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**Original Research Article**

# Study of glomerular filtration rate in patients with metabolic syndrome

**Prakash K. G., Rashmi S.***

Department of Medicine, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India

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***Correspondence:**
Dr. Rashmi S.,
E-mail: rashmi.912@gmail.com



## ABSTRACT

**Background:** Chronic kidney disease is a major risk factor for end stage renal disease, cardiovascular events and death. Various studies have shown an association between metabolic syndrome and CKD. Even mild renal insufficiency increases the risk for cardiovascular events. This study was conducted to detect CKD in its early stages which are characterized by mildly reduced GFR in patients with metabolic syndrome.
**Methods:** This is a cross sectional study of 60 patients, 30 with metabolic syndrome diagnosed on the basis of IDF criteria and 30 controls. EGFR was calculated using the CKD-EPI formula and the results between the two groups was analysed using chi square test for statistical significance.
**Results:** In this study conducted on 60 patients, age distribution was between 20 and 60 years. Male to female ratio was 1:1.06. 26.66% of the cases had normal GFR while among the controls, 46.66% had normal GFR. Out of the 30 cases, 53.33% had mildly reduced GFR while out of the controls, 23.33% had mildly reduced GFR. This association between metabolic syndrome and mildly reduced EGFR was found to be significant ($p \leq 0.05$).
**Conclusions:** The results of this study showed that metabolic syndrome is associated with a mildly reduced GFR and hence early detection of these risk factors is essential for treatment and prevention of CKD.

**Keywords:** Chronic kidney disease, Glomerular filtration rate, Metabolic syndrome

## INTRODUCTION

The metabolic syndrome (syndrome X, insulin resistance syndrome) consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease (CVD) and diabetes mellitus (DM).[1]

The major features of the metabolic syndrome include central obesity, hypertriglyceridemia, low levels of high-density lipoprotein (HDL) cholesterol, hyperglycemia, and hypertension.[1] According to IDF criteria, diagnosis of metabolic syndrome is made when three out of these five parameters are satisfied, with abdominal obesity being present compulsorily.[2] Metabolic syndrome is associated with increased cardiovascular morbidity and mortality. Various studies have shown that metabolic syndrome is associated with renal impairment. Metabolic syndrome is associated with decreased GFR and chronic kidney disease.

Chronic kidney disease is defined as abnormality of kidney structure or function present for more than 3 months and has been classified based on cause, GFR and albuminuria[3]. It has been identified as a major risk factor for end stage renal disease, cardiovascular events and death.

Even mild renal insufficiency increases the risk of cardiovascular events. Early CKD is characterized by a mildly decreased glomerular filtration rate and its estimation can therefore be used in the early diagnosis of CKD. There have been studies regarding the association of metabolic syndrome with CKD. However not many studies have been conducted to study the association between metabolic syndrome and mildly reduced GFR which is defined as a GFR of 60-90ml/min/1.73m$^2$.

The prevalence of metabolic syndrome is increasing to epidemic proportions in many developed and developing countries.

Many studies have demonstrated the impact of metabolic syndrome on evolution of CKD and highlighted the importance of targeting metabolic syndrome for prevention of renal disease and premature death.[4]

Clinical studies have shown that by the time the overt signs of renal involvement such as proteinuria and reduced GFR occur, structural damage has already been established. It is thus critical to detect the earliest changes and devise suitable therapeutic interventions.[5]

Therefore this study is being undertaken to know the association of metabolic syndrome with early chronic kidney disease and also to study the relationship of various components of metabolic syndrome and reduction in glomerular filtration rate in order to detect those at high risk for development of chronic kidney disease. This is helpful in appropriate modification and treatment of the various risk factors and thereby helping in prevention or delaying the development of end stage renal disease.

## METHODS

This was a cross sectional study conducted on both inpatients and outpatients at Medicine department at hospitals attached to BMCRI. It was conducted from the period of August 2018 to May 2019. Patients were screened and diagnosed as having metabolic syndrome based on the IDF criteria for metabolic syndrome. The patients with pre-existing renal and cardiac diseases, those aged over 60 years were excluded and a total of sixty patients were included in the study.

Demographic data, thorough history and clinical examination was done and recorded in a questionnaire. Height and weight was measure and BMI calculated. Abdominal obesity was measured by recording abdominal girth. Haematological investigations like Fasting blood sugar, lipid profile and renal function tests were performed. The EGFR was calculated from the serum creatinine levels using the Chronic Kidney Disease Epidemiology collaboration formula.[3]

The IDF criteria for metabolic syndrome has been shown in table 1.[2]

Subjects who were included in the study were

- Adult patients aged 18 to ≤60 years of either sexes.
- Patients clinically suspected or diagnosed as having metabolic syndrome, according to IDF criteria.
- Adults ≤60years without metabolic syndrome as control group.
- Patients willing to give written informed consent to the study.

Patients aged >60years, those who were previously diagnosed to have kidney disease like nephritis, renal failure, renal transplant patients were excluded from the study.

Patients with pre-existing cardiovascular diseases like heart failure, coronary heart disease also formed part of the exclusion criteria.

**Table 1: IDF criteria for metabolic syndrome.**

| Criteria | Defining level |
|---|---|
| Blood pressure | Systolic BP≥130mmhg or diastolic BP≥85mmhg<br>or treatment of previously diagnosed hypertension |
| Triglycerides | ≥150mg/dl<br>or specific treatment for this lipid abnormality |
| HDL cholesterol<br>Men<br>Women | <40mg/dl<br><50mg/dl<br>or specific treatment for this lipid abnormality |
| Fasting glucose | ≥100mg/dl<br>or previously diagnosed type 2 diabetes |

Central obesity defined as waist circumference with ethnicity specific values, for South Asian population-men≥90cm and women≥80cm.

Plus, any two of the following four factors,

If BMI is more than 30kg/m$^2$, central obesity can be assumed and waist circumference does not need to be measured.

Subjects were classified into two groups based on the presence of metabolic syndrome. Both the groups, with and without metabolic syndrome, were studied for reduced GFR which was calculated from the CKD-EPI formula.

CKD-EPI equation [6]

$GFR = 141 \times [\min(Scr/k),1)^{\alpha} \times \max(Scr/k),1)^{-1.209}] \times 0.993^{age} \times 1.018$[ if female] x 1.159 [if black]

where, α is -0.329 for females and -0.411 for males, Min indicates minimum of Scr/k or 1, and max indicates maximum of Scr/k or 1, K= 0.7 if female and 0.9 if male, Scr= serum creatinine.

They were further classified into groups based on their GFR. A GFR of >110ml/min/1.73m$^2$ was considered as hyperfiltration. Mildly reduced GFR was defined as a GFR between 60-90ml/min/1.73m$^2$. A GFR of 90-110ml/min/1.73m$^2$ was considered as normal.[3]

***Statistical analysis***

Data was entered in the excel spreadsheet. Descriptive statistics like mean, standard deviation and percentages were calculated. Chi square test was used to compare the qualitative variables between the groups using SPSS software version 2.0. Multiple linear regression analysis was done to study the association of various factors of metabolic syndrome with the GFR.

## RESULTS

A total of sixty patients were studied, 29 males and 31 females. Our study population consisted predominantly of middle-aged subjects.

Age distribution of the subjects is enclosed in figure 1.

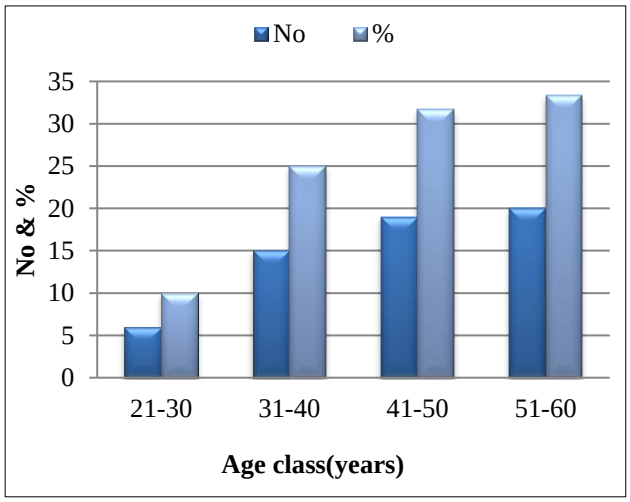


**Figure 1: Age wise distribution of subjects.**

Among the various components of metabolic syndrome, elevated fasting blood glucose was the most common risk factor (76.6% among cases, 10% among the controls), followed by dyslipidemia and hypertension in both the groups. Among the patients with metabolic syndrome, 26.6 percentage had normal GFR and 53.3 percentage had mildly reduced GFR.

Whereas among the patients without metabolic syndrome, 46.6 percentage had normal GFR and 23.3 percentage had mildly reduced GFR.

The percentage of patients with mildly reduced GFR and normal GFR was compared between both the groups using chi square test and the difference was found to be statistically significant (p=0.05) (Figure 2).

Metabolic syndrome causes mildly reduced GFR. However, in our study, it was seen that the components of metabolic syndrome did not affect the GFR independently. Multiple linear regression analysis was done to study the same with EGFR as the dependent variable. The standardised coefficient beta was -0.81, -2.12 and -0.05 for FBS, triglycerides and BMI respectively which implied a negative association with GFR.

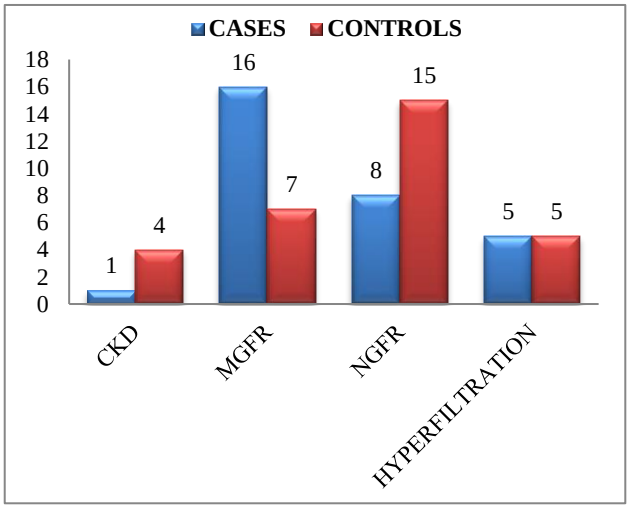


**Figure 2: Distribution of the subjects based on EGFR.**

**Table 2: Multiple linear regression analysis.**

| | Unstandardized Coefficients | | Standardized Coefficients | t | p value |
|---|---|---|---|---|---|
| | B | Std. Error | Beta | | |
| (Constant) | 25.947 | 41.238 | | 0.629 | 0.532 |
| FBS | -0.039 | 0.064 | -0.081 | -0.605 | 0.548 |
| TG | -0.173 | 0.112 | -0.212 | -1.539 | 0.130 |
| HDL | 0.034 | 0.052 | 0.088 | 0.660 | 0.512 |
| BMI | -0.399 | 1.262 | -0.051 | -0.316 | 0.753 |
| Abdominal circumference | 1.176 | 0.604 | 0.322 | 1.945 | 0.057 |

Dependent Variable: EGFR

HDL showed a positive correlation with GFR with a beta value of 0.08. It can be inferred that metabolic syndrome rather than the individual components affect the GFR. (Table 2). A multiple linear regression was calculated to predict EGFR based on FBS, TG, HDL, BMI and Abdominal circumference. Predicted EGFR = 25.94 - 0.039 (FBS) -0.173 (TG) + 0.034(HDL) – 0.399 (BMI) + 1.17 (Abdominal Circumference).

## DISCUSSION

Measurement of EGFR is helpful in early detection of CKD. In this study comprising of patients with and without metabolic syndrome, EGFR was calculated using the CKD-EPI formula among both the subgroups.

It can be said that the various studies conducted on the association between GFR and metabolic syndrome have yielded broadly consistent results that metabolic syndrome is a risk factor for reduced GFR, independent of age , sex or other potential confounders.

In our study too, it was seen that metabolic syndrome is independently associated with a mildly reduced GFR.

A study by Wen Hu et al further supports this. In their study in Chinese population, it was found that metabolic syndrome was associated with a mildly reduced GFR following a multivariable adjustment.[7] Another study by Hui Song et al also proves the same.[8]

However, studies have yielded mixed results for the association between various components of metabolic syndrome and GFR.

For example, in the study by Wen Hu et al, it was seen that FBS and HbA1C levels had a positive correlation with GFR and triglycerides, waist circumference had a negative correlation.[7]

In another study conducted by Kitiyakara C et al on metabolic syndrome and CKD in a Southeast Asian cohort of 3795 subjects, it was seen that only high blood pressure had an association with GFR.[9]

A study by Chen et al, reported a positive association between high blood pressure, reduced HDL, high triglycerides and GFR in a study conducted on 6217 US adults.[10]

In a study by Hui Song et al, it was seen that metabolic syndrome was related to the reduced GFR and that elevated blood pressure, low HDL and elevated FBS were independently associated with reduced GFR.[8]

In contrary to the above reports, our study showed that there was no significant correlation between EGFR and the components of metabolic syndrome.

Multiple linear regression analysis was done to verify the effect of various factors of metabolic syndrome on EGFR. Negative beta values were obtained for triglycerides and hypertension and positive values were obtained for HDL and fasting plasma glucose levels, thus implying their effect on metabolic syndrome, though this was not statistically significant. This could be due to the complex interplay of the components of metabolic syndrome and the basic pathological process of metabolic syndrome which is insulin resistance and inflammatory response.

The disparity among different studies could probably be due to the variable study population and demographic characteristics. One of the limitations of our study is the limited sample size and large population based studies are needed to ascertain these findings. Also, this study was largely based on the calculation of EGFR than the measurement of albumin-creatinine ratio. However this could probably reflect the early dysfunction rather than structural damage to the kidneys which is pathognomonic of early CKD.[11]

## CONCLUSION

Metabolic syndrome is a risk factor for mildly reduced GFR. The various components of metabolic syndrome have an independent effect on GFR, though not statistically significant in our study. It can be said that, amongst the various parameters, EGFR is one of the important ones to be monitored in a patient with metabolic syndrome in order to detect CKD at the earliest stage.

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