International Journal of Research in Medical Sciences
Khan M et al. Int J Res Med Sci. 2025 Jan;13(1):27-32
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20244090

Original Research Article

A comparative analysis of adiponectin and soluble CD36 levels between diabetic and non-diabetic metabolic syndrome patients

Mansura Khan[1], M. Sohrab Alam[1], Nadia Siddiquee[2], Jesmin Nur[1], Zeenat Farzana Rahman[1], Mohammad Moniruzzaman[1]*

[1]Department of Immunology, BIRDEM General Hospital, Dhaka, Bangladesh
[2]Department of Physical Medicine and Rehabilitation, BIRDEM General Hospital, Dhaka, Bangladesh

Received: 20 November 2024
Accepted: 18 December 2024

***Correspondence:**
Dr. Mohammad Moniruzzaman,
E-mail: drmonirbirdem@gmail.com

ABSTRACT

Background: Metabolic syndrome refers to a constellation of interrelated metabolic risk factors that promote the development of type-2 diabetes mellitus (T2 DM) and cardiovascular diseases (CVD). The purpose of this study was to compare the serum levels of adiponectin and soluble CD36 between diabetic and non-diabetic metabolic syndrome patients. The aim of this study was to compare the serum levels of adiponectin and soluble CD36 between diabetic and non-diabetic metabolic syndrome patients.

Methods: This cross-sectional analytical study, conducted at the Outpatient Department and Department of Immunology at BIRDEM General Hospital over 12 months, included 80 participants: 60 with metabolic syndrome (30 type-2 diabetic and 30 non-diabetic) and 20 healthy controls. Participants underwent clinical examinations, anthropometric measurements and blood tests for serum analysis of adiponectin and soluble CD36 using ELISA and immunonephelometry. Data were analyzed using nonparametric tests (Mann-Whitney U test, Levene's test) and correlation analyses (Pearson and Spearman) with $p<0.05$, using SPSS version 20.

Results: Metabolic syndrome patients had higher weight, BMI, waist circumference and blood pressure compared to healthy subjects. Adiponectin and soluble CD36 levels were significantly lower in metabolic syndrome patients, with differences between diabetic and non-diabetic groups. Adiponectin negatively correlated with waist circumference, blood pressure and triglycerides, while soluble CD36 positively correlated with waist circumference, diastolic blood pressure and triglycerides.

Conclusions: In conclusion, our study highlights that adiponectin and soluble CD36 levels are significantly altered in diabetic versus non-diabetic metabolic syndrome patients, suggesting their potential as biomarkers for metabolic syndrome.

Keywords: Adiponectin, Diabetes mellitus, Metabolic syndrome, Soluble CD36

INTRODUCTION

Metabolic syndrome is a cluster of interrelated metabolic risk factors that occur together more frequently than by chance and are thought to directly contribute to the development of type-2 diabetes mellitus (T2 DM) and cardiovascular diseases (CVD), both of which are among the leading and most lethal non-communicable diseases globally. The key risk factors include abdominal obesity, elevated fasting plasma glucose, high blood pressure, high triglycerides and low levels of high-density lipoprotein cholesterol.[1] Abdominal obesity and insulin resistance are considered the primary underlying factors of the syndrome, which is why it is also referred to as “Insulin resistance syndrome”.[2] The presence of metabolic syndrome significantly increases the likelihood of developing T2 DM, making it a strong predictor of the condition's onset.[3] Additionally, individuals with metabolic syndrome are twice as likely to die from and three times more likely to suffer from, a heart attack or stroke compared to those without the syndrome.[2] Obese individuals and those with pre-existing diabetes also experience double the risk of CVD when metabolic syndrome is present.[4]

The prevalence of metabolic syndrome varies globally, influenced by factors such as population age, ethnicity and the diagnostic criteria used. Epidemiological studies indicate a high rate of this syndrome in Bangladesh as well. For example, a recent cross-sectional analytical study at BIRDEM General Hospital found that the overall prevalence of metabolic syndrome among newly diagnosed T2 DM patients was 79%, 81% and 68% according to NCEP-ATP III, WHO and IDF criteria, respectively.[5]

From both clinical and public health standpoints, there is a compelling need to identify individuals with metabolic syndrome who are at heightened risk of developing type-2 diabetes mellitus (T2 DM) and cardiovascular diseases (CVD) in the near future. Researchers have found that the risk factors associated with metabolic syndrome are linked to chronic, subclinical, low-grade systemic inflammation.[6]

Some researchers have coined this inflammatory state as “metaflammation”, referring to inflammation triggered by metabolic disturbances.[7] Given these findings, it can be hypothesized that the levels of biomolecules associated with these risk factors may aid in the diagnosis of metabolic syndrome. Among the molecules identified, adiponectin is one such biomarker.[8,9]

Adiponectin is a multifunctional protein that is exclusively secreted by adipose tissue into the bloodstream and is present in high concentrations in plasma. It has insulin-sensitizing effects and is regarded as a key factor in the development of metabolic syndrome.[10] Several prospective studies have shown that low levels of adiponectin are linked to insulin resistance, elevated insulin levels and an increased risk of developing type-2 diabetes mellitus (T2 DM). As a result, low serum adiponectin levels could serve as an indicator of metabolic syndrome.

CD36, also known as platelet glycoprotein 4, is a protein encoded by the CD36 gene. It is an integral membrane protein expressed in various tissues and plays multiple roles. In muscle, liver and fat tissues, CD36 is involved in the uptake of fatty acids and research has shown a link between higher CD36 expression and insulin resistance.[11] A soluble form of CD36 has been identified in the blood, reflecting the expression of CD36 in tissues and potentially serving as a marker for insulin resistance and atherosclerosis.[12]

These findings suggest significant associations between higher levels of soluble CD36 in serum, reduced insulin sensitivity, obesity, inflammation and a potential risk for future atherosclerosis. The purpose of this study was to compare the serum levels of adiponectin and soluble CD36 between diabetic and non-diabetic metabolic syndrome patients.

The aim of this study was to compare the serum levels of adiponectin and soluble CD36 between diabetic and non-diabetic metabolic syndrome patients.

METHODS

Study type

This was cross-sectional analytical study.

Study place

The study was conducted at the Outpatient Department (OPD) and the Department of Immunology of BIRDEM General Hospital, Dhaka, Bangladesh.

Study duration

The study was done over a 12-month period.

Sample size

The study included 80 subjects: 60 patients diagnosed with metabolic syndrome (30 type-2 diabetic and 30 non-diabetic) and 20 healthy controls.

Inclusion criteria

Age 18 years or older. Diagnosis of metabolic syndrome based on the 'Consensus Definition' of metabolic syndrome, which includes the presence of three or more of the following conditions.

Elevated waist circumference. Triglycerides of 150 mg/dl or higher. HDL-cholesterol of less than 40 mg/dl for men and less than 50 mg/dl for women. Blood pressure of 130/85 mmHg or higher. Fasting glucose of 100 mg/dl or higher. Healthy subjects without metabolic syndrome.

Exclusion criteria

Pregnancy, acute or chronic inflammatory diseases (e.g., cancer, autoimmune diseases, chronic kidney disease). Recent surgery, age less than 18 years.

Ethical approval

Institutional approval was obtained from the IRB of BIRDEM General Hospital, adhering to the Helsinki Declaration. Informed written consent was obtained from all participants to ensure privacy and confidentiality. Participants were interviewed, clinically examined and underwent routine hematological tests.

Anthropometric measurements included height, weight and waist circumference, measured with participants in light clothing and no shoes. BMI was calculated and waist circumference was measured midway between the lowest rib and iliac crest after normal expiration. A 5 ml random blood sample was collected from each participant, transported to the Department of Immunology, centrifuged at 3000 rpm for 15 minutes and serum was stored at -80°C for further analyses. Fasting plasma glucose and lipid profile data were collected from patient reports. Adiponectin was measured using the ELISA method (Biosensis Inc., Australia) with a quantitative sandwich ELISA on a 96-well plate. Soluble CD36 was measured using the ELISA method (Aviscera Bioscience Inc., USA) with a quantitative sandwich ELISA on a 96-well plate.

Stastical analysis

Data were expressed as median and interquartile range, with a p-value<0.05 considered statistically significant. Nonparametric tests (Levene's test, Mann Whitney U test) and correlation analyses (Pearson and Spearman coefficients) were conducted using SPSS version 20.

RESULTS

A total of 80 subjects were included in the study: 60 patients with at least three criteria of the 'Consensus Definition' of metabolic syndrome, with a mean age of 43.34±10.93 years and 20 healthy subjects with a mean age of 42.0±10.64 years. Among the study population, males and females were equally represented (50% each, 30 individuals). Most of the patients belonged to the 34–43 years age group (50%).

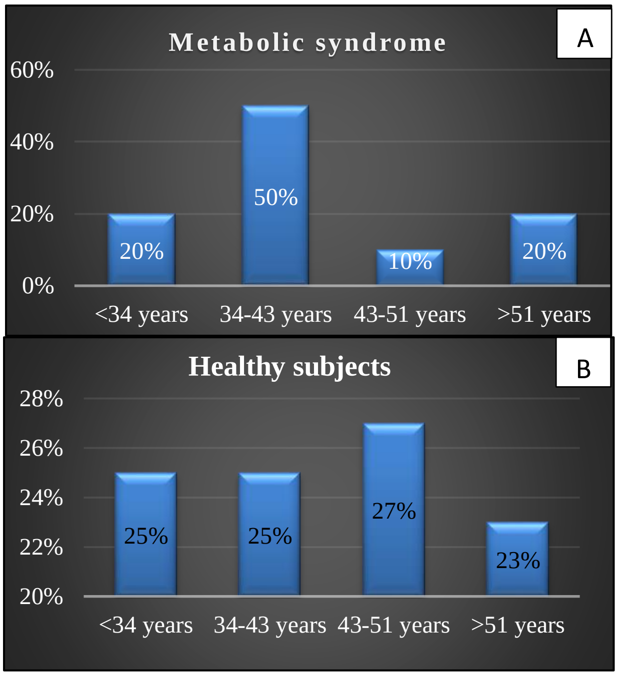

Figure 1 (A and B): Age group distribution of patients and healthy subjects.

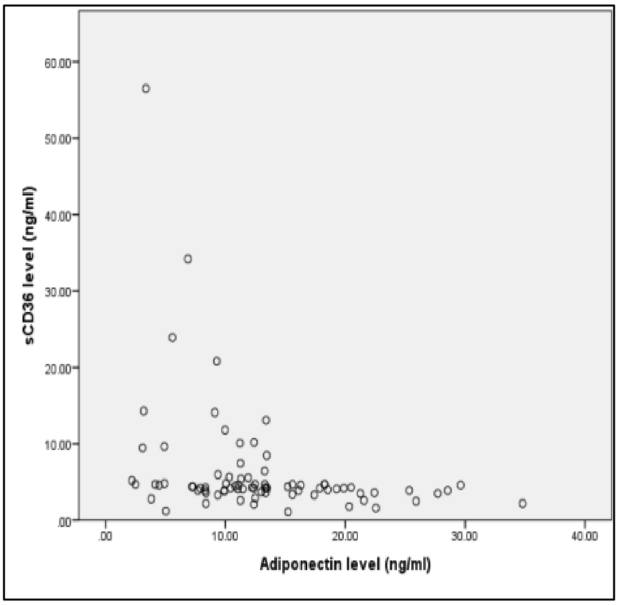

Figure 2: Scatter diagram of association between adiponectin and soluble CD36.

There were significant differences between patients with metabolic syndrome and healthy subjects in terms of weight (p<0.001), BMI (p<0.001), waist circumference (p<0.001), blood pressure (p<0.001), fasting plasma glucose (p=0.001), triglycerides (p=0.013), total cholesterol and LDL (p<0.001) and HDL (p=0.012).

Due to the non-homogeneous distribution of soluble CD36 data, a nonparametric Mann-Whitney U test was used to compare groups. The test revealed statistically significant differences in adiponectin, soluble CD36.

Due to non-homogeneity in soluble CD36 distribution, a Mann-Whitney U test was conducted. Statistically significant differences were found in adiponectin and soluble CD36 levels between diabetic and non-diabetic metabolic syndrome patients (p<0.05).

Pearson correlation analysis showed a significant negative correlation of adiponectin with waist circumference (WC), systolic and diastolic blood pressure (SBP and DBP) and triglycerides (TG). A significant positive correlation was observed between adiponectin and high-density lipoprotein (HDL).

As soluble CD36 data were skewed, Spearman correlation analysis was used. Significant positive correlations were found between soluble CD36 and waist circumference (WC) (rs=0.345, p=0.002), diastolic blood pressure (DBP) (rs=0.361, p=0.001) and triglycerides (TG) (rs=0.275, p=0.014).

Spearman correlation analysis showed a significant negative correlation of adiponectin with soluble CD36 (rs=-0.405, p<0.001).

Table 1: Distribution of anthropometric measurements, clinical and biochemical status in study subjects.

Variables	Diagnosis	Number	Mean±Std. Deviation	P value
Height (cm)	Met. Syndrome	60	162.26±9.11	0.470
	Healthy subjects	20	160.51±9.99	
Weight (kg)	Met. Syndrome	60	70.60±12.34	<0.001
	Healthy subjects	20	55.70±12.62	
BMI (kg/m²)	Met. Syndrome	60	26.67±3.13	<0.001
	Healthy subjects	20	21.42±3.23	
WC (cm)	Met. Syndrome	60	93.94±8.58	<0.001
	Healthy subjects	20	78.50±9.38	
SBP (mmHg)	Met. Syndrome	60	136.42±14.64	<0.001
	Healthy subjects	20	114.50±7.59	
DBP (mmHg)	Met. Syndrome	60	82.92±9.45	<0.001
	Healthy subjects	20	70.75±7.66	
FBG (mmol/l)	Met. Syndrome	60	7.62±3.94	0.001
	Healthy subjects	20	4.55±0.40	
HbA1C (%)	Met. Syndrome	60	7.12±2.11	<0.001
	Healthy subjects	20	4.63±0.29	
TG (mg/dl)	Met. Syndrome	60	326.32±325.70	0.013
	Healthy subjects	20	139.55±19.16	
TC (mg/dl)	Met. Syndrome	60	238.87±66.57	<0.001
	Healthy subjects	20	191.70±22.43	
LDL (mg/dl)	Met. Syndrome	60	161.80±57.26	<0.001
	Healthy subjects	20	104.90±33.35	
HDL (mg/dl)	Met. Syndrome	60	39.23±6.73	0.012
	Healthy subjects	20	43.50±5.53	

Table 2: Significance of serum adiponectin and soluble CD36 levels in patients and healthy subjects.

Markers	Study Group	Median	Interquartile Range	U	Z	Sig. (2-tailed) (p-value)
Adiponectin	MS	10.38	5.09	30	-6.33	<0.001
	Healthy	20.87	8.23			
Soluble CD36	MS	4.60	2.39	249	-3.90	<0.001
	Healthy	3.75	1.68			
	Healthy	3.23	0.00			

Table 3: Significance of serum adiponectin and soluble CD36 in diabetic and non-diabetic metabolic syndrome patients.

Markers	Study Group	Median	Interquartile Range	U	Z	Sig. (2-tailed) (p-value)
Adiponectin	MS with DM	11.60	4.32	281	-2.49	0.013
	MS without DM	20.87	8.23			
Soluble CD36	MS with DM	4.20	2.09	266	-2.72	0.006
	MS without DM	3.75	1.68			
	MS without DM	3.23	0.00			

Table 4: Correlation of adiponectin with parameters of metabolic syndrome.

		WC	SBP	DBP	FPG	TG	HDL
Adiponectin level	**Pearson correlation coefficient (r)**	-0.651	-0.385	-0.51	-0.201	-0.253	0.256
	Sig. (2-tailed) (P value)	<0.001	<0.001	<0.001	0.074	0.024	0.022

Table 5: Correlation of soluble CD36 with parameters of metabolic syndrome.

		WC	SBP	DBP	FPG	TG	HDL
Soluble CD36 level	**Spearman correlation coefficient (rs)**	0.345	0.192	0.361	0.104	0.275	-0.206
	Sig. (2-tailed) (P value)	0.002	0.087	0.001	0.36	0.014	0.067

DISCUSSION

The metabolic syndrome is a cluster of interrelated risk factors for type-2 diabetes (T2 DM) and cardiovascular disease (CVD). Individuals with metabolic syndrome have up to a five-fold higher risk of developing diabetes compared to those without the condition.[13] Additionally, individuals with metabolic syndrome have twice the risk of death and are three times more likely to suffer a heart attack or stroke compared to those without the condition.[2]

Approximately 20-25% of the world's adult population is affected by metabolic syndrome.[14] An increasing trend has also been observed in Asian countries, with a meta-analysis indicating that around 10-13% of adults in Asia had metabolic syndrome in 2007.[15] Epidemiological studies have revealed a high prevalence of this syndrome in Bangladesh as well. A cross-sectional study by Billah et al, in both urban and rural Bangladeshi populations reported a prevalence rate of 38.78% in 2010.[16] Additionally, a cross-sectional study at the outpatient department of BIRDEM General Hospital by Hossain et al.[5] found that the prevalence of metabolic syndrome among newly diagnosed type-2 diabetic subjects was 79%, 81% and 68%, according to modified ATP III, WHO and IDF criteria, respectively.

In this cross-sectional analytical study, a total of 80 subjects were included, with 60 patients meeting at least three criteria of the 'Consensus Definition' of metabolic syndrome. The mean age of the patients was 43.34±10.93 years. The remaining 20 subjects were healthy controls with a mean age of 42±10.64 years. The gender distribution among the study population was equal, with 50% male (30 subjects) and 50% female (30 subjects). The majority of patients (50%) fell within the 34 to 43-year age group, which may suggest an increasing trend of metabolic syndrome in younger age groups in Bangladesh. In this study, we found significant differences between patients with metabolic syndrome and healthy subjects in several key parameters. These included weight ($p<0.001$), BMI ($p<0.001$), waist circumference ($p<0.001$), blood pressure ($p<0.001$), fasting plasma glucose ($p=0.001$), triglycerides ($p=0.013$), total cholesterol, LDL ($p<0.001$) and HDL ($p=0.012$). These findings are logical, as metabolic syndrome is characterized by a combination of these clinico-biochemical factors, which contribute to its pathophysiology.

CD36, located on the surface of muscle, liver and fat tissues, plays a crucial role in the uptake of fatty acids. Several studies have indicated a relationship between elevated CD36 expression in these tissues and insulin resistance. Insulin resistance, commonly observed in overweight individuals and those genetically predisposed to metabolic syndrome, is also linked to atherosclerosis, which is thought to result from chronic low-grade inflammation. Recently, a soluble form of CD36 has been identified in the blood, reflecting tissue CD36 expression and potentially serving as a marker for insulin resistance and atherosclerosis.[12] In line with previous research, a study by Handberg et al, in 2011 found that soluble CD36 levels were significantly higher in patients with metabolic syndrome compared to healthy subjects (4.6±3.9 vs 3.8±3.2, $p=0.006$).[9] Similarly, in our study, we observed that soluble CD36 levels were significantly higher in patients with metabolic syndrome compared to healthy subjects (4.6±2.93 vs 3.75±1.68, $p<0.001$). This supports the notion that elevated soluble CD36 levels are associated with metabolic syndrome and its underlying patho-physiological mechanisms.

According to the consensus definition of metabolic syndrome, waist circumference, fasting plasma glucose, systolic blood pressure, diastolic blood pressure, triglycerides and high-density lipoprotein (HDL) levels are key diagnostic criteria. Several studies have explored the correlation between these parameters and the levels of adiponectin and soluble CD36.Stojanovic et al, found a negative correlation between adiponectin levels and waist circumference ($r=-0.437$, $p<0.001$).[17] In our study, we also observed a significant negative correlation between adiponectin levels and waist circumference ($r=-0.651$, $p<0.001$).

Additionally, adiponectin levels were negatively correlated with both systolic ($r=-0.385$, $p<0.001$) and diastolic blood pressure ($r=-0.51$, $p<0.001$), triglycerides ($r=-0.253$, $p=0.024$) and positively correlated with HDL ($r=0.256$, $p=0.022$). These findings align with those of other authors, further supporting the role of low adiponectin levels as a predictor of metabolic syndrome. On the other hand, soluble CD36 showed a significant positive correlation with waist circumference ($r_s=0.345$), triglycerides ($r_s=0.275$, $p=0.014$) and diastolic blood pressure ($r_s=0.361$, $p=0.001$). This suggests that higher soluble CD36 levels may be associated with central obesity, increased triglycerides and elevated blood pressure, which are hallmark features of metabolic syndrome.

In our study, we sought to examine the relationship between adiponectin and soluble CD36 levels in individuals with metabolic syndrome, comparing diabetic and non-diabetic patients. Our analysis found a significant negative correlation between adiponectin and soluble CD36 ($r_s=-0.405$, $p<0.001$). These results indicate that in metabolic syndrome, lower adiponectin levels are associated with higher soluble CD36 levels, which may reflect the underlying inflammatory and metabolic disturbances characteristic of the condition.

While this study offers valuable insights, some factors may influence the generalize ability of the findings. The sample size was constrained by time and budget and the use of a single ELISA kit may have impacted measurement consistency. Additionally, the cross-sectional design and single-center setting limit the broader applicability and reliance on a single biomarker measurement restricts the assessment of diagnostic consistency over time. These considerations should be kept in mind when interpreting the results.

CONCLUSION

This study demonstrates significant differences in serum levels of adiponectin and soluble CD36 between patients with metabolic syndrome and healthy controls, with metabolic syndrome patients exhibiting lower adiponectin and higher soluble CD36 levels. Notably, we identified distinct variations in these markers between diabetic and non-diabetic metabolic syndrome patients, suggesting a potential differentiator between the two groups. Furthermore, adiponectin levels showed significant negative correlations with key metabolic syndrome parameters, including waist circumference, blood pressure and triglycerides, while soluble CD36 levels were positively correlated with waist circumference, diastolic blood pressure and triglycerides. These findings support the potential of adiponectin and soluble CD36 as valuable biomarkers for metabolic syndrome, particularly for distinguishing between diabetic and non-diabetic subsets in the Bangladeshi population.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung and blood institute; American heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. Circulation. 2009;120(16):1640-5.
2. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. The lancet. 2005;16;365(9468):1415-28.
3. Sattar N, McConnachie A, Shaper AG, Blauw GJ, Buckley BM, de Craen AJ, et al. Can metabolic syndrome usefully predict cardiovascular disease and diabetes? Outcome data from two prospective studies. The Lancet. 2008;7;371(9628):1927-35.
4. Meigs JB, Rutter MK, Sullivan LM, Fox CS, D'Agostino Sr RB, Wilson PW. Impact of insulin resistance on risk of type 2 diabetes and cardiovascular disease in people with metabolic syndrome. Diabetes care. 2007;1;30(5):1219-25.
5. Hossain MS, Rahaman MZ, Banik S, Sarwar MS, Yokota K. Prevalence of the metabolic syndrome in diabetic patients living in a coastal region of Bangladesh. Int J Pharma Sci Res. 2012;1;3(8):2633.
6. Hanley AJ, Festa A, D'Agostino Jr RB, Wagenknecht LE, Savage PJ, Tracy RP, et al. Metabolic and inflammation variable clusters and prediction of type 2 diabetes: factor analysis using directly measured insulin sensitivity. Diabetes. 2004;1;53(7):1773-81.
7. Hotamisligil GS. Inflammation and metabolic disorders. Nature. 2006;14;444(7121):860-7.
8. Ryo M, Nakamura T, Kihara S, Kumada M, Shibazaki S, Takahashi M, et al. Adiponectin as a biomarker of the metabolic syndrome. Circulation journal. 2004;68(11):975-81.
9. Handberg A, Højlund K, Gastaldelli A, Flyvbjerg A, Dekker JM, Petrie J, et al. investigators. Plasma sCD36 is associated with markers of atherosclerosis, insulin resistance and fatty liver in a nondiabetic healthy population. Journal of internal medicine. 2012;271(3):294-304.
10. Matsuzawa Y, Funahashi T, Kihara S, Shimomura I. Adiponectin and metabolic syndrome. Arteriosclerosis, Thrombosis and Vas Biol. 2004;1;24(1):29-33.
11. Koonen DP, Jacobs RL, Febbraio M, Young ME, Soltys CL, Ong H, et al. Increased hepatic CD36 expression contributes to dyslipidemia associated with diet-induced obesity. Diabetes. 2007;1;56(12):2863-71.
12. Handberg A, Levin K, Højlund K, Beck-Nielsen H. Identification of the oxidized low-density lipoprotein scavenger receptor CD36 in plasma: a novel marker of insulin resistance. Circulation. 2006;12;114(11):1169-76.
13. Grundy SM. Metabolic syndrome: connecting and reconciling cardiovascular and diabetes worlds. J Am Coll Cardiol. 2006;21;47(6):1093-100.
14. Alberti G, Zimmet P, Shaw J, Grundy SM. The IDF consensus worldwide definition of the metabolic syndrome. Brussels: Int Diab Feder. 2006;23(5):469-80.
15. Nestel P, Lyu R, Low LP, Sheu WH, Nitiyanant W, Saito I, et al. Metabolic syndrome: recent prevalence in East and Southeast Asian populations. Asia Pacific J Clin Nutr. 2007;1;16(2):1.
16. Billah SM, Jahan MS, Jesmine S, Keobouahome B, Watanabe Y, Kinoue T. Metabolic Syndrome in Bangladesh using NCEP adult treatment panel III Criteria. Jpn J ClinEcol. 2011;20(1):61-70.
17. Stojanović S, Deljanin-Ilić M, Ilić S, Petrović D, Đukić S. The significance of adiponectin as a biomarker in metabolic syndrome and/or coronary artery disease. Vojnosanitetski pregled. 2015;72(9):779-84.

Cite this article as: Khan M, Alam MS, Siddiquee N, Nur J, Rahman ZF, Moniruzzaman M. A comparative analysis of adiponectin and soluble CD36 levels between diabetic and non-diabetic metabolic syndrome patients. Int J Res Med Sci 2025;13:27-32.