Comparison of different renal function tests for detecting renal dysfunction in patients with Metabolic Syndrome

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Abstract
Background: Several renal function tests (RFTs) are used to detect renal dysfunction. Their relative reliability in detection of renal dysfunction in metabolic syndrome (MS) is unknown.
Objective: To compare different renal function tests for detection of renal dysfunction in patients with MS.
Material and Methods: The material comprised 279 adult patients with MS diagnosed according to NCEP: ATP-III criteria. RFTs done in all patients were serum creatinine, serum urea, creatinine clearance, eGFR and urine protein.
Results: Serum creatinine and serum urea were above normal in 32.26% of patients. Patients with eGFR below normal were 73.84%. Creatinine clearance was below normal in 61.29%. 18.99% of total subjects tested positive for urine protein.
Conclusion: Prevalence of renal dysfunction was high (73.84%) in patients with MS. eGFR appeared to be the best indicator of renal dysfunction.
Keywords: Metabolic syndrome, renal dysfunction, renal function test.

Introduction
Metabolic syndrome (MS) is a cluster of biochemical and anthropometric abnormalities. Different criteria have been proposed by different agencies for diagnosis of MS. NCEP: ATP-III criteria are followed most commonly in India. Complications of MS can be cardiac, hepatic and renal[1]. Renal dysfunction is identified by using different renal function tests. Serum urea, serum creatinine, creatinine clearance, eGFR and detection of proteins in urine are common RFTs. Chronic kidney disease (CKD) is defined by indicators of kidney damage imaging or elevated serum creatinine or elevated serum urea or decreased creatinine clearance or decreased eGFR[2]. CKD can be classified into five stages using Kidney Outcomes Quality Initiative (KDOQI) guidelines using thresholds of eGFR within the CKD range or evidence of structural renal changes e.g. proteinuria. National Institute for Health Excellence (NICE) have suggested that stage 3 be subdivided into 3a and 3b reflecting increasing CVD risk[3].
Material & Methods

The sample comprised of 279 patients with MS residing in a rural area of Rajasthan. Diagnosis of MS was based on NCEP:ATP-III criteria\(^4\). Blood samples were drawn in fasting state from the subjects under aseptic condition after obtaining their consent. Ethical clearance was obtained from the institutional ethical committee of NIMS University, Jaipur (Ref.no. NIMSUNI/IEC/2017/23-7). Fasting plasma glucose (FPG) was estimated by glucose oxidase method\(^5\), fasting plasma triglycerides (FPTG) were estimated by an enzymatic method\(^6\) and plasma HDL cholesterol (PHDLc) was estimated by an enzymatic method\(^7\). Anthropometric data were collected through direct measures. Body mass index (BMI) was calculated by body weight in kg divided by height in meter squared. Blood pressure (BP) was measured using standard mercury sphygmomanometer. Renal function tests (RFTs) done were serum creatinine by Jaffe’s method\(^8\), serum urea by urease method [9], creatinine clearance by Coxxcfaft G formula (online calculator)\(^10\), eGFR by MDRD equation\(^11\) and proteinuria by dipstick method. The data were statistically analyzed using statistical package for social sciences (SPSS) version-20.

Results

The total numbers of patients were 279 (143 males and 136 females). Serum creatinine was above normal in 32.26% of patients. Serum urea was above normal in 32.26% of patients. Patients with eGFR below normal were 73.84%. Creatinine clearance was below normal in 61.29%. 18.99% of the total patients tested positive for urine protein (Table-1 & Fig-1).

Table-1: Number and percentage of patients with MS having abnormal renal function tests

| RFTs                          | Male | Female | Total |
|-------------------------------|------|--------|-------|
| N %                           | N %  | N %    |       |
| Total Patients                | 143  | 51.25  | 136   | 48.75 | 279 | 100  |
| Positive urine protein        | 29   | 20.28  | 24    | 17.65 | 53  | 18.99|
| Serum creatinine above normal | 50   | 34.96  | 40    | 29.41 | 90  | 32.26|
| Serum urea above normal       | 49   | 34.27  | 41    | 30.15 | 90  | 32.26|
| Creatinine clearance below normal | 77   | 53.84  | 94    | 69.12 | 171 | 61.29|
| eGFR below normal             | 91   | 63.64  | 115   | 84.56 | 206 | 73.84|

According to eGFR, majority of patients were in G2 stage followed by G1, G3a, G3b, G4 and G5 (Table-2 & Fig-2).
Table-2: Renal dysfunction in patients with metabolic syndrome according to eGFR.

| eGFR stages | Male (N=145) | Female (N=136) | Total (N=279) |
|-------------|-------------|----------------|--------------|
| N           | %           | N              | %            |
| >90 G1      | 52          | 36.36          | 21           | 15.44       | 73            | 26.16         |
| 89-60 G2    | 43          | 30.07          | 48           | 35.29       | 91            | 32.62         |
| 59-45 G3a   | 12          | 8.39           | 25           | 18.38       | 37            | 13.26         |
| 44-30 G3b   | 16          | 11.19          | 16           | 11.76       | 32            | 11.47         |
| 29-15 G4    | 9           | 6.29           | 13           | 9.56        | 22            | 7.89          |
| <15 G5      | 11          | 7.69           | 13           | 9.56        | 24            | 8.6           |

Fig.-2: Comparison of eGFR stages

Discussion
Developing countries are major reservoirs of renal dysfunction. The incidence of renal dysfunction is rising rapidly in India also\cite{12,13}. It has been reported that India is likely to face an awful CKD/end-stage renal disease (ESRD) burden, with 25–40% of its population being at risk\cite{14}. CKD has been recognized as a risk factor for ESRD which are among the leading causes of death in developing countries. MS is an important cause of renal dysfunction. Different RFTs were compared in MS patients in the present study. Decreased eGFR by MDRD equation was found to be the most sensitive indicator of MS.

Patients with eGFR below normal were 73.84% while patients with decreased creatinine clearance were 61.29%. Patients with serum creatinine and serum urea above normal were approx 32%. Stages of eGFR also give information about the severity of renal dysfunction whereas serum creatinine and serum urea do not give information like eGFR. It has been reported earlier that the most of patients in G3 and G4 stages had four and five MS components, while in G2 stage, the presence of three MS components was predominant\cite{15}.

Conclusion
Prevalence of renal dysfunction was high (73.84%) in patients with MS, and 8.6% subjects were found in the 5th stage of kidney disease according to eGFR scaling. eGFR appeared to be the best indicator of renal dysfunction. Further, proteinuria was found only in the 5th stage of CKD.

References
1. Jennifer L. Kuk, Chris I. Ardern. Age and Sex Differences in the Clustering of Metabolic Syndrome Factors Association with mortality risk. Diabetes Care 2010; 33(11): 2457-2461.
2. KDOQI. Chronic Kidney Disease: Evaluation, Classification, and Stratification 2002.
3. NICE. CG73 Chronic kidney disease: full guideline: 2008; [6th June 2012]. The published full clinical guideline on chronic kidney disease including recommendations and methods used.

4. Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult treatment panel -III). Circulation. 2002;10(6):3143-3421.

5. Trinder P. Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. Annals of Clinical Biochemistry.1969; 6(2):24-30.

6. Fletcher MJ. A colorimetric method for estimating serum triglycerides. Clinica Chimica Acta, 1968; 45(22):393-398.

7. Abell LL, Levy BB, Brodie BB, Kebndall FE. A simplified method for the estimation of total cholesterol in serum. Biological Chemistry.1952; 19(5):357-363.

8. Butler AR. Jaffé reaction mechanism debated. Clinical Chemistry.1977; 23(3):613-614.

9. Chaney AL, Marbach EP. The number of reagents for color production in urease activity. Clinical Chemistry.1962; 8(2):130-136.

10. Cockcroft D, Gault MD. On line calculator for Creatinine Clearance using Cockcroft-Gault Equation., Nephron, 16:31-41, 1976.

11. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: A new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999;130(6):461–470.

12. Nugent RA, Fathima SF, Feigl AB, Chyung D. The burden of chronic kidney disease on developing nations: A 21st century challenge in global health. NephronClin Pract. 2011;118:269–77.

13. Agarwal SK, Srivastava RK. Chronic kidney disease in India: Challenges and solutions. Nephron Clin Pract. 2009; 111:197–203.

14. Srinath Reddy K, Shah B, Varghese C, Ramadoss A. Responding to the threat of chronic diseases in India. Lancet. 2005;366:1744-9.

15. Raikou VD and Gavriil S. Metabolic syndrome and chronic renal disease. Diseases. 2018; (6):12.1-12.