Original Article

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Biochemistry Section

Prevalence of Metabolic Syndrome and Urinary Albumin to Creatinine Ratio as a Predictor of Cardiovascular Disease in Metabolic Syndrome Patients

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ABSTRACT

Introduction: Metabolic Syndrome (MetS) is a condition that increases the risk of cardiac disease, diabetes, hypertension and may be associated with microalbuminuria.

Aim: To investigate the prevalence of metabolic syndrome and to determine albumin to creatinine ratio as a predictor of cardiovascular disease in metabolic syndrome.

Materials and Methods: This was a hospital based cross-sectional study conducted from February 2019 to January 2020 in the Department of Biochemistry and Outpatient Department of Muzaffarnagar Medical College, Muzaffarnagar, Uttar Pradesh. Out of enrolled 795 subjects, 452 were male and 343 were female. The prevalence of metabolic syndrome was calculated on the basis of metabolic syndrome criteria. Anthropometric parameters like age, weight, height, blood pressure and the biochemical parameters including fasting blood sugar, triglyceride, Lipid Accumulation Product (LAP), urinary albumin, serum creatinine and urinary Albumin to Creatinine Ratio were measured in study population. SPSS version 16 was used for statistical analysis and student independent sample t-test was used for comparing differences amongst the variables. A p-value less than 0.05 was considered as statistically significant.

Results: Out of 795 subjects, 152 patients (19.12%) were hypertensive, 85 patients (10.69%) were diabetic and 29 patients (3.65%) were hypertensive with diabetic. The prevalence of metabolic syndrome was around 18.11% (144 subjects), out of which 52.78% were female and 47.22% were male. Out of 144 Metabolic Syndrome subjects, 23 subjects were diabetic, 32 were hypertensive, 14 were diabetic with hypertensive and 75 were others. The mean levels of urinary albumin creatinine ratio were increased significantly in metabolic syndrome subjects and the increase in urine Albumin to Creatinine Ratio (uACR) was more in metabolic syndrome subjects having Diabetes and Hypertension both.

Conclusion: The present study concluded that the microalbuminuria is associated with metabolic syndrome. The microalbuminuria was found to be more significant in metabolic syndrome subjects who were diabetic with hypertensive as compared to diabetic or hypertensive alone.

Keywords: Diabetes, Dyslipidemia, Hypertension, Lipid accumulation product, Microalbuminuria, Obesity

INTRODUCTION

The metabolic syndrome reflects metabolic and vessel risk factor viz., hormone resistance, cardiovascular disease, hypertension, central avoirdupois, pre-diabetes or polygenic disease, hyperinsulinaemia and dyslipidemia [1]. Sedentary lifestyle, sugar sweetened beverage consumption and increased portion sizes all may lead to obesity. Rising rates of electronic device use and time spent watching television may be correlated with increased risk of obesity [2]. There are various definitions and criteria of metabolic syndrome [3-6] and it is agreed that a combination of three or more components, waist circumference, elevated triglycerides, low HDL-c, raised blood pressure and elevated fasting blood glucose must be present. International Diabetes Federation (IDF) proposed a new definition of metabolic syndrome in April 2006 [6].

The Albumin-to-Creatinine Ratio (ACR) is associated with endothelial dysfunction and other health outcomes. Urinary albumin excretion has been associated with accrued Insulin Resistance (IR) [7], hypertension, vascular inflammation, blood vessels stiffness [8], nonalcoholic fatty liver disease, kidney disease, cardiovascular events, and mortality, throughout the biological range, even at levels traditionally considered normal (<30 mg/gm) [9].

According to the initial data from a observational study [10], the ACR may have some role in predicting a future risk of diabetes and also on the observed benefits of angiotensin receptor blockers and angiotensin-converting enzyme inhibitors reducing the development to diabetes because of antiproteinuria effects [11]. However, Diabetes Prevention Program (DPP) did not prove that microalbuminuria is an independent predictor of future risk of diabetes according to the follow-up information [12]. Microalbuminuria independently associated with metabolic syndrome, however studies on the association between microalbuminuria and different components of metabolic syndrome, to some extent, are conflicting. Hence, the aim of the present study was to investigate the prevalence of metabolic syndrome and to determine the ACR as a marker of cardiovascular disease in metabolic syndrome.

MATERIALS AND METHODS

This hospital based cross-sectional study was conducted in the Department of Biochemistry and Outpatient Department of Muzaffarnagar Medical College and Hospital, Muzaffarnagar from February 2019 to January 2020. Permission from the Ethical Committee (MMC/PO/2019/54) and informed consent were taken from every subject prior to the study. The sample size was calculated by using the prevalence rate of Metabolic Syndrome in Western UP (11.17%) [13].

Inclusion criteria: The patients were selected on the basis of metabolic syndrome criteria proposed by IDF 2006 [14] within the age group of 20 to 65 years. Subjects taking anti-hypertensive drugs or hypoglycaemic drugs were considered to have high BP or a high fasting glucose level, respectively. The cut-off value for fasting blood glucose was >120 mg/dL and for systolic blood pressure was 146 mm of Hg and diastolic blood pressure was 92 mm of Hg in patients taking hypoglycaemic and anti-hypertensive drugs, respectively.

Exclusion criteria: Patients with acute and chronic nephritis, severe uncontrolled hypertension, congestive cardiac failure, chronic cigarette smokers, chronic alcoholism, pregnancy, fever, severe exercise, psychological stress and any other chronic disease were excluded from the study.

Weight was measured in Kilogram by an electronic weighing machine (Commercial scale). Height was recorded in centimeter using a height scale. Abdominal girth was measured using a measuring tape and was recorded in centimeter. The level of measurement was midway between lower costal margin and iliac crest which approximately correspond to mid umbilicus level. The tape was held in parallel to the floor and without compression of the skin at normal expiration.

Blood Pressure

The measurement of blood pressure was taken in sitting posture after resting for minimum of 10-15 minutes. Three consecutive reading were recorded at an interval 2-5 minutes on the same day or in subsequent OPDs before final conclusion of high blood pressure.

Blood Sample Collection

The individuals were requested for overnight fast. Blood was taken from anticubital vein in a single disposable syringe. Sample was centrifuged and serum was separated. Fasting plasma glucose level and lipid parameters were done by enzymatic method by using automated analyser.

Urine Sample Collection and Processing

For the screening of urinary albumin and urinary creatinine concentration, first morning void (timed) Quantitative midstream urine sample was taken. Urinary Albumin (BCG method) and Creatinine (Jaffe's method) were estimated by using automated analyser (CPC Turbo Chem 100).

Urine Albumin Creatinine ratio (uACR)=Urinary Albumin (mg/dL)/ Urinary Creatinine (gm/dL).

STATISTICAL ANALYSIS

SPSS version-16 was used for Statistical analysis. Student's independent sample t-test was used to determined the statistical differences between the groups and p-value less then 0.05 considered as statistically significant.

RESULTS

[Table/Fig-1] showed the general characteristics of total study population as well as metabolic syndrome subjects. The present study included 795 subjects out of which 452 were male and 343 were female. Out of the 795 subjects, 152 (19.12%) subjects were hypertensive, 85 (10.69%) were Diabetic and 29 subjects (3.65%) were Diabetic with hypertension and others 529 (66.54%). The prevalence of metabolic syndrome was found to be 18.11% (144 subjects, 76 were female and 68 were male). Out of 144 metabolic syndrome subjects, 23 were diabetic (15.97%), 32 were Hypertensive (22.22%), 14 were hypertensive with diabetic (9.72%) and 75 subjects were others (52.09%).

[Table/Fig-2] showed the mean level of anthropometric and other biochemical parameters in general population. The mean levels of fasting blood glucose, waist circumference, BMI, waist-to-height ratio and triglyceride were found to be increased significantly in male subjects as compared to female subjects while the mean levels of diastolic and systolic blood pressure were found to be increased insignificantly in male as compared to female subjects. In the present study, significantly decreased level of HDL-c was found in female subjects as compared to males whereas LAP was found to be significantly increased in female subjects as compared to male subjects.

[Table/Fig-3] represented the mean value of demographic and biochemical parameters in metabolic syndrome in both male and female subjects. Significant increase was found in Waist Circumference, waist to height ratio, fasting blood sugar and LAPs in male subjects as compared to female subjects.

[Table/Fig-4] represented the mean value of uACR, urine creatinine and Urine albumin in Diabetic, Hypertensive, diabetic with hypertensive and other subjects who are MetS subjects. The increases in above parameters were more in subjects who were diabetic with hypertensive as compared to hypertensive or diabetic alone.

Total study subjects (N=795; M/F=452/343)				Metabolic syndrome (n=144 (18.11%); M/F=68/76			
Hypertension	Diabetes	Diabetes with hypertension	Other*	Hypertension	Diabetes	Diabetes with hypertension	Other**
152 (19.12%)	85 (10.69%)	29 (3.65%)	529 (66.54%)	32 (22.22%)	23 (15.97%)	14 (9.72%)	75 (52.09%)

[Table/Fig-1]: General characteristics of total study population and metabolic syndrome subjects.
*They may be pre-diabetes, pre-hypertensive, obese or healthy individual
**They are metabolic syndrome obese subjects and might be pre-diabetic or pre-hypertensive

S. No.	Variables	Male (452)	Female (343)	p-value
1	WC (cm)	85.67±6.16	95.96±7.37	**<0.001**
2	WC to Height (WHt) ratio (%)	0.55±0.05	0.57±0.51	**<0.001**
3	BMI (Kg/m^2)	26.61±3.38	24.28±3.24	**<0.001**
4	SBP (mm of Hg)	121±8.29	122.34±8.44	**0.02**
5	DBP (mm of Hg)	79.41±8.98	80.70±10.43	>0.05
6	HDL-c (mg/dL)	49.04±9.59	45.31±8.04	**<0.001**
7	TG (mmol/L)	1.62±0.32	1.55±0.37	**0.006**
8	FBS (mg/dL)	83.91±15.29	93.20±37.48	**<0.001**
9	Lipid Accumulation Product (LAP)	46.0±16.97	50.31±20.9	**<0.001**
10	Urine albumin (mg/dL)	52.76±60.08	58.66±66.41	0.19
11	Urine creatinine (gm/dL)	1.47±0.94	1.56±1.01	0.19
12	uACR (mg/gm)	30.04±12.17	31.06±13.89	0.27

[Table/Fig-2]: Represents demographic and biochemical parameters in study subjects.
WC: Waist circumference, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HDL-c: High density lipoprotein cholesterol, TG: Triglycerides, FBS: Fasting blood sugar, uACR-: urine Albumin to creatinine ratio.

S. No.	Parameters	Male (68)	Female (76)	p-value
1	WC (cm)	104.48±4.79	94.61±4.89	**0.001**
2	WC to height (WHt) ratio (%)	0.062±0.027	0.58±0.034	**0.001**
3	BMI (Kg/m^2)	27.22±3.06	27.86±3.37	0.24
4	SBP (mm of Hg)	130.16±8.77	128.8±7.60	0.32
5	DBP (mm of Hg)	84.61±6.23	83.08±4.83	0.10
6	HDL-c (mg/dL)	41.52±6.93	41.93±7.57	0.73
7	TG (mmol/L)	1.29±0.28	1.90±0.25	0.60
8	FBS (mg/dL)	126.96±72.27	100.01±21.72	**0.0025**
9	Lipid Accumulation Product (LAP)	77.15±16.83	70.27±15.62	**0.01**
10	Urine albumin (mg/dL)	183.74±47.98	181.63±40.36	0.77
11	Urine creatinine (gm/dL)	3.53±0.41	3.52±0.42	0.94
12	uACR (mg/gm)	52.86±15.73	52.18±12.81	0.77

[Table/Fig-3]: Shows biochemical and demographical parameters in metabolic syndrome.
WC: Waist circumference, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HDL-c: High density lipoprotein, TG: Triglycerides, FBS: Fasting blood sugar

Variables		Metabolic syndrome (144)			
		Others (75)	HTN (32)	DM (23)	DM with HTN (14)
Urine albumin (mg/dL)	Mean	173.55	180.31	190.56	283.77
	SD	24.07	12.69	13.92	56.90
	p-value	-	0.14	**0.001**	**<0.0001**
Urine creatinine (gm/dL)	Mean	3.40	3.44	3.58	3.96
	SD	0.49	0.42	0.64	0.63
	p-value	-	0.69	0.16	**0003**
uACR (mg/gm)	Mean	52.61	53.25	54.13	73.02
	SD	11.23	8.70	8.65	16.41
	p-value	-	0.77	0.55	**<0.0001**

[Table/Fig-4]: Shows the values of uACR, Urine Albumin and Creatinine in different group of metabolic subjects.
S=statistically significant, NS=statistically nonsignificant when metabolic syndrome subjects having DM (Diabetes Mellitus), HTN (Hypertension), DM and HTN with both compared with group no having DM as well as HTN

DISCUSSION

Microalbuminuria predicts increase in cardiovascular diseases and diabetic nephropathy [15] which are the main causes of morbidity and mortality. Metabolic syndrome is found to be highly prevalent worldwide, especially in affluent countries [16]. In the present study, the mean value of LAP in total study population was more in female subjects as compared to male subjects and it was statistically significant, while the mean value of LAP in male metabolic syndrome subject was more as compared to female metabolic syndrome subjects and it was statistically significant. LAP is a simple and better clinical indicator for the prediction of metabolic syndrome as compared to waist to height ratio and BMI [17].

In the present study, out of total studied subjects 10.69% were diabetic, 19.12% were hypertensive and 3.65% subjects were diabetic with hypertension. As per IDF guideline, the prevalence of metabolic syndrome was around 18.11% (8.55% were in males and 9.55% in female) and 15.97% metabolic subjects having diabetes, 22.22% having HTN and 9.72% metabolic syndrome subjects having diabetic as well HTN both. In the present study, many of the metabolic syndrome subjects were not having diabetes as well as hypertension but they were obese and may be pre-hypertensive and pre-diabetic and they were not further categorised. A researcher in their study found the prevalence of metabolic syndrome was around 19.18% and in their study, the number of female metabolic syndrome subjects were more and they concluded that female were more prone to develop metabolic syndrome as compared to male subjects [17].

In the present study, the uACR magnitude was found to be increased in metabolic syndrome. This magnitude was more elevated in metabolic subjects having DM with HTN, DM or HTN alone, respectively. The results suggested that uACR may have a significant role in predicting the metabolic syndrome subjects due to their pronicity to CVD and the severity was more in patient of DM with HTN as compared to DM or HTN alone. The level of uACR was increased in patients with metabolic syndrome, may be for the reason that earlier management for MetS should be started to prevent the progression of chronic kidney disease and other cardiovascular disease. Many researchers in their studies showed positive association between urinary albumin and increased cardiovascular risk [18,19].

Hypertension can speed up the diabetic nephropathy and can cause microalbuminuria [20]. It is also being considered as an independent risk factor for diabetic neuropathy [21]. Microalbuminuria is used to predict renal disease in patients with high risk of progression to renal failure [15]. It is no surprise that low creatinine clearance was shown to have a significant association with microalbuminuria.

The kidneys filter wastes and extra fluids from blood, and they use a lot of blood vessels for this. The nephrons do not receive the required oxygen and nutrients because of the damage of blood vessels. Raised blood pressure may narrow the arteries around the kidneys and weaken or harden them. Due to this, kidneys lose their ability to filter blood because arteries unable to deliver enough blood to the kidney tissue and the nephrons do not receive the oxygen and nutrients. There are multiple risk factors for microalbuminuria and studies have shown poor glycaemic control and increased duration of diabetes, and increased creatinine as important risk factors [22].

Metabolic syndrome causes endothelial dysfunction, chronic inflammation, increased leakage of macromolecules and these are further aggravated by Diabetes and Hypertension in metabolic syndrome. Endothelial dysfunction may precede microalbuminuria. Endothelial glycocalyx forms a barrier to protein permeability in both systemic and glomerular capillaries. The presence of microalbuminuria implies dysfunction of the glomerular filtration barrier. This study showed that microalbuminuria is common condition in metabolic syndrome and was found much more in subjects having diabetes and hypertension [23].

A researcher wrote an article on microalbuminuria, cardiovascular disease and hypertension and concluded that low grade microalbuminuria is associated with CVD [24]. Metabolic syndrome and microalbuminuria, both have been associated to CVD [25]. Both metabolic syndrome and microalbuminuria may cause small vessel disorders through endothelial dysfunction that makes an individual susceptible to organ damage [26]. Excessive fat accumulation and changes in the synthesis and secretion of adipokines might be the causative factor for the development of type 2 diabetes, hypertension and CVD [27].

Limitation(s)

The study had small population size so a study with large sample should be conducted to verify the results of the present study.

CONCLUSION(S)

In conclusion, the prevalence of metabolic syndrome was around 18.11% and in this study, the dominancy of female was noted in metabolic syndrome. The present study revealed a strong relationship between microalbuminuria and cardiovascular risk in metabolic syndrome, diabetes and hypertension. Hence, the management in early stage of metabolic syndrome may include estimation of uACR in all patients to prevent cardiovascular disease.

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