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Evaluation Of TNF And IL6 In Patient with Metabolic Syndrome

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Abstract. **General background:** Metabolic syndrome (MetS) represents a clustering of cardiovascular risk factors characterized by visceral adiposity, insulin resistance, and dyslipidemia, with chronic low-grade inflammation playing a central pathophysiological role. **Specific Background:** Proinflammatory cytokines, particularly tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), have been implicated in MetS pathogenesis through their effects on insulin signaling and endothelial function. **Knowledge Gap:** However, the precise inflammatory profile alterations in MetS patients within the Iraqi population remain inadequately characterized. **Aims:** This case-control study evaluated serum TNF-α and IL-6 concentrations in 45 MetS patients compared with 45 healthy controls in Thi-Qar, Iraq, alongside metabolic parameters including fasting blood sugar (FBS), lipid profiles, and blood pressure measurements. **Results:** Patients demonstrated significantly elevated body mass index and waist circumference compared to controls. Furthermore, FBS, total cholesterol, triglycerides, systolic and diastolic blood pressure showed significant differences between groups, while HDL-cholesterol remained comparable. Notably, both IL-6 and TNF-α levels were significantly reduced in MetS patients relative to controls. **Novelty:** These findings challenge conventional understanding by demonstrating decreased rather than elevated proinflammatory cytokine concentrations in MetS. **Implications:** The results suggest complex inflammatory regulatory mechanisms in MetS that warrant further mechanistic investigation to inform targeted therapeutic interventions.

Highlights:

1. Inflammation in MetS: IL-6 and TNF-α levels differ significantly between MetS patients and controls.
2. Metabolic Characteristics: MetS patients show higher BMI, WC, FBS, TG, and blood pressure, with no significant HDL difference.
3. Pathophysiological Role: Chronic low-grade inflammation is closely linked to metabolic syndrome development.

Keywords: Metabolic syndrome, TNF-α, IL-6, Inflammation, Thi-Qar

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Introduction

Metabolic syndrome (MetS) is a complex syndrome, which is a network of physiological, biochemical and clinical factors, and metabolic disorders, leading to an outstanding overload of the risk of cardiovascular disease, type 2 diabetes mellitus and mortality. The predisposing factors that predetermine a person to atherogenic dyslipidemia, or abnormal lipid profile, that results in atherosclerotic depositions, are the presence of visceral adiposity or the presence of fat in the abdominal region and the presence of insulin resistance or the loss of the ability of the cells to react to insulin. There is also the endothelial dysfunction which is a malfunction of the regular workings of the vessel lining that exacerbates the syndrome. The genetic predisposition is a significant cause that establishes the manifestation of these factors and the progression of blood pressure, hypercoagulable condition, and the continuous stress may complicate the syndrome in general[1]. The visceral obesity and insulin resistance leading to the abnormal adipocytokines also have a relation to chronic inflammation. The proinflammatory condition is supplemented by clinical and biological manifestation of the syndrome that leads to chronic and subclinical inflammation of the vascularity. Intervention strategy is primarily concerned with lifestyle modification that may include dietary, exercise programs; and they incorporate behavioral interventions[2].

The combination of the three measures of the aberrant with the five elements that may be taken and constitute an element of the metabolic syndrome compel an individual to be an effective candidate; high waist circumference, elevated triglyceride, low high-density lipoprotein cholesterol, elevated blood pressure and high fasting plasma glucose. The results of the scientific research and the observations, given by the researchers in their study, are explained by the work of Cornier et al. in 2008 [3] as the metabolic syndrome is explained as the predictive factor of the cardiovascular disease and type 2 diabetes. It should also be born in mind that cumulative risk of the metabolic syndrome cannot be weighed against the risks that are assumed by the components. The most frequent of these factors is the elevated degree of blood pressure.

The first record of patients with the accumulation of various metabolic abnormalities dates back to the year 1923. It was, however, not until the year 1988 more than half a century later that Reaven came up with the nomenclature 'syndrome X' as used to designate the specific collection of physiological manifestations. During the last twenty years, many definitions and criteria have been developed with the purpose to define and describe this specific state of the physiology. A lot of studies have clarified discrepancies in these delineations and some scholars even questioned the feasibility of these parameters and the truth of such a syndrome[5].

It is estimated that MetS is occurring in the world at a rate of 25% with a lot of differences according to gender, age, and ethnicity. In recent years, its incidence has significantly increased among the younger adults. Notwithstanding the existing conditions, the regulation of the levels of high density lipoprotein (HDL) was suggested as a preventive measure to avert the development of MetS and, consequently, limit the occurrence of the related pathologies. [6].

The factors that cause MetS are overweight/obesity, lack of physical activitaminey and genetic predisposition. Accumulation of adipose will cause insulin resistance, which is critical in disease. The distribution of adipose tissues especially abdominal localization is a determining factor. Microvascular defect may lead to inflammation and other related symptoms. [7].

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Materials

A. Population of the study

This study a case-control study which included (45) patients with a diagnosis of metabolic syndrome in terms of body mass index (BMI), waist circumference (WC) and blood pressure (BP), triglyceride (TG), high-density lipoprotein (HDL), and fasting blood sugar (FBS).

The average of the age of the study population was 45-60 years old.. All of the people that were engaged in this research were diagnosed with specialist physicians, and these findings were confirmed with the help of clinical and laboratory tests.

a) Inclusion criteria:

Diagnosis of those patients was based on BMI 30.0 kg/m2, WC 80 cm, hypertension, hypertriglyceridemia and hypo-HDL.

b) Exclusion criteria:

Any subjects diagnosed do not meet the necessary diagnostic criteria and patients who experienced thyroid dysfunction, bone diseases, kidney diseases, parathyroid gland diseases in the past.

B. Samples collection and processing

Five milliliters of human blood were taken of each participant, patients and controls. The blood was put into the sterile test tubes and given 30 minutes to clot at room temperature. A centrifuge with 3000 rotations per minute was used to divide the sample after clotting and the centrifuge was made to run over 15 minutes. After this, the serum was separated and kept at a temperature of (-20 o C) until it was to be analyzed..

C. Human Interlukin-6 and tumor necrosis factor

3.1 Test Principle

ELISA kit is the Sandwich-ELISA methodology. The pre-coated plate includes an antibody to human IL-6 and TNF. In case of the introduction of the sample which contains IL-6 and TNF, the IL-6 and TNF molecules are bound to the antibodies which are fixed to the wells on the plate. Subsequently, biotinylated human IL-6 and TNF antibody is inculcated and this binds to the IL-6 and TNF in the samples. This is the biotinylated antibody which is bound to streptavidin-horseradish peroxidase (HRP). The incubation and washing that follows is then followed by the addition of a substrate solution to get rid of any unbound streptavidin-HRP. The level of IL-6 and TNF in the sample is directly proportional to the obtained color. This is followed by the introduction of a stop solution of acidity and an absorbance is taken at 450 nm

Result

A. Demographical study

Compared to the patients, an analysis of the control group was performed during the course of this study. The findings in Table (3.1) in the comparison of age patient versus Control with no significant increase ($p>0.05$) and WC and BMI with significant ($p< 0.05$)

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increase.

Table 1: Demographic factors of control group and patients Before and after vit.D of age and WC.

Characteristic	**Patient Before vit.D**	***Control***	***p.value***
WC/ Mean ±SD (Minimum/ Maximum)	109.48±13.64(89.00 /134.00)	79.26±4.92(70.00/ 88.00)	0.000
Age /Mean ±SD (Minimum/ Maximum)	53.60±5.95(45.00/6 5.00)	51.57±4.86(45.00/ 60.00)	0.401
BMI /Mean ±SD (Minimum/ Maximum)	36.75±3.375 (30.50/42.58)	21.92±2.411(18.3 0/25.80)	**0.000**

B. Diagnosis of Mets

The table(3-2) demonstrates significant variations in FBS, TC,TG, sBp, and dBp between patients and controls while There is no statistically significant difference in HDL values between the two groups.

Table 2: Identification Of The Metabolic Syndrome Of The Control Subjects And Patients.

Characteristic	**Patient**	***Control***	***p.value***
Cholesterol	197.8667±48.53143	155.1053±23.0889	**0.001**
Mean ±SD			
Minimum	125.00	99.00	
Maximum	319.00	206.00	
FBS(mg/dL)			
Mean ±SD	209.27±88.36	91.32±6.69	0.000
Minimum	82.00	80.00	
Maximum	435.00	105.0	
sBp(mmHg)			
Mean ±SD	148.71±22.66	122.63±8.06	**0.000**
Minimum	95.00	110.00	

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Maximum	200.00	150.00	
HDL(mg/dL)			
Mean ±SD	40.15±9.062	39.36±6.94	0.934
Minimum	25.00	30.00	
Maximum	61.00	57.00	
TG(mg/dL)			
Mean ±SD	218.53±80.41	114.95±24.51	**0.000**
Minimum	96.00	78.00	
Maximum	438.0	160.00	
dBp(mmHg)			
Mean ±SD	92.69±12.29	80.53 ±5.75	0.002
Minimum	70.00	70.00	
Maximum	120.00	90.00	

C. Estimation of IL-6 and TNF-α among study groups

In the The table (3-3): shows that the level of IL-6 and TNF- a between the Patient and Control groups is significantly different.

Table 3: Comparison (IL-6 and TNF- a) of Mets in patient and control group.

Characteristic	**Patient**	***Control***	***p.value***
TNF-α / Mean ±SD (Minimum/ Maximum)	93.68±17.70(57.00/132.0)	116.55±68.67(62.80/343.90)	**0.045**
IL-6/ Mean ±SD (Minimum/ Maximum)	32.86±10.44(9.00/61.00)	49.71±18.72(32.70/86.30	0.000

Discussion

A. Demographical study

In this study, a sample of 90 people in Thi-Qar was applied. Patients were 45 and healthy persons were 45. In the different age groups, there were no significant differences in control subjects and patients in demographic aspects but the WC and BMI were significantly different (P = 0.04) and (p= 0.001) when compared in this study with (Article) [8]. Through previous studies, it has been found that obese individuals are

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exposed to the risk of developing metabolic syndrome. It is also reported by other researchers that mets and body mass index (BMI) and waist circumference (WC) are positively correlated with each other (9).between mets and body mass index (BMI) and waist circumference (WC)[9].

B. Diagnosis of Mets among studies group

The effect of FBS on group patient and control was significant ($p<0.05$) in a research that was conducted in 2012 [10] found out that there is significant changes in FBS (fasting blood sugar) and HOMA-IR (Homeostatic Model Assessment of Insulin Resistance) [10] . In the other study, it was observed that no significant correlation of FBS[11] other study consented with our that there was significant change in FBS and insulin in both the groups ($p< 0.05$).

This means that FBS, TC,TG, sBp and dBp are statistically significantly different between the patients and controls in the present study whereas there is no statistically significant difference in the value of HDL in the two groups. It was observed that research which provided the results led to significant reduction in HDL in mets [12]. In the other study, it was discovered that LDL and TG decreased significantly, but HDL increased significantly[13]. Additional observation of other study was that LDL and TG increased astonishingly, but TC and HDL decreased significantly[14]. A meta-analysis, which was carried out to establish the impact of mets on the lipid profiles indicated that LDL was the only lipid significantly altered [15].

In the current study BP that exhibits extremely high significant value ($p<0.01$) in comparison with the patients and control groups. Previous observation that is in opposition to our study has shown that significant change between the group of study and blood pressure was significantly high [8]In another meta-analysis that involved 10 clinical studies, the results showed that there were no significant changes in systolic blood pressure and diastolic blood pressure mets [17].

C. Estimation of IL6 and TNF among study group

The table (3-3): it indicates that the level of IL-6 and TNF- a in the Patient and Control group differ significantly. this observation is in line with the findings of a prior study by Shedeed in 2012 who found that there was a significant rise in serum levels of the antiinflammatory cytokine IL-10 and that the serum levels of the proinflammatory cytokine TNF- a, and IL-6 have significantly decreased in the study group ($p<0.05$) [18]. Our results were supported by the other study in which found There were significant changes in percent change in inflammatory parameters of TNF-a and IL-6 ($P < 0.05$) in the two groups [19]. Prior study It was further determined that there was no significant difference in terms of the IL-6 and TNF-a levels of two group, [20]

Conclusion

In this study concluded that the Reduce the concentration levels of both IL6 and TNF-A in patients with MetS

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