

Hyperglycemia and Hypertension are Associated as Parallel Risk Factors in Metabolic Syndrome at the Onset of Renal Dysfunction: A Cross-Sectional Study in a Rural Population of Northern India

Gajraj S Yadav¹, Prerna Singh², Rajesh B Ramteke³

^{1,2}Assistant Professor, Department of Biochemistry, Raipur Institute of Medical Sciences (RIMS), Raipur

³Associate Professor, Department of Forensic Medicine & Toxicology, Raipur Institute of Medical Sciences (RIMS), Raipur

Received: 28-10-2022 / Revised: 30-11-2022 / Accepted: 20-12-2022

Corresponding author: Dr Gajraj S Yadav

Conflict of interest: Nil

Abstract

Background: Studies were scanty in the rural population related to metabolic syndrome (MS) and renal dysfunction.

Objective: To assess risk component of MS and its association in renal dysfunction of patients with metabolic syndrome in rural population.

Materials and Methods: The study sample of 279 adult patients (143 male and 136 female) with metabolic syndrome, residing in a rural area of Jaipur district. The metabolic syndrome was defined as the presence of three or more of the following: elevated blood pressure, low high-density lipoprotein cholesterol level, high triglyceride level, elevated glucose level, and abdominal obesity. Blood samples were analyzed for serum urea, serum creatinine, eGFR.

Results: (FPG and hypertension) Patients with serum urea above normal was 32.26% (male and female ratio was 1.2:1). Patients with serum creatinine above normal were 32.26% (male and female ratio was 1.25:1). Patients with eGFR below normal were 73.84% among them 32.62%, 13.26%, 11.47%, 7.89%, and 8.6% patients were reported under kidney disease stages of 2nd, 3rd a, 3rd b, 4th and 5th according to eGFR stages.

Conclusion: Prevalence of renal dysfunction is high in patients with complication of uncontrolled & prolonged hyperglycemia and hypertension associated as parallel risk factors of MS components.

Keywords: Metabolic syndrome, Renal dysfunction, eGFR, Rural population.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Metabolic syndrome is a cluster of its five criteria. The combinations of MS component is not definite universally, the presence of minimum three components combinations are different in a locality, sex, race, urban, rural population, and used as a dichotomous outcome. Most of the MS components are

also associated with age. Age and sex differences in patients with MS are expressed in the different metabolic syndrome combinations are associated with mortality risk [1]. Moreover, ageing is assumed as an outer risk factor associated with all five MS criteria in a random manner, such

associations are found in developing complications with heart, liver, and renal dysfunction [2]. However, renal dysfunction is a serious public health problem around the world [3-7]. Co-occurring of component of MS may risk factors for renal dysfunction including hyperglycemia, hypertension, dyslipidemia and central obesity in a MS patient [8]. Studies in last decade emerged on the relationship between MS and renal dysfunction [9-11]. and focused on incidence rate of MS and renal dysfunction is increasing annually, presenting a serious threat to life and health [12]. Someone suggested that metabolic syndrome is a heterogeneous entity, may mask the differential associations with health risk [13]. It is clear that the combination of metabolic syndrome criteria and its encountered numbers are different between the sexes and progressive age [14]. Some previous studies are enlightened the goal to achieve the numbers and combination of MS criteria in the progression of MS complications [15]. This study aimed to explore the susceptible pioneer combination of MS criteria at the onset of renal dysfunction.

Materials and Methods

The study comprised 279 adult patients with MS residing in the rural area in Jaipur (Rajasthan) India. All participants were asked to fill a structured proforma, taking into account the educational, employment status including age and sex. They were subjected to detailed physical examination with special importance to anthropometrics. Weight was recorded using a standard electronic weighing machine. Height was recorded to the nearest 1cm. Body mass index (BMI) was calculated using the formula, $\text{weight (kg)/height(m}^2\text{)}$. Waist circumference measured at the minimum circumference between the lowest rib and the upper lateral border of the right iliac crest over light clothing using a flexible measuring tape without any pressure to the body surface and recorded to the nearest 0.1cm. Blood

pressure was taken in sitting position five minutes apart with the arms resting on a surface [16] with the help of trained nursing staff in the presence of a resident doctor. Urine collected from all individuals and assessed using 5-parameter dipstick for urine protein. The results of dipsticks proteinuria were visually read and compared with the given standard results and recorded as nil, trace, +1, +2, +3 and +4. Urine creatinine and urea were also analyzed [17,18]. Blood was drawn in the fasting state of all participants for quantitative estimation of plasma creatinine (PC) [17], urea was estimated by urease method [18] and fasting plasma glucose (FPG) [19]. fasting plasma tryglyceride (FPTG) [20]. and Plasma high-density lipoprotein cholesterol (PHDLc) [21]. all biochemical analysis was performed using the fully automated biochemistry analyzer (Human) at central laboratory of biochemistry in NIMS hospital and Research affiliated to National Institute of Medical Science and Research, Jaipur;. Fasting plasma glucose was tested by the Glucose Oxidase-Peroxidase method [22] and creatinine was analyzed by the Jaffe's method [17] both FPTG and PHDL-C were analyzed by enzymatic method [20,21]. Glomerular filtration rate was estimated (eGFR) in all subjects using MDRD formula [22]. The data statistically analyzed by using the software SPSS version-20 (IBM), and data has reported as mean \pm standard deviation (SD). $P < 0.05$ was considered as statistically significant. The study was approved by Institutional Ethical Committee (Ref-NIMSUNI/IEC/2017/23-7) of NIMS University, Jaipur.

Result

This study comprised 279 adult patients with MS residing in the rural area in India. Males were 51.25% (143) and females were 48.75% (136). Age was 50.37 ± 13.99 years. Male was 49.77 ± 13.77 years and female was 50.98 ± 14.26 years. BMI was high in female (26.12 ± 3.82) with compare to male

(25.69±3.5). The total educated subject was 65.87% (N=181) and physically active (working) subject was 71.33% (N=199), in both parameters male percentage was high. WC was high in female (93.76±6.11cm) with compare to male (86.14±7.92cm). Females were more hypertensive than males. FPG and FPTG were high in males with compare to

females. HDLc was found low in males with compare females. S. Creatinine, S. Urea, and eGFR were found high in males with compare to females but more females (9.56%, N=13) were fall into the 5th stage of eGFR with compare to males (7.69%, N=11). Total 8.6% (N=24) subjects were found at CKD under the 5th stage of eGFR (Table-1).

Table 1

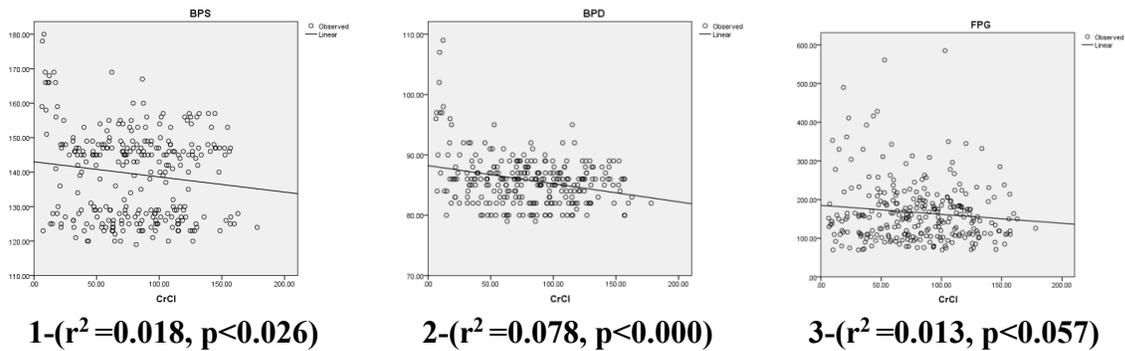
Base line Parameter	Male	Female	Total
N	143 (51.25%)	136 (48.75%)	279 (100%)
Age (Year)	49.77±13.77	50.98±14.26	50.37±13.99
Height (Met)	1.75±0.07	1.63±9.27	1.69±0.09
Weight (Kg)	77.36±9.27	68.87±9.27	73.22±10.04
BMI	25.69±3.5	26.12 ±3.82	25.9±3.66
Educated (%)	74.83% (107)	54.41% (74)	65.87% (181)
Uneducated (%)	25.17% (36)	45.59% (62)	35.13% (98)
Working (%)	79.72% (114)	62.5% (85)	71.33% (199)
Not working (%)	20.28% (29)	37.5% (51)	28.67% (80)
WC (cm)	86.14±7.92	93.76±6.11	82.31±10.01
FPG (mg/dl)	169.27±72.65	163.88±86.79	166.64±79.76
FPTG (mg/dl)	191.83±72.29	189.87±67.75	190.87±69.99
HDLc(mg/dl)	36.35±7.23	38.08±8.66	37.19±7.99
BPSys (mmHg)	138.83±12.45	140.16±13.34	139.48±12.88
BPDias (mmHg)	85.58±4.37	86.05±3.97	85.81±4.18
S. Creatinine (mg/dl)	1.72±2.06	1.51±1.5	1.62 ±1.81
S. Creatinine (above normal & %)	3.22±2.69 N=50 (34.96%)	3.04±2.09 N=40 (29.41%)	3.14±2.59 N=90 (32.26%)
S. Urea (mg/dl)	57.16±60.8	49.88±48.69	53.61±55.26
S. Urea (above normal & %)	112.66±77.85 N=49 (34.27%)	104.4±59.57 N=41 (30.15%)	108.9±69.86 N=90 (32.26%)
U. Protein (Dipstick)	20.28%(29)	17.65%(24)	18.99%(53)
U. Protein (+1 to +4)	9.8% (14)	9.56% (13)	9.89% (27)
eGFR (Mean)	72.92±34.82	58.89±28.84	66.08±32.75
eGFR (>90)	36.36% (N=52)	15.44% (N=21)	26.16% (N=73)
eGFR (<90)	63.64% (N=91)	84.56% (N=115)	73.84% (N=206)
eGFR (<15)	7.69% (N=11)	9.56% (N=13)	8.6% (N=24)

A correlation was found highly significant at the 0.01 level (2-tailed) between BP (diastolic) and RFT (CrCl, UrCl, eGFR), FPG and RFT (UrCl). The correlation was found significant at the 0.05 level (2-tailed) between BP (Systolic) and RFT (CrCl and eGFR) (Table-2).

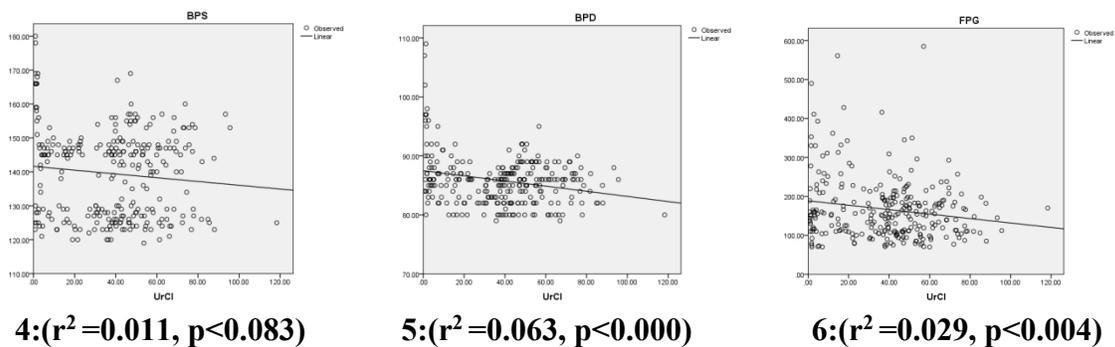
Table 2

Correlation is significant at the 0.01 level (2-tailed)		
Correlation between		p-value
BP & PG	RFT	
BP(Dias)	CrCl	0.000
BP(Dias)	UrCl	0.000
BP(Dias)	eGFR	0.000
FPG	UrCl	0.004
Correlation is significant at the 0.05 level (2-tailed)		
Correlation between		p-value
BP & PG	RFT	
BP(Sys)	CrCl	0.026
BP (Sys)	eGFR	0.015
FPG	eGFR	0.041

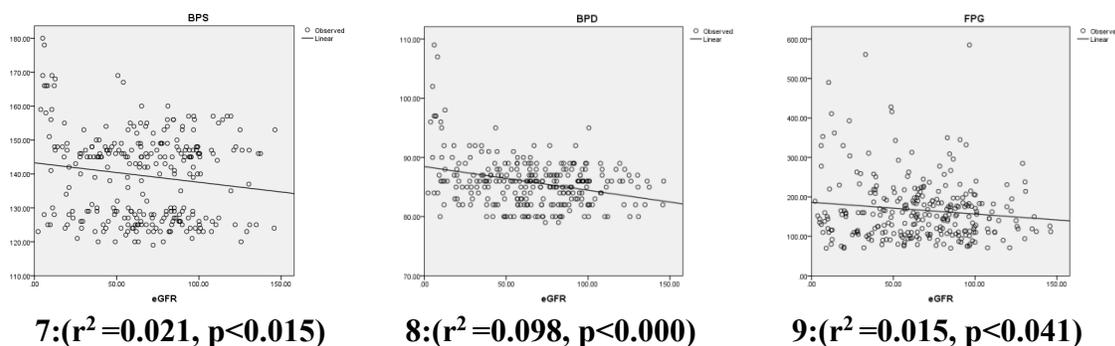
Regression curves were estimated between RFTs and BP (Sys & Dias), FPG (Graph-1 to 9).



Graph 1 to 3: RFT (CrCl) and BP (Sys & Dias), Fasting Plasma Glucose (FPG/BFS)



Graph 4 to 6: RFT (UrCl) and BP (Sys & Dias), Fasting Plasma Glucose (FPG/BFS)



Graph 7 to 9: RFT (eGFR) and BP (Sys & Dias), Fasting Plasma Glucose (FPG/BFS)

Discussion

This is a hospital-based study on patients who are residing in the rural area in India. Moreover, several hospital-based studies were on the prevalence of CKD in India [23]. Moreover, population-based studies are few and mostly done in urban India [24]. All concerned studies were focused on the effect of MS component on CKD.

Hyperglycemia and hypertension are associated parallel risk factors found significant in this study. In a other study, hypertension and hyperglycemia came out to be the most effective predictors of CKD in subjects with MS. Several population-based studies supported the effect of MS on CKD even after adjusting for the influences of diabetes, hypertension, age, and gender [25].

In another population-based study from south India, found the high prevalence of CKD in the rural population similar to this hospital-based study that records 4.41% of proteinuria [26] unlike this study found proteinuria 9.89%. In another study, using random cluster sampling method across the city of New Delhi, using MDRD eGFR of 60 ml/min/1.73 m², the prevalence of decreased GFR < 60/ml/min/1.73 m² was 4.2% [23].

The prevalence of renal dysfunction using MDRD eGFR <60 ml/min in our hospital-based study was 41.22% and the prevalence of CKD in our study was 8.6% those with decreased <15 eGFR at the 5th level of eGFR stage. The major difference in decreased eGFR might be due to different sampling

method. Reports of 2017 and 2016 from USA and China respectively, renal replacement economic burden is increasing gradually [27-29].

To control the economic burden in renal replacement, it is important to understand the relationship between MS and CKD. This study is a step ahead like recent study of china, assess early identification of risk factors such as hyperglycemia and hypertension in patients with MS will help to reduce the possibility of renal replacement [30].

Conclusion

This study points to the growing prevalence of CKD even in the rural areas in India. There is a strikingly increasing prevalence of lifestyle diseases such as hyperglycemia and hypertension in the Indian villages, similar to that in the western countries. There was a statistically significant relationship of CKD with hypertension and hyperglycemia.

On regression analysis, hyperglycemia and hypertension were found to be predictive for CKD. Prevalence of renal dysfunction is high in patients with complication of uncontrolled and prolonged hyperglycemia and hypertension associated as parallel risk factors of MS component.

Acknowledgement:

This is an original work carried out in medical biochemistry department at NIMS

University, Jaipur-303121, Rajasthan, India. The work was recommended by scientific committee (Ref-NIMS/FOMAA/2017/06) and approved by Institutional Ethical Committee (Ref-NIMSUNI/IEC/2017/23-7) of NIMS University, Jaipur.

The authors are thankful to moral support in the publication. Heartily thanks to the patients who volunteered for this study. All the facilities of this research work was provided by NIMS University.

References

1. Jennifer L. Kuk, Chris I. Arden. Age and Sex Differences in the Clustering of Metabolic Syndrome Factors Association with mortality risk. *Diabetes Care*. 2010;33(11): 2457-2461.
2. Ford ES, Giles W H, Dietz W H. Prevalence of the metabolic syndrome among US adults: findings from the Third National Health and Nutrition Examination Survey. *JAMA*. 2002; 287:356–359.
3. Zhang L, Zhao MH, Zuo L, et al. China Kidney Disease Network (CK-NET) 2016 annual data report. *Kidney Int Suppl*.2020;10(2):e97e185.
4. Murphy D, McCulloch CE, Lin F, et al. Trends in prevalence of chronic kidney disease in the United States. *Ann Intern Med*. 2016;165(7):473–481.
5. Jonsson AJ, Lund SH, Eriksen BO, Palsson R, Indridason OS. The prevalence of chronic kidney disease in Iceland according to KDIGO criteria and age-adapted estimated glomerular filtration rate thresholds. *Kidney Int*. 2020;98(5):1286–1295.
6. Zhang L, Wang F, Wang L, et al. Prevalence of chronic kidney disease in China: a cross-sectional survey. *Lancet*. 2012;379(9818):815–822.
7. Glassock RJ, Warnock DG, Delanaye P. The global burden of chronic kidney disease: estimates, variability and pitfalls. *Nat Rev Nephrol*. 2017;13(2):104–114.
8. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*. 2009;120(16):1640–1645.
9. Pammer LM, Lamina C, Schultheiss UT, et al. Association of the metabolic syndrome with mortality and major adverse cardiac events: a large chronic kidney disease cohort. *J Intern Med*. 2021;290(6):1219–1232.
10. Lea JP. Metabolic syndrome, CKD progression, and death: the good, the bad, and the ugly. *Clin J Am Soc Nephro*. 2013;8(6):893–895.
11. Comini LO, de Oliveira LC, Borges LD, et al. Individual and combined components of metabolic syndrome with chronic kidney disease in individuals with hypertension and/or diabetes mellitus accompanied by primary health care. *Diabetes Metabol Syndr Obes*. 2020;13:71–80.
12. Yun HR, Kim H, Park JT, et al. Obesity, metabolic abnormality, and progression of CKD. *Am J Kidney Dis*. 2018;72(3):400–410.
13. Zhang L, Zuo L, Wang F, et al. Metabolic syndrome and chronic kidney disease in a Chinese population aged 40 years and older. *Mayo Clin Proc*. 2007;82(7):822–827.
14. Chen J, Muntner P, Hamm LL, et al. The metabolic syndrome and chronic kidney disease in U.S. adults. *Ann Intern Med*. 2004;140(3):167–174.
15. Wang Y, Sun B, Sheng LT, et al. Association between weight status, metabolic syndrome, and chronic kidney disease among middle-aged and elderly Chinese. *Nutr Metab Cardiovasc Dis*. 2020; 30(11):2017–2026.

16. McLain LG. A statement of the committee of the American Heart Association to review. American heart journal.1976; 92(5):634-647.
17. Dumas BT, Watson WA, Biggs HG. Albumin standards and the measurement of serum albumin with bromocresol green. Clinica Chimica Acta. 1971; 31(1): 87-92.
18. Boronat M, Bosch E, Lorenzo D, Quevedo V, Lopez-Rios L, Riano M et al. Prevalence of determinants of the metabolic syndrome among subjects with advanced nondiabetes-related chronic kidney disease in Gran Canarian. Renal Failure. 2015; 38(7):198-203.
19. Wong Y, Cook P, Roderick P, Somani BK. Metabolic syndrome and kidney stone disease: A systematic review of literature. Journal of Endourology. 2016; 30(5): 246-53.
20. Trinder P. Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. Annals of Clinical Biochemistry.1969; 6(2):24-30.
21. Chaney AL, Marbach EP. The number of reagents for color production in urease activity. Clinical Chemistry.1962;8(2): 130-136.
22. Nesto R W. Obesity: A major component of the metabolic syndrome. Texas Heart Institute journal. 2005;32(1):387-389.
23. Singh NP, Ingle GK, Saini VK, Jami A, Beniwal P, Lal M, et al. Prevalence of low glomerular filtration rate, proteinuria and associated risk factors in North India using Cockcroft-Gault and Modification of Diet in Renal Disease equation: An observational, cross-sectional study. BMC Nephrol. 2009; 10:4.
24. Agarwal SK, Dash SC, Irshad M, Raju S, Singh R, Pandey RM. Prevalence of chronic renal failure in adults in Delhi, India. Nephrol Dial Transplant. 2005; 20:1638-42.
25. Thomas G, Sehgal AR, Kashyap SR, Srinivas TR, Kirwan JP, Navaneethan SD. Metabolic Syndrome and Kidney Disease: A Systematic Review and Meta-analysis. Clin J Am Soc Nephrol. 2011; 6:2364-73.
26. Mani MK. Experience with a program for prevention of chronic renal failure in India. Kidney Int Suppl. 2005;94: S75-8.
27. Saran R, Robinson B, Abbott KC, et al. US renal data system 2019 annual data report: epidemiology of kidney disease in the United States. Am J Kidney Dis. 2020;75(1Suppl 1): A6-A7.
28. Levey AS, Atkins R, Coresh J, et al. chronic kidney disease as a global public health problem: approaches and initiatives - a position statement from Kidney Disease Improving Global Outcomes. Kidney Int. 2007;72(3):247-259.
29. Zhang L, Zhao MH, Zuo L, et al. China Kidney Disease Network (CK-NET) 2016 annual data report. Kidney Int Suppl. 2020;10(2): e97-e185.
30. Hua Xiao, Xiaofei Shao, Peichun Gao, Hequn Zou, Xinzhou, Zhang. Metabolic syndrome components and chronic kidney disease in a community population Aged 40 years and older in southern china: A cross-sectional study. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2022; 15:839-84.