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Biochemical Profile of Metabolic Syndrome Leading to Chronic Kidney Disease

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Abstract

Background: Metabolic syndrome (MetS) is defined by a cluster of interconnected factors that directly increase the risk of coronary heart disease (CHD), other forms of cardiovascular atherosclerotic diseases (CVD), and diabetes mellitus type 2 (DMT2). Chronic kidney disease (CKD) and metabolic Syndrome (MS): CKD and MetS are worldwide public health problems and increasing in incidence and lead to significant cardiovascular and stroke related morbidity and mortality. All individual components of the MetS are leading to CKD and development of Albuminuria and decreased GFR. [6] Several studies have discussed the relationship between MS and CKD and found Metabolic Syndrome and CKD share a complex, bidirectional relationship. **Subjects and Methods:** This is a Hospital based observational study was conducted in the Department of Biochemistry, among the patients who met with the Criteria of metabolic syndrome. Body Mass Index (BMI) will be calculated by dividing the subject's weight in kilograms by the square of his or her height in meters. The blood pressure will be measured using manual mercury sphygmomanometer. Two recordings will be taken in the sitting position at an interval of 5 minutes. The average of the two readings will be taken as the final measurement. Metabolic syndrome will be diagnosed by the presence of three or more of the five criteria of the World Health Organization. CKD will be defined according to the Modification of Diet in Renal Disease (MDRD) - eGFR formula. **Results:** Class-I obesity patients were major participants of the study, but there was no big difference from normal to abnormal eGFR. In normal eGFR cases, 77.8% of the study subjects having HTN where as in abnormal eGFR cases, HTN was present in 90.5% of the subjects. It was showing statistically significant (p=0.04). In normal eGFR cases, 82.3% of the study subjects having DM where as in abnormal eGFR cases, DM was present in 96.8% of the subjects. It was showing statistically significant. Around 86.9% of the patients were having abnormal Triglycerides fulfilling the inclusion criteria of metabolic syndrome, and one third of them were having CKD, It was also showing statistically significant (0.28). Approximately 80% of patients were having abnormally low HDL levels in who included in this study, probably statistically HDL level could not determined. **Conclusion:** The current study provides new and important information regarding the relationship between the metabolic syndrome and risk of CKD in a representative sample of adult population and suggests that prevention and treatment of the metabolic syndrome should be an important priority for reducing the prevalence of CKD and its associated disease burden in adult population. Several studies have examined the association between insulin resistance, metabolic syndrome, and risk of CKD. In conclusion, our study indicates that the metabolic syndrome is a strong and independent risk factor for CKD in general adult population. In addition, there is a graded relationship between the number of the metabolic syndrome components and risk of CKD.

Keywords: Metabolic syndrome, Coronary heart disease, Chronic kidney disease.

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Introduction

Metabolic syndrome (MetS) is defined by a cluster of interconnected factors that directly increase the risk of coronary heart disease (CHD), other forms of cardiovascular atherosclerotic diseases (CVD), and diabetes mellitus type 2 (DMT2).[1] The term "metabolic" refers to the biochemical processes involved in the body's normal functioning.[2] The term "metabolic syndrome" is used to describe a cluster of conditions including increased blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol or triglyceride levels.[3] Recently, other abnormalities such as chronic pro-inflammatory and pro- thrombotic states, non-alcoholic fatty liver disease and sleep apnea have been added to the entity of the syndrome, making its definition even more complex.[4]

Chronic kidney disease (CKD) and metabolic Syndrome (MS): CKD and MetS are worldwide public health problems and increasing in incidence and lead to significant cardiovascular and stroke related morbidity and mortality.[5] All individual components of the MetS are leading to CKD and development of Albuminuria and decreased GFR.[6] Several studies have discussed the relationship between MS and CKD and found Metabolic Syndrome and CKD share a complex, bidirectional relationship.[7]

The pathophysiology of this condition is not well understood. However, some data suggest that MS is an

independent cause of CKD.[8] The risk of renal disease in individuals with MetS can be related to the presence of two factors: Hypertension and hyperglycemia.[9] Treatment of hypertension and hyperglycemia reduces kidney disease, as does treating hyperlipidemia with statins.[10] In addition, obesity and MetS are independent predictors of CKD. Not only is MetS associated with incident CKD but also with its progression. Microalbuminuria and CKD is also considered as independent cardiovascular risk factors.[11] Metabolic Syndrome is also a higher CVD risk factor at all stages of CKD from early renal insufficiency to end-stage renal disease.[12]

Cross-sectional studies show an association of the MetS and prevalent CKD; however, one cannot draw conclusions as to which came first – the MetS or the kidney disease. Observational studies suggest a relationship between MetS and incident CKD, but they also demonstrate the development of MetS in patients with established CKD. These observations suggest a bidirectional relationship.[13]

Subjects and Methods

This is a Hospital based observational study was conducted in the Department of Biochemistry, among the patients who met with the Criteria of metabolic syndrome.

Inclusion Criteria

- Age: 30 to 70 years.
- Patients with central obesity i.e. BMI >30kg/m2.
- Patients with Systemic Blood Pressure ≥ 140/90 mmHg or on treatment of previously diagnosed hypertension
- Patients with fasting plasma glucose (FPG): >100 mg/dl (5.6 mmol/L) or on treatment for diagnosed type 2 Diabetes Mellitus.
- Patients with Dyslipidemia i.e. : Triglycerides (TG) : ≥150mg/dl
- Or HDL-C: ≤ 35mg/dl (male) : ≤ 39mg/dl (female)
- ANY OF THE ABOVE THREE PARAMETERS MEETING THE INCLUSION CRITERIA IN A PATIENT WILL BE TESTED FOR SERUM CREATININE and GFR <60ml/min/1.73m2 according to MDRD formula.

Exclusion Criteria

- Patients less than 30 years and more than 70 years of age.
- BMI <29.9kg/m2
- Patients with missing measurements for any component of the metabolic syndrome or renal functions.
- Pregnant women.

Method

Body Mass Index (BMI) will be calculated by dividing the subject's weight in kilograms by the square of his or her height in meters.

The blood pressure will be measured using manual mercury sphygmomanometer. Two recordings will be taken in the sitting position at an interval of 5 minutes. The average of the two readings will be taken as the final measurement.

A 5ml of fasting blood sample will be collected and it will be centrifuged at 3000rpm for 10min and the serum is used for analysis of metabolic syndrome biochemical profile and eGFR.

Metabolic syndrome will be diagnosed by the presence of three or more of the five criteria of the World Health Organization. CKD will be defined according to the Modification of Diet in Renal Disease (MDRD) - eGFR formula.

Data Analysis

Statistical analysis of the data will be performed by using Microsoft Excel and Statistical Package for Social Sciences (SPSS) version 17. Data will be represented in the form of frequencies, percentages and mean ± SD with the help of tables and graphs.

Results

Class-I obesity patients were major participants of the study, but there was no big difference from normal to abnormal eGFR. [Table 2]

In normal eGFR cases, 77.8% of the study subjects having HTN where as in abnormal eGFR cases, HTN was present in 90.5% of the subjects. It was showing statistically significant (p=0.04). [Table 3]

In normal eGFR cases, 82.3% of the study subjects having DM where as in abnormal eGFR cases, DM was present in 96.8% of the subjects. It was showing statistically significant. [Table 4]

Around 86.9% of the patients were having abnormal Triglycerides fulfilling the inclusion criteria of metabolic syndrome, and one third of them were having CKD, It was also showing statistically significant (0.28). [Table 5]

Approximately 80% of patients were having abnormally low HDL levels in who included in this study, probably statistically HDL level could not determined. [Table 6]

Table 1: Baseline characteristics of the study participants

Variable		eGFR				P-value
		Normal		Abnormal		
		Mean/Count	SD/%	Mean/Count	SD/%	
Age		45.5	6.7	54.5	6.2	<0.001
Sex	Female	48	53.3%	30	47.6%	0.51
	Male	42	46.7%	33	52.4%	
Height		156.5	9.0	158.1	9.0	0.3
Weight		79.7	10.3	82.0	9.7	0.2
BMI		32.4	1.4	32.5	1.3	0.6
HTN	Normal	10	11.1%	6	9.5%	0.04
	Abnormal	70	77.8%	57	90.5%	

						0.04
DM	Normal	16	17.7%	2	3.2%	0.06
	Abnormal	74	82.3%	61	96.8%	0.06
TG		257.0	68.6	251.5	72.0	0.6
HDL		34.0	3.5	34.7	3.6	0.2
Sr.Creat @ base		1.2	0.2	1.4	0.4	<0.001
Sr.Creat at 3m		1.1	0.1	1.7	0.3	<0.001

Table 2: eGFR in relation to Obesity Class

Obesity	eGFR				Total		P-value
	Normal		Abnormal				
	Count	%	Count	%	Count	%	
Class-1	83	92.2%	57	90.5%	140	91.5%	0.77
Class-2	7	7.8%	6	9.5%	13	8.5%	
Total	90	100.0%	63	100.0%	153	100.0%	

Table 3: eGFR in relation to Hypertension

BP	eGFR				Total		P-value
	Normal		Abnormal				
	Count	%	Count	%	Count	%	
Non HTN	20	22.2%	6	9.5%	16	10.5%	0.04
HTN	70	77.8%	57	90.5%	137	89.5%	
Total	90	100.0%	63	100.0%	153	100.0%	

Table 4: eGFR in relation to Diabetes

FBS >110/ DM	eGFR				Total		P-value
	Normal		Abnormal				
	Count	%	Count	%	Count	%	
Non DM	16	17.7%	2	3.2%	8	5.2%	0.006
DM	74	82.3%	61	96.8%	145	94.8%	
Total	90	100.0%	63	100.0%	153	100.0%	

Table 5: eGFR in relation to Triglycerides

TG	eGFR				Total		P-value
	Normal		Abnormal				
	Count	%	Count	%	Count	%	
Normal	14	15.5%	6	9.5%	20	13.1%	0.28
Abnormal	76	84.5%	57	90.5%	133	86.9%	
Total	90	100.0%	63	100.0%	153	100.0%	

Table 6: eGFR in relation to HDL

HDL	eGFR				Total		P-value
	Normal		Abnormal				
	Count	%	Count	%	Count	%	
Normal	15	16.7%	15	23.8%	30	19.6%	0.31
Abnormal	75	83.3%	48	76.2%	123	80.4%	
Total	90	100.0%	63	100.0%	153	100.0%	

Discussion

Chen et al analyzed data on 7,800 participants with MetS in the NHANES III who were followed for over 21 years. Individuals with the MetS were at 2.6-fold greater risk of incident CKD (defined as eGFR, 60 mL/min) than individuals without MetS. The risk of CKD increased with the number of MetS components from an odds ratio (OR) of 1.89 in adults with one MetS component to 5.85 in adults with all five components. The risk of microalbuminuria among adults with MetS was double that of adults without. The risk of microalbuminuria also increased in a step-wise fashion with the number of MetS components.[14]

In a Cross-sectional study by Palaniappan al,[15] using NHANES III criteria, incidence of microalbuminuria was greater in both women (OR 2.2; 95% CI 1.44– 3.34) and men (OR 4.1; 95% CI 2.45–6.74) with MetS than without MetS.

Hoehneret al,[16] correlated the MS profile and microalbuminuria in a cross sectional study of American Indians from Wisconsin and Minnesota and concluded that individuals with three or more metabolic syndrome traits had a 2.3-fold increased odds of having microalbuminuria compared with a control group without the syndrome.

In a cross-sectional study of 15,160 Chinese adults, Chen et al found that the multivariate-adjusted ORs (95% CI) of CKD and elevated serum creatinine in participants with MetS compared to those without the MetS were 1.64 (1.16–2.32) and 1.36 (1.07–1.73), respectively. Compared to those without any components of the MetS, the multivariate-

adjusted ORs (95% CI) of CKD were 1.51 (1.02–2.23), 1.50 (0.97–2.32), 2.13 (1.30–3.50), and 2.72 (1.50–4.93) for those with one, two, three, and four or five components, respectively. The corresponding multivariate-adjusted ORs (95% CI) of elevated serum creatinine were 1.11 (0.88–1.40), 1.39 (1.07–2.04), 1.47 (1.06–2.04), and 2.00 (1.32–3.03) respectively.[17]

Tanaka et al from Japan, MetS predicted CKD in 6,980 Japanese adults participating in a screening program. There was a linear association between the number of MetS components and prevalent CKD (adjusted OR 1.54 and 95% CI 1.287–1.85; P, 0.0001).[18]

Similar results were found in the Korean population, in a retrospective study of 60,921 healthy adults; prevalence of CKD was greater in those with MetS (11.0% versus 6.3%; P, 0.001) than those without MetS. This prevalence increased with the number of components of the MetS, and this association persisted after multivariate adjustment with OR was 1.680 (95% CI 0.566–1.801).[19]

In a similar study of 118,924 individuals in China, Sun et al reported that MetS was predictive of CKD defined by incident proteinuria (HR 1.39; 95% CI 1.24– 1.36) and stage 3 or lower eGFR (1.37; 95% CI 1.3–1.44).[20]

Thomas et al performed a meta-analysis that assessed the relationship between MetS and CKD in eleven prospective observational studies with 30,146 individuals. OR for the association of the MetS (using NCEP-ATPIII definition) and CKD (defined as eGFR<60 mL/min per 1.73 m2) was 1.55 (95% CI 1.34– 1.80). The strength of the association increased as the number of MetS components increased (trend P-value =0.02).[21]

Conclusion

The current study provides new and important information regarding the relationship between the metabolic syndrome and risk of CKD in a representative sample of adult population and suggests that prevention and treatment of the metabolic syndrome should be an important priority for reducing the prevalence of CKD and its associated disease burden in adult population. Several studies have examined the association between insulin resistance, metabolic syndrome, and risk of CKD. In conclusion, our study indicates that the metabolic syndrome is a strong and independent risk factor for CKD in general adult population. In addition, there is a graded relationship between the number of the metabolic syndrome components and risk of CKD.

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