EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 9
Issue: 6
289-292
Year: 2022

A STUDY OF CORRELATION OF THE PARAMETERS OF RENAL FUNCTION TESTS WITH THE PARAMETERS OF METABOLIC SYNDROME

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Article Received on 12/04/2022 **Article Revised on 02/05/2022** **Article Accepted on 22/05/2022**

ABSTRACT

Background: Metabolic syndrome is a cluster of various metabolic abnormalities which lead to an increase in all cause mortality in the general population mostly due to cardiovascular and cerebrovascular events. It has been proposed that these metabolic abnormalities can also lead to renal dysfunction. This study was done to assess the renal functions parameters in Indian population patients with metabolic syndrome. **Methods:** This study was conducted at a university hospital with 200 participants. 100 patients had metabolic syndrome and 100 patients were taken as controls (Age, Sex, BMI matched). Serum Urea, serum Creat, 24 hour urine protein was measured in all the participants. The results were analysed using the chi square test. **Results:** We compared the findings in all the patients. A thorough physical examination, BMI etc was done in all the participants. There was a significant difference in all the renal parameters i.e. S.Urea, S.Creat, eGFR, 24 hour urine protein in the study population when compared with the control population. 68 patients in the study group had altered renal parameters and 15 participants in the control group had altered renal parameters. On comparing the individual parameters, there was a significant correlation between fasting blood glucose (p=0.03), systolic blood pressure (p=0.01) and diastolic blood pressure (p=0.036). **Conclusion:** There is significant derangement of renal parameters in obese individuals with metabolic syndrome when compared to obese without metabolic syndrome. There is an individual association of the parameters of metabolic syndrome with the renal function parameters.

INTRODUCTION

Metabolic syndrome is also known as "Syndrome X" is a group of conditions that occur together like insulin resistance, dyslipidemia, and hypertension which promote the development of Renal disease.[1] Metabolic syndrome is defined if a patient has any three of the following:

- Weight circumference more than 40 inches in men and more than 35 inches in women.
- Triglycerides more than 150 milligrams per decilitres of blood(mg/dL)
- High-density Lipoprotein (HDL) less than 40 mg/dL in men and less than 50 mg/dL in women.
- Increased fasting blood glucose of more than or equal to 100 mg/dL
- Systolic blood pressure of 130 mmHg or higher and/or diastolic of 85 mmHg or higher.[2]

Metabolic syndrome is usually associated with an increased risk of coronary artery disease, diabetes, hepatic steatosis, and cancers.[3] On top of that, there is a notable association between Metabolic syndrome and chronic kidney disease in certain groups of the population.[4][5]

MetS has been clearly associated with CKD markers which includes reduced glomerular filtration rate (<60mL/min), proteinuria and/ or microalbuminuria, and histopathological markers such as tubular atrophy and fibrosis.

Each component of MetS has been associated with both, CKD incidence and progression.

-Insulin resistance may be the most important risk factor. It leads to inflammation, leading to oxidative stress and renal insufficiency. Raised insulin levels stimulate

insulin-like growth factor 1 (IGF-1) production, which increases connective tissue growth factor, thus causing fibrosis in the diabetic state.
-Obesity may lead to increased secretion of pro-inflammatory cytokines by adipose tissue, such as:

a. Leptin which may lead to increased intra renal expression of transforming growth factor-beta leading to glomerulosclerosis.
b. TNF-alpha which may lead to production of reactive oxygen species that can in turn lead to renal endothelial cell dysfunction, mesangial expansion and fibrosis.
c. Anti-inflammatory hormones like adiponectin may be reduced in MetS leading to vascular intima thickening and smooth muscle cell proliferation. Its vascular effects may extend to CKD.

Obesity also leads to increased glomerular volume, podocyte hypertrophy, and mesangial matrix expansion preceding CKD. So, it is feasible to assume that chronic renal disease could be the result of the presence of these cytokines in the setting of metabolic syndrome.[6][7] Usually, there is a preponderance of oxidative stress in obesity which may stimulate the production of angiotensin-2 which may progressively cause glomerular fibrosis by increasing synthesis of TGF-ß and plasminogen activator inhibitor-1. Obesity also stimulates increased expression of Na-K-ATPase on renal tubules and dampens the response of natriuretic hormones which in turn promote salt and water retention and causes glomerular hyperfiltration and renal fibrosis.[8]

Statins, fibrates, and renin-angiotensin system antagonists allow for targeting specific MetS components including diabetes, hyperlipidemia, hypertension and microalbuminuria. In combination with aggressive lifestyle modification, there is potential for reducing MetS, CKD, and CVD mortality. Understanding the genetic and environmental factors that impact the relationship between CKD and MetS is also important. While awaiting further studies, awareness of the association between MetS and CKD is important. This should prompt early implementation of lifestyle changes and aggressive control of blood pressure and lipids, which may improve cardiovascular outcomes as well.

Study was done to assess and establish the relationship between parameters of renal function in obese patients with metabolic syndrome compared to that of obese patients without metabolic syndrome.

MATERIALS AND METHODS

This study was conducted in a university hospital with 200 patients. Detailed history and physical examination was done for all the participants. The inclusion criteria included all patients with age >25 years of age and age < 55 years of age. Both males and females were taken for the study. Exclusion criteria included, pregnant patients, patients with endocrine conditions like thyroid disorder, diabetes mellitus, Cushing's disease etc. Patients with Serum Creat >1.4mg/dl, serum Urea >40 were excluded from the study. Patients with structural deformities in kidney were excluded from the study. Patients with other conditions like heart conditions, Post MI, cardiomyopathy, Liver diseases etc. were excluded from the study.

Vitals examination was done with systolic, diastolic blood pressure and pulse rate measurements. Blood pressure was measured by the standard Omron Oscillometer 907. Waist circumference was measure in all the participants and the findings were noted in inches.

Blood investigations were done for all the participants. The blood investigations included CBC, total cholesterol panel, Renal function tests with Serum Creatinine and Serum Urea level. GFR was calculated based on the formula Cockcroft- Gault formula and was expressed as eGFR. All the findings were entered in a table and statistical analysis was done on the data. P value of <0.05 was declared to consider a significant correlation between the parameters.

RESULTS

The results of our study are showed in the tables below.
The baseline characteristics of the study population are shown in the table 1.

Table 1: Baseline characteristics of the study population.

Variables	Cases	Controls
	Mean ± Standard Deviation	Mean ± Standard Deviation
Age (years)	42.16 ± 10.22 years	43.18 ± 11.24
Gender	58% Males	58% Males
Fasting blood glucose (mg/dl)	119.25 ± 22.24	88.48 ± 14.22
Waist circumference (inches)	92.56 ± 6.8	86.42 ± 7.1
Systolic blood pressure (mmHg)	139.56 ± 14.66	125.26 ± 11.12
Diastolic blood pressure(mmHg)	89.99 ± 7.42	84.12 ± 6.98
Serum triglycerides(mg/dl)	185.66 ± 16.98	138.97 ± 18.44
Serum HDL (mg/dl)	41.26 ± 6.45	48.45 ± 8.24
Blood Urea(mg/dl)	29.45 ± 6.99	21.22 ± 4.56
Serum creatinine(mg/dl)	1.28 ± 0.78	0.87 ± 0.36
eGFR (ml/min/1.73m^2)	78.45 ± 14.16	86.99 ± 9.97

Average age of the participants in the cases group was 42.16 ± 10.22 years and in the controls group was 43.18 ± 11.24. There were 58% males in the study group as well as the controls group to avoid any gender bias. Fasting blood glucose levels were 119.25 ± 22.24 mg/dl and 88.48 ± 14.22 mg/dl in the study and the control group respectively. Waist circumference was 92.56 ± 6.8 inches and 86.42 ± 7.1 inches in the study and the control group respectively. Systolic blood pressure was 139.56 ± 14.66 mmHg and 125.26 ± 11.12 mmHg in the study and the control group respectively. Diastolic blood pressure was 89.99 ± 7.42 mmHg and 84.12 ± 6.98 mmHg in the study and the control group respectively.

Serum triglycerides levels were 185.66 ± 16.98 mg/dl and 138.97 ± 18.44 mg/dl in the study and the control group respectively. Serum HDL levels were 41.26 ± 6.45 mg/dl and 48.45 ± 8.24 mg/dl in the study and the control group respectively. Blood Urea levels were 29.45 ± 6.99 mg/dl and 21.22 ± 4.56 mg/dl in the study and the control group respectively. Serum creatinine levels were 1.28 ± 0.78 ml/min/1.73m^2 mg/dl and 0.87 ± 0.36 ml/min/1.73m^2 in the study and the control group respectively. eGFR was 78.45 ± 14.16 and 0.87 ± 86.99 ± 9.97 in the study and the control group respectively.

Table 2: Renal function tests in cases vs controls.

	Cases	Controls
Blood Urea(mg/dl)	29.45 ± 6.99	21.22 ± 4.56
Serum creatinine(mg/dl)	1.28 ± 0.78	0.87 ± 0.36
eGFR(ml/min/1.73m^2)	78.45 ± 14.16	86.99 ± 9.97
24 hour urinary protein	242 ± 84	122 ± 36

Table 3: Correlation of parameters of Renal function tests with parameters of metabolic syndrome.

Metabolic parameters	Serum Urea		Serum Creatinine		eGFR		24 hour urine protein	
	Correlation coefficient	P value	Correlation coefficient	P value	Correlation coefficient	P value	Correlation coefficient	P value
Age (years)	0.756	0.07	0.645	0.078	-0.522	0.066	0.536	0.059
Fasting blood glucose (mg/dl)	0.862	0.03	0.647	0.045	-0.468	0.047	0.648	0.04
Waist circumference (inches)	0.654	0.08	0.454	0.07	-0.612	0.06	0.645	0.065
Systolic blood pressure (mmHg)	0.894	0.01	0.794	0.01	-0.784	0.05	0.684	0.045
Diastolic blood pressure(mmHg)	0.948	0.036	0.835	0.04	-0.875	0.04	0.764	0.042
Serum triglycerides(mg/dl)	0.668	0.07	0.568	0.06	-0.788	0.065	0.874	0.045
Serum HDL (mg/dl)	0.228	0.06	0.214	0.055	-0.149	0.05	0.788	0.046

The correlation of the parameters of renal function tests are shown in the table 3(above). From the above table, it can be inferred that there is a correlation between the parameters of the metabolic syndrome with the parameters of the renal function tests. Not all the parameters had a significant correlation with the parameters of the renal function tests.

Fasting blood sugar was strongly and siginifanctly associated with the parameters of the renal function tests. P value was 0.03, 0.045,0.047 and 0.04 for serum Urea, serum Creatinine, eGFR and 24 hour urine protein respectively. eGFR had a negative correlation and it showed that with the increase in the increase in the other parameters, there was a reduction in eGFR of the patients.

Systolic blood pressure and diastolic blood pressure was strongly and siginifanctly associated with the parameters of the renal function tests. P value was 0.01, 0.01,0.05 and 0.045 for serum Urea, serum Creatinine, eGFR and 24 hour urine protein respectively. eGFR had a negative correlation and it showed that with the increase in the increase in the other parameters, there was a reduction in eGFR of the patients.

Other parameters did not have a statically significance as the p value was >0.05.

DISCUSSION

Our study included a total of 200 patients (100 patients had metabolic syndrome and 100 patients were taken as controls). We found that the presence of MetS was associated with the decline of renal function in cases when compared to controls. Many parameters of the metabolic syndrome show adverse correlation with renal function tests. But a statistical significanct difference was not found among all the parameters. The patients with metabolic syndrome have a higher risk of developing CKD.

There was a significant difference in all the renal parameters i.e. S.Urea, S.Creatinine, eGFR, 24 hour urine protein in the study population when compared with the control population. 68 patients in the study group and 15 participants in the control group had altered renal parameters. eGFR was 78.45 ± 14.16 and 86.99 ± 9.97 in the study and the control group respectively.

On comparing the individual parameters, there was a significant correlation between fasting blood glucose (p=0.03), systolic blood pressure (p=0.01) and diastolic

blood pressure (p=0.036). Fasting blood sugar was strongly and siginifanctly associated with the parameters of the renal function tests. P value was 0.03, 0.045,0.047 and 0.04 for serum Urea, serum Creatinine, eGFR and 24 hour urine protein respectively. eGFR had a negative correlation and it showed that with the increase in the increase in the other parameters, there was a reduction in eGFR of the patients.

Because diabetes and hypertension are both addressed by the definition of MetS and are the leading causes of CKD and ESRD, the relative contribution of the individual components of MetS to CKD risk is of interest. In this analysis, apart from elevated BP and fasting glucose, we found an increased risk for development of reduced eGFR for each individual component of MetS. This meta-analysis of individual components was done to explore the differential effect of individual components in the presence of MetS, and thus the risk estimates should be interpreted in the context of MetS. Although hypertriglyceridemia and low HDL cholesterol levels have been previously associated with increased risk for CKD, these factors are often overlooked in clinical practice. Our results suggest that these could be potential targets for reducing the risk of CKD.

The relationship between MetS and CKD is biologically plausible. Visceral obesity is highly correlated with insulin resistance, and indices of visceral obesity may be more sensitive predictors of kidney disease than BMI. Adipose tissue is a significant source of inflammatory and immunomodulatory factors, and the interaction between adipocytes and macrophages may contribute to insulin resistance and many of the features that characterize MetS. Our review demonstrated a higher risk of developing reduced eGFR with obesity. With the increasing problem of obesity across the globe, the burden of MetS is expected to rise rapidly.

Compelling data have indicated that metabolic syndrome increases the risk of CKD. Experimental studies have suggested that metabolic syndrome may induce CKD via multiple mechanic pathways. While we are waiting for randomized clinical trial and even new drug development in treating metabolic syndrome to reduce risk of CKD, current key strategies should include prevention and treatment of obesity and insulin resistance. Lifestyle modification particularly including low sodium diet and increasing physical activity would be important approaches. At the present, early identification of metabolic syndrome and treatment of individual components of metabolic syndrome may reduce the risk of CKD. However, these approaches need be further tested in large randomized clinical trial to verify their effect on reducing CKD risk.

CONCLUSION

There is significant derangement of renal parameters in obese individuals with metabolic syndrome when compared to obese without metabolic syndrome. There is an individual association of the parameters of metabolic syndrome with the renal function parameters. FBS, systolic and diastolic blood pressure had a significant association with the parameters of the renal function tests.

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