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Article

Gelatinase-Associated Lipocalin, Nitric Oxide, and Total Antioxidant Capacity in Patients with Metabolic Syndrome in Kirkuk Governorate

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Abstract: Metabolic syndrome (MetS) is a constellation of related cardiometabolic risk factors which increases the likelihood of developing cardiovascular diseases. NGAL, a 25 kDa protein released by neutrophils is associated witih various inflammatory and metabolic diseases. It has recently been demonstrated that all these diseases are primarily due to an increased burden of oxidative stress (OS) resulting from a switch in redox regulation. It appears that oxidative stress is the cause and even result of obesity and associated diseases. the present study conducted in kirkuk governorate during the period from December 2024 to June 2025, a measurement of the neutrophil gelatinase-associated lipocalin (NGAL) levels and lipid profile concentrations as well as total antioxidant capacity(TAC),, nitric oxide (NO), fasting serum glucose(FSG), glycated hemoglobin (HbA1c) and homocysteine that were done in 62 subjects with metabolic syndrome group and 30 healthy control group aged between (20–60) years old for both groups. It was found that: compared to the control group, average blood serum levels of Neutrophil gelatinase-associated lipocalin NGAL, FSG, LDL-B, TG concentrations of (LDL), VLDL and cholesterol and HbAc1 in people suffering with MS were statistically higher ($p \leq 0.05$). Results Serum NO, HDL as well as TAC were significantly decreased ($p \leq 0.05$) in patients with MetS than healthy controls.

Keywords: MetS, NGAL, lipid profile.nitric oxide, total antioxidant capacity.

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1. Introduction

The centre of the argument on metabolic syndrome (MetS) is whether abdominal obesity should or should not be a necessary presence [1]. Insulin resistance syndrome, dysmetabolic syndrome and syndrome X are other synonyms of metabolic syndrome. A medical diagnosis requires three of the five criteria in the revised definition to be met [2]. The variables as strict criterium as possible including low levels of HDL cholesterol, triglycerides, arterial blood pressure, fasting blood glucose and the waist circumference were all entered in the model. Sex and ethnicity-specific values are derived, as there were concerns regarding the differences in baseline waist circumference between the sexes and ethnic groups. Immune cells (IC) and adipocytes, hepatocyte, as well as other organs such as the kidney, prostate gland, and pancreas produce neutrophil gelatinase-associated lipocalin (NGAL) [3]. Under inflammatory and metabolic conditions adipocytes show high amounts of NGAL. NGAL is involved in carcinogenesis and increases inflammatory conditions along with high blood pressure, obesity, diabetes mellitus (DM), and metabolic disorders including insulin resistance. There was an association between SBP and plasma NGAL (4).

NOS derived from L-arginine is a source of NO production in the epithelium by NO synthesis. In this case, NO production may be inhibited by an absence of L-arginine, reduced enzyme activity and a decrease in the concentration of important cofactor [5].

Hypoxia of the tissue and blood decreased by 8 Chronic A Comparisons of the amounts of expression for eNOS and iNOS in kidney diseases [6]. The production of NO has been found to be decreased in patients with MetS. Furthermore, the late stage of disease is promoted by apoptosis and production of reactive oxygen species (ROS). In fact, reductions in oxidative stress and depletion of the antioxidant defence system (especially TAC) have been documented here in subjects with MetS due to an impaired mitochondrial respiratory system [7]. The near wall of the artery is subjected to oxidative stress and inflammation due to atherosclerosis. Inflammation can lead to oxidative stress, and oxidative stress can in turn trigger inflammation with subsequent cellular damage; hence they are linked [8]. Studies show that damage created by atherosclerotic vessels in the blood stream is caused by increased glucose and elevated cholesterol levels in those with this pathologic condition known as insulin resistance. One of the most important causes of hypertension is oxidation of the low density lipoprotein (LDL). Too much oxidized LDL can damage blood vessels and produce plaque and foam cells, which can contribute to atherosclerosis. Antioxidant defenses Antioxidative defense systems consist of several components: enzymes and inorganic substances which have the function of removing free radicals or preventing them, or failing that reducing their negative effects on living organisms [9]. Each of the antioxidants has a complex methodology requiring much time and costly experimentation. In this way it is possible to infer the total Antioxidant capacity (TAC) of a patient from the blood or serum, which then provides some information about the drought level of anti-oxidants inside a body. In studies of antioxidant systems the enzymatic one was a significant factor controlling ROS level [10]. The first line of defense is nitric oxide (NO) that consists TAC. To evaluate the enzymatic antioxidant system, we propose an antioxidant enzyme for this purpose taken from scientific literature. Very few studies have compared the levels of antioxidant in MetS patients 11.

The Aim of the Study:

The goal of the study is to evaluate the role of serum TAC, NO and NGAL in female metabolic syndrome (MetS) subjects with diabetes.

2. Materials and Methods

Study design and idividuals

A total of 62 patients (32 females, and 30 males) with metabolic syndrome (MetS) were recruited from Kirkuk Teaching Hospital, Azadi Teaching Hospital, and private physicians' clinics over the period from December 2024 to June 2025. They were -compared with 30 healthy subjects as a control group (15 females =+ 15 males) and their age ranged from 20 –to60years.

Measurements of biochemical variables

5ml fasting vein blood samples were taken and centrifuged after 20 minutes in 3000 rpm, serum was separated immediately or stored at -70 °C for further analysis.Whole blood sample with EDTA were used for the detection of HbA1c..NGAL、NO、 total antioxidant capacity (TAC)Value were measured by method of ELISA kit (Cloud-Clone Corp\ USA). Lipid profile and fasting serum glucose (FSG) were measured using a spectrophotometer, the device that employs standard colorimetric methods (Diamond Diagnostics, Egypt) and AF1.QS_4 producing to measure the amount of HbA1c in the sample.

Statistical analysis

Data were analysed by ANOVA test using SPSS software version 26. Mean ± SD was considered to represent each of the study parameters. Correlation between two biomarkers was analyzed using Pearson's correlation coefficient. Figures are prepared with the Microsoft Excel program.

3. Results and Discussion

Table 1. Demographics of the patients with MetS and healthy controls in sex, age, and BMI. The results indicated that no important differences ($p \leq 0.05$) were found between the

patients and control subjects and significant differences (p≤ 0.05) were observed for BMI of the MetS patients and healthy controls [12].

Table 1. Demographic characteristics of the study

Group	MetS patients	Healthy controls	P-value
Sex			
(Males %)	30	15	----
(Females %)	32	15	
Total	62	30	
Age (years) Mean ± SD	49.19 ± 16.21	48.25 ± 12.40	0.651
BMI ((Kg/m²) Mean ± SD	33.25	24.10	0.001

(p≤ 0.05) significant

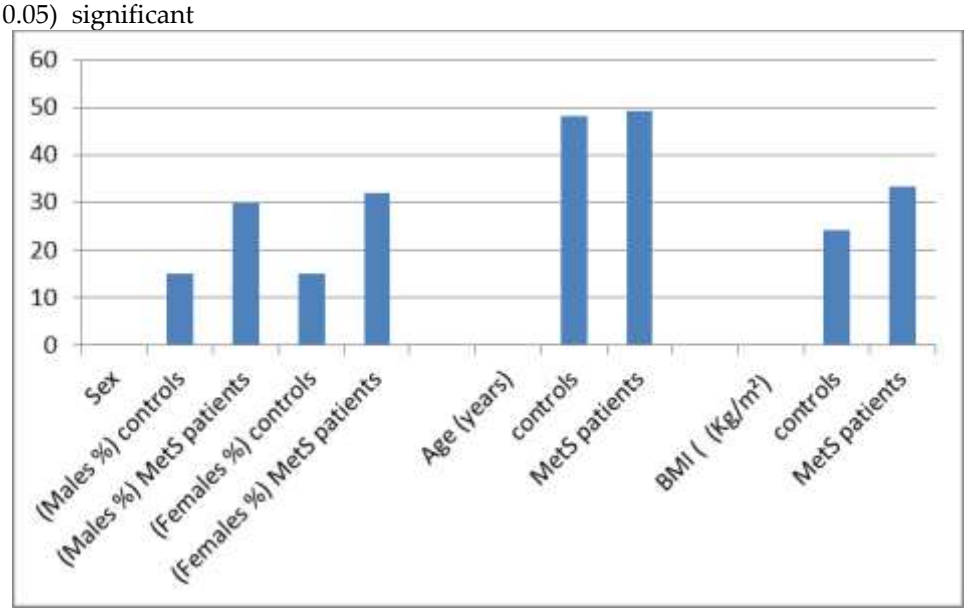


Figure 1. Participants demographic data

Neutrophil gelatinase-associated lipocalin, Total antioxidant capacity (TAC), Nitric oxide(NO), fasting serum glucose (FSG) and glycated hemoglobin (HbA1c) were investigated in the current study in this case of MetS compared to the control subjects as shown in Figure 1[13]. The mean blood levels of NGAL, FSG and HbA1c among patients with MetS were significantly higher (p≤ 0.05) than those in the control subjects as presented in Table 2. Nitric oxide (NO), and total antioxidant capacity (TAC) were significantly decreased (p≤ 0.05) in MetS patients compared to control [14].

Table 2. The serum levels of NGAL, TAC, NO, FSG and HbA1c % among the different study groups.

Parameters	Metabolic syndrome Patients (MetS) (mean ± SD) n= 60	Healthy controls (mean ± SD) n= 30	P- Value
NGAL(Pg/ml)	569.04 ± 23.92	110.21 ± 17.59	0.003
TAC (mμ/l)	1.63 ± 0.05	3.49 ± 0.12	0.001
NO (μmol/l)	4.31 ± 0.07	8.96 ± 0.14	0.001
FSG (mg/dL)	266.14 ± 7.43	92	0.000

HbA1c %	7.72	4.1%	0.001

P ≤ 0.05 significant

Table 3. shows the significant difference (P ≤ 0.05) of the concentrations of serum lipid profile between patients with metabolic syndrome and control group. The levels of MDA, LDL, VLDL, TG in patients with MetS Comparing with controls were significantly (P ≤ 0.05) higher; however, the mean of HDL concentration was recorded to be significantly decreased (P ≤ 0.05) in these patients when compared with normal individuals [15]. The cholesterol level was not significantly higher (P > 0.05) for MetS patients than in healthy individuals [16].

Table 3. Comparison of lipid profile among Patients with MetS vs. control group.

Parameters	Metabolic syndrome Patients (MetS) (mean ± SD) n= 62	Healthy controls (mean ± SD) n= 30	P- Value
Cholesterol (mg/dL)	169.03 ± 5.78	164.45 ± 8.65	0.075
Triglycerides (mg/dL)	199.47 ± 6.42	131.34 ± 7.83	0.001
HDL (mg/dL)	36.76 ± 4.63	53.56 ± 5.29	0.001
LDL (mg/dL)	139 ± 5.54	86.23 ± 7.21	0.000
VLDL (mg/dL)	45.84 ± 3.56	21.03 ± 2.01	0.003

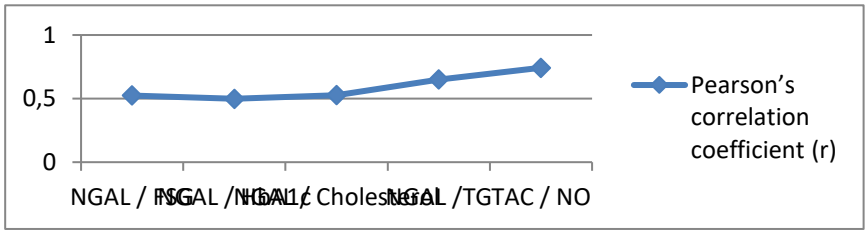
Table 4. The rate of correct diagnosis by single markers to distinguish the MetS patients from Controls.

Parameters	Control vs. patients				
	Cut off	AUC	Sensitivity	Specificity	P
NGAL	≥ 274.92	0.88	90.0%	85%	0.001
TAC	≥ 1.53	0.47	87.9%	89%	0.521
NO	≥ 4.25	0.79	80.3%	77%	0.001

AUC: Area under the ROC curve. P > 0.05 non significant . P ≤ 0.05 significant.

Table 5. NGAL, NO, and TAC correlations with some parameters in patients with metabolic syndrome.

Parameters	Pearson's correlation coefficient (r)	P-value
NGAL / FSG	0.524	0.004
NGAL / HbA1c	0.498	0.001
TAC / FSG	- 0.646	0.032
TAC / HbA1c	- 0.398	0.012
NO / FSG	- 0.297	0.021
NO / HbA1c	- 0.813	0.001
NGAL / Cholesterol	+ 0.527	0.023
NGAL /TG	+ 0.649	0.001
TAC / Cholesterol	- 0.256	0.017
TAC TG	- 0.650	0.006
NO / Cholesterol	- 0.528	0.010
NO / TG	-0.648	0.001
NGAL / TAC	- 0.312	0.003
NGAL / NO	- 0.616	0.001
TAC / NO	+ 0.741	0.031



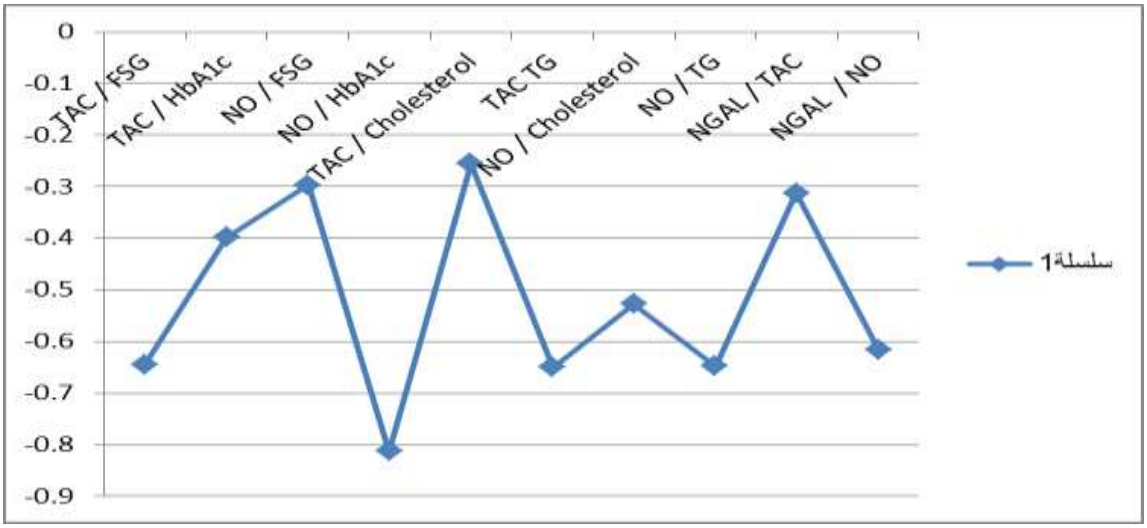


Figure 2. Correlation Values Between Oxidative Stress Markers and Biochemical Parameters

As it is follows from obtained data the results found in patients with MMM are as much as comparable to those published by Tomczak et al. who established analogous connections of NGAL and components of metabolic syndrome among hypertensive individuals [17]. Another study also found higher serum NGAL levels in hypertensive patients (Table 4).

This study agrees with previous Singer et al. 's observation that the NGAL concentrations in both control and ELISA groups were presented significantly higher [18].

Besides, NGAL was involved in inflammation and is elevated in metabolic diseases which power arterial hypertension, obesity, diabetes, and metabolic syndrome [19]. This article describes the current knowledge on NGAL and its implication in several diseases and phenotypes, including cardiovascular and renal disordersTable 5.

By some studies, the amounts of NGAL in serum could be predicted and found to be correlated to metabolic disturbances, which is induced by obesity [20]. NGAL is independently related to SBP, as well as to dyslipidemic disorders or insulin resistance. The mechanism by which NGAL may play a role in the pathophysiology of obesity is unknown [21].

With metabolic syndrome (MetS), decreased nitric oxide (NO) levels and bioavailability contribute to the characteristic biometabolic and cardiovascular disarrays. Besides its numerous beneficial effects, NO is crucial for the regulation of dilatation/relaxation of blood vessels, inhibition of platelet aggregation and as an antioxidant [22]. One crucial component of the MetS is endothelial dysfunction, which is associated with changes in NO signaling (Figure 2).

NOS supplements with the NOS cofactor tetrahydrobiopterin (BH4) or substrate sepiapterin could also be considered as potentially preventing uncoupling to reduce oxidative stress in humans. BH4 can improve endothelial dysfunction in patients with hypertension, CAD and hypercholesterolaemia [23]. These pre-clinical studies do so, however, despite two or more randomized controlled trials that have definitively excluded

the possibility of an improved circulatory fate from folate supplementation, and in the absence altogether of evidence for either BH4 or analogous compounds on CVD morbidity and mortality [24].

These data of the present study that hypertensive patients have lower TAC, NO and higher NGAL compared to controls is in line with previous findings by Mousa et al. and Yarube et al., which indicated that the antioxidant capacity and NO of hypertensive subjects were decreased [25]. The increased circulating NGAL in patients with CVDs may indicate higher nitric oxide (NO) production that can be involved on the starting and progression of atherosclerosis. A pilot study performed by Shademan et al [26] A significantly lower TAC in participants with CVDs than healthy individuals was found. Additional studies have also proposed a relationship between CVDs and low total antioxidant capacity. In addition, it was demonstrated that NGAL levels presented significantly higher values in individuals with CVDs. As NGAL was significantly higher in patients with atherosclerosis who had difficulty vs. without, Mahreen et al. provided indication that it could be a predictor for diabetic complications. All these studies refer to a potential relationship between high NGAL, atherosclerosis and reduced NO and TAC [27].

TG/HDL, LDL/HDL and non-HDL/HDL can be used for diagnosis of MetS in the Iranian population according to the results of the Iranian survey. It is important to determine some useful criteria with which to distinguish healthy adults from those suffering from MetS, since early identification of the syndrome could prevent serious complications. Based on NCEP ATP III criteria, the findings of the study indicated that TG/HDL-C was superior to the non-HDL ratio and LDL-C/HDL-C for predicting metabolic syndrome in elderly individuals [28].

The association in Met had also been found by other lipid profiles. S. Kimm et al. revealed that TC/HDL-C, LDL-C/HDLC, B TG/HDL-C and TG and HDL" werenot only significantly associated with the number of metabolic syndrome components^ insulin resistance839 ^ aogTFansformed proteins described as quartiles (homeostatic model assessment)UP affiliations. Markers based on both single and combined ratios may predict the risk for CVD better than single lipid markers such as TG or HDL-C [29].

These results are in agreement with the present study. There are some limitations of this trial that should be considered. First, the response rate as usual with other traditional community-based studies in Iraq was very low (35%). However, the relatively high number of participants allowed finding associations between these lipid profile related MetS variables. Second, the effect of visceral adiposity on MetS might have been underestimated because the cross-sectional design has low power to exclude the causal role of lipid parameters and factors associated with the MetS. The generalizability of the findings may therefore be limited by demographic characteristics and how patients are referred [30]. The present study suggests that within a larger population, specific lipid profiles are associated with traits of MetS. Temporal stability of metabolic syndrome inpatients based on compiled criteria Valtteri Kankaanpää et al. 2 Healthcare professionals can more easily apply lifestyle modifications whenMetS patients are identifiable. In such background, the utility of LDL-C/HDL- C ratio or TG/HDL-C ratio described in this paper for usage is simple and helpful. Further research with the use of populations is necessary to explore a link between lifestyle changes and lipid metabolism [31].

4. Conclusion

The diagnostic capabilities of metabolic syndrome are being improved by new scores based on NGAL, NO and TAC. Indeed NGAL is itself the pathogenetic factor of the metabolic syndrome[29] and NO is an oxidant stress signal/and angiogenic marker. Moreover, TAC accentuates the involvement of oxidative stress in metabolic syndrome

development. demonstrated significant correlation between lipid profiles MetS level and adult MetS in Iraqi community.

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