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Original Research

Sirtuin 1, but not Osteocalcin, Correlates with Lipid Accumulation Product, Visceral Adiposity and Atherogenicity Indices in Newly Diagnosed Prediabetes-Metabolic Syndrome Patients

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Abstract

Introduction: Osteocalcin (OCN) and Sirtuin 1 (SIRT1) are intricately involved in metabolic syndrome (MetS) and prediabetes (PreDM) anomalies and derangements. In a heterogeneous pool of nondiabetic and preDM MetS recruits, adiposity, atherogenicity and blood indices, SIRT1 and OCN were compared to the respective parameters in normoglycemic and lean controls. Further testing of putative relationships between indices and markers was performed in 59 patients with MetS. **Material and Methods:** In this cross-sectional study, comparisons and correlations were undertaken for biomarkers, adiposity, atherogenicity and hematological indices in 29 MetS-normoglycemic and 30 newly diagnosed drug-naive MetS-preDM patients versus 29 lean, healthy and normoglycemic controls. ANOVA and Spearman rank correlations were used for statistical comparisons. **Results**: OCN level (OCN; ng/mL) was significantly higher in normoglycemic MetS vs. both MetS-PreDM and controls (28.13±1.22 and 26.02±3.2 vs. 23.3±3.19, P<0.001 respectively). In contrast, the circulating level of SIRT1 (ng/mL) was lower in both normoglycemic and preDM MetS vs. healthy controls (1.42±0.47 and 1.64±0.58 vs. 3.88±0.95; P<0.001, respectively). Except for fasting plasma glucose and glycated hemoglobin (A1C), no further intergroup discrepancy could be identified between normoglycemic-MetS and preDM-MetS. Notably, adiposity indices and the atherogenicity index of plasma were significantly higher in both MetS (normoglycemic and preDM) groups vs. controls. The LDL-C/HDL-C ratio, visceral adiposity index, and waist/hip ratio were higher only in MetS-preDM vs. controls. In the MetS pool (n=59), OCT, but not SIRT1, was associated reciprocally with fasting glycemia and A1C, monocyte/lymphocyte ratio, but proportionally with HC. In the same MetS pool, SIRT1 correlated significantly positively with TG, lipid accumulation product, visceral adiposity index and the atherogenicity index of plasma. **Conclusions:** OCN and SIRT1 may reciprocally participate in the development of MetS and preDM; both biomarkers may be putatively surrogate diagnostic/prognostic tools for metabolic anomalies prediction/prevention and pharmacotherapy.

Keywords: Sirtuin 1, osteocalcin, prediabetes and metabolic syndrome, adiposity, hematology and atherogenicity indices.

Introduction

Diabetes mellitus (DM) is a constellation of progressive metabolic and endocrine derangements and anomalies [1]. Individuals with prediabetes (PreDM) have a glycosylated hemoglobin (HbA1C) value of 5.7–6.4%, impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT). PreDM, as a risk factor for cardiovascular disease (CVD) and diabetes, correlates with abdominal obesity, hypertension (HTN), atherogenic dyslipidemia, and visceral obesity [1]. As stated by the International Diabetes Federation (IDF) [2], MetS is principally identified by central obesity (measured by waist circumference (WC) in relevance to gender and ethnicity) with two

or more anomalies of MetS components. MetS is heterogeneous due to its components' diversity, including dropped high-density lipoprotein cholesterol (HDL-C), raised triglyceride, raised blood pressure (BP) and/or raised fast blood glucose (FBG) levels [3].

Sirtuin 1 (SIRT1) belongs to the NAD+-dependent histone deacetylases (HDAC) family that prevents DNA transcription. In general, sirtuins predominantly regulate metabolism through their regulation of inflammation, oxidative stress and mitochondrial function, thus improving insulin resistance and T2DM. SIRT1 levels have an inverse relationship with cardiac performance and inflammatory cytokines in subcutaneous abdominal fat in overweight prediabetic patients [4]. SIRT1 can also be involved in the diversity of neurodegeneration, tumors, cardiomyopathies, arrhythmias, hypertension, dysregulation of insulin secretion from the pancreatic β-cells, endothelial dysfunction, atherosclerosis, MetS, obesity with fatty liver, DM, and dyslipidemia [5].

As a serum marker of bone formation, osteocalcin (OCN) is produced by osteoblasts. Low serum osteocalcin concentration is associated with lower bone remodeling and/or decreased bone quality in T2DM women with osteoporosis. The osteopontin-osteocalcin (OCN)–osteoprotegerin hormone triad involved in bone remodeling may affect glucose metabolism in preDM before overt T2DM occurs. Serum OCN concentration is negatively correlated with FPG, insulin resistance, and HbA1C. Furthermore, MetS is related to abdominal obesity, dyslipidemia, hyperglycemia, and hypertension and is substantially associated with osteoporosis. Contradictory reports delineated the lack of interaction among the skeletal bone-derived factors (OCN, Fibroblast growth factor 23, neutrophil gelatinase-associated lipocalin, Lipocalin–2) with visceral obesity and body mass index (BMI) [6–7]. This study aimed to compare and correlate Osteocalcin (OCN) and Sirtuin 1 (SIRT1) plasma levels, a set of clinical parameters, MetS related-adiposity, atherogenicity and hematological indices between normoglycemic MetS and newly diagnosed drug-naive prediabetic MetS patients vs. lean, apparently healthy and normoglycemic controls.

Material and Methods

Study design

This cross-sectional study was conducted to examine the comparison and relation between plasma levels of OCN and SIRT1 in three groups of the Jordanian population:

1. Control group: 29 participants were apparently healthy and lean (BMI < 25 kg/m^2), and did not have hyperglycemia. A1C < 5.7%, and FPG < 100 mg/dL [1] were mainly considered for comparison purposes;
2. MetS-normoglycemic group: 29 participants; patients with central obesity plus ≥ 2 MetS components [1, 2] were either overweight (BMI > 25 kg/m^2) or obese (BMI > 30 kg/m^2). A1C < 5.7%, FPG < 100 mg/dL;
3. MetS-PreDM group: 30 participants; prediabetic patients were overweight or obese with central obesity plus ≥ 2 MetS components [2], but necessarily defined as drug-naive subjects (Figure 1).

Individuals with any of the following criteria were excluded from the study:

- Fasting for less than 12 hours.
- Females who are breastfeeding or pregnant.
- Any previous treatment with antidiabetic, antihyperlipidemic, or antihypertensive agents.
- Clinical evidence of autoimmune or life-threatening disease (drug abuse/alcohol/recently diagnosed with an untreated endocrine disorder).
- Patients with autoimmune or chronic inflammatory diseases.
- Obesity secondary to endocrine disorders, other than DM.

Study sample size

Sample size had been calculated by the following formula [8]:

$$N = \frac{2 \times SD^2 \times (z_\alpha + z_\beta)^2}{\Delta^2}$$

Where:

N: Sample size

Z_α: Type one error= 1.96 when α = 5%

Z_β: Type two error= 1.28 when β= 10%

SD = Standard deviation of OCN from Magalhães et al. [9a] study; equals 4.60 ng/mL

Δ = the difference between OCN levels in the MetS group vs. the control group in this observational study equals to 3.91 ng/mL. Thus, the minimum required number of participants per each group was 29 for OCN (Figure 1).

Clinical setting and metabolism-related indices

All ethical principles for medical research relating to human subjects were obligatory. The study was approved by the Scientific Research Committee of the School of Pharmacy and Deanship of Scientific Research at the University of Jordan approved the study. Further approval was obtained from the Jordan University Hospital Institutional Review Board (IRB) according to human and animal rights and Helsinki Declaration [9b]. Demographic data, as well as anthropometric measurements and lab tests, were obtained from each participant.

Consequently, adiposity, atherogenicity and blood indices were calculated as the following:

- Waist-to-hip ratio (WHR)=waist circumference (cm)÷ hip circumference (cm) [10];
- Waist-to-height ratio (WHtR)=waist circumference (cm)÷height (cm) [11];
- Conicity index (CI)=WC (cm)÷0.109*square root of (weight(kg)÷height(m)) [12];
- Body adiposity index (BAI)= (HC (cm) /(height (m)1.5))–18 [13];
- Lipid accumulation product (LAP) [14];
- Male LAP= (WC (cm)–65) × (TG (triglycerides) concentration (mM));
- Female LAP= (WC (cm) – 58) × (TG concentration (mM));
- Visceral adiposity index (VAI) [15];
- Male VAI=WC (cm)÷39.68+(1.88*BMI) *(TG concentration÷1.03)* (1.31÷HDL-C);
- Female VAI =WC (cm)÷36.58+(1.89*BMI) *(TG concentration÷0.81)* (1.52÷HDL-C);
- Atherogenic index of plasma (AIP)= Log10 (TG concentration/HDL-C) [16];
- Total cholesterol/HDL-C (TC/HDL-C) ratio = Total cholesterol ÷ HDL- C [17];
- LDL-C/HDL-C ratio =LDL-C ÷ HDL-C [18];
- Non-HDL-C=total cholesterol-HDL-C [18];
- Platelet-to lymphocyte ratio (PLR)= Platelets counts÷ Lymphocytes counts [19];
- Neutrophil-to-lymphocyte ratio (NLR)= Neutrophils counts ÷ Lymphocytes counts [19];
- Monocyte-to-lymphocyte ratio (MLR)= Monocytes counts ÷ Lymphocytes counts [20];

Statistical analysis

All study participants were organized accordingly to the study groups. Data were entered and tested through IBM SPSS©statistics 22 (SPSS, Inc., USA). Gender variation between the groups was analyzed utilizing the Chi-square test. Results were expressed as mean ±SD. The One-Way Analysis of Variance (ANOVA) test was used to contrast continuous dependent variables across the study groups. To assess the strength and direction of the association between continuous variables in MetS groups, which contain both normoglycemic and prediabetic MetS subjects, we used the Spearman's rank correlation coefficient.

Results

Demographic data

All study participants were Jordanians. Females were the majority of patients, representing 72.72% of all study population, and the gender was not distributed homogeneously between the three study groups but with no marked discrepancies between the 3 groups (Table 1). On the contrary, the age had vital variations between study groups (P< 0.001).

Clinical, adiposity, atherogenicity, and hematological indices

Both MetS groups (normoglycemic and preDM) had significantly higher values of DBP (P< 0.001), SBP (P< 0.001), TG (P< 0.001), and

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Table 1: Comparison of anthropometric and clinical parameters, adiposity, atherogenicity, and hematological indices as well as metabolic risk biomarkers in study participants.

Gender					
Gender	**Total Sample**	**Control Group**	**Normoglycemic-MetS Group**	**MetS-PreDM Group**	**#P-value**
Female, N (%)	64 (72.72%)	22 (75.86%)	23 (79.3%)	19 (63.3%)	0.334
Male, N (%)	24 (26.1%)	7 (24.13%)	6 (20.70%)	11 (36.6%)	
Total	88 (100%)	29 (100%)	29 (100%)	30 (100%)	
Age					
					***P-value**
Age (years, Mean ±SD)	49.72±1.17	44.39±2.05	49.07±2.00	55.68±1.51	**<0.001**
Clinical characteristics					
	Control, group N=29 Mean±SD#	**MetS group, N=29 Mean±SD#**	**MetS-PreDM, group. N=30 Mean±SD#**	**P[1]-value**	**P[2]-value**	**P[3]-value**
SBP (mmHg)	117.1±2.23	138.17±1.64	137.42±3.06	**<0.001**	**<0.001**	1
DBP (mmHg)	73.03±1.86	86.47±1.56	85.42±2.26	**<0.001**	**<0.001**	1
FBG (mg/dL)	85.31±1.40	88.53±1.72	112.57±3.45	1	**<0.001**	**<0.001**
A1C (%)	5.08±0.07	5.28±0.06	6.22±0.13	0.408	**<0.001**	**<0.001**
TG (mg/dL)	92.82±5.49	201.68±16.89	210.93±25.64	**<0.001**	**<0.001**	1
LDL-C (mg/dL)	129.65±6.07	143.87±6.12	142.21±7.23	0.380	0.519	1
HDL-C (mg/dL)	59.33±2.26	44.00±2.05	47.19±3.07	**<0.001**	**0.003**	1
TC (mg/dL)	195.80±6.26	208.60±7.32	218.03±8.40	0.673	0.105	1
Non-HDL-C (mg/dL)	136.46±6.96	164.59±6.35	170.84±7.86	**0.019**	**0.003**	1
Adiposity indices						
WC (cm)	87.23±1.81	107.1±1.96	107.66±2.30	**<0.001**	**<0.001**	1
HC (cm)	99.13±1.53	116.73±2.00	115.19±2.29	**<0.001**	**<0.001**	1
BMI (Kg/m^2)	23.20±0.34	33.85±1.04	33.10±1.23	**<0.001**	**<0.001**	1
WHR	0.88±0.01	0.92±0.01	0.94±0.01	0.083	**0.004**	0.847
WHtR	0.54±0.01	0.67±0.01	0.67±0.02	**<0.001**	**<0.001**	1
CI	1.30±0.02	1.34±0.01	1.36±0.02	0.424	0.057	1
BAI	29.92±0.78	39.66±1.24	38.77±1.71	**<0.001**	**<0.001**	1
LAP	29.09±3.09	108.99±10.79	102.91±11.90	**<0.001**	**<0.001**	1
VAI	1.33±0.12	3.95±0.45	5.38±1.76	0.252	**0.024**	1
Atherogenicity indices						
AIP	0.19±0.04	0.63±0.05	0.62±0.07	**<0.001**	**<0.001**	1
TC/HDL-C	3.47±0.20	4.90±0.20	6.12±1.32	0.617	0.058	0.835
LDL-C/HDL-C	2.40±0.17	3.37±0.15	3.59±0.43	0.053	**0.01**	1
Non-HDL-C/ HDL-C	2.48±0.20	3.90±0.20	5.16±1.32	0.621	0.051	0.773

Table 1: *Continued*

Clinical characteristics						
	Control, group N=29 Mean±SD#	**MetS group, N=29 Mean±SD#**	**MetS-PreDM, group. N=30 Mean±SD#**	**P[1]-value**	**P[2]-value**	**P[3]-value**
Hematological indices						
RDW-CV (%)	14.4±0.23	14.45±0.18	14.62±0.25	1	1	1
PLT count (× 10^9/L)	273.03±12.36	274.50±11.42	271.23±8.92	1	1	1
Monocytes%	5.63±0.28	5.31±0.24	5.40±0.24	1	1	1
Neutrophils%	57.39±1.12	57.39±1.59	59.82±1.72	1	0.755	0.769
Lymphocytes%	33.49±1.17	33.14±1.27	30.20±1.46	1	0.23	0.348
MLR	0.17±0.01	0.17±0.01	0.21±0.03	1	0.432	0.288
NLR	1.81±0.10	1.87±0.13	2.53±0.43	1	0.174	0.253
PLR	8.46±0.49	8.79±0.57	10.33±1.08	1	0.257	0.479
Metabolic risk biomarkers						
OCN (ng/mL)	23.3±3.19	28.13±1.22	26.02±3.2	**<0.001**	**0.01**	0.38
SIRT1 (ng/mL)	3.88±0.95	1.42±0.47	1.64±0.58	**<0.001**	**<0.001**	0.786

Note: P-value was obtained by ANOVA test. For gender we obtained the P-value using the Chi-Square test. Pairwise comparisons were done through Bonferroni adjustment.
P-value <0.05 are **bold**. P[1:] normoglycemic MetS group versus control, P[2:] MetS-PreDM versus control, P[3:] MetS-PreDM versus MetS normoglycemic. AIP: atherogenicity index of plasma, BAI: body adiposity index, CI: conicity index, DBP: diastolic blood pressure, FPG: fasting plasma glucose, A1C: glycosylated hemoglobin A1C, HC: hip circumference, HDL-C: high density lipoprotein-cholesterol, LAP: lipid accumulation product, LDL-C/HDL-C: low density lipoprotein cholesterol–to-high density lipoprotein cholesterol ratio, LDL-C: low density lipoprotein-cholesterol, MLR: monocyte-to-lymphocyte ratio, NLR: neutrophil-to-lymphocyte ratio, non-HDL-C/HDL: non high density lipoprotein–to-high density lipoprotein ratio, non-HDL-C: non-high density lipoprotein cholesterol, OCN: Osteocalcin, PLR: platelet-to-lymphocyte ratio. PLT: platelets, RDW: red cell width, SBP: systolic blood pressure, SIRT1: Sirtuin 1, TC/HDL-C: total cholesterol–to-high density lipoprotein cholesterol ratio, TC: total cholesterol, TG: triglycerides, WC: waist circumference, WHR: waist–to-hip ratio, WHtR: waist–to-height ratio.

non-HDL-C (P1= 0.019, P2= 0.003) than the control group and significantly lower values of HDL-C (p1< 0.001, p2= 0.003) in contrast to control group. However, in contrast to other clinical characteristics, the MetS-PreDM group presented significantly higher values of FPG and HbA1C than both normoglycemic MetS group and control group (P< 0.001) (Table 1). Also, both MetS groups (normoglycemic and PreDM) had a significantly higher value of adiposity indices, namely BMI, WC, HC, WHtR, BAI, and LAP than the control group (P< 0.001). Outstandingly, WHR and VAI had a significantly higher value in the MetS prediabetic group compared to controls (P<0.05). As for hematologic parameters, all the parameters failed to report any significant variability evidence in all the study groups (P>0.05). Interestingly, in our atherogenicity indices, as shown in Table 1, both normoglycemic MetS and MetS-PreDM groups had significantly higher AIP in comparison to the control group (P< 0.001), meanwhile the LDL-C/HDL-C ratio was significantly higher in MetS-PreDM compared to the control group (P<0.05).

SIRT1 and OCN plasma levels

OCN level (OCN; ng/mL) was significantly higher in normoglycemic MetS vs. both MetS-PreDM and controls (28.13±1.22 and 26.02±3.2 vs.

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23.3±3.19, P<0.001 respectively). In contrast, the circulating level of SIRT1 (ng/mL) was lower in both normoglycemic and preDM MetS vs. healthy controls (1.42±0.47 and 1.64±0.58 vs. 3.88±0.95; P<0.001, respectively) (Table 1).

SIRT1 and OCN Correlations

As shown in Table 2, in the MetS pool of participants (N=59), no OCN-SIRT1 relation could be disclosed. No molecular metabolic risk biomarker was related to the subclinical inflammation indicator RDW-CV. With the exception of HC, OCN notably lacked positive interdependence with any of the adiposity indices. SIRT1 was associated with the LAP and VAI adiposity indices directly, but inversely with PLT in the same pool of MetS participants (rs=0.303, rs=0.323, rs=0.286, rs=0.275, rs=0.275, rs=–0.314, respectively, P<0.05). Substantially, SIRT1 was proportionally associated with the triad of TG, TG/HDL-C and AIP. Nevertheless, OCN did not relate to any of the lipid profile parameters (non-HDL-C inclusive) or any of their atherogenicity indices. OCN related reciprocally with FPG, A1C, monocytes, and its MLR (rs=0.266, rs= –0.376, rs=–0.317, rs=–0.359, rs=–0.309, respectively, P<0.05). SIRT1 lacked marked relatedness with the glycemic control or any of blood indices;

The supplementary describes the relationships between clinical, adiposity, atherogenicity, and hematological parameters in the 59 MetS (Pre-DM and normoglycemic) recruits (Supplementary).

Discussion

In our heterogeneous pool of nondiabetic and prediabetic MetS recruits (n=59), metabolism-related adiposity, atherogenicity and blood indices, and molecular metabolic risk biomarkers SIRT1 and OCN were compared vs. the respective parameters in normoglycemic and lean controls. Further testing of putative relationships between indices and markers was also conducted in 59 participants from the MetS group. In a study by Calabrese et al. [21], the analysis of lymphocytes revealed a significant reduction of the SIRT1 expression in T2DM patients in a striking dissimilarity to our study. Effectively western blot analysis of peripheral blood mononuclear cell's SIRT1 in MetS patients with the ATP III criteria by De Kreutzenberg et al. [22] revealed significantly lower levels of SIRT1 expression in MetS vs. non–MetS subjects. Our study also showed a novel finding that SIRT1 is associated with TG, LAP, VAI, TG/HDL-C ratio, AIP, and PLT in the pool of MetS participants.

Former studies illustrated that plasma OCN concentrations were reduced in diabetic patients, so evidently, OCN might be a hopeful predictive marker to estimate the T2DM risk. In a cross-sectional study by Bador et al. [23], the plasma concentration of OCN was compared between IDF defined-MetS participants that were segregated into diabetic and nondiabetic. Their study found a significant relationship between lower OCN plasma levels, and higher FPG and homeostasis model assessment of insulin resistance (HOMA-IR) in MetS patients with DM vs. those without DM. Compared to ours, these results showed that MetS-Pre-DM (unlike normoglycemic-MetS) subjects had substantially higher HbA1C and FPG values with lower OCN plasma levels. Also, the results of Bao et al. [24] were effectively comparable with our findings [24]. Study subjects were divided into four groups according to quartiles of serum osteocalcin levels: 25th percentile (less than 13.11 ng/mL), 25–50th percentile (13.12 - 16.17 ng/mL), 50 –75th percentile (16.18 - 19.88 ng/mL) and 75th percentile (more than 19.89 ng/mL). Bao et al. revealed a decreasing trend in serum osteocalcin levels that accompanied increases in FPG, 2hPG, A1C, and HOMA-IR levels [24].

Conflicting results in the association of OCN with adiposity, hypertension, and dyslipidemia were delineated. Xu et al. [25] investigated the relationship between serum OCN levels and blood pressure in non-hypertensive and hypertensive groups from a Chinese population. The serum OCN level in their study was not associated with blood pressure in women nor with DBP in men, but it was associated significantly with SBP in men [25]. However, this association disappeared after adjustment for BMI, WC, blood

Table 2: Osteocalcin and Sirtuin 1 correlations in MetS (both normoglycemic and PreDM) participants (N=59).

Clinical parameters											
			SBP (mm Hg)	**DBP (mm Hg)**	**FBG (mg/dL)**	**A1C (%)**	**TG (mg/dL)**	**LDL-C (mg/dL)**	**HDL-C (mg/dL)**	**TC (mg/dL)**	**Non-HDL-C (mg/dL)**
Normoglycemic and PreDM MetS	**OCN (ng/mL)**	R	0.227	0.148	**-0.376**	**-0.317**	0.118	0.078	0.138	0.128	0.113
		P-value	0.084	0.263	**0.003**	**0.014**	0.372	0.558	0.298	0.336	0.395
	SIRT1 (ng/mL)	R	0.138	0.173	0.062	0.136	**0.303**	-0.083	-0.087	-0.011	0.052
		P-value	0.297	0.191	0.639	0.303	**0.020**	0.531	0.510	0.933	0.696
Adiposity indices											
			WC (cm)	**HC (cm)**	**CI**	**BMI (Kg/m²)**	**BAI**	**WHR**	**WHtR**	**LAP**	**VAI**
Normoglycemic and PreDM MetS	**OCN (ng/mL)**	R	0.166	**0.266**	0.147	0.211	0.228	-0.010	0.202	0.250	0.068
		P-value	0.208	**0.042**	0.267	0.108	0.082	0.937	0.125	0.057	0.608
	SIRT1 (ng/mL)	R	0.119	0.123	0.160	0.051	0.085	0.017	0.109	**0.323**	**0.286**
		P-value	0.369	0.354	0.226	0.704	0.522	0.896	0.413	**0.013**	**0.028**
Atherogenicity indices											
			OCN (ng/mL)	**SIRT1 (ng/mL)**	**Non-HDL-C/HDL-C ratio**	**TG/HDL-C ratio**	**TC/HDL-C ratio**		**LDL-C/HDL-C ratio**		**AIP**
Normoglycemic and PreDM MetS	**OCN (ng/mL)**	R	1.000	0.105	0.002	0.056	0.003		-0.060		0.056
		P-value		0.429	0.985	0.674	0.981		0.649		0.674
	SIRT1 (ng/mL)	R	0.105	1.000	0.076	**0.275**	0.075		-0.008		**0.275**
		P-value	0.429		0.566	**0.035**	0.572		0.952		**0.035**
Hematological indices											
			RDW-CV %	**PLT count**	**Monocytes %**	**Neutrophils %**	**Lymphocytes %**		**MLR**	**NLR**	**PLR**
Normoglycemic and PreDM MetS	**OCN (ng/mL)**	R	0.160	0.048	**-0.359**	0.077	0.012		**-0.309**	0.039	-0.063
		P-value	0.227	0.721	**0.005**	0.562	0.930		**0.017**	0.772	0.635
	SIRT1 (ng/mL)	R	-0.034	**-0.314**	-0.204	0.080	-0.036		-0.131	0.068	-0.095
		P-value	0.801	**0.015**	0.120	0.544	0.787		0.323	0.608	0.473

Spearman's correlation coefficient [®] was used, R=0.1-.0.29 small relationship, R=0.3-0.49 moderate relationship, R>0.5 high relationship. AIP: atherogenicity index of plasma, BAI: body adiposity index, CI: conicity index, DBP: diastolic blood pressure, FPG: fasting plasma glucose, A1C: glycosylated hemoglobin A1C, HC: hip circumference, HDL-C: high density lipoprotein-cholesterol, LAP: lipid accumulation product, LDL-C/HDL-C: low density lipoprotein cholesterol–to-high density lipoprotein cholesterol ratio, LDL-C: low density lipoprotein-cholesterol, MLR: monocyte-to-lymphocyte ratio, NLR: neutrophil-to-lymphocyte ratio, non-HDL-C/HDL: non high density lipoprotein–to-high density lipoprotein ratio, non-HDL-C: non-high density lipoprotein cholesterol, OCN: Osteocalcin, PLR: platelet-to-lymphocyte ratio. PLT: platelets, RDW: red cell width, SBP: systolic blood pressure, SIRT1: Sirtuin 1, TC/HDL-C: total cholesterol–to-high density lipoprotein cholesterol ratio, TC: total cholesterol, TG: triglycerides, WC: waist circumference, WHR: waist–to-hip ratio, WHtR: waist–to-height ratio.

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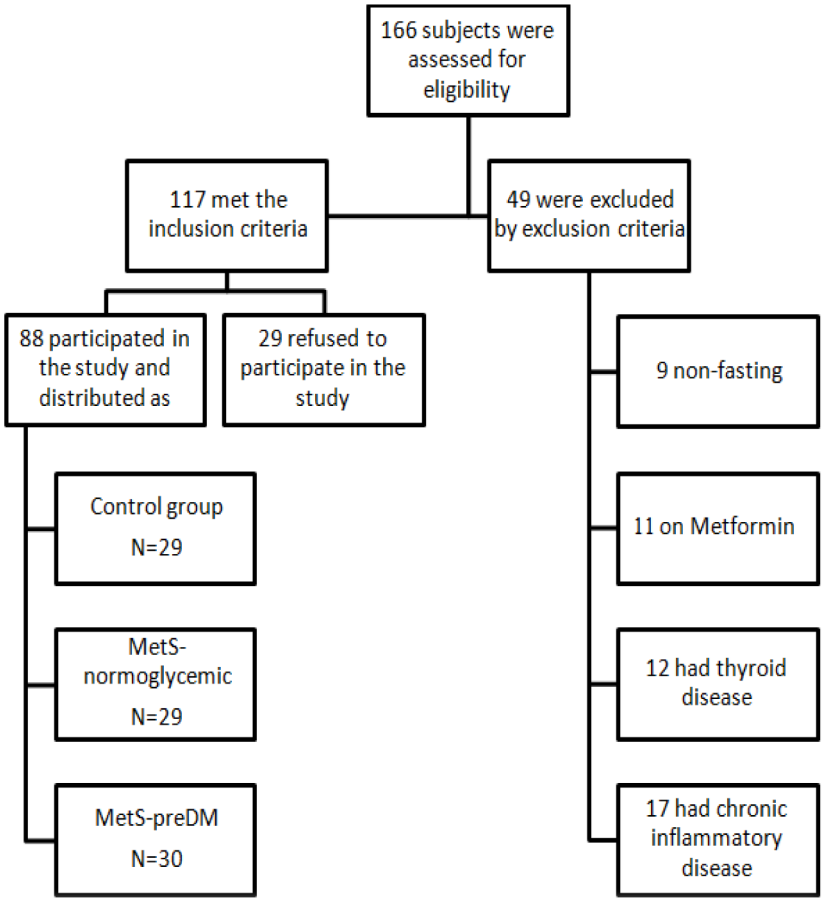

Figure 1: Recruitment process flow chart.

glucose, and HOMA-IR. The opposite finding was observed in the study of Magalhães et al. [9]. There was a significant association between serum OCN levels and SBP, BMI, WC, and FBG in a Brazilian population with and without MetS.

Similarly, the study results of Bao et al. indicated that serum OCN levels correlated with all the anthropometric indices of obesity: SBP, FPG, 2-h plasma glucose (2hPG), HbA1C, HOMA-IR, TC, TG, and free fatty acids [24]. In accordance with our study, the serum OCN concentrations were not associated with SBP, DBP, TG, LDL-C, HDL-C, TC, WC, or BMI in MetS patients. However, they were correlated with FBG, consistent with the results of Bador et al. [23]. Moreover, none of the above studies examined the correlation of serum OCN levels with atherogenicity and hematological indices. Nevertheless, our results revealed that plasma OCN concentrations correlated with MLR and monocytes. Regarding the limitations of our study, it must be noted that no causality relationship may be concluded with the cross-sectional study design, which includes a single time point for sampling biomarkers and subsequent determination and that recruiting a larger sample size was hindered owing to financial restrictions.

Conclusions

We found that OCN levels were significantly higher in MetS vs. healthy non-MetS controls; the circulating level of SIRT1 was lower in both groups: normoglycemic and PreDM-MetS vs. healthy controls. Also,

WC, HC, BMI, WHtR, BAI, LAP, and AIP were significantly higher in both MetS (non- and PreDM) groups vs. controls. The LDL-C/HDL-C ratio, VAI, and WHR were greater in MetS-PreDM (but not normoglycemic MetS) vs. lean recruits. OCN correlated positively with HC, but reciprocally with FPG, A1C, monocytes, and MLR. SIRT1 associated proportionally with TG, TG/HDL-C ratio, and AIP, LAP, and VAI, but inversely with PLT in the same pool of MetS participants.

However, except for FPG and HbA1C, no further intergroup variation could be identified between the MetS groups. Also, no OCN-SIRT1 relation could be detected in the 59 MetS participants (normoglycemic and PreDM).

No biomarker (OCN/SIRT1) correlated with SBP, DBP, LDL-C, HDL-C, TC, non-HDL-C, WC, CI, BMI, BAI, WHR, WHtR, non-HDL-C/HDL-C ratio, TC/HDL-C ratio, LDL-C/HDL-C ratio, RDW-CV%, neutrophils, lymphocytes, NLR, and PLR.

Conflict of Interest

The authors declare no conflict of interest.

References

1. (a)American Diabetes Association (ADA). Standards of medical care in Diabetes–2019. *Diabetes Care*. 42 (Supplement 1): S13–S28, 2019; (b) Tabák AG, Herder C, Rathmann W, Brunner EJ, Kivimäki M. Prediabetes: A high-risk state for developing diabetes. *Lancet*. 379(9833): 2279–2290, 2012.
2. International Diabetes Foundation (IDF). Worldwide definition of the metabolic syndrome. *The IDF consensus worldwide definition of the Metabolic Syndrome*, 1–19, 2006.
3. Stern M P, Williams K, Gonzalez-Villalpando C, Hunt KJ, Haffner S.M. Does the metabolic syndrome improve identification of individuals at risk of type 2 diabetes and/or cardiovascular disease? *Diabetes Care*. 27: 2676–2681, 2004.
4. (a)Zupkovitz G, Tischler J, Posch M, Sadzak I, Ramsauer K, Egger G, Grausenburger R, Schweifer N, Chiocca S, Decker T, Seiser C. Negative and positive regulation of gene expression by mouse histone deacetylase 1. *Mol Cell Biol*. 26(21): 7913–7928, 2006; (b) Choudhary C, Kumar, C., Gnad, F., Nielsen, M.L., Rehman, M., Walther, T.C., Olsen, J.V., and Mann, M. Lysine acetylation targets protein complexes and co-regulates major cellular functions. *Science*, 325 (5942): 834–840, 2009. (c) Seto, E., and Yoshida, M. Erasers of histone acetylation: the histone deacetylase enzymes. *Cold Spring Harbor Persp Biol*. 6(4): a018713, 2014; d) Sardu C, Pieretti G, D'Onofrio N, Ciccarelli F, Paolisso P, Passavanti MB, Marfella R, Cioffi M, Mone P, Dalise AM, Ferraraccio F, Panarese I, Gambardella A, Passariello N, Rizzo MR, Balestrieri ML, Nicoletti G, Barbieri M. Inflammatory cytokines and SIRT1 levels in subcutaneous abdominal fat: relationship with cardiac performance in overweight pre-diabetics patients. *Front Physiol*. 9:1030, 2018; (e) Kitada M, Ogura Y, Monno I, Koya D. Sirtuins and type 2 diabetes: role in inflammation, oxidative stress, and mitochondrial function. *Front Endocrinol* (Lausanne). 10:187, 2019.
5. (a)Kumar A, Chauhan S. How much successful are the medicinal chemists in modulation of SIRT1: A critical review. *Eur J Med Chem*., 119: 45–69, 2016; (b) Kane AE, Sinclair DA. Sirtuins and NAD+ in the development and treatment of metabolic and cardiovascular diseases. *Circ Res*. 123(7), 868–885, 2018.
6. (a) Oosterwerff MM, van Schoor NM, Lips P, Eekhoff EM. Osteocalcin as a predictor of the metabolic syndrome in older persons: a population-based study. *Clin Endocrinol*. 78(2): 242–247, 2013; (b) García-Martín A, Cortés-Berdonces M, Luque-Fernández I, Rozas-Moreno P, Quesada-Charneco M, Muñoz-Torres M. Osteocalcin as a marker of metabolic risk in healthy postmenopausal women. *Menopause*. 18(5), 537–541, 2011; (c) Bador KM, Wee LD, Halim SA, Fadi MF, Santhiran P, Rosli NF, Mustafa N. Serum osteocalcin in subjects with metabolic syndrome and central obesity. *Diabetes Metab Syndr*. 10(1 Suppl 1):S42-S45, 2016; (d) De Pergola G, Triggiani V, Bartolomeo N, Nardecchia A, Giagulli VA, Bruno I, Caccav, D, Silvestris F. Independent relationship of osteocalcin circulating levels with obesity, type 2 diabetes, hypertension, and HDL-cholesterol. *Endocr Metab Imm Dis - Drug Targets*. 16(4), 270–275, 2016; (e) Xu Y, Ma X, Xion, Q, Hu X, Zhang X, Yuan Y, Bao Y. Association between serum osteocalcin level and blood pressure in a Chinese population. *Blood Press*. J. 27(2), 106–111, 2016.
7. (a)*Raška I Jr, Rašková M, Zikán V, Škrha J.* Prevalence and Risk Factors of Osteoporosis in Postmenopausal Women with Type 2 Diabetes Mellitus. *Cent Eur J Public Health*. 25(1):3–10, 2017; (b) Urano T, Shiraki M, Kuroda T, Tanaka S, Urano F, Uenishi K, Inoue S. Low serum osteocalcin concentration is associated with incident type 2 diabetes mellitus in Japanese women. J Bone Miner Metab. 36(4):470–477, 2018;(c) Daniele G, Winnier D, Mari A, Bruder J, Fourcaudot M, Pengou Z, Hansis-Diarte A, Jenkinson C, Tripathy D, Folli F. The potential role of the osteopontin-osteocalcin-osteoprotegerin triad in the pathogenesis of prediabetes in humans. *Acta Diabetol*. 55(2):139–148, 2018; (d) Xu Y, Ma X, Pan X, He X, Xiao Y, Bao Y. Correlations between serum concentration of three bone-derived factors and obesity and visceral fat accumulation in a cohort of middle aged men and women. *Cardiovasc Diabetol*. 2018; 17(1):143.
8. Chow S-C, Shao J, Wang H. Sample Size Calculations in Clinical Research 2nd edition. *Biometrics*. 64(4):1307–1308, 2009
9. (a)Magalhães KB, Magalhães MM, Diniz ET, Lucena CS, Griz L, Bandeira F. Metabolic syndrome and central fat distribution are related to lower serum osteocalcin concentrations. *Ann Nutr Metab*. 62(3): 183–188, 2013; (b) Shakibapour N, Dehghani Sani, F, Beigoli S, Sadeghian H, Chamani J. Multi-spectroscopic and molecular modeling studies to reveal the interaction between propyl acridone and calf thymus DNA in the presence of histone H1: binary and ternary approaches. *J Biomol Struct Dyn*. 37(2): 359–371, 2019.
10. World Health Organization (WHO), Waist Circumference and Waist–Hip Ratio: Report of a WHO Expert Consultation. Geneva, 1–31. Available at http://apps.who.int/iris/bitstream/handle/10665/44583/9789241501491_eng.pdf;jsessionid=74FEA674E1A79EB9FF1DDEE0BDB39B09?sequence=1 (2008). Last accessed April 17th, 2018.
11. Hsieh SD, Yoshinaga H. Waist/height ratio as a simple and useful predictor of coronary heart disease risk factors in women. *Intern. Med*. 34(12):1147–1152, 1995
12. Valdez R. A simple model-based index of abdominal adiposity. J. *Clin. Epidemiol*. 44(9):955–956, 1991
13. Bergman RN, Stefanovski D, Buchanan TA, et al. A Better Index of Body Adiposity. *Obesity*. 19(5):1083–1089, 2011.

 https://doi.org/10.46389/rjd-2020-1034

14. Kahn HS, Valdez R. Metabolic risks identified by the combination of enlarged waist and elevated triacylglycerol concentration. *Am. J. Clin. Nutr*. 78:928–934, 2003
15. DeNino WF, Tchernof A, Dionne IJ, et al. Contribution of abdominal adiposity to age-related differences in insulin sensitivity and plasma lipids in healthy non-obese women. *Diabetes Care*. 24(5): 925–932, 2001
16. Dobiasova M. AIP—atherogenic index of plasma as a significant predictor of cardiovascular risk: from research to practice. *Vnitrn Lek*. 52(1): 64–71, 2006
17. Ascaso J, González Santos P, Hernández Mijares A, et al., Management of dyslipidemia in the metabolic syndrome. Recommendations of the Spanish HDL Forum. Am. J. *Cardiovasc. Drugs*. 7(1): 39–58, 2007
18. Virani, S.S. Non-HDL cholesterol as a metric of good quality of care: opportunities and challenges. *Texas Heart Inst*. J. 38(2): 160–162, 2011.
19. Ural, MU., Sehitoglu, I., BayogluTekin, Y., KirSahin, F., Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios in patients with endometrial hyperplasia and endometrial cancer. *J. Obstetr. Gyn. Res*. 41(3): 445–448, 2015
20. Ji, H., Li, Y., Fan, Z., et al., Monocyte/lymphocyte ratio predicts the severity of coronary artery disease: a syntax score assessment. *BMC Cardiovasc. Dis*. 17(1):1–8, 2017
21. Calabrese V, Cornelius C, Leso V, Torvato-Salinaro A, Ventimiglia B, Cavallaro M, Scuto M, Rizza, S, Zanoli L, Ner, S, Casellino P. Oxidative stress, glutathione status, sirtuin and cellular stress response in type 2 diabetes. *Biochim ET Biophys Acta*. 1822: 729–736, 2012
22. De Kreutzenberg SV, Ceolotto G, Papparella I, Bortoluzzi A, Semplicini A, Dalla Man C, Cobelli C, Fadini GP, Avogaro A. Downregulation of the longevity-associated protein sirtuin 1 in insulin resistance and metabolic syndrome: potential biochemical mechanisms. *Diabetes*. 59(4):1006–1015, 2010
23. Bador KM, Wee LD, Halim SA, Fadi MF, Santhiran P, Rosli NF, Mustafa N. Serum osteocalcin in subjects with metabolic syndrome and central obesity. *Diabetes & Met Syndr*. 10(1 Suppl 1): S42–45, 2016.
24. Bao Y, Ma X, Yang R, Wang F, Hao Y, Dou J, Jia W. Inverse relationship between serum osteocalcin levels and visceral fat area in chinese men. *J Clin Endocrinol Metab*. 98(1): 345–351, 2013.
25. Xu Y, Ma X, Xiong Q, Hu X, Zhang X, Yuan Y, and Bao Y. Association between serum osteocalcin level and blood pressure in a Chinese population. *Blood Press J*. 27(2): 106–111, 2016.

Supplementary

It demonstrates correlations between clinical, adiposity, atherogenicity, and hematological parameters in MetS group as the following:

Age: Age correlated positively with WC, CI, WHtR, FBG, and A1C, but negatively with DBP.
Both A1C and FBG correlated positively with each other.

Adiposity indices

Weight: Weight associated positively with WC, HC, BMI, WHtR, LAP, and RDW-CV%.
Height: Height correlated inversely with BMI, BAI, and WHtR.
WC: WC associated positively with weight, HC, CI, BMI, BAI, WHR, WHtR, and LAP.
HC: HC correlated disproportionally with WHR, but positively with weight, WC, BMI, BAI, WHtR, LAP, and RDW-CV%.
CI: CI associated positively with WC, WHR, and WHtR.
BAI: BAI associated positively with HDL-C, WHtR and RDW-CV%.
WHtR: WHtR correlated negatively with height but positively with LAP, BMI and HDL-C.

Atherogenicity indices

TG: TG associated positively with LAP, TC, Non-HDL-C, Non-HDL-C/HDL-C ratio, VAI, TC/HDL-C ratio, LDL-C/HDL-C ratio, TG/HDL-C ratio, and AIP.
LAP: LAP associated positively with TC, Non-HDL-C, Non-HDL-C/HDL-C ratio, VAI, TC/HDL-C ratio, LDL-C/HDL-C ratio, TG/HDL-C ratio, and AIP.
LDL-C: LDL-C correlated positively with Non-HDL-C/HDL-C ratio, TC/HDL-C ratio, LDL-C/HDL-C ratio, and PLT.
HDL-C: HDL-C correlated inversely with Non-HDL-C/HDL-C ratio, VAI, TC/HDL-C ratio, LDL-C/HDL-C ratio, TG/HDL-C ratio, and AIP, but positively with PLT.
TC: TC correlated positively with LDL-C, HDL-C, Non-HDL-C, Non-HDL-C/HDL-C ratio, TC/HDL-C ratio, LDL-C/HDL-C ratio, and PLT.
Non-HDL-C and Non-HDL-C/HDL-C ratio: they associated positively with each other and with LDL-C, VAI, TC/HDL-C ratio, LDL-C/HDL-C ratio, TG/HDL-C ratio, and AIP.
VAI: VAI correlated positively with TC/HDL-C ratio, LDL-C/HDL-C ratio, TG/HDL-C ratio, and AIP.
TC/HDL-C ratio and LDL-C/HDL-C ratio: both they positively correlated with each other.

Blood indices

MLR, NLR, and PLR: They correlated negatively with lymphocytes and positively with each other and with neutrophils.

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Supplementary correlations of adiposity, clinical, atherogenicity, and hematological parameters in the MetS groups (Both normoglycemic and pre-diabetic) participants (N=59).

		Age (years)	Weight (kg)	Height (cm)	WC (cm)	HC (cm)	CI	BMI (kg/m^2)	BAI	WHR
Age (years)	R	1.000	–0.067	–0.332	0.281	0.059	0.438	0.010	0.232	0.197
	P-value		0.612	**0.010**	**0.031**	0.658	**0.001**	0.938	0.077	0.134
Weight (kg)	R	–0.067	1.000	0.398	0.720	0.647	–0.164	0.701	0.223	–0.015
	P-value	0.612		**0.002**	**0.000**	**0.000**	0.213	**0.000**	0.089	0.909
Height (cm)	R	–0.332	0.398	1.000	–0.071	–0.147	–0.226	–0.269	–0.714	0.105
	P-value	**0.010**	**0.002**		0.591	0.267	0.085	**0.040**	**0.000**	0.430
WC (cm)	R	0.281	0.720	–0.071	1.000	0.771	0.416	0.779	0.570	0.269
	P-value	**0.031**	**0.000**	0.591		**0.000**	**0.001**	**0.000**	**0.000**	**0.039**
HC (cm)	R	0.059	0.647	–0.147	0.771	1.000	0.113	0.805	0.750	–0.313
	P-value	0.658	**0.000**	0.267	**0.000**		0.393	**0.000**	**0.000**	**0.016**
CI	R	0.438	–0.164	–0.226	0.416	0.113	1.000	–0.056	0.174	0.590
	P-value	**0.001**	0.213	0.085	**0.001**	0.393		0.676	0.187	**0.000**
BMI (kg/m^2)	R	0.010	0.701	–0.269	0.779	0.805	–0.056	1.000	0.765	–0.106
	P-value	0.938	**0.000**	**0.040**	**0.000**	**0.000**	0.676		**0.000**	0.423
BAI	R	0.232	0.223	–0.714	0.570	0.750	0.174	0.765	1.000	–0.298
	P-value	0.077	0.089	**0.000**	**0.000**	**0.000**	0.187	**0.000**		**0.022**
WHR	R	0.197	–0.015	0.105	0.269	–0.313	0.590	–0.106	–0.298	1.000
	P-value	0.134	0.909	0.430	**0.039**	**0.016**	**0.000**	0.423	**0.022**	
WHtR	R	0.329	0.387	–0.563	0.832	0.710	0.421	0.816	0.868	0.127
	P-value	**0.011**	**0.002**	**0.000**	**0.000**	**0.000**	**0.001**	**0.000**	**0.000**	0.338
SBP (mmHg)	R	–0.136	0.082	–0.026	0.075	0.060	0.088	0.092	0.057	0.048
	P-value	0.304	0.539	0.844	0.572	0.650	0.509	0.489	0.671	0.716
DBP (mmHg)	R	–0.290	–0.031	0.165	–0.157	–0.100	–0.053	–0.149	–0.188	0.038
	P-value	**0.026**	0.815	0.211	0.236	0.452	0.692	0.259	0.153	0.775
FBG (mg/dL)	R	0.268	–0.155	0.064	–0.028	–0.085	0.183	–0.176	–0.064	–0.019
	P-value	**0.040**	0.240	0.633	0.836	0.522	0.166	0.182	0.630	0.889
A1C%	R	0.337	0.046	0.010	0.193	0.040	0.177	0.039	0.028	0.088
	P-value	**0.009**	0.727	0.942	0.144	0.765	0.180	0.767	0.836	0.510
TG (mg/dL)	R	–0.083	0.053	0.087	–0.054	–0.011	–0.118	–0.025	–0.039	–0.038
	P-value	0.530	0.691	0.513	0.684	0.933	0.375	0.850	0.767	0.775
LAP	R	0.007	0.303	–0.053	0.352	0.334	0.098	0.339	0.284	0.073
	P-value	0.959	**0.020**	0.692	**0.006**	**0.010**	0.458	**0.009**	**0.029**	0.584
LDL-C mg/dL	R	0.131	–0.161	–0.342	–0.012	0.006	0.029	0.051	0.243	–0.075
	P-value	0.321	0.224	**0.008**	0.931	0.967	0.829	0.699	0.064	0.573
HDL-C (mg/dL)	R	0.034	–0.141	–0.412	0.100	0.175	0.117	0.183	0.354	–0.080
	P-value	0.796	0.288	**0.001**	0.450	0.184	0.378	0.165	**0.006**	0.549
TC (mg/dL)	R	0.074	–0.201	–0.325	–0.099	–0.078	–0.013	–0.005	0.177	–0.053
	P-value	0.575	0.126	**0.012**	0.458	0.559	0.919	0.972	0.180	0.691

		Age (years)	Weight (kg)	Height (cm)	WC (cm)	HC (cm)	CI	BMI (kg/m²)	BAI	WHR
Non-HDL-C (mg/dL)	R	0.109	–0.195	–0.317	–0.133	–0.131	–0.069	–0.011	0.148	–0.037
	P-value	0.413	0.139	**0.014**	0.316	0.321	0.601	0.935	0.263	0.779
RDW-CV%	R	–0.031	0.276	–0.122	0.249	0.370	–0.139	0.424	0.319	–0.129
	P-value	0.817	**0.034**	0.355	0.058	**0.004**	0.293	**0.001**	**0.014**	0.332

		WHtR	SBP (mmHg)	DBP (mmHg)	FBG (mg/dL)	A1C %	TG (mg/dL)	LAP	LDL-C (mg/dL)	HDL (mg/dL)
Age (years)	R	0.329	–0.136	–0.290	0.268	0.337	–0.083	0.007	0.131	0.034
	P-value	**0.011**	0.304	**0.026**	**0.040**	**0.009**	0.530	0.959	0.321	0.796
Weight (kg)	R	0.387	0.082	–0.031	–0.155	0.046	0.053	0.303	–0.161	–0.141
	P-value	**0.002**	0.539	0.815	0.240	0.727	0.691	**0.020**	0.224	0.288
Height (cm)	R	–0.563	–0.026	0.165	0.064	0.010	0.087	–0.053	–0.342	–0.412
	P-value	**0.000**	0.844	0.211	0.633	0.942	0.513	0.692	**0.008**	**0.001**
WC (cm)	R	0.832	0.075	–0.157	–0.028	0.193	–0.054	0.352	–0.012	0.100
	P-value	**0.000**	0.572	0.236	0.836	0.144	0.684	**0.006**	0.931	0.450
HC (cm)	R	0.710	0.060	–0.100	–0.085	0.040	–0.011	0.334	0.006	0.175
	P-value	**0.000**	0.650	0.452	0.522	0.765	0.933	**0.010**	0.967	0.184
CI	R	0.421	0.088	–0.053	0.183	0.177	–0.118	0.098	0.029	0.117
	P-value	**0.001**	0.509	0.692	0.166	0.180	0.375	0.458	0.829	0.378
BMI (kg/m²)	R	0.816	0.092	–0.149	–0.176	0.039	–0.025	0.339	0.051	0.183
	P-value	**0.000**	0.489	0.259	0.182	0.767	0.850	**0.009**	0.699	0.165
BAI	R	0.868	0.057	–0.188	–0.064	0.028	–0.039	0.284	0.243	0.354
	P-value	**0.000**	0.671	0.153	0.630	0.836	0.767	**0.029**	0.064	**0.006**
WHR	R	0.127	0.048	0.038	–0.019	0.088	–0.038	0.073	–0.075	–0.080
	P-value	0.338	0.716	0.775	0.889	0.510	0.775	0.584	0.573	0.549
WHtR	R	1.000	0.109	–0.179	–0.060	0.148	–0.049	0.346	0.158	0.283
	P-value		0.413	0.175	0.653	0.264	0.713	**0.007**	0.231	**0.030**
SBP (mmHg)	R	0.109	1.000	0.692	–0.086	0.053	–0.049	–0.013	–0.015	0.180
	P-value	0.413		**0.000**	0.519	0.691	0.711	0.923	0.910	0.172
DBP (mmHg)	R	–0.179	0.692	1.000	–0.139	–0.007	0.115	0.032	–0.007	0.068
	P-value	0.175	**0.000**		0.294	0.960	0.385	0.808	0.959	0.607
FBG (mg/dL)	R	–0.060	–0.086	–0.139	1.000	0.736	–0.055	–0.145	–0.136	–0.046
	P-value	0.653	0.519	0.294		**0.000**	0.678	0.272	0.303	0.730
A1C %	R	0.148	0.053	–0.007	0.736	1.000	–0.062	–0.087	–0.023	0.064
	P-value	0.264	0.691	0.960	**0.000**		0.642	0.515	0.864	0.629
TG (mg/dL)	R	–0.049	–0.049	0.115	–0.055	–0.062	1.000	0.865	0.104	–0.335
	P-value	0.713	0.711	0.385	0.678	0.642		**0.000**	0.431	**0.009**
LAP	R	0.346	–0.013	0.032	–0.145	–0.087	0.865	1.000	0.134	–0.224
	P-value	**0.007**	0.923	0.808	0.272	0.515	**0.000**		0.311	0.088

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		WHtR	SBP (mmHg)	DBP (mmHg)	FBG (mg/dL)	A1C %	TG (mg/dL)	LAP	LDL-C (mg/dL)	HDL (mg/dL)
LDL-C mg/dL	R	0.158	–0.015	–0.007	–0.136	–0.023	0.104	0.134	1.000	0.424
	P-value	0.231	0.910	0.959	0.303	0.864	0.431	0.311		**0.001**
HDL-C (mg/dL)	R	0.283	0.180	0.068	–0.046	0.064	–0.335	–0.224	0.424	1.000
	P-value	**0.030**	0.172	0.607	0.730	0.629	**0.009**	0.088	**0.001**	
TC (mg/dL)	R	0.086	–0.036	–0.001	–0.044	–0.001	0.312	0.300	0.842	0.453
	P-value	0.518	0.785	0.991	0.740	0.991	**0.016**	**0.021**	**0.000**	**0.000**
Non-HDL-C (mg/dL)	R	0.057	–0.058	–0.012	–0.124	–0.099	0.426	0.401	0.846	0.197
	P-value	0.668	0.660	0.927	0.348	0.456	**0.001**	**0.002**	**0.000**	0.135
Non-HDL-C/ HDL-C ratio	R	–0.153	–0.191	–0.041	–0.040	–0.105	0.647	0.506	0.268	–0.657
	P-value	0.246	0.148	0.759	0.762	0.427	**0.000**	**0.000**	**0.040**	**0.000**
VAI	R	–0.041	–0.130	0.019	–0.093	–0.126	0.897	0.803	–0.007	–0.607
	P-value	0.760	0.326	0.885	0.482	0.340	**0.000**	**0.000**	0.960	**0.000**
TC/ HDL-C	R	–0.151	–0.190	–0.041	–0.039	–0.105	0.649	0.508	0.267	–0.658
	P-value	0.252	0.149	0.759	0.770	0.430	**0.000**	**0.000**	**0.041**	**0.000**
LDL-C/ HDL-C	R	–0.177	–0.189	–0.020	–0.020	–0.037	0.475	0.343	0.449	–0.548
	P-value	0.180	0.151	0.880	0.879	0.779	**0.000**	**0.008**	**0.000**	**0.000**
TG/ HDL-C ratio	R	–0.168	–0.111	0.063	–0.061	–0.107	0.886	0.723	–0.061	–0.686
	P-value	0.203	0.404	0.637	0.646	0.420	**0.000**	**0.000**	0.645	**0.000**
AIP	R	–0.168	–0.111	0.063	–0.061	–0.107	0.886	0.723	–0.061	–0.686
	P-value	0.203	0.404	0.637	0.646	0.420	**0.000**	**0.000**	0.645	**0.000**
RDW-CV%	R	0.248	–0.051	–0.173	–0.045	0.019	–0.041	0.107	–0.091	0.073
	P-value	0.058	0.700	0.189	0.734	0.886	0.756	0.418	0.492	0.584
PLT count ($\times 10^9$/L)	R	–0.092	0.116	0.025	–0.110	–0.164	–0.059	–0.089	0.276	0.321
	P-value	0.490	0.380	0.851	0.406	0.214	0.655	0.504	**0.035**	**0.013**
Monocytes %	R	–0.173	–0.277	–0.264	0.084	–0.042	–0.111	–0.195	–0.119	–0.201
	P-value	0.191	**0.034**	**0.043**	0.527	0.751	0.403	0.138	0.368	0.126

		TC (mg/dL)	Non-HDL (mg/dL)	Non-HDL-C/ HDL-C ratio	VAI	TC/ HDL-C ratio	LDL-C/ HDL-C ratio	TG/ HDL-C	AIP	RDW-CV%
Age (years)	R	0.074	0.109	0.062	0.008	0.065	0.122	–0.043	–0.043	–0.031
	P-value	0.575	0.413	0.639	0.952	0.627	0.359	0.746	0.746	0.817
Weight (kg)	R	–0.201	–0.195	–0.013	0.027	–0.016	–0.070	0.073	0.073	0.276
	P-value	0.126	0.139	0.925	0.840	0.905	0.597	0.581	0.581	**0.034**
Height (cm)	R	–0.325	–0.317	0.103	0.092	0.099	0.099	0.224	0.224	–0.122
	P-value	**0.012**	**0.014**	0.440	0.490	0.454	0.457	0.089	0.089	0.355
WC (cm)	R	–0.099	–0.133	–0.153	–0.032	–0.153	–0.171	–0.103	–0.103	0.249
	P-value	0.458	0.316	0.246	0.811	0.246	0.195	0.439	0.439	0.058
HC (cm)	R	–0.078	–0.131	–0.208	–0.022	–0.208	–0.223	–0.102	–0.102	0.370
	P-value	0.559	0.321	0.114	0.868	0.114	0.089	0.441	0.441	**0.004**
CI	R	–0.013	–0.069	–0.161	0.000	–0.159	–0.109	–0.123	–0.123	–0.139
	P-value	0.919	0.601	0.223	0.998	0.229	0.410	0.354	0.354	0.293
BMI (kg/m^2)	R	–0.005	–0.011	–0.131	–0.071	–0.132	–0.189	–0.123	–0.123	0.424
	P-value	0.972	0.935	0.323	0.591	0.320	0.151	0.352	0.352	**0.001**
BAI	R	0.177	0.148	–0.147	–0.058	–0.145	–0.160	–0.186	–0.186	0.319
	P-value	0.180	0.263	0.265	0.660	0.272	0.226	0.159	0.159	**0.014**
TG (mg/dL)	R	0.312	0.426	0.647	0.897	0.649	0.475	0.886	0.886	–0.041
	P-value	**0.016**	**0.001**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	0.756
LAP	R	0.300	0.401	0.506	0.803	0.508	0.343	0.723	0.723	0.107
	P-value	**0.021**	**0.002**	**0.000**	**0.000**	**0.000**	**0.008**	**0.000**	**0.000**	0.418
LDL-C mg/dL	R	0.842	0.846	0.268	–0.007	0.267	0.449	–0.061	–0.061	–0.091
	P-value	**0.000**	**0.000**	**0.040**	0.960	**0.041**	**0.000**	0.645	0.645	0.492
HDL-C (mg/dL)	R	0.453	0.197	–0.657	–0.607	–0.658	–0.548	–0.686	–0.686	0.073
	P-value	**0.000**	0.135	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	0.584
TC (mg/dL)	R	1.000	0.930	0.259	0.084	0.258	0.289	0.039	0.039	–0.058
	P-value		**0.000**	**0.048**	0.526	**0.049**	**0.027**	0.772	0.772	0.665
Non-HDL-C (mg/dL)	R	0.930	1.000	0.524	0.296	0.523	0.540	0.259	0.259	–0.063
	P-value	**0.000**		**0.000**	**0.023**	**0.000**	**0.000**	**0.047**	**0.047**	0.638
Non HDL-C/ HDL-C ratio	R	0.259	0.524	1.000	0.779	1.000	0.929	0.823	0.823	–0.088
	P-value	**0.048**	**0.000**		**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	0.507
VAI	R	0.084	0.296	0.779	1.000	0.781	0.630	0.963	0.963	–0.013
	P-value	0.526	**0.023**	**0.000**		**0.000**	**0.000**	**0.000**	**0.000**	0.922
TC/ HDL-C	R	0.258	0.523	1.000	0.781	1.000	0.929	0.824	0.824	–0.088
	P-value	**0.049**	**0.000**	**0.000**	**0.000**		**0.000**	**0.000**	**0.000**	0.508
LDL-C/ HDL-C	R	0.289	0.540	0.929	0.630	0.929	1.000	0.660	0.660	–0.151
	P-value	**0.027**	**0.000**	**0.000**	**0.000**	**0.000**		**0.000**	**0.000**	0.253

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		TC (mg/dL)	Non-HDL (mg/dL)	Non-HDL-C/ HDL-C ratio	VAI	TC/ HDL-C ratio	LDL-C/ HDL-C ratio	TG/ HDL-C	AIP	RDW-CV%
TG/ HDL-C ratio	R	0.039	0.259	0.823	0.963	0.824	0.660	1.000	1.000	–0.061
	P-value	0.772	**0.047**	**0.000**	**0.000**	**0.000**	**0.000**			0.648
AIP	R	0.039	0.259	0.823	0.963	0.824	0.660	1.000	1.000	–0.061
	P-value	0.772	**0.047**	**0.000**	**0.000**	**0.000**	**0.000**			0.648
RDW-CV%	R	–0.058	–0.063	–0.088	–0.013	–0.088	–0.151	–0.061	–0.061	1.000
	P-value	0.665	0.638	0.507	0.922	0.508	0.253	0.648	0.648	
PLT count ($\times 10^9$/L)	R	0.329	0.218	–0.123	–0.183	–0.126	–0.085	–0.189	–0.189	0.015
	P-value	**0.011**	0.097	0.353	0.166	0.342	0.521	0.151	0.151	0.910

		PLT count	Monocytes %	Neutrophils %	Lymphocytes %	MLR	NLR	PLR	OCN (ng/mL)	SIRT1 (ng/mL)
HC (cm)	R	0.068	–0.194	0.052	–0.011	–0.150	0.042	0.055	0.266	0.123
	P-value	0.607	0.140	0.694	0.935	0.255	0.751	0.678	**0.042**	0.354
FBG (mg/dL)	R	–0.110	0.084	0.005	–0.035	0.059	0.026	0.007	–0.376	0.062
	P-value	0.406	0.527	0.968	0.793	0.657	0.843	0.958	**0.003**	0.639
A1C %	R	–0.164	–0.042	0.083	–0.129	0.005	0.123	0.002	–0.317	0.136
	P-value	0.214	0.751	0.530	0.330	0.969	0.353	0.986	**0.014**	0.303
TG (mg/dL)	R	–0.059	–0.111	0.153	–0.151	–0.003	0.173	0.090	0.118	0.303
	P-value	0.655	0.403	0.247	0.253	0.979	0.190	0.499	0.372	**0.020**
LAP	R	–0.089	–0.195	0.083	–0.052	–0.127	0.086	0.007	0.250	0.323
	P-value	0.504	0.138	0.532	0.693	0.336	0.518	0.961	0.057	**0.013**
LDL-C mg/dL	R	0.276	–0.119	–0.197	0.183	–0.235	–0.187	–0.022	0.078	–0.083
	P-value	**0.035**	0.368	0.135	0.165	0.073	0.157	0.867	0.558	0.531
HDL-C (mg/dL)	R	0.321	–0.201	0.163	–0.128	–0.069	0.134	0.240	0.138	–0.087
	P-value	**0.013**	0.126	0.216	0.336	0.601	0.313	0.067	0.298	0.510
TC (mg/dL)	R	0.329	–0.124	–0.079	0.066	–0.170	–0.072	0.082	0.128	–0.011
	P-value	**0.011**	0.348	0.551	0.618	0.197	0.585	0.539	0.336	0.933
VAI	R	–0.183	–0.051	0.045	–0.034	–0.033	0.063	–0.043	0.068	0.286
	P-value	0.166	0.701	0.737	0.798	0.805	0.634	0.748	0.608	**0.028**
TG/HDL-C ratio	R	–0.189	–0.014	0.040	–0.054	–0.002	0.071	–0.042	0.056	0.275
	P-value	0.151	0.918	0.763	0.686	0.987	0.595	0.750	0.674	**0.035**
AIP	R	–0.189	–0.014	0.040	–0.054	–0.002	0.071	–0.042	0.056	0.275
	P-value	0.151	0.918	0.763	0.686	0.987	0.595	0.750	0.674	**0.035**
RDW-CV%	R	0.015	–0.096	0.167	–0.139	0.046	0.152	0.225	0.160	–0.034
	P-value	0.910	0.469	0.207	0.295	0.731	0.250	0.087	0.227	0.801

		PLT count	Monocytes %	Neutrophils %	Lymphocytes %	MLR	NLR	PLR	OCN (ng/mL)	SIRT1 (ng/mL)
PLT count (× 10^9/L)	R	1.000	0.148	0.060	–0.141	0.177	0.109	0.611	0.048	–0.314
	P-value		0.265	0.651	0.288	0.180	0.410	**0.000**	0.721	**0.015**
Monocytes %	R	0.148	1.000	-.273	0.037	0.704	–0.121	0.067	–0.359	–0.204
	P-value	0.265		**0.037**	0.783	**0.000**	0.360	0.616	**0.005**	0.120
Neutrophils %	R	0.060	–0.273	1.000	–0.928	0.416	0.972	0.735	0.077	0.080
	P-value	0.651	**0.037**		**0.000**	**0.001**	**0.000**	**0.000**	0.562	0.544
Lymphocytes %	R	–0.141	0.037	–0.928	1.000	–0.635	–0.983	–0.824	0.012	–0.036
	P-value	0.288	0.783	**0.000**		**0.000**	**0.000**	**0.000**	0.930	0.787
MLR	R	0.177	0.704	0.416	–0.635	1.000	0.555	0.612	–0.309	–0.131
	P-value	0.180	**0.000**	**0.001**	**0.000**		**0.000**	**0.000**	**0.017**	0.323
NLR	R	0.109	–0.121	0.972	–0.983	0.555	1.000	0.796	0.039	0.068
	P-value	0.410	0.360	**0.000**	**0.000**	**0.000**		**0.000**	0.772	0.608
PLR	R	0.611	0.067	0.735	–0.824	0.612	0.796	1.000	–0.063	–0.095
	P-value	**0.000**	0.616	**0.000**	**0.000**	**0.000**	**0.000**		0.635	0.473

Spearman's correlation coefficient (R) was used, R=0.1-.0.29 small relationship, R=0.3–0.49 moderate relationship, R>0.5 high relationship. WC (cm), HC (cm), BMI (Kg/m^2), A1c (%), TG (mg/dL), LDL-C (mg/dL), HDL-C (mg/dL), MPV (fL), RDW-CV (%), OCN (ng/mL), SIRT1 (ng/mL). WC: waist circumference, HC: hip circumference, WHR: waist-to-hip ratio, WHtR: waist-to-height ratio, CI: conicity index, BAI : body adiposity index, A1c: glycated hemoglobin A1C, TG: triglyceride, LDL-C: low density lipoprotein-cholesterol, HDL-C: high density lipoprotein-cholesterol, RDW: red cell distribution width, MPV: mean platelet volume, MLR: monocyte-to-lymphocyte ratio, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, AIP: atherogenicity index of plasma, TC/HDL-C: total cholesterol-to-high density lipoprotein cholesterol ratio, LDL-C/HDL-C: low density lipoprotein cholesterol-to-high density lipoprotein cholesterol ratio.

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