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RESEARCH ARTICLE

METABOLIC SYNDROME VERSUS ITS INDIVIDUAL COMPONENTS AND ANGIOGRAPHIC SEVERITY OF CORONARY ARTERY DISEASE.

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Key words:-
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Abstract

Background: Metabolic syndrome (MetS) is a cluster of metabolic traits that confer high risk for coronary artery disease (CAD). This study aimed to assess the relationship between MetS components and severity of CAD .

Methods : Eighty six patients underwent elective coronary angiography, calculation of the metabolic risk score and laboratory evaluation. Patients divided into two groups according to the presence of MetS: group A; 64 patients with ≥ 3MetS components and group B; 22 patients with< 3 components. Assessment of CAD severity using Gensini score.

Results:- There were significant difference between the both groups concerning body mass index, high blood pressure, triglyceride, high density lipoprotein, fasting blood glucose (FBG), serum insulin, insulin resistance and Genseni score ($P < 0.05$) . Significant positive correlation between MetS score and Genseni score ($P< 0.000$). Multivariate analysis showed that MetS itself did not predict the presence of CAD ($p= 0.49$), howevere some individual component of MetS show significant predictive value; namely, high FBG > 110 mg/dl (OR 23.748, $p<0.001$), high TGs > 150 mg/dl (OR 7.35, $p =0.012$) and high blood pressure(OR 6.07, $p= 0.02$).

Conclusion: - Fasting blood glucose**,** high triglyceride and blood pressure were independent predictors CAD rather than metabolic syndrome itself. FBG was the most independent factor that predicts CAD.

Introduction:-

Metabolic syndrome (MetS) remains a heterogeneous disorder with multiple factors that commonly cluster together. This heterogeneity creates a challenge for its definition. [1] Different diagnostic criteria were ideintified; World Health Organization (WHO), National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATP III), and the International Diabetes Federation (IDF). Each organization defines MetS and its required components somewhat differently, suggesting that estimates of MetS prevalence in the same population could differ according to the MetS definition used. [2] MetS according to NCEP/ATP III; refers to a constellation of five risk factors. These include out-of-range waist circumference [for women >35 inches (89cm); men>40 inches (102 cm)], triglyceride levels above 150 mg/dL, low high-density lipoprotein (HDL) cholesterol levels [women <50mg/dL; men <40mg/dL, high blood pressure [>130/85mmHg], and an elevated fasting blood sugar level [>100 mg/dL]. An individual with at least three of these risk factors qualifies as having MetS .[3] Patients with MetS have an estimated relative risk (RR)

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of 2.35 (2.02–2.73) for CVD, their RR for CVD mortality after adjusting for diabetes and conventional risk factors is estimated 1.39 (1.03–1.86). [4] Even among individuals with angiographically significant coronary artery disease (CAD), the hazard ratio for cardiovascular events is much greater in those with MetS compared with those without **.[5]**

Objective:-
The study aimed to assess the relationship between MetS components and CAD severity and to determine the most predictive risk factor for CAD in patients with metabolic syndrome.

Patients and methods:-

Participants were 86 patients with an evidence of suspected CAD whom were scheduled for elective coronary angiography 48(55.8%) males and 38(44.2%) females. Patients with previous PCI, CABG, patients on chronic hemodialysis, and systemic diseases were excluded**.**

All patients are subjected to full history taking including risk for CAD assessed using standard questionnaires Height and weight were measured. BMI was calculated by the formula, BMI= Body weight (Kg)/ Height (m2) (The Quetelet Index). [6] Waist circumference was measured in standing subjects midway between the inferior lateral margin of the ribs and the superior lateral border of the iliac crest. Systolic and diastolic blood pressure was measured three times in seated resting subjects by certified staff according to a standard protocol. Hypertension was defined as systolic blood pressure ≥140 and/or diastolic ≥90 mmHg or use of antihypertensive medication.

Laboratory work up:-
Venous sampling was collected in the early morning after an overnight fasting prior to elective coronary angiography for fasting plasma glucose (FPG), Fasting serum triglyceride level (TG), Fasting serum high-density lipoprotein level (HDL), Fasting serum insulin and insulin resistance was evaluated by the homeostatic model assessment (HOMA). HOMA index= [{fasting insulin (U/mL)} × {fasting glucose (mmol/L)}] / 22.5. [7]

Calculation of metabolic syndrome score:-
Using NCEP/ATP III, those who had ≥3 of 5 components were classified as having MetS. [3] The patients were divided into two groups according to MetS for each patient.

Coronary angiography:-
All patients had undergone coronary angiography. Digital coronary angiograms were analyzed offline with an automated edge detection system (Philips Integris 5000, Netherland) and patients with proved CAD were included in the study. Calculation of Gensini score for each patient and percent diameter stenosis (DS) expressed as 25, 50, 75, 90, 99, and 100 was scored as 1, 2, 4, 8, 16, and 32, respectively. Then the score was multiplied by × 0.5, × 1, × 1.5, × 2.5, or × 5 according to the segment where the lesion was located. After the score of each lesion was calculated, they were all added together to produce the severity score for the entire coronary system. [8]

Ethics:-
Informed parental consent was obtained to be eligible for enrollment into the study. The study was done according to the rules of the Local Ethics Committee of Faculty of Medicine, Zagazig University, Egypt.

Statistical analysis:-
SPSS 20 (SPSS Science, Chicago, IL, USA) for Windows was used for statistical analysis. Continuous variables are presented as mean± standard deviation (SD), and categorical variables as percentages. Comparison of categorical and continuous variables between the two groups was performed using chi-square test and independent sample t test, respectively. Linear regression analysis was used to test univariate relations. A P value <0.05 was considered statistically significant.

Results:-

Patients were divided according to the components of MetS into group (A); with ≥3 components of MetS (64 patients, 74.4%) and group (B) who have < 3 components of MetS (22 patients, 25.6%). 48 patients were males (55.8%) and 38 patients were females (44.2%). Age of the patients was 55.48±6.22 years, 31 patients (36%) were current smokers, 45 patients (52.3%) were hypertensive, 51 patients (59.3%) were diabetic and 44 patients (51.2%)

had positive family history of CAD. The weight was 81.14±12.57 kg and the height was 1.68±9.37cm. Demographic and risk factors for CAD were comparable between both groups with no significant statistical difference regarding age, sex, smoking, height or risk factors for CAD (hypertension, diabetes, and positive family history) (table1).

Table 1:- Demographic data and risk factors in the two study groups.

Variable		Group (A) (n=64)	Group (B) (n=22)	P-Value
Age X ±SD		56.11 ± 6.45	53.68± 5.20	0.115
Gender	**Female**	32(50%)	16(72.7%)	0.133
	Male	32(50%)	6(27.3%)	
HTN		36(56.3%)	9(40.9%)	0.229
DM		41(64.1%)	10(45. 5%)	0.140
Smokers		20(31.2%)	11(50%)	0.130
Family History		30(46.9%)	14(63.6%)	0.220

There was a significant statistical difference between both groups regarding clinical and biochemical characteristics; weight, BMI, high blood pressure, all were significantly higher in-group A ($p<0.05$). (Table 2).

Table 2 :- Clinical Characteristics of both studied groups.

Variable X ±SD	Group (A) (n=64)	Group (B) (n=22)	P-Value
Height	168±10.1	170± 6.65	0.211
Weight	84.88±11.22	70.27± 9.78	0.000
BMI	30.191±3.3238	24.191± 3.3208	0.000
High BP	48(75%)	11(50%)	0.036

Regarding the biochemical variants of MetS; statistically, there was a significant difference between the two groups; TG, HDL, FBG, the fasting serum insulin and HOMA index. They were all significantly higher in group A ($p <0.05$) (table 3).

Table 3:- Biochemical characteristics of both studied groups.

Variable X ±SD	Group (A) (n=64)	Group (B) (n=22)	P-Value
TG	193.20 ± 57.49	155.27± 41.63	0.006
HDL	51.88 ± 15.33	64.55± 17.89	0.002
FBG	170.80 ± 75.68	109.05±61.721	0.001
fasting serum insulin	14.73 ± 10.43	9.74 ± 6.93	0.014
insulin resistance	3.5 ±2.4	2.8 ±1.7	0.014

Regarding the angiographic criteria*:* In Group (A); 50 patients (78.1%) had significant CAD while there were 14 patients (21.9%) who had normal or non-significant CAD. Ten patients had single vessel disease (15.6%), 21 patients had two vessels disease (32.8%), 19 patients had three vessels disease (29.7%). Gensini score for this group was 52.65±38.93.

In Group (B); there were 6 patients with significant CAD (27.3%), only 1 of them had single vessel disease (4.5%), 3 patients had two vessels disease (13.6%) and 2 patients had three vessels disease (9.1%). There were 16 patients (72.7%) with normal or non-significant CAD. Gensini score for this group was 11.93 ± 21.35. We demonstrated a significant difference between both groups regarding the presence of CAD and Genseni score ($p< 0.05$) (Table 4).

Table 4:- Coronary angiographic Characteristics of both studied groups.

Group (A) (n=64)	**Group (B) (n=22)**	**P-Value**	
Geneni score	52.65 ± 38.93	11.93 ± 21.35	0.000
CAD	50(78.1%)	6(27.3%)	0.000
Single vessel disease	10(15.6%)	1(4.5%)	
Two vessels disease	21(32.8%)	3(13.6%)	
Three vessels disease	19(29.7%)	2(9.1%)	
Normal or minimal	14(21.9%)	16(72.7%)	0 .000

There were statistically significant positive correlation between metabolic syndrome score and Genseni score ($p<0.05$) (Table 5, Figure 1).

Table 5:- Correlation between metabolic syndrome score and Genseni score.

	R	**P**
Metabolic syndrome score and Genseni score	0.499	0.000

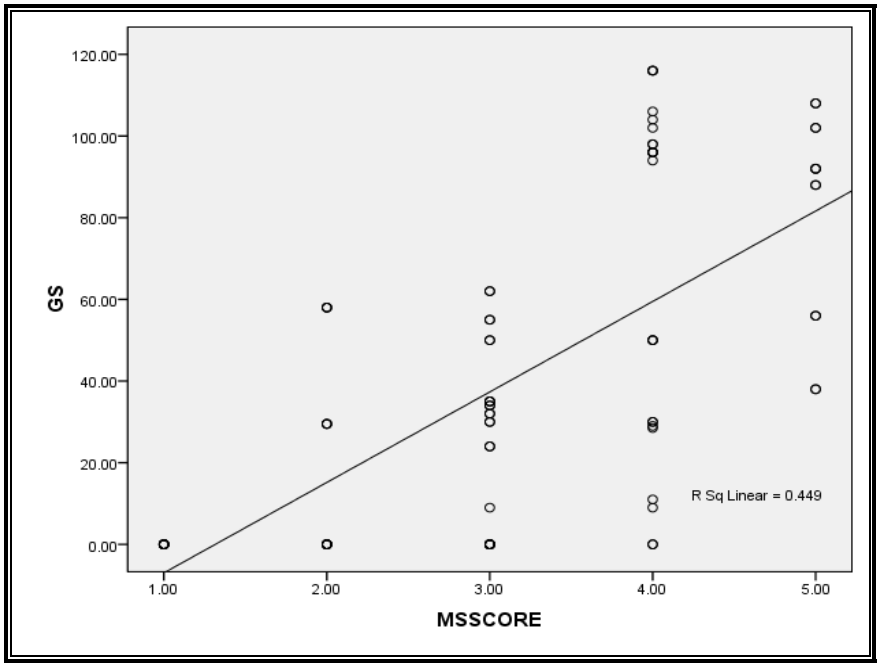

Figure 1:- A scatter diagram is showing significant positive correlation between metabolic syndrome score and Gensini score.

Multivariate regression analysis showed that metabolic syndrome itself did not predict the presence of CAD (OR 0.451, p = 0.489). Instead some individual component of metabolic syndrome show significant predictive value; namely, high FBG more than 110 mg/dl (OR 23.748,p< 0.001), high TGs > 150 mg/dl (OR 7.349,p = 0.019) and high blood pressure > 130/ 85 mmHg (OR 6.074,p= 0.023). FBG is the most independent factor that predicts CAD. (Table 6).

Table 6:- Multiple clinical and biochemical parameters as determinants of angiographic coronary artery disease in multivariate logistic regression analysis.

Metabolic syndrome component	**OR**	**P. value**
HDL	1.379	0.692
TG	7.349	0.019
BP	6.074	0.023
FBG	23.748	0.000
BMI	3.147	0.259
MetS	0.451	0.489

Discussion:-

MetS is defined by a constellation of an interconnected physiological, biochemical, clinical, and metabolic factors that directly increases the risk of atherosclerotic cardiovascular disease and all-causes mortality.[9] In spite being only a cluster of clinical risk factors metabolic syndrome (MetS) has been recognized as independent predictor of cardiovascular diseases . [10] A handful of previous studies have reported the prevalence of metabolic syndrome among patients with CAD. Although many definitions for metabolic criteria had been published, still it is debatable which component of it is the most predictive for patients' vulnerability to CAD. The current study demonstrated a highly statistically significant difference between both groups regarding body weight and BMI. This results in agreement with Wormser et al. and Flegal et al. [11, 12] Mansour et al. [13] found that BMI was higher in Egyptian patients with both metabolic syndrome and CAD but statistically insignificant. Mohsen Ibrahim et al. [14] explained this discordance to be due to the high prevalence of abdominal obesity in Egyptians.

We found a statistical significant difference between both groups regarding the high blood pressure >130/85 mmHg (p=0.036).This result agrees with the previous studies provided that high BP is a major and independent cardiovascular risk factor, and hypertension tends to cluster with other metabolic risk factors. [15] Hypertensive individuals tend to have systemic endothelial dysfunction and chronic subclinical inflammation; [16] about half of patients with essential hypertension have insulin resistant. [17] This concludes that hypertension now is increasingly recognized as a powerful risk for cardiac and cerebrovascular events. [18] Many other studies such as Takatoshi et al, showed the clinical importance of the metabolic syndrome itself regardless of hypertension which presence was independent of other potential confounders in multivariate analysis. This further confirms the importance of high blood pressure >130/85 mmHg as strong risk factor of CAD in such cases. [19] Patients with metabolic syndrome (group A) had high levels of the triglyceride(TG), high density lipoprotein (HDL) and fasting blood glucose (FBG), compared to group B (less than 3 components). These finding were in agreement with Mansour et al. and Kim et al. [13,15]

Mottillo et al. demonstrated that visceral adipose tissue is an active endocrine organ that produces several bioactive derivatives including pro inflammatory and pro thrombotic adipokines, and this change is associated with each individual component of MetS. The close relationships among the different components of the syndrome make it difficult to understand what the hidden exact criminal that initiate the atherosclerotic process. [20]

In our present study, we compare the level of serum insulin and HOMA index (as a marker of insulin resistance) in the two groups. It was found that there was statistical significant difference regarding fasting serum insulin and HOMA index, being significantly higher in group A. Haffner et al. [21] stated that insulin resistance is an independent risk factor for cardiovascular disease; its presence can lead to macrovascular complications before other features of metabolic syndrome.

We identified that not only CAD is highly prevalent in the patients with metabolic syndrome, but also its severity is more in such cases; Genseni score was higher in metabolic syndrome group. In addition, there was a significant positive correlation between Metabolic syndrome score and Genseni risk score. This agrees with Yavuz et al, who confirmed such a relation.[22]

Patients with metabolic syndrome have more extensive coronary lesions and poorer collateral circulation than those without metabolic syndrome. Hadaegh et al, demonstrated that all MetS definitions were associated with the increased risk of CAD [23].Plaques in subjects with MetS harbor more lipid content and more calcification. [24] Other studies found that patients with and without metabolic syndrome did not differ in the prevalence of CAD. [15] These discrepancies may be due to the difference between different metabolic syndrome criterion used, different ethnicity and age of the study population in different studies . These discrepancies confirm the opinion that metabolic syndrome definition may vary according to ethnic background.

A multivariate regression analysis was done and we found that metabolic syndrome itself did not predict the presence of CAD in our cases (OR 0.451, p =0.489). Instead some individual component of metabolic syndrome show significant predictive value; namely, high FBG more than 110 mg/dl (OR 23.748,p<0.001), high TGs > 150 mg/dl (OR 7.349,p =0.019) and high blood pressure > 130/ 85 mmHg (OR 6.074,p=0.023).

In our study, FBG, TGs and high blood pressure more than 130/ 85 mmHg are considered independent factors that can predict CAD rather than metabolic syndrome itself. FBG was the most independent factor that can predict CAD. Nearly the same deduction was noted in many studies that tried to reach the exact and most valuable criterion of metabolic syndrome that links to CAD. In the secondary analysis of the prospective West of Scotland Coronary

Prevention Study, Metabolic syndrome was not a significant predictor of CAD when adjusted for its component factors in a multivariate model. It was suggest that the syndrome itself conveys no greater information than the sum of its component risk factors. [25] In agreement with our work, other study concluded that diabetes and high FBG not the metabolic syndrome itself predicted the severity and extent of CAD. [26] Other studies high lightened the value of blood pressure and stated that elevated blood pressure for CAD events and high FBG for CAD remained as independent predictors in all definitions**. [27]**

Conclusion:-

FBG, high TGs and high blood pressure were independent predictors CAD rather than metabolic syndrome itself. FBG was the most independent factor that predicts CAD.

Recommendation:-

More workout is needed to solve the issue of different definitions of metabolic syndrome concerning the difference in patients ethnic profile as well as clinical and biochemical profile.

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Declaration of interest:-

The authors declare that there is no conflict of interest.

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