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Original Research Article

Role of serum Cystatin C as a marker of early nephropathy in metabolic syndrome: a case control study

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ABSTRACT

Background: The metabolic syndrome (MS) has become a significant public health problem and patients with MS are at higher risk for developing renal diseases. Serum Cystatin C suggested as a sensitive endogenous marker than creatinine for slight changes in GFR could be useful marker in MS.
Methods: A total of 200 subjects were included. New International Diabetes Federation (IDF) definition of MS was used as inclusion criteria. Patients excluded were those with hypo/hyperthyroidism, on glucocorticoids, statins and fibrate, malignancy, cirrhosis, active liver disease and conditions affecting abdominal girth. Serum Cystatin C, insulin, creatinine, triglycerides, high density lipoproteins-cholesterol (HDL-C), fasting glucose, Urinary microalbumin and Urinary creatinine were estimated by standard method.
eGFR and HOMA-IR (homeostasis model assessment of insulin resistance) were calculated. The primary outcome assessed was the occurrence of early nephropathy in MS and the secondary outcome included evaluation of early nephropathy by serum Cystatin C and eGFR. Appropriate statistical test was applied by using SPSS Version 21 software.
Results: Fasting insulin levels and insulin resistance were significantly raised in MS cases. eGFR (MDRD) was lower in the MS cases (72.59±8.79mL/min/1.73m^2) vs non-MS (130.34±40.75 mL/min/1.73m). Urinary microalbumin levels and serum cystatin C were significantly increased in MS and the cystatin c levels showed significant positive correlation with urinary microalbumin and negative correlation with eGFR.eGFR was found to be lower in the microalbuminuric than normoalbuminuric groups.
Conclusions: Serum Cystatin C levels are higher in MS and can be useful, practical, non-invasive biomarker for evaluation of early renal involvement in MS.

Keywords: Cystatin C, Case control study, Early nephropathy, Marker, Metabolic syndrome

INTRODUCTION

The metabolic syndrome (MS) ,with core components of abdominal obesity, dyslipidaemia, hypertension, and insulin resistance(IR), has become a significant public health problem, and its prevalence is likely to increase.[1]

Recent epidemiologic analysis have found that patients with the MS are at higher risk for developing renal diseases ,thereby allowing the identification of a target population that may benefit from therapeutic strategies at an early stage.[2] Because the kidney plays a major role in the metabolism of low molecular-mass plasma proteins, it was postulated that their serum levels might reflect

changes in glomerular filtration rate (GFR). Among these proteins, Cystatin C, a cysteine protease inhibitor has been suggested as a sensitive endogenous serum marker for changes in GFR.[3] It is freely filtered at the level of the glomerulus and virtually all is reabsorbed and metabolized by the proximal tubular cells. It is produced at a constant rate by nucleated cells and released into bloodstream with a half-life of 2 hr. Its concentration is almost totally dependent on GFR. Creatinine is a useful endogenous marker of renal filtration or GFR, but inference of GFR from the serum creatinine level alone is complicated by the differing rates of creatinine production between persons, mainly because of variations in muscle mass.[4] In one meta-analysis, serum Cystatin is clearly superior to serum creatinine as a marker of GFR. Thus, Cystatin could be a useful tool in patients with MS who are at higher risk of CKD. One of the important uses of elevated Cystatin C in patients with metabolic syndrome is detection of a slight glomerular filtration rate impairment not yet detected by serum creatinine variations. Serum Cystatin C levels capture the gradient of kidney function among persons who do not meet conventional definitions of CKD (creatinine eGFR <60 ml/min/1.73m^2).

The term "preclinical kidney disease" has been defined as creatinine eGFR >60 ml/min/1.73m^2 with Cystatin C levels ≥1.0mg/L. This group is at higher risk for development of creatinine eGFR <60ml/min/1.73m^2 as well as CVD and mortality outcomes.[5] When Coll et al, compared controls with 10 patients with hypertension and proteinuria, serum cystatin was the marker that showed significant differences, whereas creatinine did not.[6]

Thus, slight variations in GFR are more easily detected by cystatin than by serum creatinine, and it offers better diagnostic efficacy, which could be especially useful in patients with MS. Cystatin C is a promising measure of GFR that may be an alternative or a complement to serum creatinine.[7]

Early identification of at-risk individuals using appropriate screening methods would greatly help in preventing or postponing the onset of CKD. There is paucity of information in Indian context regarding association of MS and Cystatin C in spite of the fact that CKD are common in patients of MS which itself is increasing in Indian urban population. Therefore, this present study was conducted to evaluate the association of serum Cystatin C with MS which may help to identify a pre-clinical state of kidney function that is not detected usually with serum creatinine or estimated GFR.

METHODS

We conducted a Case control hospital-based study wherein we screened all patients with clinical diagnosis of MS.

Inclusion criteria

New International Diabetes Federation (IDF) definition of metabolic syndrome was used. According to the new IDF definition, for a person to be defined as having the metabolic syndrome they must have: Central obesity with ethnicity specific values (waist circumference Female≥ 80cm, Male≥ 90cm(INDIANS) *If BMI is >27kg/m^2, (Asians) central obesity can be assumed and waist circumference does not need to be measured.[8] plus any two of the following four factors Triglycerides ≥150mg/dL (1.7mmol/L) or specific treatment for this lipid abnormality HDL cholesterol <40mg/dL (1.03mmol/L) in males <50mg/dL (1.2mmol/L) in females or specific treatment for this lipid abnormality Blood Pressure Systolic BP ≥130 or diastolic BP ≥85mmHg or treatment of previously diagnosed hypertension Fasting Plasma Glucose (FPG) ≥100mg/dL (5.6mmol/L) or previously diagnosed type 2 diabetes. If above 5.6mmol/L or 100mg/dl, OGTT is strongly recommended but is not necessary to define presence of the syndrome. Microalbuminuria: albumin to creatinine ratio ≥30mg/g or urinary albumin excretion rate ≥20µg/min. Early nephropathy criteria: if GFR is 60-89ml/min/1.73m^2 with microalbuminuria. Microalbuminuria: albumin to creatinine ratio ≥30mg/g or urinary albumin excretion rate ≥20µg/min.

Exclusion criteria

We excluded those with hypo or hyperthyroidism, on glucocorticoid, statins and fibrate therapy, those with malignancy, cirrhosis, active liver disease due to viral infection and conditions affecting abdominal girth e.g. Pregnancy, ascites, gross abdominal tumours, organomegaly etc. Clinical examination with anthropometric measurements which included measurement of waist circumference at level of anterior superior iliac spine, hip circumference and blood pressure in supine position was recorded. Following12 to 14 hours fasting, blood sample was collected by venepuncture in all subjects into a plain vial (3ml) and sugar vial (2ml). It was allowed to clot for 30-60 minutes. Serum was separated by centrifuging for 5 minutes at room temperature. Some of the serum was used for insulin, HDL-C and triglycerides estimation. Sugar vial sample was used for fasting blood glucose estimation. Remaining of the serum was stored at -80ºC until other tests were done for estimation of Cystatin C levels. Early morning mid-stream spot urine sample was collected in sterile vial and stored at 2 to 8 degree Celsius for up to 72 hrs for estimation of urine microalbumin. Serum Cystatin C was estimated by ELISA. Serum creatinine, triglycerides (TG), high density lipoproteins-cholesterol (HDL-C) and fasting glucose estimation were done by standard methods on Clinical Chemistry Analyser (Beckman Coulter DXC 800, USA). Serum insulin was estimated by Electro-chemiluminescence Immunoassay. Urine microalbumin was estimated by turbidimetric method.

Urine creatinine by standard method on Clinical Chemistry Analyser.

eGFR=186 x Sr creatinine$^{-1.154}$ x age$^{-0.023}$x 0.742 if female.

HOMA–IR (homeostasis model assessment of insulin resistance) was calculated by-

HOMA-IR= serum glucose (mg/dl) × plasma insulin (µIU/ml)/405.

Estimation of Cystatin C levels

Human Cystatin C ELISA kit manufactured by EIAab was used. The microtiter plate provided in this kit has been pre-coated with an antibody specific to Cystatin C. Standards or samples were then added to the appropriate microtiter plate wells with a biotin-conjugated polyclonal antibody preparation specific for and Avidin conjugated to Horseradish Peroxidase (HRP) is added to each microplate well and incubated. Then a TMB substrate solution was added to each well. Only those wells that contain, biotin-conjugated antibody and enzyme-conjugated Avidin exhibited a change in colour. The enzyme-substrate reaction was terminated by the addition of a sulphuric acid solution and the colour change is measured spectrophotometrically at a wavelength of 450 nm ±2nm. The concentration of in the samples was then determined by comparing the O.D. of the samples to the standard curve.

Calculation of results

The duplicate readings for each standard, control, and sample were averaged and subtracted the average zero standard optical density. A standard curve was created by reducing the data using computer software capable of generating a four parameter logistic (4-PL) curve-fit. As an alternative, a standard curve was constructed by plotting the mean absorbance for each standard on the x-axis against the concentration on the y-axis and draws a best fit curve through the points on the graph.

Statistical analysis

The primary outcome assessed was the occurrence of early nephropathy in metabolic syndrome and the secondary outcome included evaluation of early nephropathy by serum Cystatin C and eGFR. Appropriate statistical test applied by using SPSS Version 21 software Spearmen's and Pearson's (wherever applicable) correlation coefficient was calculated for evaluating the strength of association between each components of metabolic syndrome and Cystatin C. A p value <0.05 was considered significant.

RESULTS

A total of 200 subjects were recruited with their consent. The percentage of male and female in metabolic syndrome were 22.5% and 27.5% respectively. The prevalence of metabolic syndrome was maximum in the 41-50 years age group. The biological and clinical characteristics of the study population like BMI, waist circumference, WHR fasting plasma glucose, systolic blood pressure, diastolic blood pressure, HDL-C and triglycerides are depicted in Table 1. All characteristics were found to be significantly higher (p<0.05) in cases as compared to controls (Table 1). Also, we compared cases, by IDF criteria to assess the overall frequency of components by both criteria in the Indian population (Table 2).

Table 1: Depicts the biological and clinical characteristics of study population (both case and control).

Character	Cases (N=100)	Controls (N=100)	P value
Age	49.05±5.99	48.86±6.14	0.82
BMI (Kg/m^2)	30.03±3.92	23.08±1.73	<.001
Waist circumference (cm)	95.24±8.35	79.13±5.31	<.001
WHR	0.92±0.04	0.82±0.05	<.001
SBP (mmHg)	147.66±8.43	122.85±8.06	<.001
DBP (mmHg)	94.49±5.98	78.72±5.97	<.001
FPG (mg/dl)	122.93±7.37	84.1±8.47	<.001
TG (mg/dl)	208.55±56.83	125.41±19.74	<.001
HDL-C (mg/dl)	30.66±8.39	47.05±7.51	<.001
UMB (mg/g)	56.29±64.23	11.59±8.05	<.001
Creatinine (mg/dl)	0.95±0.14	0.61±0.13	<.001
eGFR (MDRD)	72.59±8.79	130.34±40.76	<.001
Cystatin C (ng/ml)	1.55±0.47	0.77±0.12	<.001

Table 2: Frequency of components of metabolic syndrome in cases as per IDF criteria.

Number of positive components	Metabolic syndrome cases	Number of patients	Total
Three	M	6	11 (11%)
	F	5	
Four	M	8	9 (9%)
	F	1	
Five	M	31	80 (80%)
	F	49	

Parameters

Fasting insulin levels and insulin resistance were significantly raised (p<0.05) in metabolic syndrome cases in comparison to controls (Table 3). HOMA-IR had a significant positive correlation with all the components (p<0.05) except for BMI (Table 4). Creatinine clearance eGFR evaluated by MDRD formula was lower in the metabolic syndrome cases in comparison to controls (72.59±8.79mL/min/1.73m^2 vs 130.34±40.75 mL/min/1.73m^2, respectively). Urinary microalbumin

levels and serum cystatin C were significantly increased in metabolic syndrome (Table 5) and the cystatin c levels showed significant positive correlation with urinary microalbumin and negative correlation with eGFR (MDRD) (Table 7).

Table 3: Fasting insulin levels in metabolic syndrome cases and controls.

	Fasting insulin (µIU/ml)		
	Range	Median	P value
Cases (n=100)	6.00-74.00	25.00	<0.0001
Controls (n=100)	1-11	7.00	
	HOMA-IR		
	Range	Median	P value
Cases (n=100)	1.94-24.85	7.83	<0.0001
Controls (n=100)	0.16-2.66	1.45	

Table 4: Correlation coefficient (rs) of HOMA-IR with components of metabolic syndrome.

Metabolic syndrome cases HOMA-IR		
	r_s	P
BMI (kg/m^2)	-0.041	0.682
Waist circumference (cm)	0.696	<0.001
WHR	0.569	<0.001
Systolic blood pressure (mmHg)	0.862	<0.001
Diastolic blood pressure (mmHg)	0.661	<0.001
Triglycerides (mg/dl)	0.922	<0.001
HDL-C (mg/dl)	-0.852	<0.001

*r_s was calculated by using spearman correlation analysis

Table 5: Urinary microalbumin (mg/gm) values in metabolic syndrome cases and controls.

	Urinary Microalbumin (mg/gm)		
	Range	Median	P value
Cases (n=100)	0.04-264.15	32.14	<.0001
Controls (n=100)	0.04-29.50	12.19	

*Compaired by Mann Whitney U test.

Table 6: Mean and standard deviation of serum Cystatin C values in metabolic syndrome cases and controls.

Serum cystatin c (ng/ml)	Metabolic syndrome cases (n=100)	Controls (n=100)	p value
	1.55±.47	0.77±0.12	<.001

*compaired by student's t-test

Table 7: Correlation between urinary microalbumin(mg/gm), eGFR (MDRD in ml/min/1.73m^2), serum Cystatin C (ng/ml).

	Cystatin C (ng/ml)	
Urinary microalbumin (mg/gm)	r_p	0.940
	P	<.001
eGFR (MDRD in ml/min/1.73m^2)	r_p	-0.896
	P	<.001

Table 8: Comparison of eGFR and Cystatin C among controls, normoalbuminuric, and microalbuminuric cases.

Parameters	Controls	Cases	
	Normo-albuminuria (n=100)	Normo-albuminuria (n=47)	Micro-albuminuria (n=53)
ACR	11.59±8.06	9.99±8.66	97.37±64.28
eGFR	130.34±40.76	80.47±5.27*	65.60±4.09*ʒ
Cystatin C	0.769±0.115	1.18±0.135*	1.88±0.41*ʒ

*p<.001 in comparison to controls and ʒ p<0.05 in comparison to normoalbuminuric cases by one-way ANOVA followed by Turkey HSD posterior test

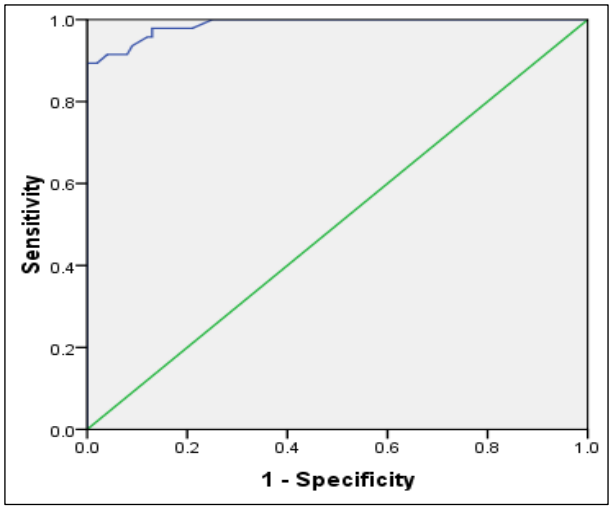

Figure 1: ROC curve showing sensitivity and specificity at different cut off values of Cystatin C for differentiating controls and normoalbuminuric metabolic syndrome (AUC:0.988, P<0.001).

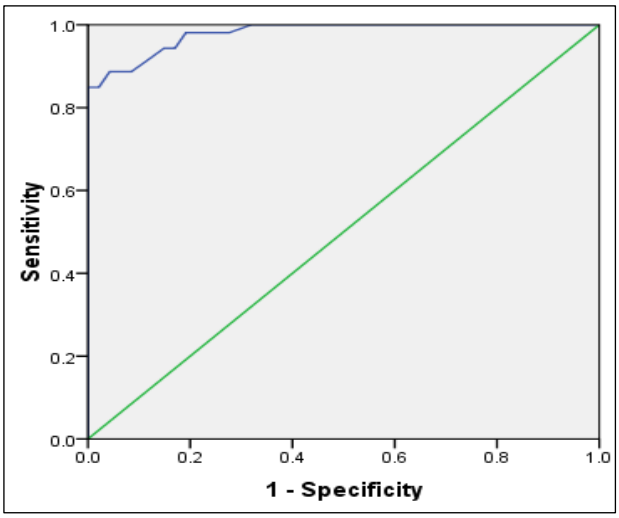

Figure 2: ROC curve showing sensitivity and specificity at different cut off values of Cystatin C for differentiating normoalbuminuric and microalbuminuric metabolic syndrome (AUC:0.980, P<.001).

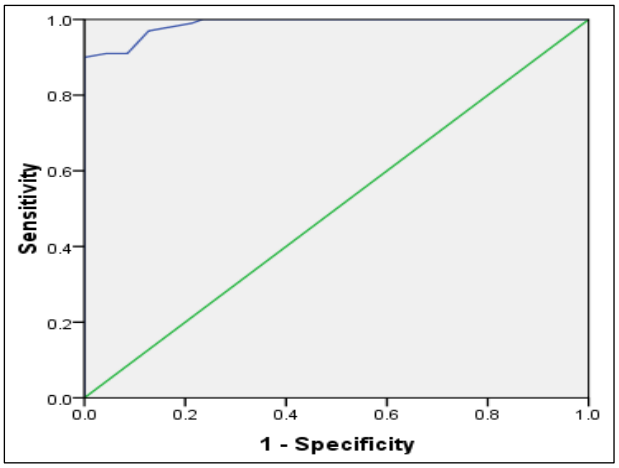

Figure 3: ROC curve showing sensitivity and specificity at different cut off values of eGFR for differentiating controls and normoalbuminuric metabolic syndrome (AUC:0.988, P<.001).

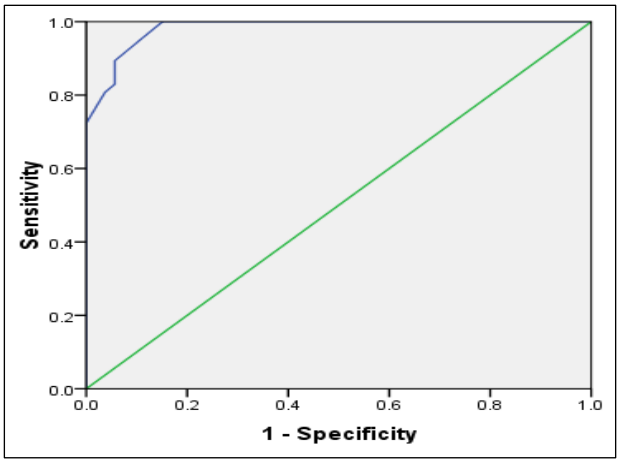

Figure 4: ROC curve showing sensitivity and specificity at different cut off values of eGFR for differentiating normoalbuminuric and microalbuminuric metabolic syndrome (AUC:0.983, P<.001).

Metabolic syndrome cases were further subcategorized into 2 groups depending on their urinary albumin excretion evaluated using the urine albumin/creatinine ratio (ACR in mg/g creatinine, i.e. urinary microalbumin): microalbuminuric and normoalbuminuric. eGFR was found to be lower in the microalbuminuric than normoalbuminuric groups. The levels of Cystatin C in serum showed stepwise increase with albuminuric levels which was significantly different according to their albuminuria (normoalbuminuria vs microalbumiuria). Receiver operating characteristics (ROC) analysis was employed to calculate the area under the curve (AUC) for the cystatin C levels of serum and eGFR to find the best cut off values for identifying early renal impairment in metabolic syndrome cases. When ROC was drawn, optimum cut off value of Cystatin C was a) 0.95ng/ml having sensitivity of 91% and specificity of 92% to differentiate between controls and normoalbuminuric metabolic syndrome. b) 1.36ng/ml having sensitivity of 90% and specificity of 90%to differentiate between normoalbuminuric and microalbuminuric metabolic syndrome and the optimum cut off value of eGFR was 71.5ml/min/1.73m^2 having sensitivity of 93% and specificity of 91% to differentiate between normoalbuminuric and microalbuminuric metabolic syndrome. Cystatin c has significant positive correlation with all parameters except for HDL-C as p value <0.05 (Table 9) on calculation of correlation coefficient.

Table 9: Correlation coefficient (rp) of cystatin C with parameters.

	Metabolic syndrome cases	
	r_p	P
Waist circumference (cm)	0.720	<.001
Waist to hip ratio	0.526	<.001
Systolic blood pressure (mmHg)	0.860	<.001
Diastolic blood pressure (mmHg)	0.618	<.001
Fasting plasma glucose (mg/dl)	0.887	<.001
Triglycerides (mg/dl)	0.928	<.001
HDL-C (mg/dl)	-0.788	<.001
HOMA-IR	0.950	<.001

Table 10: Relationship of cystatin c level adjusted with creatinine clearance (MDRD) to the number of metabolic syndrome components (IDF).

Cases	N	Mean Cystatin C (ng/ml)
No component	100	0.77±0.12
3 components	11	1.03±0.09
4 components	9	1.16±0.12
5 components	80	1.67±0.46
P value for trend	<0.001	

The Table 10 shows the progressive increase in Cystatin as a function of the number of metabolic syndrome components in the overall population, independently of serum creatinine level and creatinine clearance estimated by MDRD study equation by covariance analysis. The P value for trend was highly significant (P<0.001) for the progressive increment in the number of metabolic syndrome components.

DISCUSSION

Metabolic Syndrome is taking the course of global epidemic particularly in adults and children in India and is associated with an increased risk of chronic kidney diseases, type 2 diabetes mellitus and cardiovascular diseases. It is particularly important to effectively implement and strengthen population-based primary prevention strategies for the prevention of 'epidemic' of obesity and the metabolic syndrome in India.[9]

Insulin resistance (IR) plays a central role in the metabolic syndrome and is associated with increased risk for CKD in non-diabetic patients. However, the relationship between MS and the risk of CKD has been scarcely studied in the Indian population, therefore the aim of this study was to examine the association of MS and its components and the risk of CKD.[10]

In the National Health and Nutrition Examination Survey sample, age-adjusted prevalence of the metabolic syndrome were 24.0% and 23.4% in men and women respectively.[11] Sawant et al, illustrate marked heterogeneity in the prevalence of MS according to gender.[12] The prevalence of MS in their study in males was double as compared to females, whereas in other studies in India, MS prevalence in women was 1.5-2 times higher than in male.[13] The prevalence of metabolic syndrome increases with age both in men and women with similar results observed in our study.[14] Given that insulin resistance is an important risk factor for development of CKD, identification of subjects with insulin resistance is a strategy for identifying high-risk people for targeted preventive interventions. The homeostasis model assessment of insulin resistance (HOMA-IR) , which is developed in 1985 by Matthews and co-workers, for application in large epidemiologic investigations is most commonly used surrogate measure of insulin resistance in vivo.[15] In terms of precision (reproducibility of measure), HOMA-IR is comparable to the glucose clamp technique but inferior in terms of accuracy, but using HOMA-IR makes it possible to study a large number of subjects and with a single glucose and insulin measurement in the fasting state.[16]

Although the HOMA-IR has been widely used, its cut-off for insulin resistance has not been conclusive. In a recent study on 1,327 non-diabetic, normotensive individuals in Tehran, it was demonstrated that this cut-off should be 1.8.[17] In a study done by Esteghamati et al, in Iran it was found that insulin resistance and MS were significantly associated, and HOMA-IR levels were directly related to the number of MS components. Highest level of HOMA-IR or insulin resistance is associated with group of patients with 5 positive components. Our study showed a positive association of HOMA-IR with all parameters except for HDL-C with a highest correlation of HOMA index found with fasting TG (r_p=.922, p<.001). Jeppesen et al, in a large population based study found a positive correlation coefficient with all the parameters of metabolic syndrome except HDL cholesterol where it is negative.[18]

Moreover, studies have showed that there was a significant graded relationship between the number of metabolic syndrome components and risk of CKD. A cross-sectional survey in the Chinese population has concluded that metabolic syndrome might be an important risk factor for CKD.[19] This was consistent with the findings in our study where creatinine clearance evaluated by MDRD equation was lower in MS group than non-MS group (72.59±8.79ml/min/1.73m^2 vs 130.34±40.76 respectively, p<0.001) although the mean creatinine values were within normal range in both the groups(0.95±0.14 vs 0.61±0.13 respectively). In MS, glomerular hyper filtration leading to proteinuria has an early-onset in life, much before manifestations of cardiovascular disease; and so may be a marker of metabolic risk.[20] Chen et al, has shown that there is a graded prevalence of CKD or microalbuminuria according to the number of metabolic syndrome components.[21] This was in support with finding in our study where mean urinary microalbumin was higher in MS cases as compared to controls (56.29±64.23 vs 11.59±8.05 respectively, p<0.001).

Cystatin C might be an important marker of MS and increased renal risk associated with it. It has been shown that Cystatin C has a stronger association with mortality risk than creatinine based estimates of GFR.[22] We observed that the Cystatin C value was significantly higher in MS patients than in controls (1.55±0.47 vs 0.77±0.12ng/ml respectively, p<.001) with a progressive increase in Cystatin C as a function of the number of metabolic syndrome components (p value for trend <.001). However, it is difficult to draw any definitive conclusion concerning a cause-and-effect relationship because of the complexity of their interrelationships.

Hypertension and fasting plasma glucose levels are the individual traits of the syndrome that are associated with the greatest risk for microalbuminuria and a low GFR in the study of Chen et al. However, some data suggest that other aspects of the metabolic syndrome may play an independent role in promoting renal damage.[23] A meta-analysis of clinical trials indicates that lipid lowering preserves glomerular filtration rate and decreases proteinuria level in patients with renal disease.[24] A number of findings also indicate obesity as an independent factor for causing renal dysfunction. The multivariate analysis made by Chen et al, showed that the risk for being affected by CKD was more than twice as high in patients with increased waist circumference than in those without. BMI also was associated with an increased risk of the development of end-stage renal disease.[25] We showed that correlation of Cystatin C with BMI when adjusted with waist, (r_p= -0.002, p=0.986) was no more significant, but the correlation with waist circumference (r_p= 0.720, p<0.001) remained highly significant, showing the leading role of this parameter. Thus, patients with MS and increased Cystatin C level could have small changes in kidney function not detected by estimated glomerular filtration rate. Elevated Cystatin C level could be associated with mild renal impairment and thus, insulin resistance, which could contribute to cardiovascular risk.[26]

In our study, we compared the Cystatin C levels in MS cases by categorizing them into 2 groups depending on their different degrees of kidney damage i.e. urinary microalbumin evaluated by albumin to creatinine ratio

(ACR) (normalbuminuria and microalbuminuria) with controls (normoalbuminuric). In microalbuminuric MS ,the Cystatin C levels were significantly increased as compared to normoalbuminuric MS (1.18±0.135 vs 1.88±0.41 respectively, p<.005). An ROC analysis was also performed to calculate the area under the curve (AUC) for the cystatin C levels of serum and to find the best cut off values for identifying early renal impairment in metabolic syndrome cases .When ROC was drawn, optimum cut off value of Cystatin C was 1.36ng/ml having sensitivity of 90% and specificity of 90% to differentiate between normoalbuminuric and microalbuminuric metabolic syndrome. It was thought that this increment was probably due to the tubular phase before glomerular manifestation. This suggests that the cystatin C levels are related to subclinical tubular impairment and can be earlier measurable markers of renal involvement before onset of albuminuria in MS. In these patients, the cystatin C levels were independent factors to predict eGFR: 60-89mL/min/1.73m^2 estimated by the MDRD equation.

The routine classical evaluation of nephropathy includes appearance of microalbuminuria, decreased creatinine clearance and increased serum creatinine.[27] The finding in our study was in consistence with a previous study in T2DM where it had been reported that a decline in the renal function of patients with diabetes was not always accompanied by an increased ACR. About 20%-30% of patients with T2DM, accompanied by renal insufficiency, showed normoalbuminuria.[28] To overcome these limitations, many clinicians additionally used creatinine in evaluating such patients. However, serum creatinine also depends on creatinine production, extra renal elimination and tubular handling. Moreover, tubular involvement may precede glomerular involvement because several tubular proteins and enzymes are detectable even before the appearance of microalbuminuria and a rise in serum creatinine.[29,30] Therefore, other biomarkers for estimation of renal function have been searched for and one of them was Cystatin C. Our study results confirmed that Cystatin C could be one of the additional tubular factors which represent kidney state of diabetic patients and reinforce the importance of diagnostic value of Cystatin C among patients with metabolic syndrome. Our data also suggest that cystatin may be more than a marker of GFR as it is well correlated with components of metabolic syndrome.

It was a hospital-based study, so it may not truly reflect the actual associations of serum Cystatin C levels with nephropathy and components of metabolic syndrome in the community. It was a base line study, so follow up of patients of metabolic syndrome would not possible due to limited period of time. To generalize the results of this study, larger sample size should be required, which was not possible in this study due to limited period of time. The systemic inflammation, one of the important cause of insulin resistance and an important effect of abdominal obesity, was not measured. Thus, the more direct relationship between insulin sensitivity and inflammation in metabolic syndrome patients could not be delineated. The eGFR, estimated by the MDRD equation, did not appear to reflect actual kidney function. So, we could not conclude that which factor is more accurate or useful.

CONCLUSION

Serum Cystatin C levels are higher in metabolic syndrome and can be a useful, practical, non-invasive biomarker for evaluation of early renal involvement in metabolic syndrome cases. Progressive increase in the levels occurs as the number of metabolic syndrome components increase.

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