CORONARY ANGIOGRAPHIC FINDINGS IN PATIENTS WITH METABOLIC SYNDROME

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ABSTRACT:

Background and objectives: metabolic syndrome is a common disorder associated with increased risk of cardiovascular diseases and diabetes , its prevalence in Iraq is not well estimated , many studies relate the relation of this syndrome to coronary artery disease due to the clustering of the cardiovascular risk factors in this syndrome , for this reason we tried in our study to evaluate the relationship between this syndrome and ischemic heart disease documented by coronay angiography , furthermore we planned in our study to classify and determine the severity of different coronary lesion in this syndrome.

Patients and methods: in this study we enrolled 146 patients with lschemic heart disease, 76 of them having the criteria of metabolic syndrome and 70 patients with IHD and no metabolic syndrome were taken as controls between February 2010 to February 2011- angiography was done for all the patients, and the different types of coronary lesions and their complexity scores analyzed and reported according to the American heart association criteria and syntax scoring system.

Results &Conclusion:

The mean syntax score was significantly higher among patients with this syndrome and also, complex coronay lesions in from of, ostial, bifucational and multi vessels disease were significantly higher in this group wether they are diabetics or not in comparison to the control group.

INTRODUCTION

Metabolic syndrome is a combination of medical disorders associated with increasing incidenc of cardiovascular disease and diabetes(1). Its prevalence in Iraq is not well estimated and the prevalence of this disorder increases with age. Some studies in USA estimate its Prevalence to be up to 25 percent of American population(2). The characteristics of this syndrome include fasting hyperglycemia,hypertension,hypertryglicery demia, low HDL, and or abdominal obesity.(3)

This syndrome is also known as metabolic syndrome, syndrome x, insulin resistance syndrome, Reaven's syndrome, CHAOS syndrome in Australia. Currently there are 2 major criteria to define this syndrome

1-The international diabetes federation.(4,5)

2. The third report of the national cholesterol education program expert panel on detection, evaluation and treatment of high blood cholesterol in adult (ATP3).

The national cholesterol education program. NCEP defines metabolic syndrome when 3 or more of the following characteristics are found.(3)

1 High fasting glucose more than 110 mg/dl.

2. High blood pressure, systolic BP more than130 mm hg, diastolic blood pressure more than 85 mm hg

3. Waist circumference more than 88 cm in females and more than 102 cm in males

4. HDL cholesterol less than 50 mg/ dl

5. Fasting triglyceride more than 150 mg

The two criteria used for diagnosis of metabolic syndrome, NCEP, IDF criteria are very similar and they can highly identify the patient with metabolic syndrome if any of them has been used in the same patient, but the two main differences are that the IDF indicates central obesity has been present if the BMI is more than 30 and IDF does not depend on waist circumference. This will result in exclusion of individuals without increased waist circumference if their BMI below this range, but in the NCEP criteria we can discover these patients.

However the IDF and NCEP are much closer to each other than the previous NCEP and WHO criteria.(6)

International Diabetes Federation, IDF 2006 includes central obesity and any 2 of the following

1 . Fasting plasma glucose more than 100mg/ dl or previously diagnosed type 2 diabetes. If fasting plasma glucose more than 100mg/dl oral glucose tolerance test is highly recommended but is not necessary to define the presence of this syndrome.

2. Increased BP, systolic more than 130 or diastolic BP more than 85 mm Hg, or treatment of previously diagnosed hypertension.

3. Decreased HDL cholesterol less than 40 mg/ dl in males and less than 50 mg/dl in

females or specific treatment for this lipid abnormality .

4. Increased triglycerides more than 150 mg/ dl or specific treatment for this lipid abnormality. If the BMI more than 30 , central obesity can be assumed and waist circumference does not to be measured. In our study we depend on NCEP criteria to diagnose those patients with metabolic syndrome. The WHO criteria require presence of one of diabetes mellitus, impaired glucose tolerance,impaired fasting glucose or insulin resistance and two of the following.. 1.Blood pressure equal or more than 140/90 mmhg.2.dyslipedemia ,trigeceride equal or more than 1.695 mmol and high density lipoprotein cholesterol equal or less than 0.9 for male, equal or less than 1.0 mmol for female.3 Central obesity; waist hip ratio more than o.90 for male;more than 0.85 for female,or body mass index more than30 kg/m.4.micro albuminuria;urinary albumine excretion equal or more than20 mico gm/minute ,or albumine/creatinine ratio equal or more than 30 mg/g.

The exact etiology of this syndrome is not yet completely understood, and the pathophysiology is extremely complex, and only partially elucidated. The majority of patients are obese with sedentary lifestyle and low physical activities and excessive caloric intake and have a degree of insulin resistance. Other important factors include aging, genetics(7,8,9,10), stress and body weight. Many markers of systemic inflammation like c- reactive protein, fibrinogen, interleukin- 6, TNF- alpha, uric

acid. TNF- alpha has been shown to trigger cell signaling by interaction with TNF- alpha-receptor that may lead to insulin resistance(11) .The trigyceride is firstly elevated which result in visceral fat redistribution and resulting in insulin resistence.(12,13,14) Some theories suggest that prolonged stress can be a cause of syndrome x due to dysfunction of hypothalamic pituitary adrenal axis resulting in increase circulating cortisol level which cause increase glucose and insulin level resulting in insulin resistance, dyslipidemia,hypertension,osteoporosis(15) . This HPA axis dysfunction may explain the reported risk indication of abdominal obesity to cardiovascular disease, type2 diabetes, and stroke. Psychosocial stress also linked to heart disease. One predictor of cardiovascular disease event and related mortality is a lack of physical activity and many components of syndrome X like central obesity are associated with sedentary life and has 2 folds increase of metabolic syndrome(15,16).

It has been shown in many studies that majority of patients of type 2 diabetes or impaired of glucose tolerance,(75 percent) have metabolic syndrome(17). This will result in high prevalence of cardiovascular disease than found in patients with type 2 diabetes or IGTT without the syndrome. Probably patients with coronary heart disease have a prevalence of metabolic syndrome about half of them with nearly 37 percent of those with premature coronary artery disease will have metabolic syndrome especially in women. Changes in lifestyle like physical activity, weight reduction, nutrition may result in reduction in the prevalence of this syndrome and its expected cardiovascular complications(2). There is a lot of controversy about the real risk of metabolic syndrome to the aetiology of coronary artery disease and most of the experts believe that the increased cardiovascular risk seen in these subject is probably due to clustering of known cardiovascular risk factor however there have been many reports of increased prevalence of cerebrovasuclar accident and coronary artery disease in these subjects, most of these report have used surrogate markers for CAD(2). More over the interrelationship between the metabolic syndrome and the presence and absence of CAD and it's effect on future major adverse cardiac events remain unknown.

For this reason we tried in our study to evaluate the potential relationship between metabolic syndrome and ischemic heart disease which is angiographically significantly defined. Further more the different types of coronary lesions and it's relations to dysmetabolic syndrome in comparison to the controls has been planed in our study aiming to find any possible association between specific coronary lesion and this syndrome with the objective of reduction of such expected complication by modification of component of the syndrome X in form of weight reduction , limitation of calorie intake, enforcement of exercise, diet , and other life style modification programs.

Patients and methods :

Study design

This study is a case control study was carried out in the Iraqi center for heart diseases Baghdad. Iraq from February 2010 to February 2011

76 pateints with metabolic syndrome and ischemic heart disease according to the national cholesterol education and prevention program (NCEP) report were enrolled in this study with age range between 29years-82 years (mean age 58 y) and 45 of them are males and 31of them are females .Also 70 patients with ischemic heart disease and without metabolic syndrome were taken as controls 39 male and 31 females. The patients with dysmetabolic criteria labeled as group A and the control group labeled as group B also group A subdivide in to two sub groups

Group A1; patients with metabolic syndrome and diabetes 49 patients

Group A2; patients with metabolic syndrome and without diabetes 27 patients

All the patients were admitted to the Iraqi center for heart diseases and was diagnosed to have ischemic heart disease in form of chronic stable angina., unstable angina/NSTEMI,ST elevation MI and all of them were arranged for coronary angiography (46 patients,60%) or coronary angiography and possible intervention (30 patients,40%), after completing their investigations in form of renal function tests, lipid profile, blood sugar. Echo cardiography, and virology screen . All the patients provided written informed consent about the procedure and its possible results.

CLASSIFICATION OF METABOLIC STATUS:

The patients were divided into two main groups:

Group A included 76 patients with ischemic heart disease and metabolic syndrome Group B included 70 patients with ischemic heart disease and not fitting the criteria of metabolic syndrome.

Group A was subdivided into two minor subgroups

Group AI represent patients with metabolic syndrome and diabetes mellitus 49 patients(59 %)

Group A2 represents patients with metabolic syndrome and without diabetes mellitus 27 patients(41%).

This classification of metabolic status was based on NCEP ATP III criteria, which is based on the presence or absence of equal, or more than three of the following risk factors:

1. Waist circumference of more than 102 centimeters for male and more than 88 centimeters for women

2. Hypertension (systolic blood pressure) equal or more than 130 mm Hg, diastolic Bp equal or more than 85 mm Hg or use of antihypertensive agents.

3. Fasting blood sugar equal or more than 110 mg/ dl

4. HDL cholesterol less than 50 mg/dl

5. Triglycerides of more than 150 mg / dl

The group of patients who met the criteria of metabolic syndrome (group A, no.= 76) where subdivided into 2 minor groups consisting of group A1 (no.= 49 patients) represent the diabetic metabolic group.

And group A2 number = 27 patients represent the non diabetic group. All the patients' information were reported in the data paper (questionnaire paper) which involve name, date, age, sex, risk factors (smoking, DM. hypertension, dyslipidemia, waist circumference, BMI, height and weight. Symptoms in form of chest pain, dyspnea, ECG finding. ECHO finding, type of IHD in form of chronic stable angina, US/ NSTEMI, STEMI, Post myocardial infarction angina. Metabolic parameter in form of fasting blood sugar, lipid profile (HDL,TRIGLYCERIDE, waist circumference and BP) were also reported.

Assessment of coronary angiographic findings:

After this assessment, all patients were arranged for coronary angiography and possible intervention in form of PTCA or PTCA and stenting using transfemoral approach (95% of the patients) or brachial approach (5% of the patients) and under local anesthesia with full pressure and ECG and hemodynamic monitoring. The significance of the coronary artery lesions were assessed by interventional cardiologist using visual assessment .The presence of one or more than 50% stenosis in the coronary artery diameter was considered as a significant coronary artery disease, diameter between 20-49 % considered as a minimum coronary artery disease, less than 20% luminal narrowing was consider

as no coronary artery disease. The coronary lesions also classified according to American Heart Association criteria which regarded as one of the most popular classifications of the coronary lesions. Also in our study we. used the syntax scoring system for the assessment of the severity of the different coronary lesions..(table1) Also the complex coronary lesions were included in the present study including:

LMS disease or LMS equivalent ,Total occlusion ,Presence of thrombus ,Diffuse disease and length more than 20 mm ,Locations in extremely angulated segment , Excessive tortousity of proximal segment ,Bifurcation and trifurcation lesions, Ostial lesions ,Calcified lesions, Proximal LAD lesions ,Three or more vessel disease

The SYNTAX score is calculated by a computer program consisting of sequential and interactive self-guided questions. The algorithm consists of twelve main questions. They can be divided in two groups:The first three determine the dominance, the total number of lesions and the vessel segments involved per lesion and they appear once. The maximum number of lesions allowed is twelve and each lesion is characterized by a number, 1 to 12.

Diameter reduction

-Total occlusion x5

-Significant lesion(50-99%) x2

Total occlusion(TO)

-Age>3months or unknown +1

-Blunt stump +1

-Bridging +1

-First segment visible beyond TO +1/per

Non-visible segment

-side branch (SB)-yes,SB<1.5mm +1

-Yes, both SB<&>1.5mm+1

Characterifstic scoring

Trifurcations

-2 diseased segments +4

-3 diseased segments +5

-4 diseased segments +6

Results:

The mean age of the group A was 58±12 SD years (ranging between 29 to 82 years) and 45 of them were males (59%) and 31 of them were females (41%) . the mean age of the group B was 52±16 SD years 39 of them were males (55%) and 31 of them were females(45%)

-Prevalence of metabolic factors by metabolic status :

In this study the prevalence of hypertension was the highest a:mong the five factors used to describe the metabolic syndrome . it represent about 90% of group A and it was prevalent in about 84% of group B . increased waist circumference is the second common parameter constituting about 88% of the patients in group A. Hyperglycemia is present in about 64% while the increased triglycerides and decrease HDL range between 51-56% of the cases . In those who classified with normal metabolic status the prevalence of metabolic factors range from 13% (decreased HDL) to 84% (hypertension). Table 1 illustrates the prevalence of these metabolic risk factors .

Base line Characteristics:

Patients with ischemic heart disease and metabolic syndrome tend to be older than those who didn't fit the criteria of syndrome X (58±12 versus 52±16) and more frequently having exertional dyspnoea and low EF in comparison to the group B (23% versus 12%). dyspnea is more prominent in the group A patients, but there is no significant differences regarding the prevalence of pathological Q wave among the 2 groups 21% versus 18%, but there is significant difference in the prevalence of LV systolic dysfunction reflected by low ejection fraction (less than 50%) among group A patients in comparison to group B(23 % versus 12%) .the classical ischemic symptoms were less frequent in the group A in comparison with group B (69% versus 81%).Table 2 illustrates these baseline characteristics by metabolic status.

Prevalence of angiographic ally defined coronary artery disease:

Compared to group B ,group A revealed an increased prevalence of more complex CORONARY ARTERY DISEASE, also there is AN INCREASED prevalence of these type C lesion among patients in group A2(non diabetic metabolic group) in comparison to the control group.

According to the involvement of the anatomical sites of the coronary artery tree and complexity score of the coronary artery lesions the prevalence of the ostial and bifurcation lesions and multivessel diseases was significantly higher in the group A and subgroup A2 in comparison to group B .

1 . Ostial lesions including ostial and proximal LAD reported in 17% of group A and 22% of subgroup A2 and only 7% of group B.

2. Bifurcation lesion reported in 36% in group A and 22% in subgroup A2 and 12% in group B.

3. Three or more vessel disease was reported in 34% group A and 26% of subgroup A2 and 16% of group B .

4. Total coronary occlusion was prevalent in 14% in group A and 11% in group A2 and 8% in group B.

5. Presence of thrombus (clot containing lesion) was defined only in 5% in group A and 3% in subgroup A2 and 6% of group B.

6. Left main stem disease and left main stem equivalent was prevalent in 4% in group A and 3% in subgroup A2 and 7% in group B .

7. Presence of calcification and extremely angulated lesion location present 9% in group A 3%group A2 and 4% in group B.

8. The mean syntax score was 31% in group A and 33% in group A2 and 10% in group B.

- Table 2 demonstrates the prevalence of significant angiographically defined CAD among the different groups.
- Table 3 and 4 demonstrates the prevalence of complex lesions among the different groups using the syntax scoring system and the differences by using the mean and standard deviation of the different groups.

Table (1): The demographic data and clinical profile of the study groups

Variable	Group A	Group B	Group A1	Group A2	P value
Mean age	58±12	52±16	57±13	59±11	>0.05
gender					
Male Female	45 (59%) 31 (41%)	39 (55%) 31 (45%)	30 (61%) 19 (39%)	15 (55%) 12 (45%)	>0.05
Risk factors					
Smoking	58 (76%)	54 (77%)	38 (77%)	20 (74%)	>0.05
Hypertension	69 (90%)	59 (84%)	45 (91%)	24 (88%)	>0.05
DM	49 (64%)	32 (46%)	49 (100%)	0	
↑Waist	67 (88%)	12 (17%)	44 (89%)	23 (85%)	<0.05
↑triglyceride	43 (56%)	17 (24%)	26 (53%)	17 (63%)	<0.05
↓HDL	39 (51%)	9 (13%)	25 (51%)	14 (52%)	<0.05 <0.05
Q. wave	16 (21%)	13 (18%)	9 (18%)	7 (25%)	>0.05
EF<50%	18 (23%)	9 (12%)	11 (22%)	7 (25%)	<0.05
Classical symptoms	53 (69%)	61 (81%)	36 (73%)	17 (62%)	>0.05
Total	76	70	49	27	

A: Patient with dysmetabolic syndrome and IHD

A1: Patient with DM and dysmetabolic syndrome

B: Patient with IHD and no dysmetabolic syndrome

A2: Patient with dysmetabolic syndrome no DM

NB: * The difference is statistically significant (P value > 0.05)

**** The difference is statistically non-significant (P value < 0.05)**

Table (2): The prevalence of different coronary lesions among the study groups

Type of lesion	A (No =76)	B (No =70)	A1 (No =49)	A2 (No =27)	P value
Ostial lesions	13 (17%)	5 (7%)	7 (14%)	6 (22%)	<0.05
Bifurcation and trifurcation lesion	18 (36%)	9 (12%)	12 (24%)	6 (22%)	<0.05
3 or more vessel disease	26 (34%)	11 (16%)	19 (32%)	7 (26%)	<0.05
Total coronary occlusion	11 (14%)	6 (8%)	8 (16%)	3 (11%)	<0.05
Thrombus containing lesion	4 (5%)	4 (6%)	3 (6%)	1 (3%)	>0.05
LMS OR LMS equivalent	3 (4%)	5 (7%)	2 (4%)	1 (3%)	>0.05
Calcified & angulated lesion	7 (9%)	3 (4%)	6 (12%)	1 (3%)	<0.05
High complexity (SYNTAX) score (22 or above)	24 (31%)	7(10%)	15 (30%)	9 (33%)	<0.05
Total	76	70	49	27	

Table (3): Classification of the complex coronary lesions among the study groups using SYNTAX scoring system

Variable	Score 1*	Score II*	Score III*	Score IV*
A (76)	40 (53%)	12 (16%)	20 (26%)	4 (5%)
B (70)	59 (84%)	4 (6%)	6 (9%)	1 (1%)
A_1 (49)	28 (57%)	6 (12%)	13 (27%)	2 (4%)
A_2 (27)	11 (40%)	7 (26%)	8 (30%)	1 (4%)

Score I = 1-10

Score II = 11-21

Score III = 22-31

Score IV = >31

NB: * The difference is statistically significant (P value > 0.05)

**** The difference is statistically non-significant (P value < 0.05)**

TABLE (4): Distribution of the studied population according to SYNTAX score mean

Group	SYNTAX score (Mean ± SD)	Total no.
A	19.2 ± 8.4	76
B	11.6 ± 9.2	70
A_1	18.3 ± 9.6	49
A_2	16.3 ± 11.4	27

The difference between each of the cases means and the control mean is statistically significant difference (Z=4.87, P< 0.05)

DISCUSSION:

In this study we assessed the prevalence of different parameters used to describe the metabolic syndrome according to NCEP criteria. .in our study,hypertension was the most common component of metabolic syndrome ,occurring in about 90% of group A.this agree with other reports wich identify hypertension to be the most common parameter of metabolic syndrome.(katzamaryk;;peter t;leon,Arthur s;Wilmore,jack H;skinner,james s;Rao,D.C;Targeting the metabolic syndrome;evidence from the heritage family study'"med sci.sort. 35(10);1703 1709).also we found increased waist circumference is the second prevalent parameter.followed by DM then dyslipidemia.also the patient with metabolic syndrome tend to be older than the controls (58 years versus 52 years),and tend to express less classical ischemic symptoms in comparision to the controls(69% versus 81%),also the prevalence of left ventricular systolic dysfunction was more among group A(23% VERSUS 12)but there was no significant difference regarding the frequenct of the Q wave among the study population.The present study revealed that significant CAD (angiographically defined) tend to be highly associated with metabolic syndrome and thus increase the cardiovascular risk and major adverse cardiac events .this agreed and support the previous reports by(Alexander CM, Landsman PB, Teutsch SM, et al. NCEP-defined metabolic syndrome, diabetes and prevalence of coronary heart disease among NHANES III participants age 50 years and older. Diabetes .2003 : 52:1210-1214(Abstract/Free Full Text), which revealed that the metabolic symptom associated with CHD. Also this study shows that the increased risk of coronary artery disease also present in patients with dysmetabolic criteria regardless to the presence or absence of diabetes as it was shown in group A2. The present study supports the previous reports suggesting that the metabolic syndrome is associated with CAD and sin contrast to many previous studies which depend on reporting CAD by self report of MI or ischemic symptoms or

positive response to the angina . In our study we try to confirm this correlation and link between metabolic syndrome and CAD by significant coronary artery disease which defined angiographically. this angiographically defined CAD in our study also agree with study done by (Oscar C.Marroquin, Kevin E.Kip;David E.Kelley;Delia Johnson;Leslee J.shaw, et al, for the women's ischemic syndrome evaluation and investigators, circulation 2004;109:714-721 C2004 American Heart Association Inc) .

In comparison to the study done by (Lakka H-M, Laaksonen DF, Lakka TA, et al. the metabolic syndrome and total and cardiovascular mortality in middle aged men. JAMA.2002;288:2709-2716) which reveal the increased cardiovascular events in middle age men and dysmetabolic syndrome, our study showed this increased risk for both genders . Moreover our study reveal that the metabolic syndrome is associated with increased risk of more significant and complex coronary lesions reflected by increased the prevalence of ostial, bifurcational, multivessel disease , and high syntax score as compared with patients with normal metabolic status. This is also applied to the patients in group A2 with metabolic syndrome and without diabetes.However this study revealed lower incidence of LMS disease in patients with metabolic syndrome which is not clearly explained but might be due to restricted no. of patients taken in this study.

Conclusion

The present study shows that angiographically defined CAD is more prevalent in patient with metabolic syndrome, more over the prevalence of more complex coronary lesion reflected by syntax score and AHA criteria was also high among the patient withthis syndrome wether they are diabetic or not .also the study revealed that patient with metabolic syndrome were more frequently having LV systolic dysfunction and less frequently presented with classical ischemic symptoms. this results should generate a further future work to describe this association and expected strategies to improve or modify the risks associated with this syndrome.

Recommendations:

1,This study should generate for further future work to describe the association between metabolic syndrome and complex coronary lesions.

2.hyper tension and central obesity are the most frequent component of this syndrome and plans should be directed to modify these and other risk factors, like exercise ,diet, calorie intake which expected to result in reduction of adverse cardiac events.

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الخلاصة

بيان مدى انتشار تواجد انسداد شرايين القلب التاجية المثبتة عن طريق قسطرة القلب و الشرايين في مرضى متلازمة الايض

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متلازمة الايض هي من الامراض الشائعة و لم تكن هناك دراسة واضحة في العراق توضح مدى اصابة هؤلاء المرضى بانسداد شرايين القلب التاجية حيث ان الهدف من الدراسة هو بيان مدى الاصابة بانسدادات الشرايين التاجية لهؤلاء المرضى حيث تضمنت هذه الدراسة ١٤٦ مريض من المرضى المصابين بعدم كفاءة الشرايين التاجية و استمرت لمدة سنة كاملة حيث كان ٧٦ مريض يعاني من متلازمة الايض و عدم كفاءة الشرايين التاجية و ٧٠ مريض يعانون من عدم كفاءة الشرايين التاجية بدون متلازمة الايض جميعهم اجريت لهم قسطرة القلب و الشرايين في المركز العراقي لامراض القلب (مدينة الطب) حيث اثبتت الدراسة ان هؤلاء المرضى يعانون من انسدادات تاجية معقدة حسب معامل سينتاكس ١٩.٢ مقارنة مع المرضى الغيرمصابين بهذه المتلازمة ١١.٦ كما ان الانسدادات المتعددة (اكثر من ثلاثة شرايين) كانت اكثر شيوعا في مرضى متلازمة الايض ٣٤% مقابل ١٦% .

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