Renal functions in patients with metabolic syndrome

Augusthy A.¹, Sahu S.², Ashok Kumar J.³, Jawalekar S.⁴

¹Dr. Asha Augusthy, Associate Professor, Department of Biochemistry, Sree Narayana Institute of Medical Sciences, Ernakulam, Kerala, ²Dr. Suchanda Sahu, Associate Professor, Department of Biochemistry, All India Institute of Medical Sciences, Sijua, Bhubaneshwar, Odisha, ³Dr. Ashok Kumar Jeppu, Associate Professor, Biochemistry unit, International Medical School, Management and Science University, Shah Alam, Selangor, Malaysia, ⁴Dr. Seema Jawalekar, Professor, Department of Biochemistry, GMC, Pali, Rajasthan, India.

Corresponding Author: Dr. Asha Augusthy, Associate Professor, Department of Biochemistry, Sree Narayana Institute of Medical Sciences, Ernakulam, Kerala. Email address: asha.augusty@gmail.com

Abstract

Introduction: Metabolic syndrome consists of a constellation of metabolic abnormalities that confer increased risk of diabetes mellitus. The aim of the present study was to study renal functions in patients with metabolic syndrome.

Materials and methods: 50 controls and 50 individuals with metabolic syndrome were selected by purposive sampling technique. Waist circumference and blood pressure was measured and serum levels of fasting blood sugar, triglycerides and HDL were estimated and eGFR was calculated in controls and cases.

Results: We found that serum urea and creatinine levels were significantly increased and eGFR levels were significantly decreased in metabolic syndrome when compared to controls.

Conclusion: Our study concluded that there is significant renal dysfunction in patients with metabolic syndrome.

Keywords: eGFR, Metabolic syndrome, Renal function

Introduction

Metabolic syndrome (MetS) consists of a constellation of metabolic abnormalities that confer increased risk of diabetes mellitus. The major features of the metabolic syndrome include central obesity, hypertriglyceridemia, low HDL cholesterol, hyperglycemia and hypertension [1].

Individuals with metabolic syndrome are at increased risk for developing chronic kidney disease (CKD) [2-5]. The mechanism behind this increased risk may be due to the aggregation of known risk factors for CKD in the metabolic syndrome diagnosis. On the other hand, the metabolic syndrome diagnosis may indicate the presence of insulin resistance, which may directly increase the risk for CKD [6].

Components and consequences of MetS, including diabetes mellitus and coronary heart disease, alter renal physiology and metabolism through a cascade of various reactions [7]. For example, obesity-related early renal changes increase the glomerular filtration rate (GFR) because of increased salt reabsorption by the proximal tubule. Consequent tubuloglomerular feedback mediated reduction in afferent arteriolar resistance results in increased glomerular capillary pressure [2]. The increased GFR is a compensatory response that restores salt balance despite continued increases in tubular reabsorption but contributes to renal injury, especially if it is combined with elevated blood pressure. In addition, obesity induced sleep apnea activates sympathetic nervous system increasing the tone of the glomerular efferent arterioles and the secretion of renin and angiotensin.

In patients with MetS, mildly elevated blood pressure or mild hyperglycemia may portend an increased risk of CKD. In addition, dyslipidemia may affect the prognosis of CKD as low HDL cholesterol was shown to be a predictor of faster CKD progression[8]. Recent evidence also indicated that presence of MetS is associated with an increased risk of developing CKD.

As a matter of fact, both MetS and CKD are major global health issues with regard to the increasing prevalence of obesity and aging society [9].
The aim of this study is to find out the renal functions in metabolic syndrome.

Materials and Methods

Study design-The present study was conducted in the Department of Biochemistry, Father Muller’s Medical College after obtaining clearance from institutional ethics committee.

The study group consisted of 100 individuals selected by purposive sampling technique who had come to hospital for health check-up during a time period of two years. Informed written consent was obtained from all individual participants included in the study. This was a case-control study with a sample size of 100 patients.

Selection of subjects-50 individuals with metabolic syndrome (all patients who fulfil criteria for metabolic syndrome, according to National cholesterol education program (NCEP): ATP III 2001 for metabolic syndrome [10]and 50 controls were selected.

Exclusion criteria—Smokers, alcoholics, patients with history of liver and renal impairment were excluded from the study.

Sample and data collection—For the selected patients history was taken, physical examination was done. Waist circumference and blood pressure was measured.

Glomerular filtration rate (GFR) was estimated on the basis of serum creatinine level, with the most recent expression of the Modification of Diet in Renal Disease Study (MDRD) prediction equation for standardized serum creatinine [11]. eGFR was estimated using the recalibrated version of the four-variable MDRD study equation \( \text{eGFR (ml/min/1.73 m^2)} = \frac{186 \times \text{Scr (mg/dl)}}{1.154 \times \text{xage}^{0.203} \times 0.742 \text{ (if woman)}} \) [12]. In this study CKD was defined as eGFR< 60ml/min/1.73m2.

The criteria was set according to the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF-KDOQI).

The staging of CKD was categorized according to NKF-KDOQI criteria based on different eGFR distribution: Stage 1> 90ml/min, Stage 2:60-89ml/min, Stage 3:30-60ml/min, Stage 4:15-29ml/min and Stage 5:15ml/min[13].

Plasma fasting blood sugar (FBS), serum HDL, serum triglyceride, serum urea and serum creatinine levels were estimated. Plasma FBS was estimated using glucose oxidase peroxidase method.

Triglycerides were estimated by enzymatic colour test glucose oxidase-peroxidase method. HDL was estimated by immune-inhibition enzymatic colour test.

All estimations were done on Olympus AU 400 autoanalyzer. Statistical analysis—The data was analysed by students paired t test and Pearson’s correlation coefficient for relationship between variables.

Statistical analyses were performed with the help of SPSS software. For all statistical analyses the p value was considered to be significant when p <0.05.

Results

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Metabolic syndrome</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist circumference(cm)</td>
<td>91.56± 4.82</td>
<td>97.55± 6.72</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure (mm of Hg)</td>
<td>0120.94± 11.28</td>
<td>131.84± 14.55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm of Hg)</td>
<td>77.58± 7.05</td>
<td>82.65± 8.4</td>
<td>0.001</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>99.27± 9.15</td>
<td>111.18± 8.49</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>45.12±7.84</td>
<td>38.22±5.82</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>139.44±102.64</td>
<td>217.98±143.25</td>
<td>0.002</td>
</tr>
</tbody>
</table>

In our study we found that waist circumference, blood pressure, FBS, triglycerides were significantly increased in metabolic syndrome compared to controls. HDL cholesterol levels were significantly decreased in metabolic syndrome when compared to controls.
We also found that serum urea and serum creatinine were significantly increased in metabolic syndrome compared to controls. eGFR levels were significantly decreased in metabolic syndrome when compared to controls.

Table-3: Distribution of controls and metabolic syndrome with respect to GFR

<table>
<thead>
<tr>
<th>GFR(ml/min)</th>
<th>Controls</th>
<th>Metabolic syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1 Normal or High (&gt;90)</td>
<td>32 (64%)</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>Stage 2 Mildly decreased (60-89)</td>
<td>18 (36%)</td>
<td>30 (60%)</td>
</tr>
<tr>
<td>Stage 3 Moderately decreased (30-60)</td>
<td>-</td>
<td>11 (22%)</td>
</tr>
<tr>
<td>Stage 4 Severely decreased (15-29)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Stage 5 Kidney failure (&lt;15)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>

In metabolic syndrome 18% of patients belonged to stage I, 60% belonged to stage 2 and 22% belonged to stage 3 whereas in controls 64% belonged to stage 1 and 36% belonged to stage 2 of CKD.

Discussion

Metabolic syndrome is characterized as a cluster of metabolic disorders including central obesity, dyslipidemia, hypertension, and glucose intolerance [14]. There are some experimental and clinical evidence that implicated a causal link between increased BMI and increased risk of CKD [15, 16].

The possible mechanism for this link is through obesity-related risk factors such as hypertension, dyslipidemia, and hyperglycemia, all components of metabolic syndrome [17].

In our study we found that waist circumference, blood pressure, FBS, triglycerides were significantly increased in metabolic syndrome compared to controls. HDL cholesterol levels were significantly decreased in metabolic syndrome when compared to controls. The renal dysfunction in metabolic syndrome may be due to individual components which are risk factors for the development of CKD. One of the risk factors for CKD is obesity and it is also correlated to insulin resistance [18].

The interaction between macrophages and adipocytes which are an important source of inflammatory and immunomodulatory factors leads to insulin resistance [19]. Studies which reported obesity as a significant risk factor for eGFR<60 ml/min/1.73 m² used waist circumference rather than BMI [20-21].

In a study done by Lorraine S. Evangelista and co-workers found that general obesity and abdominal obesity were more prevalent in patients with CKD and abdominal obesity induces endocrine dysfunction or chronic inflammation thereby causing or worsening CKD [22]. Peter Stenvinkel and friends found that...
excess fat mass promotes kidney disease directly as well as indirectly through hypertension, atherosclerosis, and type 2 diabetes [23]. Another risk factor for renal dysfunction is dyslipidemia. Studies done by Muntner P et al and to Ryu et al found that both high TG and low HDL cholesterol levels were associated with a significantly increased risk of CKD.

This is in accordance with our studies which showed high TG and low HDL. Dyslipidemia is closely related to glomerular capillary endothelial and mesangial cell as well as podocyte injury, which in turn leads to mesangial sclerosis. The glomerular mesangium due to accumulation of lipoproteins can stimulate matrix production and glomerulosclerosis [24].

Ivana Mikolasevic and friends concluded that dyslipidemia is seen in patients with CKD. They observed that patients with CKD suffer from hypertriglyceridemia due to the delayed catabolism and the increased hepatic production of triglyceride-rich lipoproteins.

They also noticed that there is decreased levels of HDL due to decreased levels of Apolipoprotein A I and A II, decreased activity of lecithin–cholesterol acyltransferase and increased activity of cholesterol ester transfer protein (CETP)[25].

Studies done by Daniel E Weiner et al [26] and Gearoid M. McMahon et al [27] also found that there is significant dyslipidemia in patients with CKD.

Type 2 diabetes mellitus and hypertension are significant and common risk factors for end stage renal disease. A study done by Banach M et al concluded that insulin resistance and central obesity have been considered the main factors involved in hypertension pathophysiology associated with MS [24].

Chen et al found that the risk of CKD was 2.6 times more in MetS. In obesity and MetS there is increased levels of C-reactive protein, tumor necrosis factor-α, interleukin-6 and oxidative stress in serum and adipose tissue due to chronic low grade inflammation.

This will end up in kidney damage due to progressive loss of nephrons and decline in GFR. Each component of MetS can potentially induce renal damage[28].

One main limitation of our study is that we have not analysed cystatin C and NGAL which are latest markers for renal dysfunction.

Conclusion
In the present study renal functions were assessed in terms of serum urea, creatinine and eGFR. It was found that serum urea, creatinine and eGFR levels were significantly increased in patients with metabolic syndrome when compared with controls. eGFR levels were significantly decreased in metabolic syndrome when compared to controls. Our study concluded that there is significant renal dysfunction in patients with metabolic syndrome.

It is ideal to have periodic measurements of waist circumference, blood pressure and serum lipid profile and sugar levels to check the occurrence the metabolic syndrome which can lead to CKD.

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References


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