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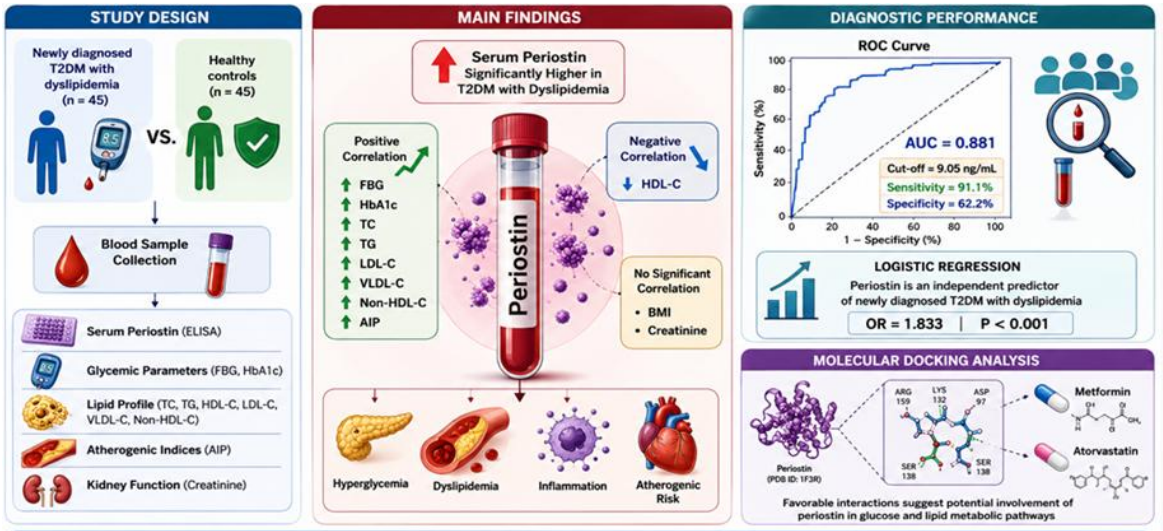
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Serum Periostin as a Novel Biomarker of Metabolic and Atherogenic Risk in Newly Diagnosed Type 2 Diabetes Mellitus with Dyslipidemia

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Graphical Abstract

Highlights

Serum periostin levels were significantly elevated in newly diagnosed T2DM patients with dyslipidemia.

Periostin was significantly associated with metabolic and atherogenic risk markers.

Serum periostin demonstrated good diagnostic performance for identifying T2DM-related metabolic risk.

ROC analysis showed an AUC of 0.881 for serum periostin.

Periostin may represent a promising biomarker of metabolic and atherogenic risk in T2DM.

ABSTRACT

Periostin has emerged as a potential marker of metabolic and cardiovascular disorders. This study investigated the relationship between serum periostin levels and metabolic abnormalities, lipid parameters, and atherogenic risk in patients with newly diagnosed type 2 diabetes mellitus (T2DM) and dyslipidemia. The interactions of periostin with commonly used metabolic drugs were also assessed using molecular docking.

Methods:

This case–control study included 45 patients with newly diagnosed T2DM and dyslipidemia and 45 healthy controls. Serum periostin was measured using an enzyme-linked immunosorbent assay. Glucose parameters, lipid profile, kidney function tests, and atherogenic indices were evaluated. Correlation analysis, receiver operating characteristic (ROC) curve analysis, and multivariate logistic regression were performed. Molecular docking assessed interactions between periostin, metformin, and atorvastatin.

Results:

Serum periostin levels were significantly higher in patients than in healthy controls. Periostin was positively correlated with fasting blood glucose, HbA1c, total cholesterol, triglycerides, LDL-C, VLDL-C, non-HDL-C, and the atherogenic index of plasma and negatively correlated with HDL-C. No significant correlation was observed with creatinine or BMI. ROC analysis showed good diagnostic performance (AUC = 0.881), with 91.1% sensitivity and 62.2% specificity at a cut-off value of 9.05 ng/mL. Multivariate logistic regression identified periostin as an independent predictor of T2DM with dyslipidemia (OR = 1.833, $p < 0.001$). Molecular docking revealed favorable interactions between periostin, metformin, and atorvastatin.

Conclusions:

Elevated serum periostin levels are associated with metabolic abnormalities and increased atherogenic risk in newly diagnosed T2DM with dyslipidemia. Periostin may

therefore be a useful biomarker for identifying early metabolic imbalance and atherogenic risk.

Keywords: Type 2 diabetes mellitus; Insulin resistance; Dyslipidemia; Glucose; Periostin; Atherogenic index.

INTRODUCTION

A global health issue, Type 2 diabetes mellitus (T2DM) has become firmly associated with the prevalence of obesity and many chronic diseases [1]. The primary cause of type 2 diabetes is defects in the action or secretion of insulin, or both, which result in lipid, protein, and carbohydrate metabolic problems [2]. In patients with diabetes, persistent hyperglycemia is linked to several pathogenic processes, such as dyslipidemia, platelet activation, and disruptions in endothelial metabolism [3]. Patients with type 2 diabetes mellitus (T2DM) are highly likely to have dyslipidemia, according to several studies. Common lipid abnormalities include elevated triglycerides (TG), increased small dense LDL-C particles, and decreased HDL-C levels, all of which are significant risk factors for cardiovascular disease [4,5]. One of the main causes of cardiovascular disease (CVD) in people with diabetes mellitus is dyslipidemia [6]. Due to westernized food patterns, obesity, population aging, decreased physical activity, and other undesirable lifestyle changes, its incidence is already significant and is still rising in many emerging nations [7]. Therefore, a thorough understanding of the essential traits and clinical profiles of patients with dyslipidemia is necessary to improve control of this condition [8].

Periostin is an extracellular matrix protein that resembles fasciclin I and is also referred to as osteoblast-specific factor 2 (OSF-2), which is encoded by the POSTN gene situated on the long arm (q arm) of human chromosome 13. It is an important part of repairing and reshaping tissues. [9,10]. It has a hydrophilic C-terminal domain and is a secreted matrix N-glycoprotein, featuring internal homologous repeats, an N-terminal signal peptide sequence, and a cysteine-rich domain [9]. The significant structural and sequence similarity of periostin with fasciclin 1 and transforming growth factor β–induced indicates involvement of periostin in cell adhesion and migration [11]. Moreover, periostin is expressed through a diverse array of transcripts generated by alternative splicing, which may exhibit distinct activities and biological purposes.

Numerous clinical conditions, including several cardiovascular diseases, such as myocardial infarction and heart failure, asthma, and Metastases of different malignancies, have been linked to the expression of periostin [12,13].

Although the evidence for the association of type 2 diabetes mellitus (T2DM) with dyslipidemia and cardiovascular complications is increasing, there is still limited knowledge of early molecular biomarkers reflecting metabolic deterioration in newly diagnosed patients. The role of periostin in early-stage T2DM with dyslipidemia has not been adequately studied, and its association with lipid abnormalities and glycemic control has not been fully revealed [9,12].

Recent evidence indicates that periostin is an extracellular matrix-associated mediator of linking metabolic stress and chronic inflammation. It has been proposed that periostin promotes metabolic dysfunction by stimulating inflammatory signaling pathways, such as nuclear factor kappa B (NF-κB), which leads to the production of pro-inflammatory cytokines and subsequent deranged insulin signaling and endothelial function, thereby favoring the development of insulin resistance and atherogenic lipid alterations [11,13,14]. In addition, periostin has been implicated in tissue remodeling and inflammatory microenvironments associated with metabolic diseases[9,12].

Clinically, the finding of periostin as a circulating biomarker might offer an early window into the metabolic deterioration before overt complications. However, the diagnostic value of periostin in newly diagnosed T2DM patients with dyslipidemia remains to be further explored. Therefore, the present study aimed to evaluate serum periostin levels and their association with glycemic parameters, lipid profile, and atherogenic indices in newly diagnosed T2DM patients with dyslipidemia. We hypothesized that high periostin levels are strongly associated with metabolic and lipid derangements and could be an early biomarker of cardiometabolic risk in this population.

METHODS

Study participants and Clinical biochemical measurements

This study included 90 participants, 45 healthy controls and 45 patients newly diagnosed with type 2 diabetes mellitus (T2DM) and dyslipidemia. Participants were recruited in 2026 from a teaching hospital and were aged 35-50 years. Demographic

and clinical parameters such as age, body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded for all subjects. Blood samples were analyzed for fasting blood glucose (FBG), glycated hemoglobin (HbA1c), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), very-low-density lipoprotein cholesterol (VLDL-C), urea and serum creatinine. Biochemical parameters were determined with a Cobas c111 analyzer (Roche Diagnostics, Germany). Non-HDL-C was calculated as:

$$\text{Non-HDL-C} = \text{TC} - \text{HDL-C}$$

Serum periostin levels were determined using a commercially available enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's instructions.

2.2.Statistical Analysis

Statistical analyses were performed using SPSS software version 23.0. Continuous variables were expressed as mean ± standard deviation (SD). Differences between the T2DM with dyslipidemia and control groups were assessed using an independent-samples t-test.

Pearson's correlation analysis was performed to assess the associations between serum periostin levels and clinical and biochemical parameters. We considered p-value < 0.05 as statistically significant.

A post hoc power analysis was performed with G*Power version 3.1.9.4. Based on an effect size (Cohen's d) of 1.476, an alpha level of 0.05, and 45 participants per group, the statistical power was calculated to be 99.9%.

Molecular Docking Analysis

Molecular docking analysis was performed to investigate the potential interaction of periostin with commonly used medications for diabetes and hyperlipidemia. The 3D structure of periostin was retrieved from the Protein Data Bank (PDB). The structures of metformin and atorvastatin were downloaded from PubChem and optimized before docking. The docking simulations were done with the MOE software. The binding affinity was evaluated by docking score and molecular interactions such as hydrogen bonds and hydrophobic contacts. As an exploratory computational approach to

investigate potential interactions between periostin and commonly prescribed metabolic drugs, molecular docking was performed in (Figure 1).

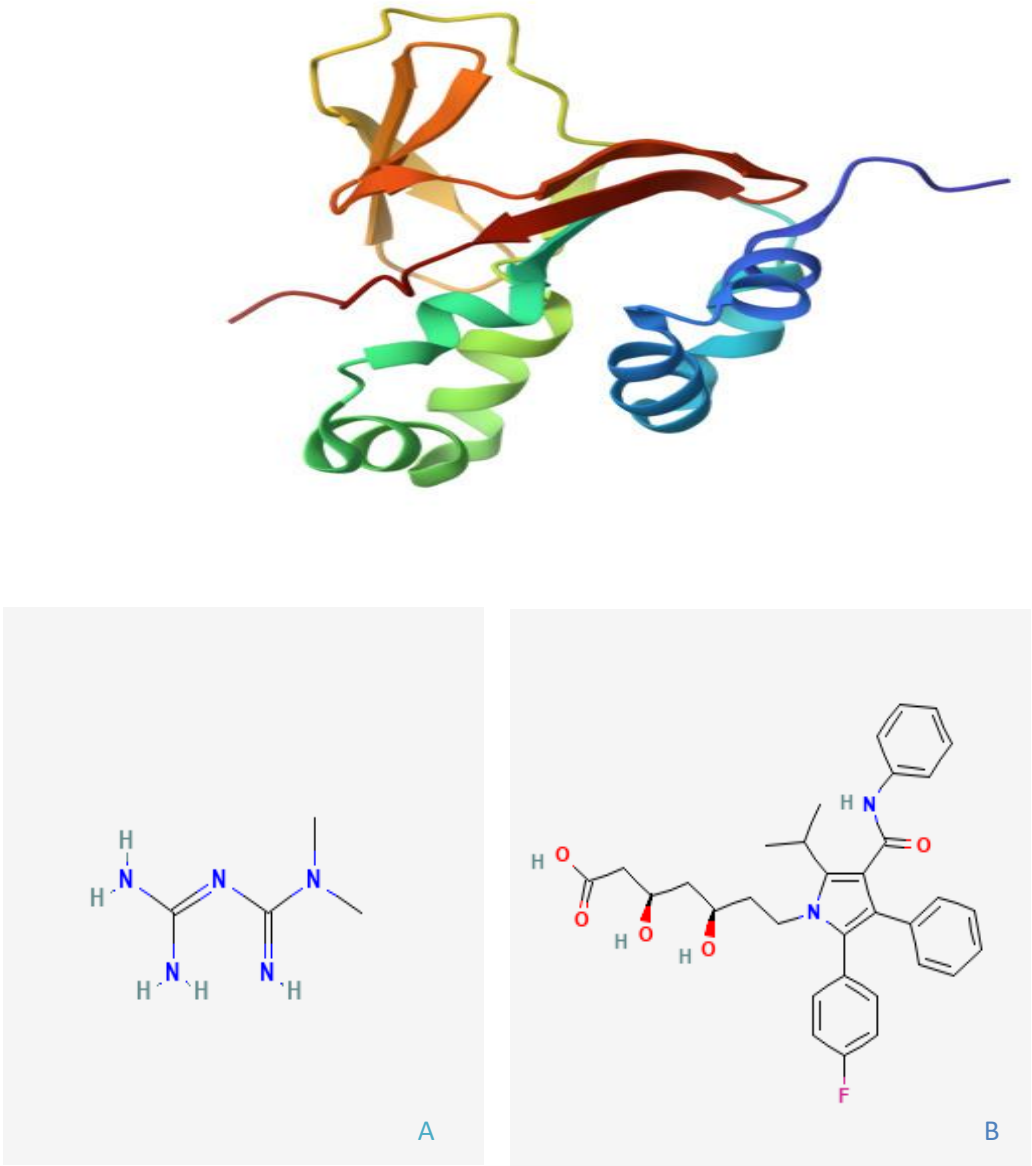


Figure 1: The three-dimensional (3D) structure of human periostin was retrieved from the Protein Data Bank (PDB) database and prepared for molecular docking studies. Selected ligands(A) Metformin and (B) Atorvastatin were downloaded in SDF format from the PubChem database and then converted to PDB format with Open Babel

software. Water molecules and co-crystallized ligands were removed from the protein structure before docking, and hydrogen atoms were added to optimize the docking process.

Although periostin is not a known pharmacological target of metformin or atorvastatin, growing evidence suggests that periostin is involved in metabolic dysfunction, inflammation, extracellular matrix remodeling, and cardiovascular complications in type 2 diabetes mellitus and dyslipidemia. Hence, molecular docking was carried out as an exploratory computational approach to investigate whether commonly prescribed metabolic drugs may theoretically interact with periostin and to provide preliminary insights into potential molecular associations. The docking results do not suggest a direct

The therapeutic target of periostin but rather provide a hypothesis for future experimental work.

RESULTS

In Table 1, Patients with type 2 diabetes mellitus (T2DM) and dyslipidemia had significantly higher levels of BMI, SBP, DBP, FBS, HbA1c, TC, TG, LDL-C, VLDL-C, and non-HDL-C than the control group ($p < 0.01$). On the other hand, the T2DM group with dyslipidemia had significantly lower HDL-C levels ($p < 0.01$). Nonetheless, both groups' urea and creatinine levels stayed within the typical physiological range (Table 1).

Table (1): Mean ±SD of clinical parameters between groups (T2DM with dyslipidemia and control)

Parameter	T2DM with dyslipidemia	Control
Number (45)	Mean ±SD	Mean ±SD
BMI (kg/m^2)	28.87±4.63**	25.77±3.32
SBP (mmHg)	140.0±10.25**	120.0±5.00
DBP (mmHg)	95.00±5.00**	75.5±5.50
FBS (mg/dl)	168.57±62.81**	79.57±6.04
HbA1C (mg/dl)	8.57±1.82**	5.25±0.46
TC (mg/dl)	231.02 ±47.68**	153.62±28.88
TG (mg/dl)	204.62 ±61.83**	99±20.38
HDL (mg/dl)	42.04±6.62**	50.79±7.92
LDL (mg/dl)	148.05±44.79**	92.288±30.32
VLDL (mg/dl)	40.92±12.36**	19.8±4.07
Non-HDL-C	144.246±3.43**	121.15±3.35

Urea(mg/dl)	34.31±8.30	30.64 ±6.67
Creatinin(mg/dl)	0.82±0.19	0.68±0.15

**: high-significant p value <0.001

Serum periostin levels were significantly elevated ($p < 0.01$) in patients with type 2 diabetes mellitus (T2DM) and dyslipidemia compared with the control group, as shown in Table 2.

Table 2: Mean ± SD of serum periostin levels in T2DM patients with dyslipidemia and the control group.

Parameter	T2DM with dyslipidemia	control
Number (45)	Mean ±SD	Mean ±SD
Periostin (ng/dl)	14.16±4.84**	8.93±1.30

**: high-significant p value <0.001

Serum periostin levels were significantly elevated ($p < 0.001$) in patients with type 2 diabetes mellitus (T2DM) and dyslipidemia compared with the control group, as shown in Table 2 and Figure 3.

Periostin and FBG, HbA1c, TC, TG, LDL-C, VLDL-C, and urea showed a strong positive correlation ($p < 0.05$) according to correlation analysis, while HDL-C showed a significant negative correlation. On the other hand, Table 3 indicates that periostin did not significantly correlate with either creatinine or BMI as show in Table 3.

Table (3): Correlation coefficient of Periostin in (T2DM with dyslipidemia) with study parameters.

Parameter	periostin level (ng/dl)	
	r	p-value

BMI (kg/m^2)	0.064	0.552
FBG (mg/dl)	0.315**	0.003
HbA1C (mg/dl)	0.383**	0.00
TC (mg/dl)	0.347**	0.001
TG (mg/dl)	0.379**	0.00
HDL (mg/dl)	-0.228*	0.03
LDL (mg/dl)	0.269*	0.01
VLDL (mg/dl)	0.379**	0.01
Non-HDL-C	0.358**	0.03
Urea (mg/dl)	0.236*	0.025
Creatinine (mg/dl)	0.093	0.384

*: p value <0.05

**: p value <0.001

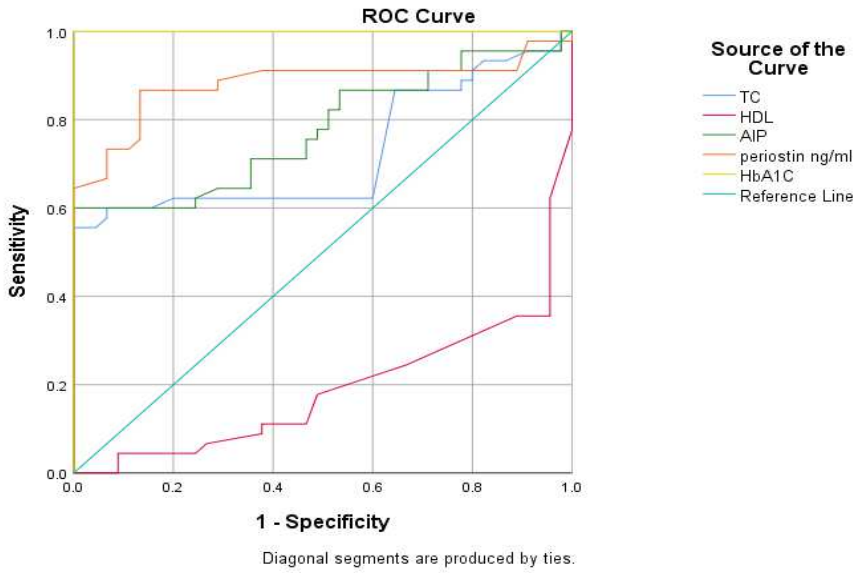


Figure 2 shows a comparative ROC curve analysis of HbA1c, Periostin, AIP, TC, and HDL-C to distinguish newly diagnosed T2DM patients with dyslipidemia from healthy controls.

HbA1c had the best diagnostic performance (AUC = 1.000), followed by serum periostin (AUC = 0.881), according to a comparative ROC analysis. When compared to AIP (AUC = 0.777) and total cholesterol (AUC = 0.725), periostin had better discrimination capacity. These results imply that periostin may be a useful biomarker for diagnosing dyslipidemia in newly diagnosed T2DM patients and may offer more information than traditional lipid markers.The comparative ROC curve analysis is presented in Figure 2.

Multivariate logistic regression analysis identified serum periostin and BMI as significant independent predictors of newly diagnosed T2DM with dyslipidemia (Table 4).

Table 4: BMI and serum periostin as predictors of newly diagnosed type 2 diabetes mellitus with dyslipidemia using multivariate logistic regression analysis

Variable	B	S.E.	Wald	df	Sig.	OR (Exp(B))
Periostin (ng/mL)	0.606	0.146	17.148	1	<0.001	1.833
BMI (kg/m²)	0.266	0.089	9.019	1	0.003	1.305
Constant	-13.811	3.155	19.164	1	<0.001	0.000

Comparative analysis showed significant differences in AIP, TC, HDL-C, and serum periostin between patients with T2DM and dyslipidemia and healthy controls (Table 5).

Table 5: AIP, TC, HDL-C, and periostin levels in T2DM patients with dyslipidemia compared to healthy controls

Parameter	t-value	p-value	Mean Difference	95% CI
AIP	-6.049	<0.001	-0.187	-0.248 to -0.125
TC (mg/dL)	-4.987	<0.001	-51.311	-71.875 to -30.748
HDL-C (mg/dL)	5.208	<0.001	7.933	4.904 to 10.963
Periostin (ng/dl)	-6.914	<0.001	-5.229	-6.748 to -3.710

The diagnostic potential of serum periostin was assessed using ROC curve analysis. The diagnostic performance was good, as indicated by the area under the curve (AUC) of 0.881. 9.05 ng/mL was the ideal cut-off value for serum periostin. The specificity was 62.2%, and the sensitivity was 91.1% at this cut-off value.The ROC curve for serum periostin is presented .The ROC curve for serum periostin is presented in Figure 2.

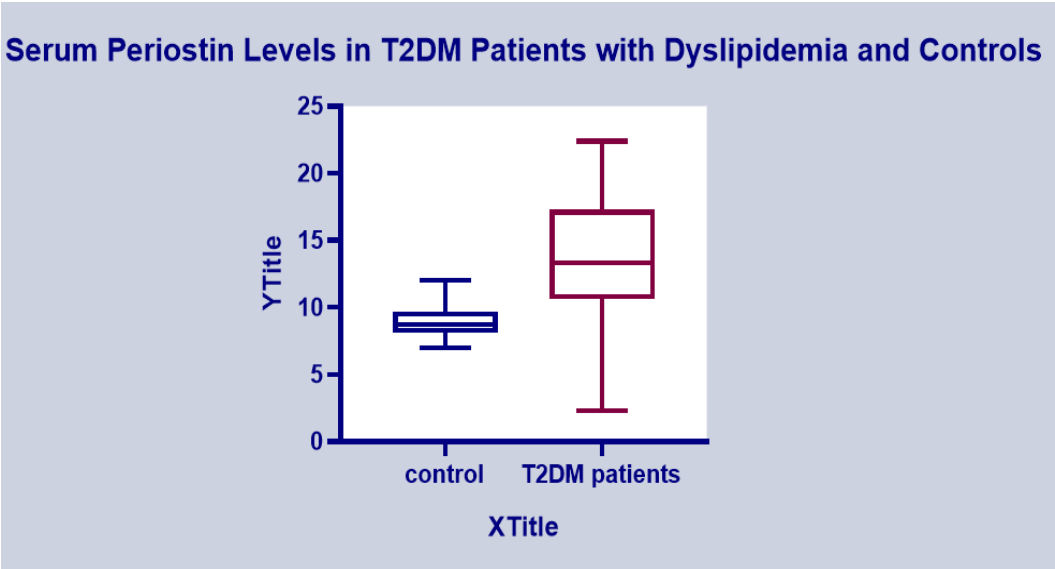


Figure 3: Serum Periostin Levels in T2DM Patients and Healthy Controls Compared

A proposed mechanism by which periostin may contribute to metabolic dysfunction and insulin resistance through extracellular matrix remodeling, integrin activation, NF-κB signaling, and induction of inflammatory cytokines is illustrated in Figure 4.

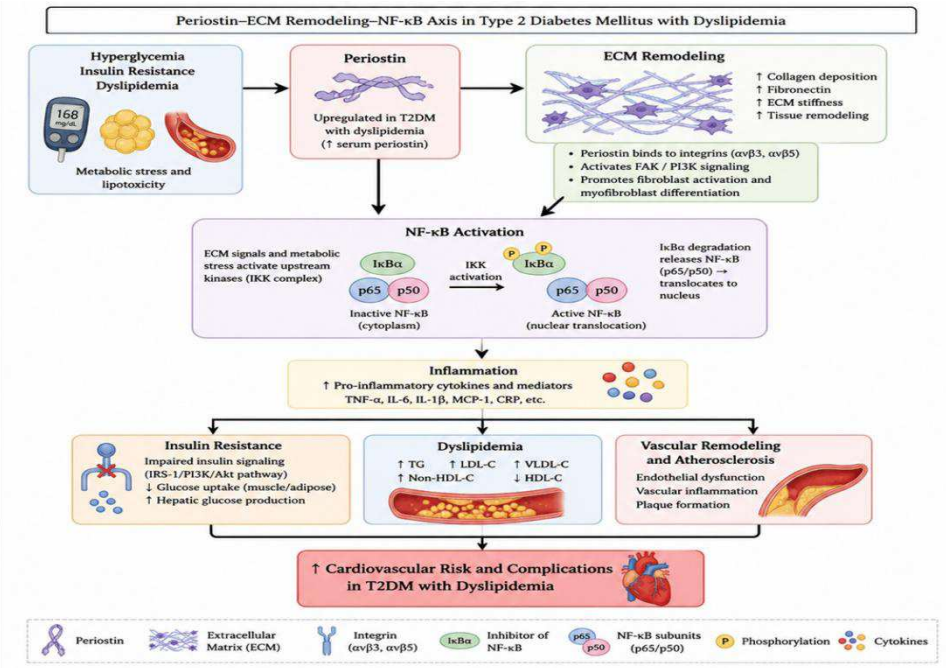


Figure 4: Proposed mechanism of Periostin-mediated signaling pathway showing its role in extracellular matrix remodeling, activation of integrin, NF-κB signaling, and subsequent induction of inflammatory cytokines leading to insulin resistance.

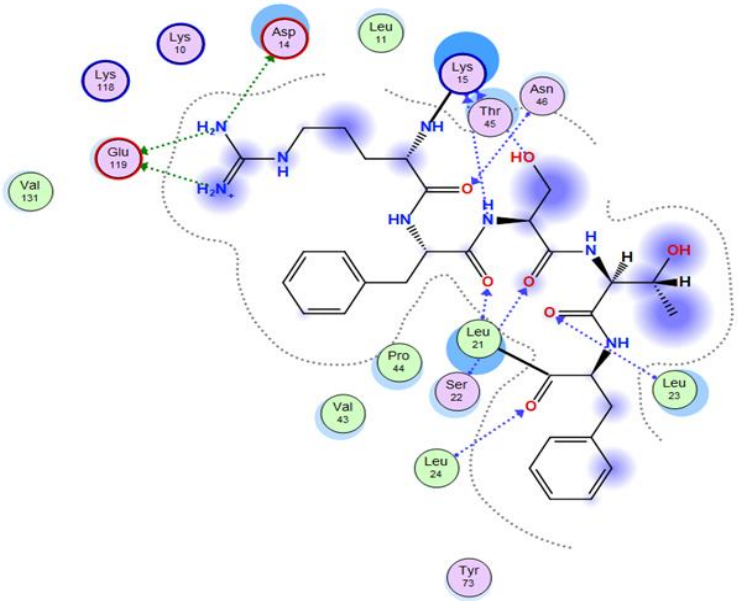


Figure 5: 2D interaction of Periostin protein with Metformin showing hydrogen bond formation and finding key active site amino acid residues involved in the stability of ligand-protein.

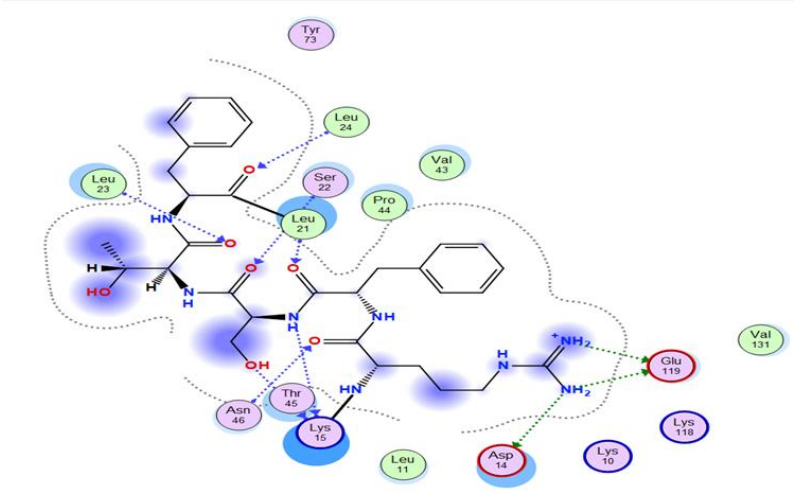


Figure 6: 2D interaction of Periostin protein with Atorvastatin showing hydrogen bond formation and finding key active site amino acid residues involved in the stability of ligand-protein.

Molecular docking analysis demonstrated that both metformin and atorvastatin could bind to periostin at the predicted binding pocket. Metformin formed hydrogen-bond interactions with key amino acid residues, indicating a moderate binding affinity toward periostin (Figure 5). In contrast, atorvastatin exhibited a higher binding affinity and a more stable docking pose, involving both hydrogen-bonding and hydrophobic interactions (Figure 6). These findings suggest that atorvastatin may interact more favorably with periostin than metformin under the simulated conditions.

Table 6: Comparative molecular docking interaction profile of Metformin and Atorvastatin with Periostin (PDB ID: 5WT7)

A comparative summary of the molecular docking scores, RMSD values, interacting residues, hydrogen bonds, ionic interactions, and interaction distances for metformin .and atorvastatin is presented in Table 6

Compound	Docking Score (kcal/mol)	RMSD (Å)	Key Interacting Residues	No. of H-bonds	No. of Ionic Bonds	Interaction Range (Å)	Strongest Interaction
Metformin	-7.05 to -7.37*	0.96–2.01*	ASP14, GLU119, LYS15, ASN46	6–8*	2–3*	2.70–3.40*	GLU119 (~-6 kcal/mol*)
Atorvastatin	-7.37	1.70	ASP14, GLU119, LYS15, LEU21, SER22, LEU23, LEU24, ASN46	11	5	2.72–3.43	GLU119 (-6.6 kcal/mol)

Comparative molecular docking analysis was performed to evaluate the binding interaction of metformin and atorvastatin with periostin (PDB ID: 5WT7). Both compounds showed good binding affinities for the predicted active site. The docking score of atorvastatin was observed as -7.37 kcal/mol with an RMSD value of 1.70 Å, showing a stable ligand-protein complex.

Interaction profiling revealed that atorvastatin formed more hydrogen bonds (n=11) and ionic interactions (n=5) than metformin. Key amino acid residues involved in binding are ASP14, GLU119, LYS15, ASN46, LEU21, SER22, LEU23, and LEU24. The most

stable interactions were observed with GLU119 and ASP14, which indicates their important role in ligand stabilization.

The novelty of the current study is the evaluation of serum periostin in newly diagnosed T2DM patients with dyslipidemia and its association with comprehensive atherogenic index (AIP) and full lipid correlation profile, which has not yet been investigated in the early stage of metabolic disease.

DISCUSSION

T2DM with dyslipidemia, a chronic multifactorial metabolic condition with a rapidly rising global incidence, is the most prevalent type of diabetes. Diabetes causes several metabolic, structural, and biochemical alterations that lead to the development of various issues resulting from diabetes[14]. Several metabolic, structural, and biochemical alterations caused by diabetes contribute to the development of complications [15]. Prevalence of T2DM with dyslipidemia is contribute by many risk factors that include a complex combination of metabolic, genetic, and environmental factors [16].. In line with other research, this study showed that individuals with type 2 diabetes mellitus and dyslipidemia had significantly higher BMIs ($p < 0.01$) than the control group [17]. It is commonly known that being overweight or obese increases the chance of developing type 2 diabetes. Although the precise mechanism by which obesity leads to T2DM and IR is still unknown, several factors, including both cell-autonomous mechanisms and inter-organ interactions, have been linked to the development of this pathological process [17]. “A highly significant increase ($p < 0.01$) in SBP and DBP was observed in T2DM patients with dyslipidemia compared with the control group, in agreement with previous studies [18]. Hypertension is frequently seen in newly diagnosed diabetes and, when combined with dyslipidemia, is associated with

a higher cardiometabolic risk profile [19]. In addition, FBS and HbA1c were significantly elevated in the T2DM group compared to controls, consistent with Kang et al. [20]. Increased FBS and HbA1c levels are primarily due to chronic hyperglycemia and insulin resistance[21]. Furthermore, there was a highly significant increase($p<0.01$) of TC, TG, LDL, VLDL, and Non-HDL-C in T2DM with dyslipidemia compared to that of the control group. Dyslipidemia is a prevalent characteristic of type 2 diabetes that raises the risk of atherosclerosis and diabetic patient mortality [22]. In newly diagnosed type 2 diabetes mellitus (T2DM) patients with dyslipidemia, increased total cholesterol (TC) and triglycerides (TG) are often linked to poor glycemic control and insulin resistance. Specifically, elevated HbA1c levels, a measure of long-term blood sugar control, are strongly correlated with higher TC, LDL-C, and TG levels[23]. This is further compounded by the presence of insulin resistance, which can lead to increased production of VLDL and subsequent elevation of TG[24]

Serum periostin levels in the diabetic patients in the current study were noticeably greater than those in the control group. Periostin levels in the blood were considerably greater in Asians with type 2 diabetes than in controls, according to a comparable study [25].

Guerrot et al. demonstrated a substantial correlation between periostin expression and the onset of experimental hypertension and associated diabetes with dyslipidemia [26]. Additionally, it was shown that periostin plays a crucial role in regulating various inflammatory microenvironments, including hepatic inflammation and atherosclerosis, by maintaining or enhancing inflammatory responses in these pathological conditions. Aggregate evidence from research analyzing serum periostin levels linked to inflammation. The strong relationship between periostin, inflammation, and metabolic problems is closely associated with diabetes, obesity, and fat metabolism [27].

The periostin role in lipid metabolism has been demonstrated in a few investigations. In their research, An, J. N. et al. found that periostin inhibition is linked to alterations in a number of lipids and lipid metabolism, while periostin ablation inhibits aging [28]. Periostin may play a role in adipose tissue metabolic dysfunction, according to another study. This is because periostin is A unique crosstalk through gradual extracellular matrix damage, and age-associated metabolic problems may be a contributing factor to impaired lipid metabolism [29]. Our research showed that serum periostin levels had a negative correlation with HDL-C and a positive correlation with TG, TC, LDL-C, and VLDL-C. These results align with those published by Luo Y. et al. [30,31]. Periostin and HDL-C were found to be negatively correlated in patients with type 2 diabetes mellitus (T2DM) and dyslipidemia. Periostin and HDL-C (high-density lipoprotein cholesterol) is not standard or established concepts. The focus in T2DM and dyslipidemia research is primarily on the relationship between HDL-C and cardiovascular risk, as well as the impact of diabetes on HDL particle composition, function, and its role in cholesterol transport. While periosteal changes are observed in conditions like osteoporosis, which can be associated with diabetes, they are not directly linked to HDL-C levels or diabetic dyslipidemia in the same way as other factors like triglycerides and LDL-C [32].

Serum periostin's area under the ROC curve (AUC) was 0.881, indicating acceptable diagnostic accuracy. An AUC between 0.8 and 0.9 indicates a significant ability of the test to distinguish between healthy and sick people, according to normal ROC analysis interpretation. This indicates that periostin may be a useful biomarker for differentiating between healthy controls and newly diagnosed type 2 diabetes mellitus patients with dyslipidemia[33].

Serum periostin and BMI were found to be significant predictors of newly diagnosed type 2 diabetes mellitus with dyslipidemia by multivariate logistic regression analysis. Significantly, periostin maintained its high correlation with metabolic disorders even after controlling for BMI (OR = 1.833, P < 0.001)[34,35].

The current investigation showed that newly diagnosed T2DM patients with dyslipidemia and healthy controls had significantly different levels of AIP, TC, HDL-C, and serum periostin. The patient group's AIP was significantly greater (P < 0.001), suggesting a higher risk of cardiovascular disease and an increased atherogenic load. According to recent research, AIP is a good indicator of insulin resistance, cardiometabolic risk, and future cardiovascular events in individuals with type 2 diabetes mellitus [36, 37].

Total cholesterol levels were significantly increased in patients compared with controls (P < 0.001), reflecting impaired lipid metabolism and the presence of diabetic dyslipidemia. Conversely, HDL-C levels were significantly lower in patients (P < 0.001), suggesting reduced reverse cholesterol transport and an increased susceptibility to atherosclerotic complications. These lipid abnormalities are characteristic features of diabetic dyslipidemia and are strongly associated with cardiovascular morbidity and mortality [38,39].

When compared to healthy controls, the T2DM with dyslipidemia group had significantly higher serum periostin levels (mean difference = 5.229 ng/mL, P < 0.001). An extracellular matrix protein called periostin is involved in inflammation, tissue remodeling, and metabolic control. There is growing evidence linking high periostin levels to cardiovascular risk, vascular damage, and metabolic dysfunction in diabetic patients. Together with the decrease in HDL-C, the notable rise in AIP, TC, and

periostin suggests that newly diagnosed T2DM patients with dyslipidemia have a very unfavorable cardiometabolic profile. These results lend credence to periostin's possible function as a biomarker in early-stage type 2 diabetes mellitus that reflects both metabolic abnormalities and cardiovascular risk [40,41].

The present study has several limitations. First, the sample size was relatively small, and all the participants were enrolled in a single center. Second, the inflammation markers, including CRP, IL-6, and TNF-α, were not measured, and therefore, the inflammatory pathways underlying periostin with metabolic disturbances could not be directly assessed. Third, the cross-sectional design of the study does not allow us to establish causal relationships between periostin and metabolic abnormalities. The present findings should be validated in future studies with larger sample sizes and multicenter recruitment.

Molecular docking analysis showed that both metformin and atorvastatin can bind to periostin at the predicted binding pocket. ... Atorvastatin showed higher binding affinity than metformin, indicating a more stable interaction with periostin. These results are consistent with prior evidence linking periostin to metabolic dysfunction, inflammation, and lipid abnormalities in type 2 diabetes mellitus. Although the docking analysis provides only computational predictions, the observed interactions are consistent with the elevated serum periostin levels detected in the present study, further supporting its potential role as a cardiometabolic biomarker [42].

Given the significant increase in serum periostin levels and the high correlation with glycemic and lipid parameters, an exploratory docking analysis was conducted to evaluate the potential of common metabolic drugs to theoretically interact with

periostin, providing a preliminary mechanistic framework to associate the clinical findings with potential molecular interactions.

Conclusion

Results of the present study suggested a possible association between periostin and cardiovascular risk factors in diabetes, as newly diagnosed patients with type 2 diabetes and dyslipidemia had significantly higher serum periostin levels compared with healthy controls. Periostin showed positive correlations with glycemic and atherogenic lipid parameters and good diagnostic performance in ROC analysis. In addition, molecular docking analysis showed that periostin had favorable interactions with commonly used metabolic drugs, which further supported its potential roles in glucose and lipid metabolic pathways. These results imply that periostin could be a promising biomarker for identifying metabolic abnormalities, atherogenic risk, and early cardiovascular complications associated with type 2 DM.

DISCLOSURES

Human subjects: Written informed consent was obtained from all participants before enrollment in the study. The study was performed in accordance with the ethical standards of the Declaration of Helsinki and was approved by the appropriate institutional ethics committee (BCSMU/0530/1118C dt. May 30, 2026).

Conflicts of interest: The authors declare no conflicts of interest.

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Other relationships: All authors have declared that there are no other relationships or activities that could influence the submitted work.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

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Nihad Kadhum Hasan: Investigation, Data curation, Validation, Writing – review and editing.

Nada Nadhim Ahmed: Investigation, Methodology, Data curation, Writing – review and editing.

Zahraa A. A. Turki: Investigation, Data curation, Writing – review and editing.

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