Original Article

Association of metabolic syndrome in type 2 diabetes patients with or without nephropathy

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Abstract

Background: Diabetes mellitus is the commonest metabolic abnormality in the world. Type 2 diabetes is the commonest form of diabetes, constituting nearly 90% of diabetic population in any country. The incidence and prevalence of Diabetes Mellitus have been increasing steadily in Bangladesh. Diabetes mellitus is the leading cause of end stage renal disease (ESRD) and accounts for approximately 40% of patients receiving dialysis globally each year. MetS occurs in 85% of the patients with type 2 diabetes mellitus (DM) and is associated with an increased prevalence of micro and macro vascular complications. So detection of nephropathy in subjects with metabolic syndrome at early stage and by creating awareness can significantly reduce mortality, morbidity and cost associated with kidney disease. Therefore, this study was conducted to compare the frequency of metabolic syndrome and its association in subjects with nephropathy and without nephropathy in type 2 diabetes in Bangladeshi population and whether subjects of MetS should be addressed for regular screening with greater emphasis or not.

Methods: This was a cross sectional comparative study done in Mymensingh Medical College Hospital and Mymensingh Diabetic Somitee, Mymensingh from March' 2014 to April' 2015. A total of 200 patients were finally enrolled by considering inclusion and exclusion criteria and the participants were divided into two groups on the basis of Albumin Creatinine Ratio (ACR) of urine and designated as group I and group II. Patients having persistent ACR of urine ≥30mg/gm (nephropathy) was defined as group I (n=49) and ACR of urine (<30mg/gm) who did not develop nephropathy was defined as group II (n=151). Type 2 diabetes patients were selected as prediagnosed type 2 diabetic patients according to World Health Organization (WHO) criteria or on antidiabetic agents (ADA).Metabolic syndrome was defined according to the criteria of modified US National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) (2001). Subjects were considered to have nephropathy if the albumin creatinine ratio (ACR) of urine was persistently ≥30mg/gm which was done on two occasions, three months apart. Simplified Modification of diet in renal disease (MDRD) study equation was used.

Results: In our study, subjects with nephropathy group were older than non nephropathy group. (χ^2= 14.35 and P = 0.001), which was statistically significant (P<0.05). Among group I, more than fifty percent (61.22%) subjects were male and rest were female (38.77%). The proportion of nephropathy was significantly higher in male than female. We also observed that, the proportion of nephropathy was highest (39.47%) among component 5 (Diabetes mellitus, Increased Blood Pressure, Decreased HDL, Increased TG, Central Obesity) group. Patients, who had metabolic syndrome, 4.45 times risk of developing nephropathy in comparison to who did not have metabolic syndrome. (OR: 4.45).

Conclusion: We found that higher the number of metabolic component, higher the risk of developing nephropathy. Diabetic subjects who had metabolic syndrome, had four times higher risk of developing nephropathy in comparison to who did not have metabolic syndrome.

Key Words: Diabetes mellitus, Metabolic syndrome, Nephropathy, Albumin creatinine ratio.

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Introduction:

Diabetes mellitus is the commonest metabolic abnormality in the world. Type 2diabetes is the commonest form of diabetes, constituting nearly 90% of diabetic population in any country. Prevalence of type 2 diabetes is increasing in most of the countries especially in developing countries.[1]The incidence and prevalence of Diabetes Mellitus have been increasing steadily in Bangladesh. Diabetes is the most feared disease because it leads to a variety of complications including end stage renal disease, cardiovascular damage and retinal abnormalities. As a consequence, a large burden is put on the National Health System of all countries around the world.[2] Diabetes mellitus is the leading cause of end stage renal disease (ESRD) and accounts for approximately 40% of patients receiving dialysis globally each year.[3] Traditional risk factors for development of diabetic nephropathy include poor glycaemic control, increased duration of disease, hypertension and smoking.[4] Recently, attention has focused on obesity being a major promoter of proteinuria and chronic kidney disease (CKD).Diabetic nephropathy is a major health problem in diabetic patients. The natural history of diabetic nephropathy has generally been viewed as a descending path from normoalbuminuria to end stage renal disease (ESRD) through an intermediate stage marked by microalbuminuria and overt proteinuria.[5] Diabetic nephropathy is observed in about 10-40% of type 2 DM patients and is traditionally diagnosed by increased albuminuria.[6] Estimated glomerular filtration rate (eGFR) is another marker of renal function, which is usually normal at the initial stages of diabetic nephropathy and begins to decrease in later stages.[7]

Metabolic syndrome (MetS) has been described as a cluster of cardiovascular risk factors such as obesity, hypertension, dyslipidemia, and hyperglycemia, which is associated with increased mortality even among subjects with a low risk cardiovascular profile.[8] MetS occurs in 85% of the patients with type 2 diabetes mellitus (DM) and is associated with an increased prevalence of micro and macro vascular complications.[9] Several groups have examined the relationship between the MetS and CKD. Hoehner correlated the metabolic syndrome profile and microalbuminuria in a cross sectional study of American Indians from Wisconsin and Minnesota.[10] After stratification, individuals with three or more MetS traits had a 2.3 fold increased odds of having microalbuminuria compared with a control group without the syndrome.The data extracted from the Third National Health and Nutrition Examination Survey database contains detailed clinical information from 6000 subjects.[11,12] Both studies found a statistical association between metabolic syndrome and microalbuminuria. There has been a significant correlation between number of metabolic syndrome factors and GFR<60 ml/min.[12] Individual traits that confer greatest risk were

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hypertension and hyperglycemia, which is not surprising, because both factors predispose to CKD pathogenesis and/or progression.[13]Hypertension and lipid abnormalities are known to be strong risk factors for the development of diabetic nephropathy.[14,15] In addition to identifying blood Pressure (BP) and hyperglycemia as risks for CKD in the metabolic syndrome, it is observed that increased waist circumference significantly correlated with microalbuminuria and Glomerular Filtration Rate (GFR) decline, suggesting that obesity may be an independent risk for CKD even and after adjusting for co morbid risks, such as BP and proteinuria.[16] It was observed that increased waist circumference significantly correlated with microalbuminuria and GFR decline[12], suggesting that obesity may be an independent risk for CKD.[17,18] Prevalence of metabolic syndrome in DM of Bangladeshi [17]Epidemiologic studies have linked the metabolic syndrome population is 81 % according to criteria of modified US National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) (2001). This study was conducted with a view to compare the frequency of metabolic syndrome and its association in subjects with nephropathy and without nephropathy in type 2 diabetes.

Rationale:

The MetS and diabetes Mellitus have both become global public health problems with increasing social and economic impact due to their high prevalence and remarkable impact on morbidity and mortality. MetS occurs in 70-80% of the patients with type 2 diabetes mellitus (DM) and about 30-45% patients with type 2 DM have micro vascular complications. Diabetic nephropathy is the leading cause of end-stage renal disease (ESRD) and accounts for approximately 40% of patients receiving dialysis globally each year. Furthermore, diabetic patients have the highest risk of morbidity and mortality when develops nephropathy. A developing country like Bangladesh has to take extra burden of cost healthcare facility to provide care to End Stage Renal Disease. So detection of nephropathy in subjects with metabolic syndrome at early stage and by creating awareness can significantly reduce mortality, morbidity and cost associated with kidney disease. Therefore, this study was conducted to compare the frequency of metabolic syndrome and its association in subjects with nephropathy and without nephropathy in type 2 diabetes in Bangladeshi population and whether subjects of metabolic syndrome should be addressed for regular screening with greater emphasis or not.

Hypothesis:

"Metabolic syndrome is a risk factor for nephropathy in type 2 diabetes patients."

Aims and objectives:

a) General objective: To compare the frequency of MetSin subjects with nephropathy and without nephropathy in type 2 diabetes.

b) Specific objectives: i) To find out the association of increased blood pressure with nephropathy in type 2 diabetes. ii) To find out the association of central obesity (waist circumference) with nephropathy in type 2 diabetes. iii) To find out the association of increased blood triglyceride (TG) level with nephropathy in type 2 diabetes. iv) To find out the association of decreased blood high density lipoprotein (HDL) level with nephropathy in type 2 diabetes.

Materials and Methods:

This was a cross sectional comparative study done in Mymensingh Medical College Hospital and Mymensingh Diabetic Somitee, Mymensingh from March' 2014 to April' 2015 to compare the frequency of metabolic syndrome and its association in subjects with nephropathy and without nephropathy in type 2 diabetes. The study participants/ study subjects were patient with type 2 diabetes who attended in outpatient department of Mymensingh Medical College Hospital and Mymensingh Diabetic Somitee, Mymensingh. Study participants/ study subjects were selected according to inclusion and exclusion criteria and then the participants were divided into two groups

on the basis of Albumin Creatinine Ratio (ACR) of urine and designated as group I and group II. Patients having persistent ACR of urine ≥30mg/gm (nephropathy) was defined as group I (n=49) and ACR of urine (<30mg/gm) who did not develop nephropathy was defined as group II (n=151).Inclusion criteria were known type 2 diabetes for > 2 years, Age> 40 years. Exclusion criteria were pregnancy, patient with gross ascites, febrile illness; very ill patient ; heart failure, urinary tract infection, and patient on steroid. Purposive sampling technique was adopted. Type 2 diabetes patients were selected as pre diagnosed type 2 diabetic patients according to World Health Organization criteria or on antidiabetic agents (ADA).

The current WHO diagnostic criteria for diabetes. Fasting plasma glucose ≥ 7.0mmol/l (126mg/dl) or Two hours after 75 gram glucose ≥ 11.1mmol/l (200mg/dl). Metabolic syndrome was defined according to the criteria of modified US National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) (2001). Patients with type 2 diabetes mellitus (DM) already fulfill one of the NCEP-ATP III diagnostic criteria, and in this study any 2 of the following criteria was taken for diagnosis of metabolic syndrome; a)Central obesity was defined as waist circumference (WC) ≥ 90 cm (male), ≥ 80 cm or (female);b)Hyper triglyceridemia was defined as triglyceridemia (≥150 mg/dl) or anti lipidaemic drug use (statin, fenofibrate); c)Low HDL cholesterolaemia was defined as <40 mg/dL (male), < 50 mg/dL (female);d)Elevated Blood pressure was defined as ≥ 130/85 mmHg (or treated for hypertension). Subjects were considered to have nephropathy if the albumin creatinine ratio (ACR) of urine was persistently ≥30mg/gm which was done on two occasions, three months apart. Simplified Modification of diet in renal disease (MDRD) study equation was used.

eGFR (ml/min/1.73m^2) = 186× (Scr)-1.154 × (Age)-0.203 × (0.742 if female).

Waist circumference was measured by using a measuring tape which was placed at the highest point of the iliac crest around the abdomen in horizontal plane and measured in centimeter (cm) at the end of expiration**.** Blood pressure was measured in sitting position on two occasions, five minutes apart using a sphygmomanometer by auscultatory method. Mean blood pressure value was taken from 2 readings. No study subjects had history of taking niacin (antilipidaemic drug).Nephropathy was confirmed by a repeat test of ACR of urine after 3 months. All data were collected and tabulated and statistically analyzed using SPSS (Statistical Package for Social Science) version 16 software. Quantitative variables were expressed as Mean ±SD, while the qualitative variables were presented as numbers and percentages. Comparison of qualitative data was done using chi-square test (χ^2). Quantitative data were compared using Independent Samples T test. Level of significance was considered as p value less than 0.05 and CI 95%. Data was presented as mean±SD. A χ^2 test was employed to determine the association between categorical variables. Prior to commencement of this study, the research protocol was approved by the local ethical committee. The aims and objectives of the study with its procedure, risk & benefits of the study was explained to the patient in easily understandable and local language & then informed verbal and written consent was taken and assured that, all information & records, would be kept confidential and the procedure was helpful for both the physicians & patients in making rational approach of the case management. Spot urine samples (about 30 ml) was collected in test tubes labeled with individual registration number for each participants and test was done for albumin and sugar by using reagent strip. Urine microscopy was done after centrifuging at 3000 r.p.m for 5 minutes and then placing the sediment with cover slip under high power of light microscope. For measurement of ACR of urine, auto analyzer (Beckman Coulter Model no Au 480, Made in Japan) machine was used. At first machine was set for measure of ACR. Then about 200 microliter urine was send to machine through sample cup. Machine

automatically received 16 microliter of urine. After 12-15 minutes the machine delivered the reading of urinary albumin (in mg/litre) and urinary creatinine (in gm/litre) in a strip. For urinary albumin and urinary creatinine the wave length were used 340 nanometer and 520 nanometer respectively. Urinary albumin was measured by end point method and urinary creatinine mas measured by fixed time kinetic method.

Then ACR of urine was calculated manually by dividing the urinary albumin value (in mg/litre) by urinary creatinine value (in gm/litre). Finally results of ACR of urine was expressed as mg/gm. Venous blood samples were collected from each examined subject, after overnight (12 hours) fasting in two separate fractions labeled with individual registration number. The first blood fraction (3ml) was collected in ethylene diaminetetracetic acid (EDTA) containing tube for glycosylated haemoglobin (HbA1c) measurement. The second blood fraction (5ml) of peripheral blood sample was collected in clean centrifuge tube without anticoagulant to separate serum for biochemical analysis of serum triglyceride, high density lipoprotein level and serum creatinine. Serum creatinine was estimated by Jaffe's alkaline method. Determination of serum triglycerides and high density lipoprotein were determined by auto analyzer (Beck man coulter machine model no Au 480, made in Japan). HbA1C was determined by the colorimetric determination of glycohemoglobininwhole blood. Renal function was further assessed by using the simplified modification of diet in renal disease (MDRD) equation to estimate glomerular filtration rate (GFR).

Observations and Results:

A total of 200 patients with type 2 DM were included in this study finally. The results were presented by following tables and graphs. The mean age of subjects in group I and II were 60±7.2 and 54±6.9 respectively (table -1). Subjects with nephropathy group were older then non nephropathy group (table-2).

The proportion of nephropathy was significantly higher in male than female (table-3). Mean waist circumference in group I and group II were 88.82±6.28 and 82.73±7.09 respectively (table-4). Mean Systolic Blood Pressure in I and group II were 135.00±12.16 and 127.48±10.11 respectively (table-5).

Mean Diastolic Blood Pressure in Group I and group II were 84.90 ±8.13 and 82.22 ±6.44 respectively (table-5). Majority of the study participants (83.50%) had hypertension and DM below 5 years (table-10). Mean HDL in Group I and group II were 41.49±3.75 and 42.84±4.77 respectively (table-7). Mean TG level in \Group I and group II were 172.76±36.05 and 153.15±18.84 respectively (table-8). The proportion of nephropathy was highest (39.47%) among component 5 (table-11c).

The proportion of nephropathy was significantly higher among metabolic syndrome group than non metabolic syndrome group (table-11d). Subjects who had metabolic syndrome were 4.45 times risk of developing nephropathy in comparison to who did not have metabolic syndrome (table-12)

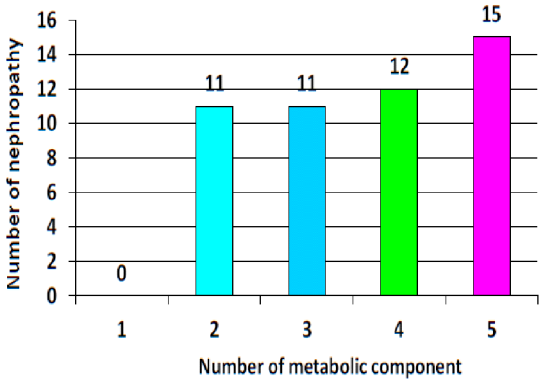

Figure 1: Simple Bar diagram showing increased frequency of metabolic component with increased frequency of nephropathy (n=49)

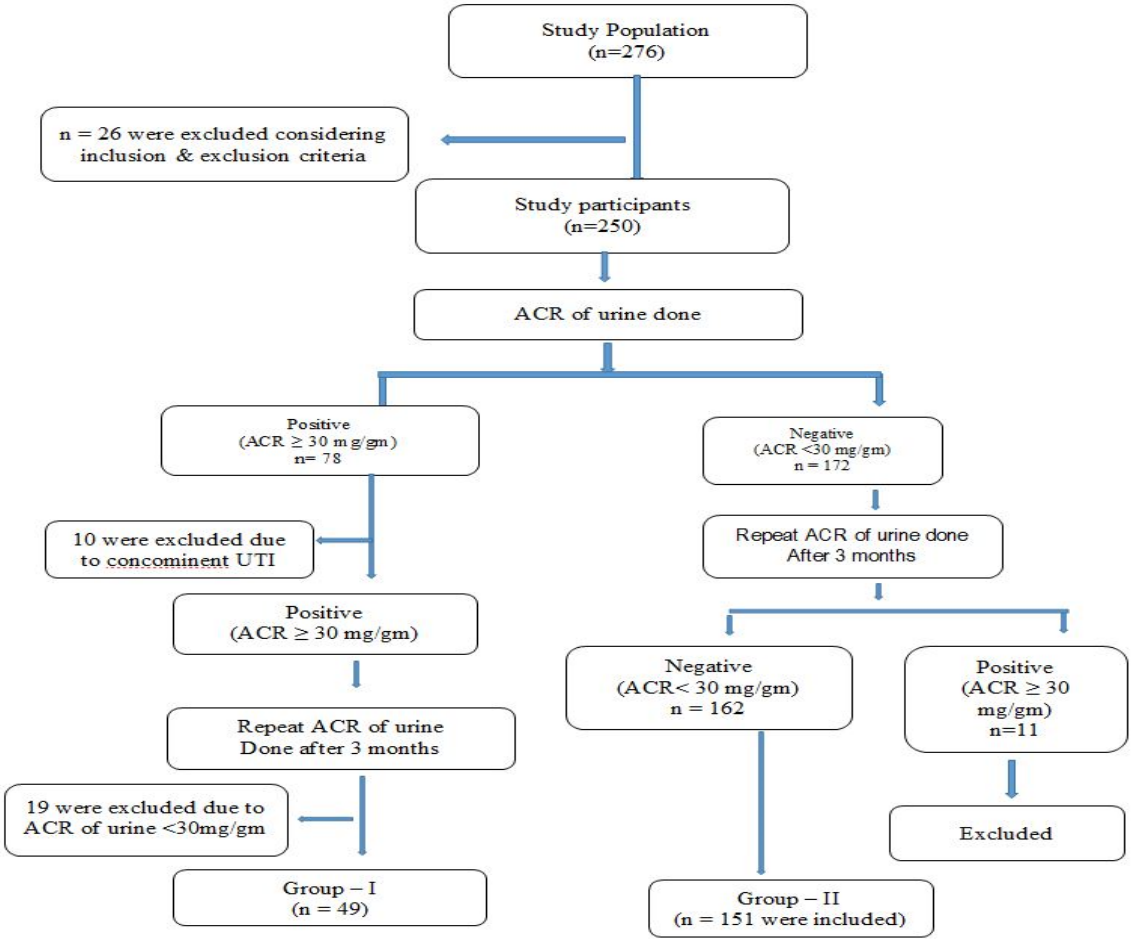

Figure: Flow chart showing sampling method and grouping

Table 1: Demographic, Anthropometric, clinical and laboratory parameters among study subjects (n=200)

Variables	**Group I (Nephropathy Present) n=49 (Mean ±SD)**	**Group II (Nephropathy Absent) n=151 (Mean ±SD)**	P value
Age (years)	60 ± 7.2	54 ± 6.9	0.001
Waist Circumference/ Central obesity (cm)	88.82±6.28	82.73±7.09	0.001
SBP(mm Hg)	135.00±12.16	127.48±10.11	0.001
DBP (mmHg)	84.90 ±8.13	82.22 ±6.44	0.019
Duration of HTN (years)	7.14±4.9	2.67± 2.0	0.001
Duration of DM (years)	13.12±3.78	6.75±2.92	0.001
HDL(mg/dl)	41.49±3.75	42.84±4.77	0.072
TG (mg/dl)	172.76±36.05	153.15±18.84	0.001
Serum Creatinine (mg/dl)	1.30±0.12	1.30±3.09	0.989
e GFR ml/min/1.73 m2	53.38±11.15	69.49±13.58	0.001
HbA1c (%)	7.60±0.81	6.88±0.45	0.001

Significant difference (P value<0.05)

Table 2: Distribution of study subjects by age group (n=200)

Age group	Group I (Nephropathy Present) n (%)	Group II (Nephropathy Absent) n (%)	χ^2	P value
41-55 years	16 (32.65%)	96 (63.58%)	14.35	0.001
56-75 years	33 (67.35%)	55 (36.42%)		
Total	49 (100.0%)	151 (100.0%)		

Table 3: Distribution of study subjects by sex (n=200)

Sex	Group I (Nephropathy Present) n (%)	Group II (Nephropathy Absent) n (%)	χ^2	P value
Male	30 (61.22%)	70 (46.40%)	3.32	0.07
Female	19 (38.77%)	81 (53.60%)		
Total	49 (100.0%)	151 (100.0%)		

Table 4: Distribution of study subjects by Central obesity (Waist Circumference) (n=200)

Variables	Group I (Nephropathy Present) n =49 (Mean ±SD)	Group II (Nephropathy Absent) n=151 (Mean ±SD	P value
Central obesity (Waist Circumference in cm)	88.82±6.28	82.73±7.09	0.001

Cut off value of Central obesity :
Male: waist Circumference ≥90 cm
Female: waist Circumference≥80 cm

Table 5: Distribution of study subjects by Systolic Blood Pressure (n=200)

Variables	Group I (Nephropathy Present) n=49 (Mean ±SD)	Group II (Nephropathy Absent) n=151 (Mean ±SD)	P value
Systolic Blood Pressure (mm Hg)	135.00±12.16	127.48±10.11	0.001

Cut off value of Systolic Blood Pressure: ≥ 130 mm Hg or on anti-hypertensive drug.

Table 6: Distribution of study subjects by Diastolic Blood Pressure (n=200)

Variables	Group I (Nephropathy Present) n=49 (Mean ±SD)	Group II (Nephropathy Absent) n=151 (Mean ±SD)	P value
Diastolic Blood Pressure (mmHg)	84.90 ±8.13	82.22 ±6.44	0.019

Cut off value of Diastolic Blood Pressure: ≥85 mmHg or on antihypertensive drug

Table 7: Distribution of study subjects by High Density Lipoprotein Level (n=200)

Variables	Group I (Nephropathy Present) n=49 (Mean ±SD)	Group II (Nephropathy Absent) n=151 (Mean ±SD)	P value
High Density Lipoprotein Level (mg/dl)	41.49±3.75	42.84±4.77	0.072

Cut off value of HDL: Male: < 40 mg/dl.
Female: <50 mg/dl.

Table 8: Distribution of study subjects by Triglyceride Level (n=200)

Variables	Group I (Nephropathy Present) n=49 (Mean ±SD)	Group II (Nephropathy Absent) n=151 (Mean ±SD)	P value
Triglyceride Level (mg/dl)	172.76±36.05	153.15±18.84	0.001

Cut off value of Triglyceride Level: ≥150 mg/dl or on treatment

Table 09: Frequency distribution of Duration of Hypertension among study subjects (n=200)

Diagnosed duration of Hypertension	Frequency (n)	Percent (%)
No HTN	5	2.50
<5 years	167	83.50
6-10 years	20	10.00
11-15 years	4	2.00
16-20 years	3	1.50
>20 years	1	0.50
Total	200	100.00

Table 11 (a): Frequency distribution of metabolic component among study subjects (n=200)

		Group I (n =49)		Group II (n=151)	
Metabolic Component		**Frequency (n)**	**Percentage (%)**	**Frequency (n)**	**Percentage (%)**
DM	Yes	49	100.00	151	100.00
Central Obesity (Waist circumference)in case of Male	Present	17	34.69	26	17.22
	Absent	13	26.53	44	29.14
Central Obesity (Waist circumference)in case of Female	Present	13	26.53	29	19.21
	Absent	06	12.24	52	34.44
TG or on treatment	High	29	59.18	60	39.74
	Low	20	40.82	91	60.26
HDL in case of male	Low	17	34.69	24	15.89
	High	13	26.53	46	30.46
HDL in case of Female	Low	10	20.41	52	34.44
	High	09	18.37	29	19.21
Increased Blood pressure or treated	Present	42	85.71	83	54.97
	Absent	07	14.29	68	45.03

Table 10: Frequency distribution of Diagnosed period of DM among Study subjects (n=200)

Diagnosed period of DM	**Frequency (n)**	**Percent (%)**
<5 years	75	37.50
6-10 years	75	37.50
11-15 years	43	21.50
16-20 years	5	2.50
>20 years	2	1.00
Total	200	100.00

Highest proportion was found in HTN>TG>WC, HDL after DM in both group I & II.

Cut off values :

DM **:** Fasting plasma glucose >7 mmol or 2 hours after 75 gram glucose orgetting antidiabetic agent

Central obesity **:** Male : Waist circumference ≥90 cm,

: Female: Waist circumference ≥80 cm

TG **:** ≥150 mg/dl or on antilipidaemic drug.

HDL **:**Male: < 40 mg/dl.

:Female: <50 mg/dl.

Blood pressure **:** ≥ 130/85 mmHg or on antihypertensive drug

Table 11 (b): Parameters of different metabolic components among subjects of metabolic syndrome. (n=104)

Metabolic Component			Mean ± SD
Central Obesity (Waist circumference)	Male	High	93.69 ± 2.78
		Low	85.66 ± 1.63
	Female	High	85.37 ± 3.29
		Low	75.0 ± 2.44
SBP	High		134.83 ± 10.06
	Low		122.5 ± 3.98
DBP	High		85.69 ± 7.28
	Low		81.67 ± 4.20
TG	High		181.80 ± 31.10
	Low		143.17 ± 3.38
HDL	Male	High	42.25 ± 1.35
		Low	36.75 ± 1.80
	Female	High	51.69 ± 0.85
		Low	42.42 ± 2.07

Cut off values :
Central obesity : Male : Waist circumference ≥90 cm,
Female: Waist circumference ≥80 cm
TG : ≥150 mg/dl or on antilipidaemic drug.
HDL : Male: < 40 mg/dl.
Female: <50 mg/dl.
Blood pressure : ≥ 130/85 mmHg or on antihypertensive drug

Table 11 (c): Frequency distribution of metabolic component group (Metabolic syndrome) in group I (With nephropathy) (n=38)

No. of metabolic component	Group of metabolic component (Metabolic syndrome)	Frequency of nephropathy n (%)
5	Diabetes mellitus, Increased Blood Pressure, Decreased HDL, Increased TG, Central Obesity.	15 (39.47%)
4	Diabetes mellitus, Increased Blood Pressure, Decreased HDL, Increased TG.	5 (13.16%)
	Diabetes mellitus, Increased Blood Pressure, Increased TG, Central Obesity.	5 (13.16%)
	Diabetes mellitus, Increased Blood Pressure, Decreased HDL, Central Obesity.	2 (5.26%)
3	Diabetes mellitus, Increased Blood Pressure, Central Obesity.	4 (10.53%)
	Diabetes mellitus, Increased Blood Pressure, Increased TG.	2 (5.26%)
	Diabetes mellitus, Decreased HDL, Central Obesity	1 (2.63%)
	Diabetes mellitus, Increased TG, Central Obesity.	1 (2.63%)
	Diabetes mellitus, Increased Blood Pressure, Decreased HDL.	3 (7.89%)

Table 11 (d): Association of component of metabolic syndrome with or without nephropathy (n=200)

Metabolic Component	Group I (Nephropathy Present) n (%)	Group II (Nephropathy Absent) n (%)	χ^2	P value
≤2 component (Metabolic syndrome absent)	11(22.45%)	85 (56.3%)	16.33	0.001
≥3 component (Metabolic syndrome Present)	38(77.55%)	66(43.7%)		
Total	49(100%)	151(100%)		

Table 12: Strength of association of metabolic syndrome and nephropathy among the study subjects. (n=200)

Risk factor	Group I (Nephropathy Present)	Group II (Nephropathy Absent)	Odds ratio (OR)
Metabolic syndrome Present	38 (77.55%)	66(43.71%)	4.45
Metabolic syndrome Absent	11 (22.45%)	85(56.29%)	
Total	49(100.00%)	151(100.00%)	

Discussion:

Over the past decades, there has been a significant worldwide increase in the incidence of diabetes mellitus.[19] The high prevalence of microvascular complications of diabetes such as diabetic nephropathy means that the number of patients with end-stage renal disease (ESRD) due to diabetes will also increase dramatically.[20] Hence, diabetes, and especially type 2 diabetes, is becoming the main reason for patients to start renal replacement therapy.[21] In general, microalbuminuria is a sensitive marker for damage induced by diabetes. In our study, nephropathy was observed significantly among patients in the higher age group [Table-2]. Chi-Square (χ^2) value was 14.35 and P value was 0.001, which was statistically significant (P<0.05). Mean age was also significantly higher among group I (nephropathy present) than group II (60±7.2 vs. 54±69, P =0.001) which was statistically significant (P<0.05). A study in Egypt, observed that nephropathy was significantly higher among higher age group, which was comparable to our study[22] Similar findings were shown in a study done in Yemen[23] & in Turkey.[24] In our study, although the proportion of nephropathy was significantly higher in male than female but we did not found statistically significant difference (χ^2=3.32, P=0.07) regarding the presence of microalbuminuria in group I and II. [Table- 3]. A study done in Albania[25] and they found similar findings to our study. In some other studies in Egypt [22,26,27] also reported similar findings to our study.

It was observed in a study[12] that increased waist circumference significantly correlated with microalbuminuria and GFR decline, suggesting that obesity may be an independent risk for CKD.[17,18] In this study, Central obesity (mean waist circumference) was significantly higher in group I (nephropathy present) than group II (88.82±6.28 vs. 82.73±7.09, p=0.001) [Table-4].This finding was significant statistically (P<0.05). In a study, done in Albania[25] were also observed similar findings to our study.

Hypertension is one of the imperative contributing factors associated with both causation and progression of renal failure.[28] Several reports have indicated the reno-protective effect of blood pressure reduction.[29] In our study, majority of the study participant (83.50%) had hypertension with duration below 5 years; In this study, we observed that, mean Systolic Blood Pressure (SBP) was significantly higher among group I (nephropathy present) than group II (135.00±12.16 vs. 127.48±10.11,p=0.001), which was statistically significant (P<0.05) [Table-5].

We also observed that, mean Diastolic Blood Pressure (DBP) was significantly higher among group I (nephropathy present) than group II (84.90 ±8.13 vs. 82.22 ±6.44, p=0.019), which was statistically significant (P<0.05) [Table-6]. In some other study done in Egypt[22], Albania[25],

Turkey[24], Nepal[30] and Yemen[23] were observed similar findings.

In our study, below 10 years diagnosed duration of diabetes was found in 75.0% of study subjects. More than 20 years diagnosed duration of diabetes was found only in 1.0% study subject. [Table -10] In this study, mean diagnosed duration of diabetes was significantly higher in group I (nephropathy present) than group II (13.12±3.78 vs. 6.75±2.92, p=0.001) [Table-1]. This finding was significant statistically (P<0.05).In some other study conducted in Yemen[23], Nepal[30], Albenia[25], Oman[31] and Turkey[24] were observed also similar findings to our study.

Plasma lipid levels have emerged as potentially important predictors of DN risk[32]. In diabetes, multiple lipid abnormalities are already present at an early stage of diabetic nephropathy.[33] In our study, we found that mean High Density Lipoprotein (HDL) Level was lower among Group I (nephropathy present) than group II (41.49±3.75 vs.42.84±4.77,p=0.072) which was not significant statistically (P>0.05) [Table -7].In a study done in Turkey[24] were also observed similar findings to our study.

In our study, we found that mean Triglyceride (TG) level was significantly higher among Group I (nephropathy present) than group II (172.76±36.05 vs. 153.15±18.84,p=0.001) which was significant statistically (P<0.05) [Table 8]. In some other study done in Egypt[22], Yemen[23] and in Iran[34] were also observed similar findings to our study. In our study, we found that mean eGFR was significantly lower among Group I (nephropathy present) than group II (53.38±11.15 vs. 69.49±13.58, p=0.001) which was significant statistically (P<0.05) [Table 1]. In a study done in Turkey[24] were also observed similar findings to our study. In our study, the lowest eGFR was found in subjects who had four and five metabolic components.

In our study, we found that mean HbA1c level was significantly higher among Group I (nephropathy present) than group II (7.60±0.81 vs. 6.88±0.45, p=0.001) which was significant statistically (P<0.05) [Table 1]. In a study conducted in Egypt[22] and another study conducted in Iran[34] were also observed similar findings to our study. In some other study in Brazil[35] they were found that the most significant risk factor for nephropathy in diabetic patient was elevated HbA1c.

In our study, we observed that the higher proportion of metabolic component was found in both group I & II in the sequence of increased blood pressure, increased serum Triglyceride level, central obesity (WC), low serum High Density Lipoprotein after DM. [Table -11 (b)]. The proportion of nephropathy was significantly higher among metabolic syndrome group than non-metabolic syndrome group (77.55% vs. 22.45%). Chi-Square (χ^2) value was 16.33 and P value was 0.001 which was statistically significant (P<0.05) [Table 11- (d)]. Increased number of individual metabolic component [(central obesity, increased TG (≥150 mg/dl), Low HDL (M <40, F<50 mg/dl, increased Blood pressure (≥130/85), DM (FBS >7 mmol/l)] was associated with increased frequency of nephropathy. [Figure -1]

We observed that, the proportion of nephropathy was highest (39.47%) among component 5 (Diabetes mellitus, Increased Blood Pressure, Decreased HDL, Increased TG, Central Obesity) group. Among component 4, (Diabetes mellitus, Increased Blood Pressure, Decreased HDL, Increased TG) group had highest (13.16%) proportion of nephropathy and among component 3, (Diabetes mellitus, Increased Blood Pressure, Central Obesity) group had highest (10.53%) proportion of nephropathy. [Table 11- (c)] Patients, who had metabolic syndrome, 4.45 times risk of developing nephropathy in comparison to who did not have metabolic syndrome. (OR: 4.45) [Table -12].

Conclusion:

We found that higher the number of metabolic component, higher the risk of developing nephropathy. Diabetic subjects who had metabolic syndrome, had four times higher risk of

developing nephropathy in comparison to who did not have metabolic syndrome.

Limitation:

Although optimum care had been tried by the researcher in every steps of this study, still some limitations existed eg the study was conducted in a selected area. So the study population might not represent the whole community; probability sampling technique could not be employed to recruit the study unit; they were selected purposively due to time & fund constraints. As a result, there might be some selection bias;we depended on the patient's previous information which might have been influenced by recall bias; renal biopsy is the gold standard diagnostic investigation which was not performed ;in spite of maximum effort by the researcher, due to time and resource limitation, the sample size was small; a larger sample size would have given a better result; culture of urine could not be done to exclude urinary tract infection; diagnosis of heart failure done clinically.

Recommendation:

We found a significant association between nephropathy with following metabolic component namely increased blood pressure, increased duration of diabetes, increased serum levels of triglyceride, and central obesity. Therefore, it is essential to provide aggressive control of above metabolic components and long term glycemic control in order to reduce and prevent the development nephropathy and thereby decrease overall morbidity and mortality. Subjects having metabolic syndrome should be screened for nephropathy. In order to obtain more information for nephropathy and its association with metabolic syndrome, prospective epidemiologic studies are needed with large sample size.

Conflicts of Interest:

This study was supported by the department of Nephrology, Mymensingh Medical College Hospital and Mymensingh Diabetic Somitee, Mymensingh.All authors have no conflicts of interest to declare.

Authors Contribution:

Research idea and study design: MSI, MI &AAC data acquisition : MSI, AAC, MA,AKSUA, MAR; SKD, GCB, MOF, RCM, MSIK; data interpretation; MSI ,AAC, MA,AKSUA, MAR; SKD, GCB, MOF, RCM, MSIK; Supervisions or mentorship : AAC; Co-guide: MI; Md Saiful Islam is the primary author and other authors contributed important intellectual content during manuscript drafting or revision accepts accountability of the overall work.

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