Cross-Sectional Correlates of Increasing Vaspin and Asymmetrical Dimethylarginine Plasma levels with Adiposity Indices and Atherogenic index of plasma in Metabolic Syndrome Subjects in Jordan

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ABSTRACT

OBJECTIVES our study aimed to investigate the correlation between plasma vaspin and asymmetrical dimethylarginine (ADMA) as well as adiposity indices, hematology indices and lipid ratios in metabolic syndrome (MetS) and Type-2 diabetes mellitus (T2DM) patients. METHODS In a cross-sectional design, 28 lean and healthy control, 29 nondiabetic MetS و and 30 MetS-Pre/T2DM drug naïve subjects were enrolled. Plasma vaspin and ADMA were measured by colorimetric-enzymatic assay and expressed as median (interquartile range). RESULTS While ADMA mean circulating levels (μM) were significantly higher in the pre/diabetic MetS group (p=0.04 vs. controls'). Similarly vaspin mean circulating levels (ng/mL) were significantly higher in the nondiabetic MetS group (with P=0.03 vs. controls'). In both MetS (non-diabetic and pre-diabetic/diabetic) groups, adiposity indices, Atherogenicity index of plasma (AIP) and mean platelet volume (MPV) were substantially higher in comparison to those of apparently healthy controls. Substantially a direct ADMA-vaspin and ADMA – waist to height ratio (WHtR) relationships were observed in the total population but none was identified in any study arm (rs= 0.309, P<0.01). Expectedly, ADMA and vaspin correlated significantly and directly with each of population's waist circumference (WC) and body mass index (BMI). Exceptionally, ADMA correlated pronouncedly and proportionally with fasting blood glucose (FBG) and HbA1C but with none of fasting lipid profile parameters (P<0.05 and P<0.01 respectively). Meanwhile, vaspin correlated significantly and directly with triglycerides (TG) and total cholesterol (TC) (rs=0.210, P<0.05 and rs= 0.206, P<0.05 respectively), AIP (rs=0.224, P<0.05), platelet count (rs=0.226, P<0.05), hip circumference (HC) (rs=0. 275, P<0.05) and body adiposity index (BAI) (rs=0.228, P<0.05). CONCLUSION Our findings substantiate that both metabolic biomarkers can be surrogate prognostic tools and putative pharmacotherapeutic targets to predict and prevent the metabolic disorders.

Keywords: Asymmetrical Dimethylearginine, Vaspin; Type 2 Diabetes Mellitus, Metabolic Syndrome, Adiposity and Hematology Indices and Lipid Ratios.

1. INTRODUCTION

The metabolic syndrome (MetS) is a cluster of pathophysiological alterations that includes the presence of hypertension, insulin resistance, dyslipidemia, and abdominal obesity. MetS is associated with increased risk of developing diabetes and cardiovascular diseases. Obesity and the chronic inflammation associated with it initiate a state of insulin resistance (IR). The secretion of chemo attractants draws immune cells into adipose tissue (AT). Increase in circulating free fatty acids (FFA) results from dysfunctional AT lipid metabolism, and this initiates inflammatory signaling cascades in the cells

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infiltrating the AT. Further inflammation exacerbates this pathological state, and disrupts the insulin signaling sequence. Defects in hepatic and skeletal muscle glucose homeostasis are caused by disruption of normal AT function, resulting in IR and ultimately the development of T2DM[1]. The rapid increase in prevalence of diabetes mellitus is a global challenge as it is estimated that by 2040, 642 million adults will be diabetic[2]. This rapid growth imposes both social and financial burdens on patient family, country and patient himself. Around 12% of global health expenditure is spent on DM according to International Diabetes Federation[2].

Asymmetric dimethylarginine (ADMA) is a naturally occurring amino acid that competitively inhibits Nitric oxide synthase (NOS) activity. It is produced by methylation of arginine residues of intracellular proteins via protein arginine N-methyltransferases (PRMTs). NOS plays a critical role in the endothelial function[3]. There are abundant experimental data that endothelial dysfunction is caused by reduced bioavailability of NO in the vascular wall[4]. The available evidence indicates that endogenous NOS inhibitors might be causally related to this process[5]. Abbasi, et al[6] a study showed that plasma ADMA concentrations are elevated in patients with type 2 diabetes when compared with a matched control group of nondiabetic individuals. ADMA has emerged as an important predictor element associated with cardiovascular risk factors, endothelial dysfunction[7], hypertension, atherosclerosis and cardiovascular mortality However, Vaspin is an adipokine isolated from visceral white adipose tissue of the Otsuka Long–Evans Tokushima Fatty (OLETF) rat, an animal model of abdominal obesity with T2DM[8]. Vaspin has been designated as a visceral adipose tissue-derived serpin because its structure is common to the serine protease inhibitor family[9]. Interestingly, exercise and treatment with insulin and the insulin sensitizer pioglitazone prevent the diabetes-related decrease in vaspin expression in visceral adipose tissue[10]. Administration of vaspin to obese mice fed with a high-fat, high-sucrose diet improves glucose tolerance and insulin sensitivity[11]. Vaspin is associated with some but not all components of MetS. Vaspin is a predictor of MetS as a single entity, independent of obesity. This relationship is largely ascribed to the effects of insulin resistance and chronic inflammation[12].

The study aimed to compare both ADMA and Vaspin plasma levels in normoglycemic MetS and pre-diabetic or newly diagnosed T2DMJordanian patients versus healthy lean individuals. Therefore, to link both ADMA and Vaspin to metabolic picture of MetS and T2DM, correlation studies were established with:

- Adiposity indices, namely, waist circumference (WC), hip circumference (HC), waist-to-hip ratio (WHR), waist-to-height ratio (WHtR), conicity index (CI) and body adiposity index (BAI);
- Inflammatory hematological indices, namely: mean platelet volume (MPV), red cell distribution width (RDW), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), and neutrophil-to-lymphocyte ratio (NLR).
- Atherogenicity indices, namely, total cholesterol-to-high density lipoprotein ratio (TC/HDL-C ratio), low density lipoprotein-to-high density lipoprotein ratio (LDL-C/HDL-C ratio) and atherogenicity index of plasma (AIP=log {TG/HDL-C}).
- Correlating ADMA and Vaspin levels to each other.

Up to researcher knowledge, this is the first time these metabolic biomarkers have been investigated in Jordanian population.

2. METHODS

2.1. Study design and settings

This was a cross-sectional study composed of 3 arms: control group of 28 healthy, normoglycemic (HbA1c<5.7%, FBS<100mg/dL) and lean (BMI<25

Kg/m2) individuals, MetS group of 29 normoglycemic patients who met international diabetes federation (IDF) criteria of MetS [13] and MetS-pre/T2DM group that included 30 prediabetic or newly diagnosed antihyperglycemic treatment-naïve MetS [13].patients with T2DM [14].

The MetS patients were recruited from the Diabetes and Endocrinology outpatient clinics whereas control individuals were recruited from the Blood Bank at the Jordan University Hospital. The approvals were obtained from the Scientific Research Committee at the School of Pharmacy in The University of Jordan, and Institutional Review Board at the Jordan University Hospital. Then, a written informed consent was provided and handed to each candidate.

Exclusion criteria

- Autoimmune or inflammatory diseases.
- Any life-threatening disease.
- Endocrine disorder other than MetS or DM.
- Previous treatment with an antihyperglycemic agent.
- Breastfeeding /Pregnancy.

2.2. Sample size calculations

Sample size was calculated using the G*power® 3.0.10 software based on study by Gurel et al[15] (Considering α=0.05, β=0.8), Number of groups: 3, considering pooled SD as 11, total sample size is 120 which means we need 30 /group.

Anthropometric measurements (WC, HC, weight and height) were taken for each participant. WC was measured by using non-stretchable standard tape over the abdomen at the midpoint between the lowest rib and the upper point of the iliac crest while the HC was measured at the level of the widest diameter around the buttocks. Fasting blood samples were taken by the nurse 10-12 hrs after meals for lipid profile, complete blood count, HbA1C% and fasting blood glucose (FBG) levels. Sandwich enzyme linked immunosorbent assay (ELISA) was implemented for both MT and CYR2 assay (My BioSource, Inc. USA).was run for ADMA and Vaspin determination.

CI was calculated as follows[16]:

$$\frac{\text{Waist circumference (m)}}{0.109\sqrt{\dfrac{\text{Body weight (kg)}}{\text{Height (m)}}}}$$

Body adiposity index (BAI) [17] = $\dfrac{\text{hip circumferemce}}{[\,(\text{Height}_{(m)})^{1.5}]-18}$

2.3. Statistical analysis

All biomarker levels were compared between the 3 studied groups. All patient variables were entered into SPSS (Statistical Package for Social Sciences) version 17. Categorical variables were analyzed using Chi-square, and continuous variables were analyzed by ANCOVA. Pearson correlation was used to assess the relation between plasma levels of ADMA and vaspin in association with metabolic risk factors. P-value <0.05 was considered statistically significant.

3. RESULTS

3.1. Clinical characteristics

Study participants were Caucasians (Jordanians). Gender was distributed homogenously among the study arms as shown in Table 1. Females constituted 52.8%while men 47.2% of the study population. Age had significant variations (P<0.001) among the study arms (Table 1). SBP, DBP, TGs and TC were significantly higher in both MetS groups vs. controls (P<0.0%). Expectedly, FBG and HbA1c% were significantly higher in pre/diabetic MetS patients vs. nondiabetic MetS and the control subjects. LDL-C was significantly higher in pre/diabetic MetS vs. controls. In both MetS groups (the

MetS and the MetS pre-diabetic/T2DM), all adiposity indices were substantially higher in comparison to those of apparently healthy controls (P<0.001), except for C-index which was significant at (P<0.05). While, WHR was not significantly different between MetS group (pre-diabetic/T2DM) vs. control where P>0.05. In the MetS-pre-diabetic/T2DM groups AIP was markedly higher in comparison to those of the apparently healthy controls (P<0.001). The TC/HDL-C ratio and LDL-C/HDL-C ratio had no significance between MetS groups (nondiabetic and pre-diabetic/diabetic) vs. control where P>0.05. In addition, MPV was markedly higher in both MetS groups (nondiabetic and pre-diabetic/diabetic; P<0.05). In the pre/T2DM MetS group, Lymphocytes were significantly higher than that in the non-diabetic MetS group (P<0.05). Exceptionally among MLR, NLR and PLR, PLR displayed higher levels in the MetS-pre /T2DM group vs. the non-diabetic MetS group (P<0.05).

3.2. ADMA and vaspin levels

Table (1) shows that ADMA plasma levels were significantly higher in MetS group (pre-diabetic/diabetic) vs. control group (P< 0.05). However, no significant differences in the levels of ADMA were detected between the nondiabetic MetS vs. controls, neither between the prediabetic/diabetic MetS vs. MetS patients (Figure 1). Vaspin levels were at significantly higher in the MetS nondiabetic group compared to controls but there was no substantial difference in its levels between both MetS groups (Figure 2).

Table (1)

Comparison of clinical characteristics, adiposity, atherogenicity and hematological indices between study groups

Demographic data							
	Control group. N=28	**MetS group. N=29**	**MetS pre/T2DM group. N=30**	**P#-value**	**P-value[1]**	**P-value[2]**	**P-value[3]**
Age years	30.79±8.7	44.5±10.9	51.8± 10.8	0.009			
Female, N (%)	17(56.7%)	14(48.3%)	16(53.3%)	0.810			
Male, N (%)	13(43.3%)	15(51.7%)	14(46.7%)				
Clinical parameters							
SBP (mm Hg)	110.8 ± 12.3	132.7± 15.1	132.3 ± 15.2		<0.001	0.009	0.497
DBP (mm Hg)	69.8 ± 9.6	79.8 ± 8.2	81.2 ± 10.9		0.042	0.02	0.641
FBG (mg/dL)	89.7 ± 6.3	90.4 ± 7.6	119.5 ± 37.9		0.874	<0.001	<0.001
HbA1c (%)	5.1 ± 0.2	5.2 ± 0.3	6.4 ± 1.1		0.938	<0.001	<0.001
TG (mg/dL)	74.8 ± 33.3	187.9 ± 89.1	204.1 ± 118.1		0.001	0.001	0.524
LDL-C[a] (mg/dL)	92.8 ± 24.9	121.8 ± 33.3	138.7 ± 39.8		0.323	0.04	0.163
HDL-C (mg/dL)	45.7 ± 8.1	43 ± 17.1	40.6 ± 12.2		0.505	0.271	0.554
TC (mg/dL)	153.8 ± 26.5	202.4 ± 40.5	220.1 ± 43.2		0.03	0.002	0.18
Adiposity indices							
WC (cm)	79.3 ± 6.3	103.5 ± 9.03	105 ± 9.6		<0.001	<0.001	0.458
HC (cm)	95.7 ± 6.5	116.1 ± 9.8	117.5 ± 11.3		<0.001	<0.001	0.134

BMI (Kg/m$^{2)}$	22.1 ± 1.8	33.5 ± 4.3	33.9 ± 5.9		<0.001	<0.001	0.339
WHR	0.83 ± 0.07	0.89 ± 0.06	0.89 ± 0.06		<0.05	<0.05	0.474
WHtR	0.47 ± 0.03	0.62 ± 0.05	0.63 ± 0.06		<0.001	<0.001	0.310
C-index	1.2 ± 0.07	1.27 ± 0.05	1.28 ± 0.06		<0.05	<0.05	0.697
BAI	25.8 ± 4.16	35.5 ± 5.6	37 ± 7.6		<0.001	<0.001	0.208
Hematologic indices							
RDW-CV%	13.4 ± 0.7	13.2 ± 2.1	13.8 ± 1.2		0.904	0.325	0.193
MPV (fL)	6.3 ± 1.1	9.2 ± 2	9.1 ± 2.4		<0.001	0.027	0.641
PLTLT count (X10^^{3}/ µL)	235 ± 46.4	274 ± 66.7	261 ± 60.5		0.098	0.253	0.661
Monocytes (X10^^{3}/ µL)	0.8 ± 0.9	0.6 ± 0.3	0.6 ± 0.6		0.852	0.511	0.561
Neutrophiles (X 10^^{3}/ µL)	5 ± 1.6	4.4 ± 1.2	6.4 ± 10.6		0.852	0.968	0.877
Lymphocytes (X10^^{3}/ µL)	2.7 ± 0.9	2.3 ± 0.5	2.7 ± 0.7		0.640	0.194	0.041
MLR	0.2 ± 0.3	0.3 ± 0.1	0.2 ± 0.1		0.571	0.409	0.112
NLR	1.97 ± 0.7	1.96 ± 0.5	2.29 ± 3		0.837	0.587	0.678
PLR	98.4 ± 42.9	125.4 ± 44.8	101.9 ± 34.7		0.251	0.505	0.043
Atherogenicity indices							
AIP	0.2 ± 0.2	0.6 ± 0.2	0.7 ± 0.2		<0.001	<0.001	0.703
TC/HDL-C ratio	3.5 ± 0.8	5 ± 1.3	6.6 ± 6.2		0.356	0.061	0.213
LDL-C/HDL-C ratio	2.1 ± 0.7	3 ± 0.96	4.4 ± 5.1		0.596	0.126	0.210
Metabolic biomarkers							
ADMA (µM)	0.21±0.107	0.25±0.151	0.33±0.160		0.226	0.049	0.269
Vaspin (ng/ml)	924.29±390.07	1281.54±641.07	1124.91±533.38		0.034	0.117	0.593

P-value obtained by ANCOVA test

[a]Covariate appearing in the model is evaluated at the following values: age=42.53.

Pairwise comparisons were done through LSD adjustment.

adjusted mean and P-value obtained by ANCOVA test

P-value <0.05 was highlighted bold

[1] MetS group vs. control, [2]MetS pre/T2DM vs. control, [3] MetS pre/T2DM vs. MetsS.

DPB: diastolic blood pressure, FBG: fasting blood glucose, HbA1C%: percent glycosylated- hemoglobin, HDL-C: high density lipoprotein-cholesterol, LDL-C: low density lipoprotein-cholesterol, MT: Melatonin, SBP: systolic blood pressure, ADMA: Asymmetrical dimethyle arginine 2, TG: triglycerides, TC: total cholesterol, WC: waist circumference, HC: hip circumference, WHR: waist-to-hip ratio, WHtR: waist-to-height ratio, C-index: conicity index, BAI: body adiposity index, RDW: red cell width, MPV: mean platelet volume, PLT: platelet, MLR: monocyte-to- lymphocyte ratio,

NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio.

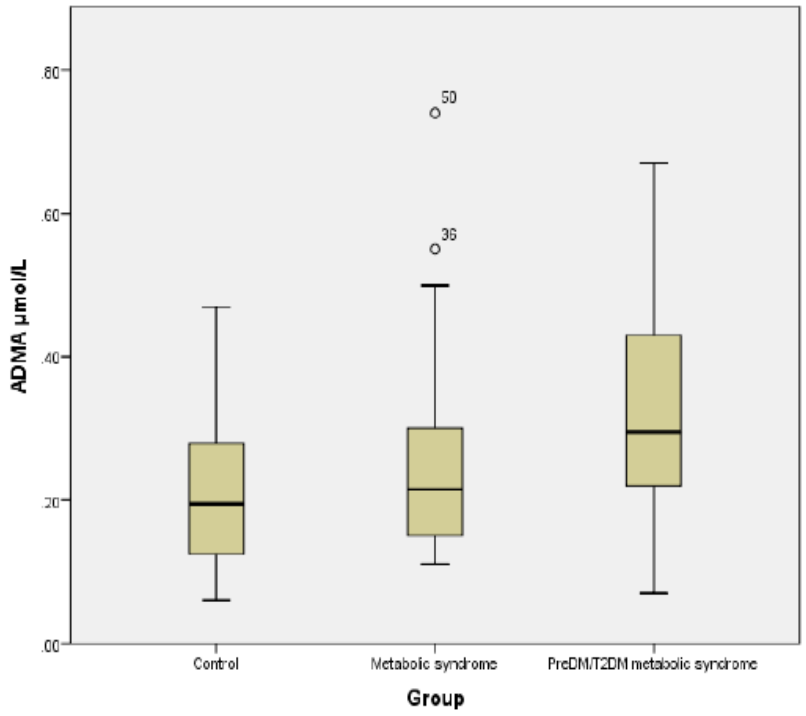

Figure (1): Levels of Asymmetrical dimethyle arginine (ADMA) in the three study groups (mean±SD)

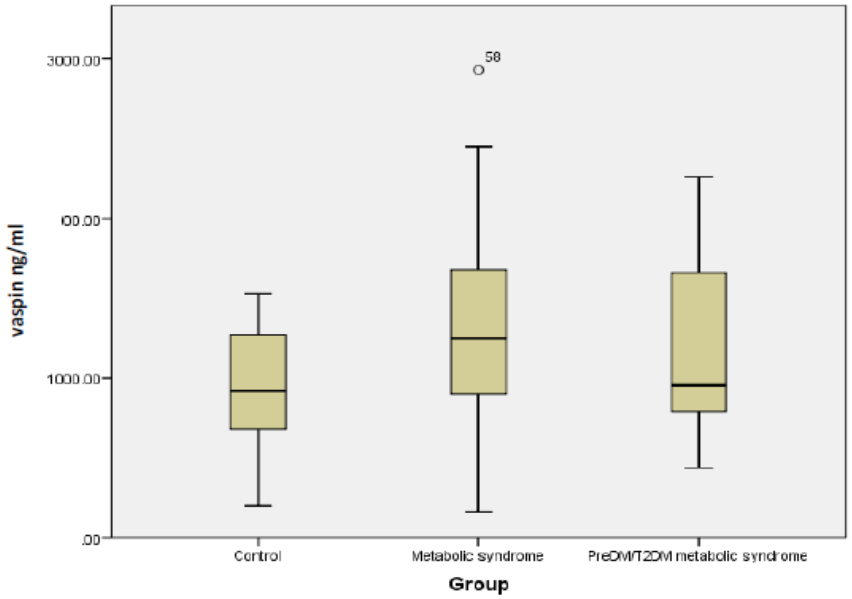

Figure (2): Levels of vaspin in the three study groups (mean±SD)

3.3. ADMA and Vaspin correlations

4. Table 2 displays that ADMA correlated significantly and directly with FBG and HbA1c.Meanwhile, vaspin correlated significantly and directly with TG and TC in the study population.ADMA correlated significantly and directly with each of population adiposity indices, namely WC, BMI and WHtR, As for as vaspin correlated significantly and directly with each of population adiposity indices, namely WC, HC, BMI and BAI. Table 2 also demonstrates that vaspin correlated significantly directly with AIP and platelet count in the total study population. ADMA and vaspin in the total population correlate directly and significantly with each other (Figure 3).

Table (2)
Asymmetrical dimethyle arginine (ADMA) and Vaspin correlations

Parameter	Correlation	TOTAL study population	
		ADMA (µM)	Vaspin (ng/ml)
Clinical parameters			
SBP (mmHg)	r	0.077	0.123
	p-value	0.480	0.255
DBP (mmHg)	r	0.078	0.048
	p-value	0.478	0.657
FBG (mg/dL)	r	0.227	-0.026
	P value	0.035	0.810
HbA1c (%)	r	0.23	-0.027
	p-value	0.008	0.804
TG (mg/dL)	r	0.114	0.210
	p-value	0.294	0.049
LDL-C (mg/dL)	r	0.199	0.166
	P value	0.066	0.125
HDL-C (mg/dL)	r	-0.168	-0.082
	p-value	0.123	0.451
TC (mg/dL)	r	0.165	0.206
	p-value	0.129	0.049
Adiposity indices			
WC(cm)	r	0.223	0.252
	p-value	0.039	0.0190
HC(cm)	r	0.197	0.275
	p-value	0.069	0.0100

Parameter	Correlation	TOTAL study population	
		ADMA (µM)	Vaspin (ng/ml)
BMI (Kg/m^2)	r	0.257	0.361
	P value	0.017	0.001
WHR	r	0.107	0.050
	p-value	0.325	0.648
WHtR	r	0.232	0.247*
	p-value	0.031	0.021
C-Index	r	0.088	-0.012
	P value	0.421	0.915
BAI	r	0.009	0.228
	p-value	0.181	0.034
Hematological indices			
RDW (%)	r	0.155	0.045
	p-value	0.153	0.677
MPV (fL)	r	0.075	0.157
	p-value	0.493	0.148
Plt count ($x10^{\wedge 3}$/ µL)	r	0.204	0.226
	P value	0.060	0.035
Monocytes ($x10^{\wedge 3}$/ µL)	r	-0.085	-0.012
	p-value	0.437	0.913
Neutophiles ($x10^{\wedge 3}$/ µL)	r	-0.052	-0.074
	p-value	0.632	0.496
Lymphocytes ($x10^{\wedge 3}$/ µL)	r	0.019	0.103
	p-value	0.859	0.341
MLR	r	-0.067	-0.047
	P value	0.541	0.667
NLR	r	-0.060	-0.111
	p-value	0.584	0.306
PLR	r	0.056	0.001
	p-value	0.612	0.993
Atherogenicity indices			
LDL-C/HDL-C	r	0.179	0.093
	p-value	0.100	0.390
TC/HDL-C	r	0.180	0.111
	p-value	0.097	0.306
AIP	r	0.178	0.224
	P value	0.101	0.037

Pearson correlation coefficient (r) was used,

r =0.1-0.29 small relationship,

r =0.3-0.49 moderate relationship,

r >0.5 high relationship.

P-value <0.05 was highlighted bold

SBP: systolic blood pressure, DPB: diastolic blood pressure, FBG: fasting blood glucose, HbA1C%: percent glycosylated- hemoglobin, HDL-C: high density lipoprotein-cholesterol, LDL-C: low density lipoprotein-cholesterol, TG: triglycerides, TC: total cholesterol, WC: waist circumference, HC: hip circumference, BMI: body mass index, WHR: waist-to-hip ratio, WHtR: waist-to-height ratio, C-index: conicity index, BAI: body adiposity index, RDW: red cell width, MPV: mean platelet volume, PLT: platelet, MLR: monocyte-to--lymphocyte ratio, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio.

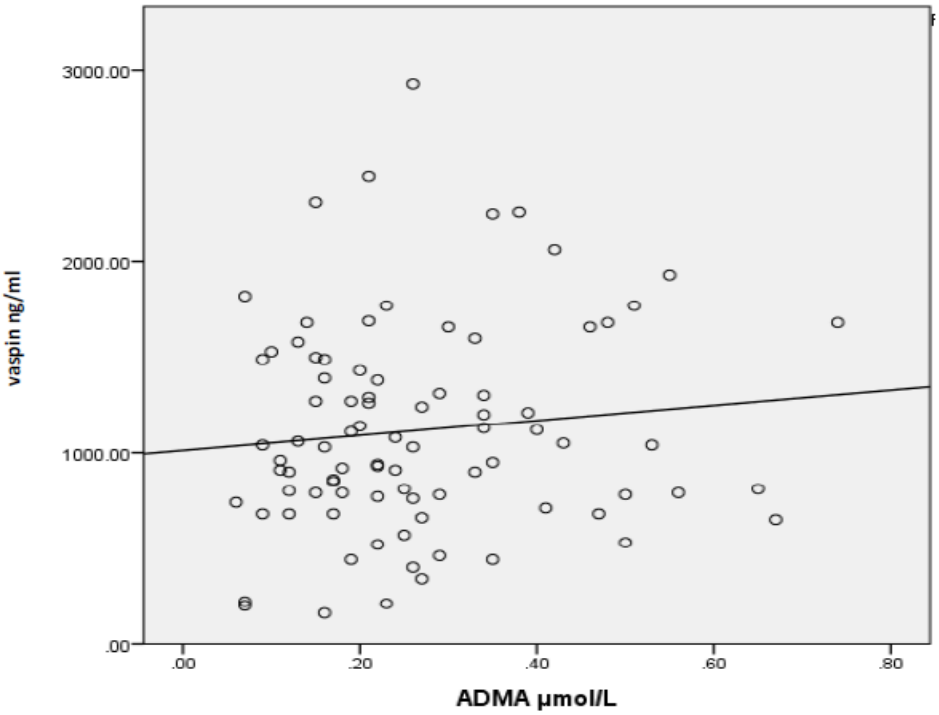

Figure (3): Asymmetrical dimethyle arginine (ADMA)-vaspin relationship in the total study population

4. DISCUSSION

In this study, we have found significant increase in plasma concentrations of ADMA in patients with pre-diabetic/T2DM with MetS vs. controls. While Palomo, et al[18] conducted a study with a design based to ATP III criteria for diagnosis of MetS and found that ADMA levels were significantly higher in individuals with MetS compared to controls[18]. However, Palomo et al[18] did not compare ADMA levels in patients with glucose intolerance distinctly from MetS and this is what makes our study different from Palomo et al[18] study.

Comparable to our study, ADMA levels have been

shown to correlate with body mass index (BMI) in the elderly according to Eid et al[19]. In addition, observational studies in subjects with obesity and insulin resistance Krzyzanowska et al[20] shows that ADMA levels are reduced after weight loss.

We also correlated ADMA levels to clinical parameter, adiposity indices, atherogenicity indices, hematologic indices and to vaspin. Interestingly, ADMA levels did not correlate with SBP or DBP in our study. This lack of association was also observed by Chirinos et al[21] in a population-based study performed in Arequipa, Peru (previous Study). These authors found an association between ADMA levels and the carotid intima-media thickness, but not with blood pressure or other hemodynamic parameters.

Unprecedentedly, our study delineated for the first time that ADMA is correlated to various adiposity indices in the total study population such as WC, BMI and WHtR (ADMA, WC: rs=0.223, P<0.05, BMI: rs=0.257, P<0.05, WHtR: rs=0.232, P<0.05).

Human studies on vaspin relationship with T2DM and/or MetS are not abundant; mostly these studies were animal or gene expression-based. In our study a significant increase in plasma concentrations of vaspin in the nondiabetic MetS group compared to control group was reported. Similar to our findings, Choi et al[22], conducted a study in 81 MetS subjects and 241 age- and sex matched non-MetS control subjects using the ELISA. Evidently plasma vaspin concentrations were significantly higher in MetS-men compared with those without (P = 0.002). There was also a positive correlation between plasma vaspin concentrations and BMI and WC Choi et al[22].

Basically visceral vaspin mRNA expression correlated with BMI, percentage of body fat, and 2-hour oral glucose tolerance test. Kloting et al[23] delineated that human vaspin mRNA expression in adipose tissue was regulated in a fat depot-specific manner and could be associated with parameters of obesity, insulin resistance, and glucose metabolism. The researchers suggested that the increase in vaspin may be a compensatory response to antagonize the action of other unknown proteases that are up-regulated in obesity and in states of insulin resistance. Hence, this up-regulation may be a defensive mechanism against insulin resistance[9].

Unprecedentedly our study could detect proportional correlations between vaspin and clinical parameters, adiposity indices, atherogenicity indices, and hematological indices. Our study found a direct correlation between vaspin and ADMA (rs= 0.309, P<0.01), in the total study population of its apparently healthy lean, pre-diabetic/diabetic and nondiabetic MetS participants. On the other hand Jung et al[24] could identify a marked reciprocal correlation when vaspin treatment in Sprague-Dawley (SD) rats was found to reduce ADMA level, thereby increasing eNOS activity and NO secretion from endothelial cells and isolated aorta. Additionally vaspin correlated significantly and inversely with (TG: rs=-0.210, P<0.05; TC: rs= -0.206, P<0.05), correlated significantly and directly with each of population adiposity indices, namely WC, HC, BMI and BAI (vaspin, WC: rs=0.252, P<0.05, HC: rs=0. 275, P<0.05, BMI: rs=0.361, P<0.001, BAI: rs=0.228, P<0.05), correlated directly with population' AIP (rs=0.224, P<0.05), and correlated significantly directly with platelet count (rs=0.226, P<0.05) in the total study population.

5. Study Limitations

This is a cross-sectional study which limits the interpretation and speculations of the results in order to obtain a cause-effect relationship between the biomarkers and obesity as well as diabetes. The inclusion of a diabetic group on medication could have provided us with further evidence of the effect of diabetes duration. Additional clues for whether a good glycemic control

could have had any influence on the circulating biomarkers may be inferred.

CONCLUSIONS

- ADMA levels exhibited an ascending order of significant elevation in the study arms (MetS-pre-diabetic/T2DM > controls).
- Vaspin levels differed among the groups being significantly higher in nondiabetic MetS patients than healthy lean individuals and this difference was significant.
- Non-diabetic MetS and pre-diabetic/diabetic MetS individuals had higher atherogenicity, inflammatory hematological and adiposity parameters compared to healthy lean participants. For most of these parameters, the highest levels were obtained in MetS pre-diabetic/T2DM.
- The ADMA and vaspin were directly associated in total study population.
- Both biomarkers exhibited correlations with a number of adiposity, hematology and atherogenicity indices.
- Lower ADMA and vaspin levels are associated with different aspects of the metabolic parameters (lipid profile, A1C, glucose level, BP). Thus, our findings supported the importance of ADMA and vaspin in MetS and T2DM pathogenesis and for potential therapeutic interventional approaches.

Conflict of interest The authors declare none.

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دراسة مقطعية لمستويات الفاسبين والأرجنين ثنائي المثل غير المتماثل في بلازما الدم لدى المرضى المصابين بمرض السكري وغير المصابين بمرض السكري ذوي المتلازمة الأيضية في الأردن

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ملخص

الأهداف

تم اقتراح الأرجنين ثنائي المثل غير المتماثل (ادما) والفاسبين على أنهما من آليات فسيولوجيا المرض لمتلازمة الأيض وداء السكري النوع الثاني. هدفت هذه الدراسة إلى المقارنة والربط بين مستويات أدما وفاسبين في البلازما، ومقارنتهما مع بعضهما البعض ومع مؤشرات السمنة، ونسب الدهون ومؤشرات الدم، للأشخاص المصابين بالمتلازمة الأيضية وما قبل السكري/ حديثي التشخيص بداء السكري النوع الثاني.

الطرق

في دراسة استهدفت ٢٨ من الأشخاص النحيفين أصحاب سكر الدم الطبيعي (المجموعة الضابطة)، و٢٩ من الأشخاص المصابين بالمتلازمة الأيضية غير المصابين بداء السكري و٣٠ من الأشخاص المصابين بالمتلازمة الدين تم تشخيصهم بالإصابة بداء السكري النوع الثاني أو ما قبل السكري. مؤشر كتلة الجسم والجنس كانا متطابقين. تم تقييم أدما وفاسبين باستخدام المقايسات اللونية. كما تم فحص الارتباطات بين هذه المؤشرات الحيوية الأيضية، فيما بينها، ومع السمنة، وتصلب الشرايين ومؤشرات الدم.

النتائج

سجل متوسط مستويات أدما (نغ/ مل) فروقات ذات دلالات إحصائية، وكان الأعلى في مجموعة مرضى المتلازمة الأيضية/ ما قبل السكري (٠,٣٢±٠,١٦، مقابل المجموعة الضابطة ٠,٢١±٠,١؛ P<٠,٠٥).

وكان متوسط متوسط مستويات فاسبين (نغ/ مل) أعلى بكثير في مجموعات المتلازمة الأيضية غير المصابين بداء السكري (١٢٨١,٥٤ ± ٦٤١,٠٧) مقابل المجموعة الضابطة (٩٢٤,٢٩ ± ٣٩٠,٠٧؛ P <٠,٠٥).

في كل من المجموعتين للمصابين بالمتلازمة الأيضية (غير المصابين بداء السكري الذين تم تشخيصهم بما قبل السكري أو داء السكري النوع الثاني)، كانت جميع المؤشرات الدهنية والاثيروجينيستي وكذلك متوسط حجم الصفائح الدموية وعددها أعلى بكثير بالمقارنة مع المجموعة الضابطة. ولوحظ وجود علاقة طردية بين مستويات أدماوفاسبين في المجموع الكلي لعينة الدراسة (rs= 0.309, P<٠,٠١).

من المتوقع، أن أدما وفاسبين يرتبطان بشكل كبير ومباشر مع كل مؤشرات السمنة في المجموع الكلي لعينة الدراسة. بشكل استثنائي، ترتبط أدما بشكل كبير ومباشر مع جلوكوز الدم الصائم rs=0.227, P<0.05 وتحليل السكر التراكمي HbA1C (rs=0.001, P<0.01) في الوقت نفسه، يرتبط فاسبين بشكل كبير ومباشر مع الدهون الثلاثية (rs=0.210, P<0.05) في المجموع الكلي لمجتمع الدراسة.

أثبتت النتائج أن أدما وفاسبين قد تكون مرتبطة ارتباطا وثيقا مع مرض السكري والمتلازمة الأيضية. وهكذا كل من المؤشرات الحيوية يمكن أن تكون أداة التشخيص والتحذير والتنبؤ ومنع حدوث المتلازمة الأيضية والاضطرابات ذات الصلة.

الكلمات الدالة: الأرجنين ثنائي المثل غير المتماثل، الفاسبين، داء السكري من النوع ٢، متلازمة الأيض، مؤشرات السمنة، أمراض الدم، نسب الدهون.

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