a valuable early biomarker for assessing and preventing cardiovascular complications in patients with Type 2 DM.

Keywords: TSP-1, Type 2 DM, cardiovascular risk factors.

INTRODUCTION

Chronic hyperglycaemia is a disorder of carbohydrate metabolism due to lack of insulin secretion or impaired insulin metabolism, or both. It affects the carbohydrates, lipids, and proteins metabolism.^[1] The organs and tissues which are

commonly affected by diabetes are liver, skeletal muscle and adipose tissue, because of insulin resistance. The severity of symptoms vary depending upon the duration and type of diabetes.^[2]Type 1 diabetes mellitus (T1DM) contributes for 5% to 10% of DM and is caused by autoimmune destruction of beta cells of islets of the

pancreas, commonly seen in children and adolescents. Here there is a complete deficit of insulin. Type 2 diabetes mellitus (T2DM) accounts about 90% of all diabetic cases, mostly seen in people more than 45 years. But now a days it is also seen in children, adolescents, and young adults due to increasing obesity, physical inactivity, and unhealthy dietary habits.^[3]

TSP-1, a trimeric 450 kDa complex structure discovered in 1971.^[4] This multifunctional glycoprotein is commonly released from macrophages, platelets, and adipocytes. It is an important mediator of obesity, inflammation & insulin resistance.^[5] It regulates the activity of macrophages and inflammatory cytokines via activation of TLR-4 signalling pathway.^[6] Besides acting as a potent modulator of inflammation via activating TGF β (Transforming growth factor β) further activates a chain of inflammatory mediators, which includes PAI-1 (Plasminogen activator inhibitor) enhancing the fibrotic changes in multiple organs.^[7] It also inhibits NO production and NO signalling pathway by interfering with Vascular Endothelial Growth Factor Pathway,^[8] TSP-1 has various domains named amino terminal domain, carboxy terminal domain, procollagen like domain. The carboxy terminal has type I; II & III repeats. The type I repeats which is known as TSR (Thrombospondin Structural Repeats) were initially found in human endothelial cell. The sequence CSVTCG present inside the TSR has specific affinity for CD36.^[9] Besides this; the carboxy terminal also has affinity for CD47, recognized as integrin associated protein (IAP). Binding of TSP 1 with CD36 and CD 47 leads to endothelial dysfunction and apoptosis and inhibition of the proliferation & migration of endothelial smooth muscle cell.^[10]

Under normal glycemic condition, the gene expression of TSP -1 is decreased by the cyclic GMP dependent protein kinase (PKG) 10. PKG inhibits the upstream stimulatory factor 2 (USF2) expression. USF2 is a glucose regulated transcription factor and it binds to the TSP-1 gene promoter. Under hyperglycaemic conditions, there is down regulation of the PKG activity, which decreases the TSP 1 expression by removing the inhibition of glucose-stimulated USF2 expression. This results in increased activation of TGF- β in mesangial cells.^[11] Raman p et al.(2007) has demonstrated that expression of TSP 1 is up regulated by high glucose treatment through the hexosamine pathway.^[12] It has been previously demonstrated that elevated glucose induces oxidative stress in vascular smooth muscle cells. This occurs via a PKC-mediated pathway that generates superoxide, which ultimately degrades the signalling protein PKG-1.^[13]

So the present study focused on estimation of the level of TSP-1 in patients with Type 2DM and to find out whether any association exists between

serum level of TSP-1, cardiovascular risk factors and Type 2 Diabetes Mellitus.

MATERIALS AND METHODS

The prospective study enrolled 80 study participants in the department of Biochemistry in collaboration with the department of General Medicine, Veer Surendra Sai Institute of Medical Sciences and Research, Burla. The study period of the present cross sectional analytical study was approximately three months. The study protocol was approved by institutional ethics committee via registration no.111-2025/I/S/T/112/Dt.03.11.2025. Written consent was obtained from each participant.

Inclusion Criteria

1. Group A- Clinically diagnosed cases of Type 2 Diabetes Mellitus within the age group of 35 to 60 years of either sex attending the OPD & IPD of general medicine department.
2. Group B- Taken from general population within 35 to 60 years.
3. Those willing to participate in study.

Exclusion Criteria

1. Patients unwilling to give consent
2. Patients with history of smoking, alcoholism, malignancy, CKD, liver diseases, acute infections, pregnancy, autoimmune disorders.

Sample size calculation

$$n = [Z(1-\alpha/2)]^2 (S1^2 + S2^2) / d^2$$

$$Z(1-\alpha/2) = 1.96 \text{ at } 95\% \text{ confidence interval, } \alpha = 0.05$$

$$S1, S2 = \text{standard deviations } (0.0043, 0.226)$$

$$d = \text{specified precision assumed} = 0.1 \text{ ng/ml}$$

By using this formula, the estimated sample size of one group will be 40.

Biochemical Analysis

Following twelve hours of fasting and taking all aseptic laboratory procedures, 7 ml of venous blood were collected from the patient's antecubital veins. The blood samples were allowed to clot and after centrifugation serum were separated out. The tests for lipid profile and FBS were done using a fully automated analyser (CobasC311, Roche Diagnostics, Mannheim, Germany) using appropriate diagnostic kits as per the manufacturer's instructions. The serum samples of thrombospondin 1 were stored at -20 degree C until further used by ELISA method. HbA1C & hsCRP were measured using standard nephelometry procedure.

Anthropometric Parameters

The anthropometric data were collected from the participants, including age, body weight, height and BMI was calculated by taking the ratio of weight (kg) and height in meters squares using Quetelet index^[14]. Blood pressure was measured using standard sphygmomanometer.

Statistical Analysis

Statistical analysis was performed with SPSS software version 21.0 (IBM Corp., Armonk, NY). The quantitative data were expressed in mean and standard deviation. Comparison of continuous

variables was done using Independent t-test. Pearson correlation coefficient was used to find out

correlations and p value<0.05 was taken for statistical significance.

RESULTS

T2DM- Type 2 Diabetes Mellitus, BMI- Body Mass Index, SBP- Systolic Blood Pressure

Table 1: Demographic profile of study subjects

VARIABLES	T2 DM(n=40)		CONTROL(n=40)		p VALUE
AGE(In Years)	53±5.2		49±2.8		.25
SEX	MALE18	FEMALE22	MALE19	FEMALE21	.35
BMI (Kg/m ²)(WHO Indian Standard)	32.2±2.6		23±1.5		<0.05*
SBP(mmHg)	168.2±18.6		128±10.5		<0.05*

P value<0.05*

Table 1 shows the demographic profile of study subjects. The study included 80 subjects of which 40 individuals (18M &22F) were Type 2 Diabetic patients and 40 individuals (19M & 21F) were

healthy subjects with mean age group 53±5.2 & 49±2.8 respectively. The mean BMI and SBP of Type2 Diabetic subjects were higher as compared to control with p<0.05.

Table 2: Biochemical parameters of Type 2 Diabetic patients & control

FBS-Fasting Blood Sugar, HbA1C-Glycated Haemoglobin, TG-Triglycerides, HDLC-High-Density Lipoprotein Cholesterol, AI- Atherogenic Index, hs-CRP High-Sensitivity C - reactive protein

VARIABLES	T2DM(n=40)	CONTROL(n=40)	p VALUE
FBS(mg/dl)	269±17.8	97±12.3	<0.05*
HbA1C(%)	8.5±2.2	3.5±1.8	<0.05*
TG(mg/dl)	170±11.8	130±20.1	<0.05*
HDL-C(mg/dl)	32±4.6	49.7±8.2	<0.05*
Atherogenic Index(AI)	0.72±0.09	0.1±1.3	<0.05*
hsCRP(mg/l)	2.8±0.3	1.1±1.2	<0.05*
TSP-1(ng/ml)	37142±3640	13920±14352	<0.05*

P value<0.05*

The result of Table-2 shows significant increase in serum TSP-1, hsCRP, TG level in Type 2 Diabetic patients as compared to control(p<0.05). There is significant decrease in serum HDL-C in diabetic patients (p<0.05).

Serum TSP-1 showed positive correlation with cardiovascular risk factors like BMI, SBP, TG,AI, hsCRP, FBS as shown in FIG:1,2,3,5,6,7.However there was a negative correlation of TSP-1with HDL-C as shown in FIG:4.

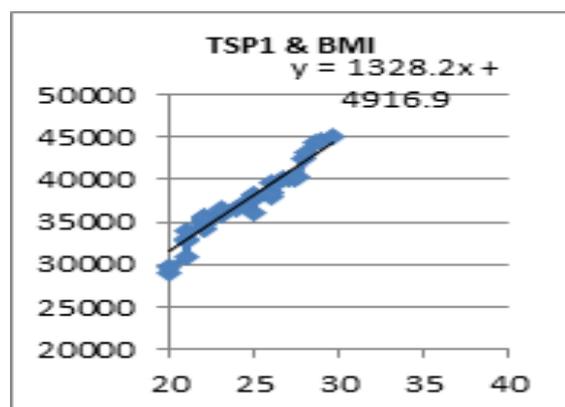


Figure 1: Correlation between TSP-1 & BMI

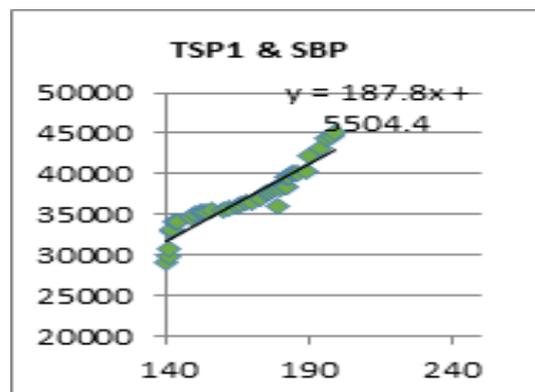


Figure 2: Correlation between TSP-1 & SBP

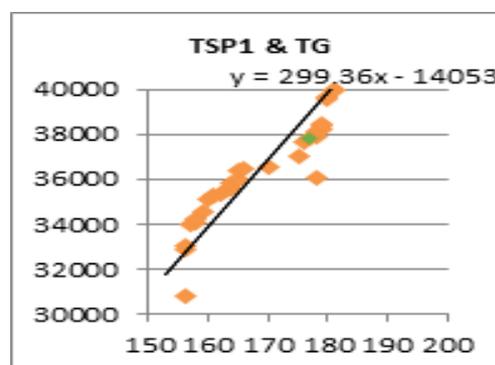


Figure 3: Correlation between TSP-1 & TG

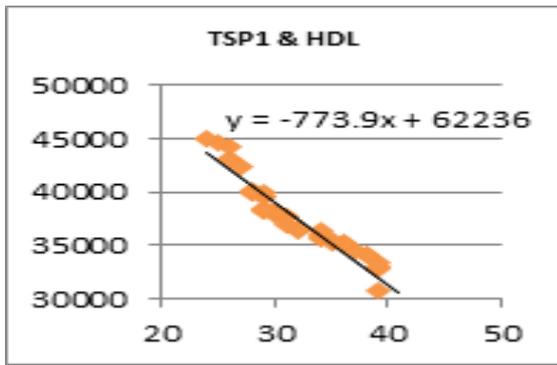


Figure 4: Correlation between TSP-1 & HDL-C

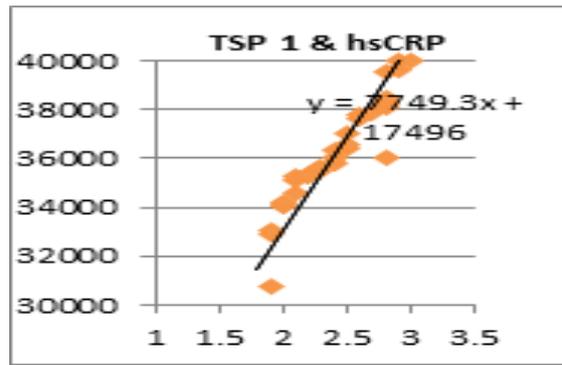


Figure 6: Correlation between TSP-1 & hsCRP

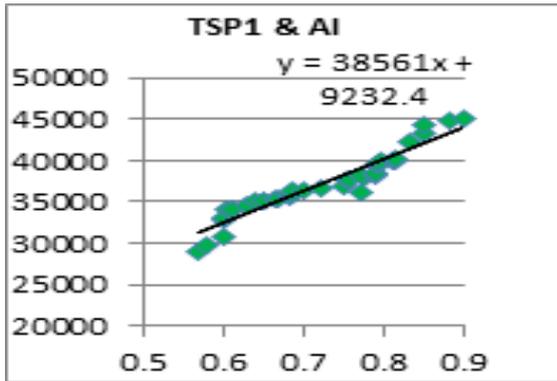


Figure 5: Correlation between TSP-1 & AI

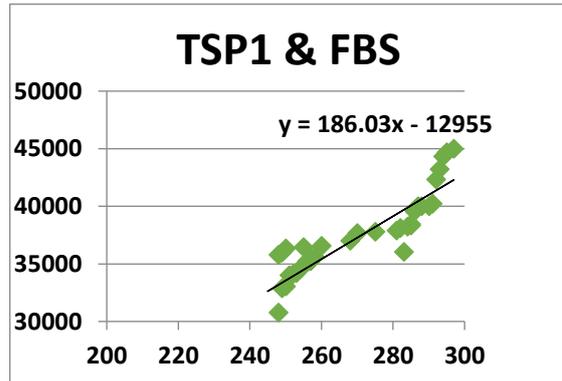


Figure 7: Correlation between TSP-1 & FBS

Table 3: Demographic & Biochemical parameters of both genders in Type 2 Diabetic patients
TSP-1Thrombospondin-1, BMI-Body Mass Index, FBS-Fasting Blood Sugar

Variables	Diabetic		P Value
	Male (n=19)	Female(n=21)	
SEX			0.35
BMI (Kg/m ²)	29.9 ±0.8	33.7 ±.8	<0.001*
FBS (mg/dl)	252 ±4.3	284 ±9.1	<0.001*
TSP-1 (ng/ml)	34251 ±2185	39867 ±2520	<0.001*

P value<0.05*

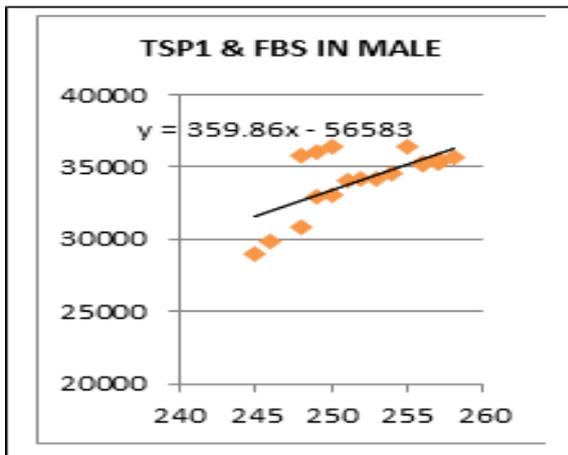


Figure 8: Correlation between TSP-1 & FBS in male

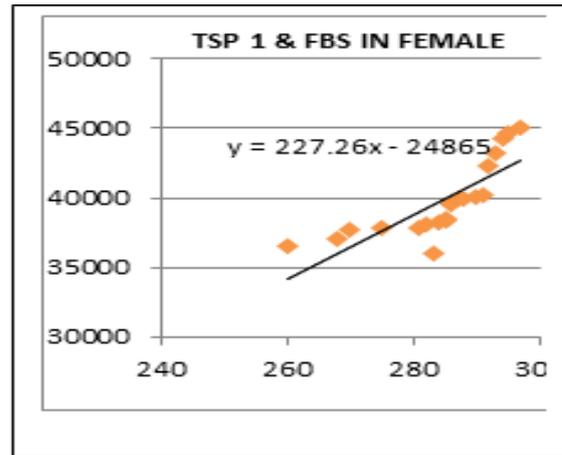


Figure 8: Correlation between TSP-1 & FBS in female

Variable	r Value
FBS in Male	0.6
FBS in Female	0.7

DISCUSSION

The glycoprotein thrombospondin (TSP)-1 is abundantly expressed in the endothelium of islets of pancreas. TSP-1 modifies the morphology of the islet cells and activates transforming growth factor (TGF) β -1.^[15] Transforming growth factor β (TGF β) is a pleuripotent cytokine which consists of TGF β 1, 2, 3, out of which TGF β 1 is the isoform found in most of the tissues. It is a powerful activator of chemotaxis and stimulates the immigration of neutrophils, lymphocytes, monocytes, and fibroblasts ultimately promoting apoptosis and hypertrophy of cardiac myocytes.^[16,17]

The present study revealed significant increase in TSP-1 in diabetic patients as compared to the healthy individuals as shown in Table-2.

Risk Level	hs-CRP Concentration (mg/L)
Low	< 1.0 mg/L
Average	1.0 to 3.0 mg/L
High	> 3.0 mg/L

In diabetic patients, high hs-CRP is associated with micro vascular complications such as kidney damage and vision loss. High level of blood sugar may induce oxidative stress, which further stimulates the production of more CRP, creating a cycle of inflammation.^[21] It also actively contributes in the pathogenesis of Atherosclerotic Cardiovascular Disease. While dyslipidemia takes part in the formation of arterial plaques, hs-CRP analyses the level of inflammation that drives plaque growth and eventual rupture.^[19-22]

The present study revealed dyslipidemia and increased Atherogenic Index (log 10= TG/HDL cholesterol) as shown in Table 2 and Fig 5. Inflammations and lipids act as synergistic partners in the progression of vascular disease. High TG levels raises the accumulation of saturated fatty acids, which triggers the NLRP3 inflammasome in macrophages resulting in the secretion of IL-1 β and insulin resistance in Type2DM.^[23]

AI is a more precise predictor of cardiovascular events than LDL-C alone, because TG change large, fluffy LDL into small, dense LDL creating a pro-thrombotic state.^[24-25]

In a healthy body, HDL (High-Density Lipoprotein) acts like a "scavenger" that removes excess cholesterol from the arteries. Generally, there is an inverse relationship between HDL and inflammation markers.

The result of Table-3 shows significant increase in serum level of TSP-1 in diabetic males as well as in diabetic females. However diabetic females show stronger positive correlation of FBS with TSP-1. Our finding coincided with the study demonstrated by AI-Kraity et al.^[26] This study involved perimenopausal female group, so reduced level of estrogen & sexual dimorphism of adipose tissue

Hyperglycaemia increases the transcription of TSP-1 by down regulating PKG & up regulating the USF2. Raman p et al.(2007) suggested that activators of Hexosamine Pathway promote the transcriptional expression of TSP-1.^[12]

Li Y et al.(2011) have also demonstrated that reduced TSP-1 have improved the glucose-insulin homeostasis, decreasing the macrophage accumulation and adipose tissue inflammation.^[18]

The present study showed significant increase in serum TSP-1, hsCRP, TG level in Type2 Diabetic patients as compared to control(p<0.05). However there is significant decrease in serum HDL-C in diabetic patients (p<0.05).

High-sensitivity C-reactive protein (hs-CRP) is a clinical biomarker used to measure chronic, low-grade inflammation associated with long-term metabolic and cardiovascular diseases.^[19, 20]

may be the reason of elevated level of BMI & serum TSP-1.^[27,28]

Study of Choi et al. (2012) has demonstrated the association of TSP-1 & Coronary heart disease and atherosclerosis.^[29] Diabetes is a risk factor for cardiovascular diseases both in males & females. However Diabetic Female are more susceptible to cardiovascular mortality.^[30] This may be due to the fact that Diabetic Females with higher BMI are more predisposed to unfavourable changes like coagulation, vascular disorder and cardiovascular risk factors than Diabetic Male.^[31]

CONCLUSION

This study demonstrates that Thrombospondin-1 (TSP-1) level is significantly elevated in patients with Type 2 Diabetes Mellitus (T2DM) compared to healthy individuals. Our findings establish an association between increased TSP-1 and elevated level of cardiovascular risk factors, like hsCRP, TG & AI. These significant positive correlations suggest that TSP-1 is closely linked to the chronic low-grade inflammation. The strong association with the atherogenic index further highlights the role of TSP-1 as a potent marker for the progression of subclinical atherosclerosis. Conversely, there is an inverse relationship between HDL and TSP 1. These results suggest that TSP-1 may serve as a valuable early biomarker for assessing cardiovascular vulnerability in T2DM patients. Further research in large scale is required to determine the therapeutic role of TSP-1 as a biomarker of cardiovascular disease in the diabetic population.

Limitations

The main limitation of the present study was its short duration as a cross-sectional analytical study.

To confirm our findings, larger scale, and longer duration studies should be conducted.

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Disclosures

Human subjects: Consent was obtained from all participants in this study. Veer Surendra Sai Institute of Medical Sciences and Research issued approval regn. no.

111-2025/I/S/T/112/Dt.03.11.2025.

Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue.

Conflicts of interest: Nil.

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Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Stuti Mishra, Sumitra Bhoi, Madhusmita Acharya, Sagnika Tripathy, Neelam B. Tirkey, Namrata Panigrahi.

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