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RESEARCH ARTICLE

Study of Serum Interleukin-18 in Metabolic and Pre Metabolic Syndromes

Mona El-Fedawy El Saied[1], Hend Maghraby Maghraby[1], Abeer Abd-Elfattah Ali[1], Nagwa Abd EL-Ghaffar Mohammed[2] and Shymaa Ramadan Mohamed[1]

1- Department of Internal Medicine. Faculty of Medicine for girls. Al-Azhar University

2- Department of Clinical and Chemical Pathology, National Research Center, Cairo, Egypt

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Corresponding Author

Mona El-Fedawy El Saied

Abstract

Background: Metabolic syndrome (MetS) is a cluster of risk factors for cardiovascular disease (CVD), including insulin resistance, obesity, hypertension, elevated triglycerides, and low levels of HDL cholesterol. Interleukin-18 (IL-18) is proinflammatory cytokine with important regulatory function in innate and acquired immune responses and control of energy homeostasis which implicated in the evolution and development of complications of MetS.

Aim of the work: To determine serum level of circulating IL-18 as a specific biomarker for distinguishing between MetS patients and pre-MetS subjects

Patients and Methods: This study was conducted on 20 patients with MetS and 40 patients with pre-MetS which divided into 20 non obese hypertensive patients and 20 obese diabetic patients. These patients compared with 25 ages and sex matched healthy volunteers. All Patients and control were subjected to full medical history, clinical examination and laboratory investigations in addition to fasting serum insulin and serum IL-18.

Results: Mean serum IL-18 was significantly higher in both pre-MetS and MetS in comparison with control group and lower in pre-MetS than MetS group. Insulin resistance was higher in MetS patients and in pre-MetS diabetic patients than controls.

There was positive correlation between mean serum IL18 and WC, serum insulin, FBG, insulin resistance and serum TG and negative correlation between mean serum IL18 and serum HDL in MetS patients and in pre-MetS diabetic patients. There was positive correlation between serum IL-18 and S.B.P in pre-MetS hypertensive patients.

Conclusion: Serum IL18 significantly increased in both MetS and pre-MetS than control but more in MetS. Circulating serum IL-18 levels could be a useful biomarker for distinguishing patients with MetS from patients with pre-MetS.

INTRODUCTION

The prevalence of MetS is dramatically increased during the past decades. MetS is a cluster of risk factors for CVD, including insulin resistance, obesity, hypertension, elevated triglycerides, and low levels of HDL cholesterol[1]. The risk of developing CVD is approximately doubled in MetS.[2]

Adipose tissue is not merely a simple reservoir of energy stored as triglycerides, but serves as an active secretory organ releasing many peptides and cytokines into the circulation. In the state of obesity, the balance between these numerous molecules is dysregulated. Enlargement of adipocytes producing more proinflammatory

cytokines (TNFα, IL-6 and IL-1 family (IL-1F) members) and less anti-inflammatory proteins, such as adiponectin, was suggested as one potential explanation. Others proposed that infiltration of inflammatory cells may represent the critical step in adipose tissue-associated inflammation, although the initial trigger(s) for accumulation of these cells remains elusive[3.]

Interleukin-18 is proinflammatory cytokine located on chromosome 11q22.2-22.3 and is a member of the IL-1 cluster[4]. Originally, IL-18 was described as an interferon-γ-inducing factor because of its strong ability to stimulate interferon-γ release with the presence of co-stimuli, such as IL-12 or lipopolysaccharide. IL18 described as an important regulator of innate and acquired immune responses. A role for IL-18 has been implicated in several autoimmune diseases, myocardial function, emphysema, MetS, psoriasis, inflammatory bowel disease, hemophagocytic syndromes, macrophage activation syndrome, sepsis, and acute kidney injury, although in some models of disease, IL-18 is protective[5].

IL-18 enhances T cell and natural killer cell maturation, as well as the production of cytokines, chemokines and cell adhesion molecules. IL-18 can promote Th1 or Th2 lineage maturation dependent on underlying genetic influences and the ambient cytokine milieu. IL- 18 promotes neutrophil activation, reactive oxygen intermediate synthesis, cytokine release, and degranulation[6].

The pathogenesis of MetS has focused on an immunologic component, with its accompanying cytokines and other inflammatory markers, to play a crucial role in the evolution and development of complications[7].

A novel function for IL-18 in control of energy homeostasis has also been described[8]. Zirlik et al[9]., and others reported that circulating levels of IL-18 in human adults directly correlate with BMI, adiposity, and insulin resistance and are elevated in obesity. Also IL-18 is implicated in the pathogenesis of several diseases which complicate the MetS components such as atherosclerosis and ischemic heart disease. These results highlight the importance of IL-18 as a potential marker of diagnostic as well as prognostic importance in MetS [10, 11].

This study was performed to determine serum level of circulating IL-18 as a specific biomarker for distinguishing between MetS patients and pre-MetS subjects.

Patients and Methods

This study was conducted on 60 patients recruited from internal medicine outpatient clinic at Al-Zhraa university Hospital from (September 2013 to May 2014) in addition to 25age and sex matched healthy volunteers.

To diagnose patients with MetS on base of American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) criteria[12].They must have 3 of following 5 criteria: Central obesity (defined as waist circumference (WC) ≥ 102 cm for men and ≥ 88cm for women. Raised triglycerides levels ≥ 150 mg/dL, or specific treatment for this lipid abnormality. Reduced HDL-cholesterol < 40 mg/dL in men, < 50mg/dL in women or specific treatment for this lipid abnormality. Raised blood pressure (systolic blood pressure (SBP) ≥130 mmHg and/or diastolic blood pressure (DBP) ≥85 mmHg), or treatment of previously diagnosed hypertension. Raised fasting plasma glucose ≥100 mg/dL, or on drug treatment for diabetes. Whereas the patients who had 1 or 2 component defined as pre-MetS subjects[12].

Patient with Chronic liver disease, chronic renal failure, autoimmune disease, malignancy and patient on corticosteroid therapy have been excluded from the study.

Informed consent was obtained from all patients and controls and approval of ethical committee of faculty of medicine for girls, Al-Azhar University was also obtained.

The patients were divided into 2 groups:

Group I: Twenty patients with MetS (13 female &7 male) their ages ranged between (44- 60 years) with mean ± SD (51.9 ± 5.55).

Group II: Forty patients with pre-MetS this group will be divided into:

Group II a: Twenty hypertensive patients non obese (9 female &11 male) their ages ranged between (47-65years) with mean ± SD (52.80±5.36).

Group II b: Twenty diabetic patients (14 female &6 male) their ages ranged between (40- 58years) with mean ± SD (46.75±5.43).

These patients will be compared to twenty five healthy volunteers (11female &14 male) their ages ranged between (40- 60 years) with mean ± SD (48.84±5.63).

All Patients and control were subjected to the following:

-Complete history taking, Full clinical examination including, Arterial Blood pressure, waist circumference, ECG.

- Laboratory investigations including:

-Complete Blood count (CBC).

- Fasting blood glucose.

-Serum triglyceride and serum HDL.

-Fasting serum insulin level.

-Serum IL-18 level by ELISA.

-Insulin resistance measured by the homeostasis model assessment (HOMA-IR) which is calculated using the following formula's[13]:

HOMA-IR = fasting blood glucose (mg/dl) x fasting serum insulin (μIU/ml)/405

Five ml of fasting (12-14 hours) venous blood samples were taken from each subject participating in the study and divided into parts: The 1st part (2ml of blood) was put into EDTA containig tube for CBC determination on Coulter Counter T890 (Coulter Counter, Harpenden, UK). The 2nd part (3 ml of blood) was put into plain tube and was left to clot and the serum was separated by centrifugation for 15 minutes at 3000 xg. The separted serum was stored at at -20℃ for determination of fasting blood glucose, serum triglyceride, serum HDL, serum insulin and serum IL-18,

The determination of serum triglyceride (TG) was performed on Hitachi auto analyzer (Hitachi 912) (Roche Diagnostics GmbH, D-68298 Mannheim, USA) by colorimetric techniques. Fasting blood glucose was determined immediately on Hitachi auto analyzer (Hitachi 912) by glucose oxidase method.

For determination of HDL-cholesterol, phosphotungestic acid and magnesium ions are used for precipitating all lipoproteins except HDL fraction that was present in the supernatant and measured by Hitachi 912 auto analyzer.

Fasting serum insulin was determined using radio immuno assay[14] (Perez-Fontan, 2004).

Serum IL-18 was determines using enzyme linked immunosorbent assay (ELISA)[15] and the kit was supplied from MBL **(MBL International** 15A Constitution Way, Woburn, USA)

Statistical Analysis

Statistical analyses were performed using (SPSS) version 16 software (Chikago,USA).

Comparison between groups was performed using paired and unpaired student's t test for quantitative data. Correlation was assessed by using the Spearman correlation coefficient. For all data $P < 0.05$ was considered significant and $P < 0.01$ was considered highly significant.

Results:

Table (1): Comparison between group I (metabolic group), group IIa (HTN group), group IIb (DM group) and control group as regard demographic data and laboratory parameters.

Variables	Group I (n=20)	Group IIa (n=20)	Group IIb (n=20)	Control group (n=25)	P_1	P_2	P_3
Waist circumference (cm)	115.2± 13.98	85.65± 5.27	104.30±10.93	87.28± 6.03	0.000**	0.000**	0.000**
S.B.P. (mmHg)	139.5± 19.59	148±10.05	114.5 ±6.86	110.4± 9.35	0.000**	0.000**	0.000**
D.B.P. (mmHg)	85± 7.61	87.5±8.51	77.5±4.44	73.2± 8.02	0.000**	0.000**	0.000**
IL-18 (pg/ml)	316.79 ±64.85	239.77±31.11	221.34±36.06	120.63 ±29.5	0.000**	0.000**	0.000**
Serum insulin (µIU/ml)	29.69±7.34	9.81±2.78	20.27±3.32	9.97±2.27	0.000**	0.122	0.000**
Insulin Resistance	9.42±3.44	2.11±0.63	7.07±1.40	2.14±0.56	0.000**	0.856	0.000**
F.B.G. (mg/dl)	127.8 ±25.93	87.1 ±5.94	142.50 ±23.77	86.72±7.13	0.000**	0.070	0.000**
HDL (mg/dl)	41.28±4.8	65±8.91	72.20±15.78	65.24±14.09	0.000**	0.131	0.945
TG (mg/dl)	213.89±56.74	106.7±27.75	115.68±19.98	111.18±20.61	0.000**	0.464	0.552

P_1 is the difference between patients with MetS, and the control group. P_2 is the difference between hypertensive patients with pre-MetS and the control group, and P_3 is the difference between diabetic patients with pre-MetS and the control group. $^{**}P < 0.01$ (highly significant), $^{*}P<0.05$ (Significant), $P > 0.05$ (non significant).

Table (2): Comparison between patients of group I (metabolic group) and group IIa (HTN group) as regard demographic data and laboratory parameters.

Variables	Group I (n=20)	Group IIa (n=20)	P

Waist circumference (cm)	115.2±13.98	85.65±8.68	0.000**
S.B.P. (mmHg)	139.5 ±19.59	148±10.05	0.095
D.B.P. (mmHg)	85±7.61	87.5±8.51	0.334
IL-18 (pg/ml)	316.79±64.85	239.77±31.11	0.000**
Serum insulin (µIU/ml)	29.69±7.34	9.81±2.78	0.000**
Insulin resistance	9.42±3.44	2.11±0.63	0.000**
FBG (mg/dl)	127.8 ±25.93	87.1 ±5.94	0.000**
HDL (mg/dl)	41.28± 4.8	65.0±8.91	0.000**
TG (mg/dl)	213.89±56.74	106.7±27.75	0.000**

*******P* < 0.01 (highly significant),* P<0.05 (Significant), *P* > 0.05 (non significant).

Table (3): Comparison between group I (metabolic group) and group IIb (DM group) as regard demographic data and laboratory parameters.

Variables	**Group I (n=20)**	**Group IIb (n=20)**	**P**
Waist circumference (cm)	115.2±13.98	104.3±10.93	0.009**
S.B.P. (mmHg)	139.5 ±19.59	114.5 ±6.86	0.000**
D.B.P. (mmHg)	85±7.61	77.5±4.44	0.001**
IL-18 (pg/ml)	316.79 ±64.85	221.34±36.06	0.000**
Serum insulin (µIU/ml)	29.69±7.34	20.27±3.32	0.000**
Insulin resistance	9.43±3.44	7.07±1.40	0.009**
FBG (mg/dl)	127.8±25.93	142.50±23.77	0.069
HDL (mg/dl)	41.28±4.8	72.20±15.78	0.000**
TG(mg/dl)	213.89±56.74	115.68±19.98	0.000**

*******P* < 0.01 (highly significant), *P<0.05 (Significant), *P* > 0.05 (non significant).

Table (4): Comparison between group IIa (HTN group) and group IIb (DM group) as regard laboratory parameters.

Variables	**Group IIa (n=20)**	**Group IIb (n=20)**	**P**

IL-18 (pg/ml)	239.77±31.11	221.34±36.06	0.092
Serum insulin (µIU/ml)	9.81±2.78	20.27±3.32	0.000**
Insulin Resistance	2.11±0.63	7.07±1.40	0.000**
FBG (mg/dl)	87.1 ±5.94	142.50±23.77	0.000**
HDL (mg/dl)	65±8.91	72.20±15.78	0.086
TG (mg/dl)	106.7±27.75	115.68±19.98	0.249

***P* < 0.01 (highly significant), *P<0.05 (Significant), *P* > 0.05 (non significant).

Table (5): Correlation between mean serum IL-18 and different studied parameters in different groups.

	IL-18		**IL-18**		**IL-18**	
	Group I		**Group IIa**		**Group IIb**	
	r	**P**	**r**	**P**	**r**	**P**
SBP			0.306	<0.05*		
WC	0.645	<0.01**	0.254	>0.05	-0.514	<0.05*
FBG	0.596	<0.01**			0.579	<0.01**
Insulin	0.597	<0.01**			0.603	<0.01**
HDL	-0.506	<0.05*			-0.567	<0.05*
TG	0.474	<0.05*			0.507	<0.05*
Insulin resistance	0.834	<0.01**			0.537	<0.05*

***P* < 0.01 (highly significant), P<0.05 (Significant), *P* > 0.05 (non significant).

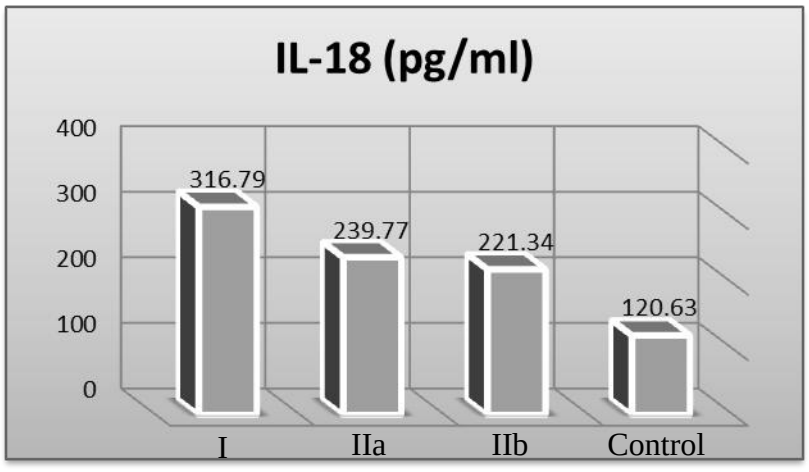

Figure 1: The mean serum IL-18 in different studied groups.

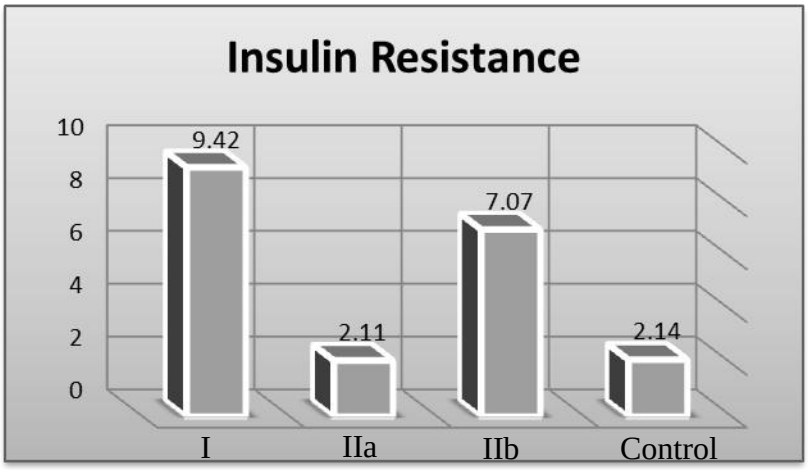

Figure 2: Insulin resistance in different studied groups.

There were highly significant increase in mean WC, mean S.B.P. and mean D.B.P in group I & IIb compared with control group.While in group IIa there was a highly significant decrease in mean WC, highly significant increase in mean S.B.P. and mean D.B.P. compared with control group (Table 1).

There were highly significant increase in mean serum IL-18, mean serum insulin, mean insulin resistance and mean FBG in group I & IIb compared with control group and the mean serum IL-18 was highly significantly increased in group IIa compared with control group. The mean serum insulin, mean insulin resistance and mean FBG has no significant difference in group IIa when compared with control. The mean serum TG was highly significantly increased while mean serum HDL was highly significantly decreased in group I compared with control group. (Table 1 & fig. 1).

There were highly significant increase in mean WC, mean serum IL-18, mean serum insulin, mean insulin resistance and mean FBG, mean serum TG and highly significant decrease in serum HDL in group I compared with group IIa. While there were no significant difference in mean S.B.P. and mean D.B.P. in group I when compared with group IIa. (Table 2, fig. 2).

There were highly significant increase in mean WC, mean S.B.P. and mean D.B.P, mean serum IL-18, mean serum insulin, mean insulin resistance and mean serum TG and highly significant decrease in serum HDL in group I compared with group IIb. While there were no significant difference in FBG in group I when compared with group IIb. (Table 3).

There were highly significant decreased in the mean WC, mean serum insulin, mean insulin resistance and mean FBG in group IIa compared with group IIb and highly significant increase mean S.B.P. and mean D.B.P in group IIa compared with group IIb. While no significant difference in serum IL-18, mean serum H.D.L. and mean serum TG in group IIa when compared with group IIb (Table 4, Fig.1).

There were positive significant correlation between serum IL-18 and WC, serum insulin, FBG, insulin resistance and serum TG, while there was negative significant correlation between serum IL-18 and serum HDL in group I and IIb. (Table 5).

There were positive significant correlation between serum IL-18 and S.B.P and positive non significant correlation between IL18 and WC in group I and group IIa (Tale 5).

Discussion:

MetS is a strong predictor of type 2 diabetes, with an increased incidence rate of 5 to7-folds. The risk of developing CVD is approximately doubled in the MetS[3]. The physiologic mechanisms linking inflammation and MetS have not been clearly defined; their association may be partly mediated by adipose tissue[16].

Inflammation is characterized by elevated levels of acute phase proteins, such as fibrinogen and C-reactive protein (CRP), and elevated levels of such cytokines as IL-6 and TNF- α. All these biomarkers, which are CV risk factors at the same time, are markedly elevated in patients with MetS and DM[17].

Interleukin-18, a recently described member of the IL-1 cytokine superfamily, is now recognized as an important regulator of innate and acquired immune responses. IL-18 is expressed at sites of chronic inflammation, in autoimmune diseases, in a variety of cancers, and in the context of numerous infectious disease[10].

This study was performed to determine serum level of circulating IL-18 as a specific biomarker for distinguishing between MetS patients and pre-MetS subjects.

In the present study, mean serum IL-18 levels were found to be significantly higher in MetS patients (group I) compared with control group. These results agreed with Hung et al.,[18] and Herman et al.,[19] as they found that IL-18 levels were increased in patients with MetS.

Zirlik et al.,[9] found that elevated IL-18 plasma levels associated with risk factors for atherosclerosis and with MetS component when IL-18 plasma levels were determined in 2231 subjects from the Dallas Heart Study to investigates whether elevated IL-18 levels adds to traditional risk factors with coronary atherosclerosis in the general population or not.

Interestingly study carried out with Presta et al.,[20] and Opstad et al.,[21] showed that polymorphisms in the IL-18 gene was associated with increased serum levels of IL-18, impaired insulin sensitivity and increased risk of having MetS.

Trøseid et al[22] found that interleukin-18 were elevated in subjects with MetS and also when the cardiovascular events were recorded among them during the next 3 years they found that IL-18 was the strongest predictor for such events in subjects with MetS. This suggests not only implication of IL-18 in pathogenesis of MetS but also in subsequent complication.

Weiss et al.,[11] and Ahmad et al.,[23] found that expression of IL-18 was increased in subcutaneous adipose tissue of subjects with MetS and they concluded that subjects with MetS have a particular inflammatory pattern in adipose tissue (AT).

Stensvold et al.,[24] found that IL-18 seem to be the best marker for inflammation in MetS. Growing evidence suggests that IL-18 plays an important role in the development of MetS. Through a cascade of reactions, IL-18 stimulates inflammation and immune responses in the human body. In rats, over expression of IL-18 protein aggravated insulin resistance and led to enhanced vascular inflammation and remodelling [25].

Everett et al.,[26] found that higher circulating levels of IL-18 were associated with increased MetS scores and to predict type 2 diabetes, cardiovascular events, and mortality. These findings suggest that IL-18 dysfunction or resistance is a novel pathophysiological mechanism underlying insulin resistance and MetS.

We found that serum IL-18 levels were highly significant elevated in group I (MetS patients) than that of group II (Pre-MetS patients). In agreement with our results Yamaoka et al.,[6] found that IL-18 levels can be useful biomarker for distinguishing patients with MetS from subjects with pre-MetS condition, and higher circulating levels of IL-18 were associated with increased MetS score.

Also Herman et al.,[19] found that the number of MetS components identified is positively correlated only with IL-18 serum levels when he studied the links between low-grade inflammation, selected serum androgens and prevalence of MetS, according to NCEP and IDF criteria, in Polish men over the age of 40.

In the present study, mean serum IL-18 levels were found to be significantly higher in hypertensive patients (Group IIa) when compared with control group. In agreement with our result Rabkin,[27] reported that circulating levels of IL-18 increased in hypertensive patients.

Krishnan et al.,[28] found that there is a growing evidence to suggest that hypertension is associated with elevated production of the IL-1 family cytokines, IL-1β and IL-18. He reported that, it is not known-(at this stage) - whether elevated levels of IL-1β and IL-18 are causes or mere consequences of chronically elevated blood pressure and/or its disease sequel such as vascular remodelling, atherosclerosis and renal dysfunction.

IL-18 promote the proliferation and migration of vascular smooth muscle cells (VSMCs), processes that are critical to the vascular remodelling associated with and contributing to hypertension. The proliferative response of cultured VSMCs to angiotensin II was blocked followings iRNA-mediated knockdown of IL-18[29.]

Experimental evidence indicates that the expression of IL-18 and/or its receptor can be induced by catecholamines or angiotensin, which are involved in the pathophysiology of hypertension[27].

In the present study, mean serum IL-18 levels were found to be significantly higher in pr -metabolic diabetic patients (group IIb) compared with control group. Also Thorand et al.,[30] and Hivert et al.,[31] found that higher circulating plasma levels of IL-18 are associated with future diabetes incidence in a healthy cohort of middle aged women. This association was independent of well-known risk factors for diabetes, including obesity and dietary intake, and novel risk factors, including levels of adipokines. This could means that IL-18 may be implicated very early in the disease process.

Another study found that IL-18 increased in the diabetic patients with microangiopathy especially nephropathy. This suggests role of IL18 in pathogenesis of type 2 diabetes and its complication[32]. Also another studies found that elevated levels of plasma IL-18 were reported in T2DM patients[33,34].

Kadoglou et al.,[35] found that diabetic patient with hypercholesterolemia have elevated concentrations of matrix metalloproteinase's (MMP-7, MMP-8), IL-18, WBC and hsCRP. Importantly, atorvastatin treatment improved lipid profile, significantly reduced the concentrations of MMP-7, MMP-8, IL-18, WBC and hsCRP.

Sabuncu et al.,[36] found that serum IL-18 concentration was elevated in diabetic patient with acute diabetic foot ulcers. However these findings don't indicate whether the IL-18 elevation is a cause or result of diabetic foot ulceration.

In this study, mean serum IL-18 was non-significantly increased in hypertensive group patients compared with diabetic group although diabetic group had higher body mass index and waist circumference (WC). This result is in accordance with Vilarrasa et al.,[37]who found that no significant differences were found in IL-18 between obese and normal-weight men and women. This incensement may be due to different degree of 'IL-18 resistance' in studied group. IL-18 resistance' was first reported in a study of Zilverschoon et al.,[38] who compared obese vs. normal weight individuals, where peripheral blood mononuclear cells from obese individuals were shown to exhibit a reduced production of interferon-γ (IFN-γ) in response to IL-18 stimulation, or may be due to genetic variation.

These results suggested that IL-18-MetS association might not be exclusively mediated by excess adiposity, and lean mass might also play a potential role. This finding is supported by Fain[39] who reported that the non fat cells in human adipose tissue contribute to most of the release of IL-18 and one study from 144 healthy men reported that fat-free mass rather than fat mass was positively associated with serum IL-18[40].

Moreover, TNF-α infusion in men enhanced IL-18 mRNA expression in muscles, but not in adipose tissues[41]. Also Circulating IL-18 was positively correlated with lean mass index (LMI) (fat free mass) after adjustment for fat mass index (FMI) in study carried out by Sun et al.,[42].

In the present study we found that there was positive correlation between mean serum IL-18 and mean waist circumference (WC) in group I (MetS patients) and in group IIb (pre-metabolic diabetic patients). Also there was

positive correlation between mean serum IL-18 and mean S.B.P in group I and in group IIa (pre-metabolic hypertensive patients).

In agreement with our result Mabrouk et al.,[43] found that obese diabetic and non diabetic subjects had significantly higher serum IL-18, resistin, and visfatin levels than lean individuals as these proinflammatory proteins were found to be released predominantly by visceral white adipose tissue macrophages.

The present study showed that there was positive correlation between mean serum IL-18 and mean serum insulin, mean FBG and mean insulin resistance in group I and in group IIb. In agreement with our result Bruun et al,[44] found that plasma IL-18 and AT-mRNA expressions of IL-18, are increased in obese compared with lean subjects and regular moderate physical activity induced an increase in insulin sensitivity paralleled by a decrease in plasma IL-18 but was without effect on adipose tissue expression of IL-18. So IL-18 is associated with obesity, insulin resistance.

Previous researchs has reported a slight correlation between IL-18 and fasting plasma glucose in T2DM[45]. and between IL-18 and fasting plasma insulin in obese women[46].

In the present study: there was positive correlation between mean serum IL-18 and mean serum TG. While there was negative correlation between mean serum IL-18 and mean serum HDL in group I and in group II b. Olusi et al.,[47] found that serum IL-18 concentration was positively correlated with serum TG and glucose concentrations in both obese and diabetic subjects after controlling for the confounding effects of age, sex, and body mass index.

Also Evans et al.,[48] and Troseid et al.,[22] found that interlukin 18 has strong relation with dyslipidemia. Cornier et al.,[49] reported that IL-18 has a negative correlation with HDL. Also another study found that significant increase in serum IL-18 levels was accompanied with significant abnormal and atherogenic lipid profile[50].

In the present study there was no significant difference in mean insulin resistance in group IIa and control group. In agreement with our result Reaven[51] reported that insulin resistance is a fundamental defect in patients with type 2 diabetes; essentially all patients with type 2 diabetes are insulin-resistant. In contrast, essential hypertension occurs in insulin-sensitive individuals, and probably only 50% of persons with essential hypertension are insulin-resistant.

Conclusion:

Serum IL18 significantly increased in both MetS and pre-MetS than control but more in MetS. Circulating serum IL-18 levels could be a useful biomarker for distinguishing patients with MetS from patients with pre-MetS.

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