Section: General Medicine

Original Research Article

ASSESSMENT OF LEVELS OF SOLUBLE CD36 IN PATIENTS WITH METABOLIC SYNDROME

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ABSTRACT

Background: Aim: Metabolic syndrome represents a cluster of interrelated metabolic risk factors that increase the likelihood of developing type 2 diabetes mellitus (T2DM) and cardiovascular diseases (CVD). The present study aimed to assess the levels of soluble CD36 (sCD36) in patients with metabolic syndrome and to explore its correlation with various metabolic parameters.

Materials and Methods: This cross-sectional analytical study included 60 participants diagnosed with metabolic syndrome. All participants underwent detailed clinical evaluation, anthropometric assessment, and biochemical analysis. Serum levels of soluble CD36 were estimated using enzyme-linked immunosorbent assay (ELISA).

Results: The mean age of the study subjects was 53.2 ± 11.2 years, and 70% were females. The mean serum CD36 concentration was 357.3 ± 193.4 ng/ml. A negative correlation was observed between CD36 and waist circumference (r = –0.022), total cholesterol (r = –0.097), triglycerides (r = –0.200), LDL (r = –0.037), VLDL (r = –0.211), HDL (r = –0.054), and WBC count (r = –0.08), indicating that higher CD36 levels were associated with lower values of these parameters. Conversely, a positive correlation was found between CD36 and age, BMI, fasting blood sugar (FBS), postprandial blood sugar (PPBS), hemoglobin (Hb), and platelet count, suggesting that CD36 levels increased in parallel with these parameters. Among participants with metabolic syndrome and T2DM, similar correlation patterns were observed. A significant difference was noted in mean VLDL, PPBS, and WBC counts between CD36 categories. Specifically, participants with CD36 > 78 ng/ml had significantly lower VLDL, higher PPBS, and lower WBC counts compared to those with lower CD36 levels.

Conclusion: The study found no significant correlation between soluble CD36 and most metabolic parameters among individuals with metabolic syndrome. However, a significant association was observed between CD36 and VLDL levels in subjects with metabolic syndrome and T2DM. A CD36 cutoff of 78 ng/ml was associated with significant differences in VLDL, PPBS, and WBC counts, suggesting its potential role as a biochemical indicator in metabolic syndrome with diabetes.

Keywords: metabolic syndrome, type-2 diabetes mellitus, cardiovascular disease, soluble CD36.

INTRODUCTION

Diabetes mellitus is a metabolic disorder of multifactorial etiology, characterized by chronic hyperglycemia and disturbances in the metabolism of carbohydrates, fats, and proteins, resulting from defects in insulin secretion, insulin action, or both.[1] Type 2 diabetes mellitus (T2DM) is often considered a consequence of metabolic syndrome, as individuals with metabolic syndrome have a five-fold increased risk of developing diabetes compared to healthy controls.[2] Insulin resistance plays a pivotal role in

the pathogenesis of metabolic syndrome, prediabetes, and T2DM. Conversely, it has been observed that approximately 70% of prediabetic individuals and 86% of patients with type 2 diabetes meet the diagnostic criteria for metabolic syndrome.[3]

CD36 is a widely expressed cell surface membrane glycoprotein that performs multiple biological functions. It acts as a facilitator of fatty acid uptake, a signalling molecule, and a class B scavenger receptor that binds a broad spectrum of ligands. These include apoptotic cells, thrombospondin-1 (TSP-1), fibrillar β-amyloid, components of Gram-positive bacterial cell walls, malaria-infected erythrocytes, and, importantly in the context of diabetes, oxidized low-density lipoprotein (ox-LDL) and advanced glycation end products (AGEs).[4]

Initially identified more than three decades ago as glycoprotein IV (GPIV) on platelet surfaces (~88 kDa),[5] CD36 was subsequently recognized as a macrophage receptor for ox-LDL and an adipocyte fatty acid transporter (FAT).[6] In insulin-resistant states, elevated plasma free fatty acid (FFA) levels impair insulin-stimulated glucose uptake in skeletal muscle, leading to hyperglycemia, hyperinsulinemia, and reduced glycogen synthesis.[7-10]

Given that CD36 functions as a transporter of long-chain fatty acids (LCFA)—particularly in muscle tissues—any dysfunction in this protein may contribute to elevated plasma fatty acid levels, decreased muscular glucose uptake, and insulin resistance.

Therefore, the present study was undertaken to evaluate the serum levels of soluble CD36 (sCD36) in individuals with metabolic syndrome and to explore its possible association with metabolic risk factors.

MATERIALS AND METHODS

Study Setting

This hospital-based cross-sectional study was conducted in the Department of General Medicine.

Study Duration

The study was conducted over a period of 18 months following approval from the Institutional Ethics Committee.

Sampling:

A total of 60 patients diagnosed with metabolic syndrome, either attending outpatient services or admitted to the hospital during the study period, were enrolled after obtaining informed consent from the patient or their attendant.

Inclusion Criteria

Patients fulfilling three or more of the following criteria were included:

1. **Central obesity:** Waist circumference > 90 cm (males), > 80 cm (females).
2. **Hypertriglyceridemia:** Triglycerides ≥ 150 mg/dl or on specific medication.
3. **Low HDL cholesterol:** < 40 mg/dl (males), < 50 mg/dl (females) or on specific medication.
4. **Hypertension:** Systolic ≥ 130 mmHg or diastolic ≥ 85 mmHg.
5. **Fasting plasma glucose:** ≥ 100 mg/dl, previously diagnosed type 2 diabetes mellitus, or on specific medication.

Exclusion Criteria

1. Pregnant or breastfeeding women.
2. Patients with a history of systemic diseases.

Methodology

1. Patients meeting the above criteria were identified as having metabolic syndrome.
2. Clinical and laboratory evaluations were performed, including:
   - Complete blood count (EDTA sample)
   - Fasting lipid profile
   - Fasting and postprandial blood glucose
   - Soluble CD36 levels

Anthropometric and Clinical Measurements

BMI and waist circumference were measured according to standard protocols.

Analytical Methods

- Serum glucose was measured in duplicate using the glucose oxidase method.
- Total cholesterol was quantified via cholesterol esterase/cholesterol oxidase/peroxidase reaction, and triglycerides via the glycerol-phosphate-oxidase/peroxidase method.
- Soluble CD36 levels were measured using a sandwich ELISA kit designed for accurate quantification in serum, plasma, cell culture supernatants, cell lysates, and tissue homogenates.

Assay Principle: CD36 in the sample binds to wells pre-coated with monoclonal CD36 antibody. A biotin-conjugated anti-human CD36 antibody is then added, which binds to the captured CD36. Following washing, streptavidin-HRP is added, binding to the biotin-conjugated antibody. After incubation and washing, a substrate solution is added, producing a color proportional to CD36 concentration. The reaction is stopped with acidic solution, and absorbance is measured at 450 nm.

Statistical Analysis: Data analysis was performed using SPSS version 22 (IBM SPSS Statistics, Somers, NY, USA).

- A p-value < 0.05 was considered statistically significant.
- Categorical data were expressed as frequencies & percentages, and continuous data as mean ± SD.
- Pearson correlation was used to assess the relationship between quantitative variables

Pearson correlation was done to find the correlation between two quantitative variables.

Correlation coefficient (r)	Interpretation
0 - 0.3	Positive Weak correlation
0.3-0.6	Positive Moderate correlation
0.6-1.0	Positive Strong correlation
0 to (-0.3)	Negative Weak correlation
(-0.3) to (-0.6)	Negative Moderate Correlation
(-0.6) to – (1)	Negative Strong Correlation

RESULTS

The study included **60 subjects** with metabolic syndrome. The **mean age** was **53.2 ± 11.2 years**, with the majority falling in the **41–50-year age group**. **Females comprised 70%** of the study population, while **males accounted for 30%**. Most participants had **Type 2 Diabetes Mellitus (97.5%)**, and **73.8% had hypertension**.

Anthropometric and Biochemical Parameters

- **Mean waist circumference:** 89 ± 5.1 cm
- **Mean BMI:** 31.7 ± 2.5 kg/m²
- **Mean total cholesterol:** 195 ± 58.7 mg/dl
- **Mean triglycerides:** 235.8 ± 174.9 mg/dl
- **Mean LDL:** 113.6 ± 39.8 mg/dl
- **Mean VLDL:** 37.5 ± 17.2 mg/dl
- **Mean HDL:** 38.5 ± 5.8 mg/dl
- **Mean FBS:** 175.2 ± 83.7 mg/dl
- **Mean PPBS:** 269.9 ± 96 mg/dl
- **Mean haemoglobin:** 11 ± 1.8 g/dl
- **Mean WBC count:** 9513.8 ± 3482.7 cells/mm³
- **Mean platelet count:** 288,755 ± 86,108 cells/mm³
- **Mean soluble CD36:** 357.3 ± 193.4 ng/ml

Correlation Analysis

- **Negative correlations** were observed between CD36 and the following parameters:
  - Waist circumference (r = -0.022)
  - Total cholesterol (r = -0.097)
  - Triglycerides (r = -0.200)
  - LDL (r = -0.037)
  - VLDL (r = -0.211)
  - HDL (r = -0.054)
  - WBC count (r = -0.08)

This indicates that as **CD36 levels increase**, these parameters tend to decrease, and vice versa, in metabolic syndrome subjects.

- **Positive correlations** were observed between CD36 and:
  - Age
  - BMI
  - FBS
  - PPBS
  - Hemoglobin
  - Platelet count

This suggests that as CD36 levels increase, these parameters also tend to increase.

- However, **most correlations were not statistically significant**, except for a **significant negative correlation between CD36 and VLDL** in metabolic syndrome subjects with Type 2 Diabetes Mellitus.

CD36 and Obesity

- **Mean CD36 levels** in overweight subjects: 346.7 ± 205.4 ng/ml
- **Mean CD36 levels** in obese subjects: 361.6 ± 190 ng/ml
- There was **no significant difference** in CD36 levels between overweight and obese participants.

CD36 Category Analysis

Participants were categorized based on CD36 levels (>78 ng/ml and ≤78 ng/ml):

- **VLDL** was significantly lower in participants with **CD36 >78 ng/ml**.
- **PPBS** was significantly higher in participants with **CD36 >78 ng/ml**.
- **WBC count** was significantly lower in participants with **CD36 >78 ng/ml**.

No significant differences were observed for other biochemical or anthropometric parameters between the two CD36 categories.

Table 1: Age distribution of subjects in the study

		Count	%
Age	<40 years	12	15.0%
	41 to 50 years	26	32.5%
	51 to 60 years	21	26.2%
	61 to 70 years	15	18.8%
	>70 years	6	7.5%
	Total	80	100.0%
	Mean ± SD	53.2 ± 11.2	

Table 2: Mean and SD of Metabolic syndrome parameters and CD36 among subjects

	Mean	SD	Minimum	Maximum	Range
Waist Circumference	89.0	5.1	82	100	18
BMI	31.7	2.5	26.4	40.9	14.5
T C	196.0	58.7	101	409	308
TG	235.8	174.9	63	1104	1041
LDL	113.6	39.8	43	217	174
VLDL	37.5	17.2	12	122	110
HDL	38.5	5.8	28	53	25
FBS	175.2	83.7	64	472	408
PPBS	269.9	96.0	107	500	393
Hb	11.0	1.8	5.4	14.6	9.2
WBC	9513.8	3482.7	3100	21000	17900
Platelet	288755.0	86108.5	128000	588000	460000
CD 36	357.3	193.4	30	650	620

Table 3: Correlation between CD 36 and parameters of metabolic syndrome

	Pearson Correlation	P value	N
CD 36	1		80
AGE	0.045	0.691	80
Waist Circumference	-0022	0.845	80
BMI	0.061	0.589	80
TC	-0.097	0.394	80
TG	-0.200	0.076	80
LDL	-0.037	0.747	80
VLDL	-0.211	0.061	80
HDL	-0.054	0.632	80
FBS	0.042	0.711	80
PPBS	0.217	0.053	80
Hb	0.075	0.510	80
WBC	-0.08	0.475	80
Platelet	0.105	0.353	80

Table 4: Correlation between CD 36 and parameters of metabolic syndrome among subjects with history of Type 2 DM

	Pearson Correlation	P value	N
CD 36	1		78
Age	0.051	0.658	78
Waist Circumference	0.005	0.964	78
BMI	0.063	0.582	78
T C	-0.093	0.416	78
TG	-0.215	0.059	78
LDL	-0.023	0.842	78
VLDL	-0.228*	0.045*	78
HDL	-0.043	0.706	78
FBS	0.054	0.637	78
PPBS	0.200	0.079	78
Hb	0.084	0.466	78
WBC	-0.103	0.370	78
Platelet	0.078	0.500	78

Table 5: Mean CD 36 values comparison with respect to BMI

		CD 36		P value
		Mean		
BMI	Overweight (n=23)	346.7	205.4	0.758
	Obese (n=57)	361.6	190.0	

Table 6: Mean metabolic parameters with respect to CD 36 at cut off value of <78 ng/ml

	CD 36				P value
	<78 ng/ml		>78 ng/ml		
	Mean		Mean		
Age	49.1	11.7	53.9	11.1	0.173
Waist Circumference	88.8	6.0	89.0	5.0	0.904
BMI	31.2	1.7	31.9	2.6	0.397
T C	203.8	50.1	194.6	60.3	0.622
TG	280.0	181.9	228.0	173.9	0.346
LDL	112.9	46.7	113.7	38.9	0.948
VLDL	48.6	26.8	35.6	14.4	0.015*
HDL	39.3	4.7	38.4	6.0	0.614
FBS	155.4	67.8	178.7	86.2	0.379
PPBS	204.6	76.9	281.5	94.8	0.01*

Hb	11.2	1.3	11.0	1.8	0.766
WBC	11508.3	4162.0	9161.8	3258.7	0.03*
Platelet	288200.0	75144.5	288852.9	88405.5	0.981

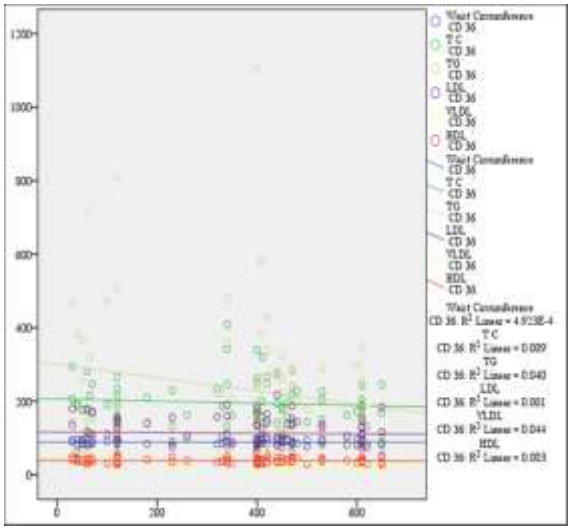

Figure 1: Scatter Plot showing Negative Correlation between CD-36 and Waist Circumference, TC, TG, LDL, VLDL, HDL

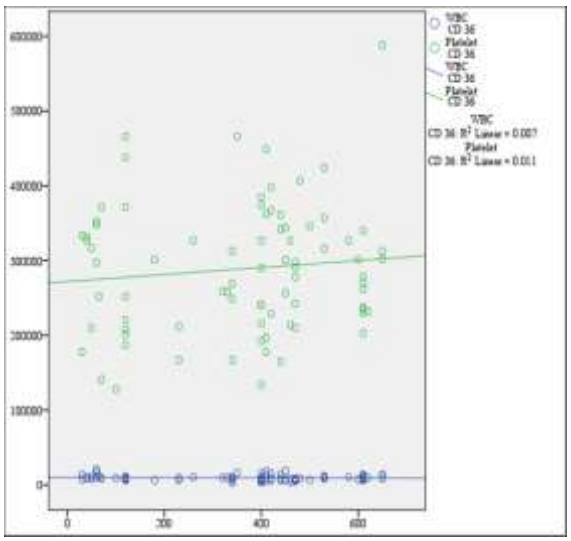

Figure 2: Scatter Plot showing Negative Correlation between CD 36 and WBC and positive correlation between CD 36 and platelet count

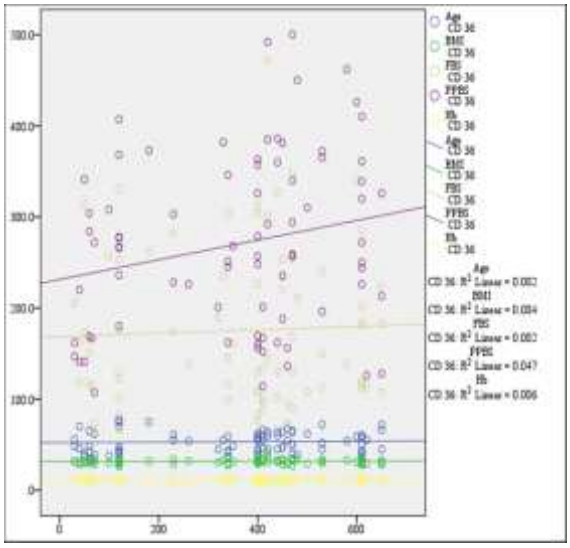

Figure 3: Scatter Plot showing Positive Correlation between CD 36 and Age, BMI, FBS, PPBS, Hb

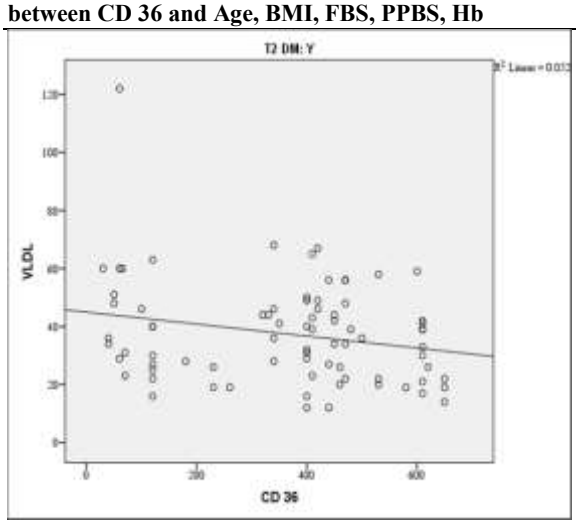

Figure 5: Scatter Plot showing Negative correlation between CD 36 and VLDL in diabetics

DISCUSSION

Circulating soluble CD36 (sCD36) has been implicated in the pathogenesis and complications of diabetes and metabolic syndrome. Previous studies have shown that serum sCD36 levels are elevated in patients with chronic kidney disease undergoing dialysis, particularly in those with type 2 diabetes. sCD36 has also been proposed as a marker of liver injury associated with insulin resistance, such as in non-alcoholic fatty liver disease (NAFLD), and correlates with insulin resistance and fatty liver even in non-diabetic populations. Similarly, elevated sCD36 has been associated with cardiovascular complications, including prediction of cardiovascular mortality in stage 5 chronic kidney disease patients and correlation with symptomatic atherosclerotic plaques, plaque instability, and adverse lipid profiles,

such as increased LDL and triglycerides and decreased HDL.

However, many earlier studies did not differentiate between membrane-bound CD36 and plasma sCD36, leaving unresolved whether circulating sCD36 derives from proteolytic cleavage of tissue-expressed CD36 or from CD36-positive microparticles (MPs) released during apoptosis. Elevated sCD36 in type 2 diabetes may reflect metabolic syndrome and serve as a surrogate marker for atherosclerosis, interacting with insulin action and inflammation, particularly in individuals with glucose intolerance. Despite these associations, effect sizes were modest, highlighting the need for cautious interpretation.

Koonen et al,[11] demonstrated that sCD36 reflects tissue CD36 expression, particularly in monocytes and macrophages, and is influenced by insulin resistance, oxidized LDL, low-grade inflammation, and hepatic steatosis. Genetic variations in the CD36 locus are linked to lipid levels, free fatty acids, insulin resistance, obesity, and coronary heart disease risk, though their effect on plasma sCD36 remains unclear. This suggests that sCD36 could potentially serve as a marker of processes central to insulin resistance and atherosclerosis in metabolic syndrome.

Knosgaard et al,[12] reported that weight loss reduces CD36 levels, supporting its role as a biochemical marker of obesity-related metabolic complications. Himoto et al. found that sCD36 levels reflected CD36 expression in Kupffer cells and were associated with obesity, independent of insulin resistance and hepatic steatosis. Griffin et al,[14] demonstrated that high glucose conditions increase macrophage CD36 expression via enhanced mRNA translation, providing a mechanism for accelerated atherosclerosis in diabetes. Zhang et al. further confirmed that elevated CD36 expression contributes to vascular complications in poorly controlled diabetic patients.

Alkhatatbeh,[16] highlighted that plasma sCD36 is largely associated with circulating MPs (CD36+MPs), which may serve as better markers of diabetes than total sCD36 protein. These MPs primarily derive from mature erythrocytes, though their precise role in diabetes pathophysiology remains under investigation. Understanding the source of sCD36 is critical, as platelet CD36 is highly resistant to proteolysis, and CD36+MPs can be traced using platelet, endothelial, and erythrocyte-specific markers.

In our study, sCD36 was measured using a commercial ELISA kit with a minimum detectable value of 78 ng/ml. Over 95% of samples exceeded this detection limit, limiting the ability to establish statistical significance. Chmielewski et al.18 reported median serum CD36 concentrations of 25.3 ng/ml in non-diabetic individuals, and ELISA kits with sensitivity around 39 ng/ml may enable more precise future studies. Variability in plasma CD36 may reflect differences in cellular expression influenced by CD36 gene polymorphisms, diet, hyperglycemia, and pharmacologic interventions such as statins, which reduce CD36 expression on monocytes.

Overall, while sCD36 has potential as a biomarker for metabolic syndrome, insulin resistance, and cardiovascular risk, its clinical utility is limited by methodological challenges, variability in detection, and the complex sources of circulating CD36.

CONCLUSION

In this study, no significant correlations were observed between soluble CD36 (sCD36) and most metabolic parameters in subjects with metabolic syndrome. However, among those with metabolic syndrome and type 2 diabetes, sCD36 showed a significant negative correlation with VLDL. Using a cutoff value of 78 ng/ml, sCD36 was associated with significant differences in VLDL, postprandial blood sugar (PPBS), and white blood cell (WBC) count. These findings suggest a potential role of sCD36 in lipid metabolism and glycemic status in this population, warranting further investigation.

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