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Original Article

Prevalence of metabolic syndrome amongst people with type 2 diabetes mellitus and its impacts on the occurrence of diabetic kidney disease

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Abstract:

Background: Prevalence of metabolic syndrome (MetS) amongst people with Type 2 diabetes mellitus (T2DM) is high. Though, diabetic kidney disease (DKD) is an increasingly important cause of morbidity and mortality worldwide, its association with MetS is not profoundly evaluated in Indian population.
Objectives: We aim to assess the prevalence of MetS and evaluate the impact of MetS on the occurrence of DKD amongst people with T2DM.
Methods: The demographic, anthropometry, blood pressure, lipids, CVD (based on ECG and history of CVD) and DKD (based on e-GFR < 60 ml/min/1.73 m^2) data of 1037 T2DM was obtained. MetS was defined by NCEP - ATP - III guidelines. Association of DKD was evaluated with other variables including MetS and its components in terms of unadjusted OR. The Odds Ratios were adjusted by considering covariates like age, gender, duration of diabetes and HbA1c in the logistic regression model.
Results: The prevalence of MetS was 86.98% (female-91.3%, male-84.5%), DKD 6.85% and CVD 13.5%. Waist circumference contributed the most to MetS (91.69%) followed by HDL-C (71.73%) and TG (63.08%). Age and duration of diabetes showed significant positive association in occurrence of DKD. OR for people with MetS to develop DKD was high in univariate and multivariate analysis, though statistically insignificant. T2DM with hypertension are at higher risk of DKD with OR 2.1957 [95% CI: 1.1618, 4.1496] versus those without hypertension (p = 0.0154).
Conclusion: Indian people with T2DM have high prevalence of MetS, where waist and low HDL-cholesterol are major contributors. MetS insignificantly, while hypertension significantly increases the risk of DKD in people with T2DM having MetS.
Keywords: India, Type 2 Diabetes Mellitus, Metabolic Syndrome, Diabetic Kidney Disease

Introduction:

The prevalence of Type 2 Diabetes is increasing globally. IDF atlas 2017 has estimated that globally 424.9 millions people have diabetes, which is expected to increase to 628.6 millions in 2045. The maximum increase will be in South East Asia. Today, China tops in the list of countries with maximum number of diabetics and India ranks at second position. But, it is projected that by 2045, India will surpass all other countries including China and will be sheltering highest number of people with diabetes globally. [1] The metabolic syndrome is a condition characterized by a special constellation of reversible major risk factors for cardiovascular disease and type-2 diabetes. It is a cluster of the risk factors, which include glucose intolerance, abdominal obesity, high triglyceride, low HDL-C and high blood pressure. [2-4] Subject with three or more than three risk factors is diagnosed with metabolic syndrome. All of these components are related to weight gain, specifically intra-abdominal/ectopic fat accumulation and a large waist circumference. It is estimated that around 20-25 percent of the World's adult population have the metabolic syndrome. People with metabolic syndrome have a five-fold greater risk of developing type-2 diabetes. [5] Each year, 3.2 million people around the world die from complications associated with diabetes. Type 2 DM, has become one of the major causes of premature illness and death, mainly through the increased risk of CVD which is responsible for up to 80 per cent of these deaths. [6-7] Apart from the cardiovascular complications, diabetes is also a leading cause of blindness, amputation and kidney failure, account for much of the social and financial burden of the disease. [8] The underlying cause of the

metabolic syndrome seems to be both insulin resistance and central obesity are considered significant factors. [9, 10] The prevalence of the metabolic syndrome and cardiovascular disease is expected to rise along with the global obesity and diabetes epidemic. [11] The International Obesity Task Force (IOTF) reports that 1.7 billion of the world's population is already at a heightened risk of weight-related, non-communicable diseases such as type 2 DM and its complications like CVD and diabetic kidney diseases. [12] Diabetic kidney diseases is also becoming an increasingly important cause of morbidity and mortality worldwide owing to an increasing prevalence of type 2 DM associated with metabolic derangement and obesity. There is considerable evidence that obesity, hypertension and other elements of the metabolic syndrome (MetS) also contribute to the progression of renal disease independent of diabetes. Diabetic Kidney Disease (DKD) is preceded by an increase in glomerular filtration rate (GFR), microalbuminuria and glomerular hypertrophy. Poor glycemic control and elevated systolic blood pressure exacerbate the proteinuria and renal injury that may culminate in end-stage renal disease. [13] Though, metabolic syndrome has shown its clear positive relationship with CVD, there is scanty Indian data available towards the association of metabolic syndrome and diabetic kidney disease. [14] In this study, we aim to look at the prevalence of metabolic syndrome, and diabetic kidney disease (DKD) amongst people with known type 2 diabetes. We also intend to see the impact of MetS and contribution of various components of MetS on the occurrence of DKD.

Methodology:

After getting Institutional Ethics Committee approval, 1037 people with known T2DM attending a tertiary care center from central India during Jan 2015 to Dec 2015 were selected. The data on demographic, anthropometry, blood pressure, lipid profile, CVD (based on ECG and past history of CVD) and DKD (based on e-GFR less than 60 ml/min/1.73 m^2) [15] was obtained. Anthropometric measurements, glycosylated hemoglobin A1c and lipids tests were carried out. Generalized obesity (BMI > 23 kg/m^2) and abdominal obesity (WC > 90 cm in men and > 80 cm in women) were defined using WHO Asia Pacific guidelines. [16] Metabolic syndrome was defined as per the National Cholesterol Education Program Adult Treatment Panel III (NCEP - ATP - III) guidelines. [17] The association of DKD was evaluated with other variables including metabolic syndrome in terms of unadjusted OR. The Odds Ratios were adjusted by considering covariates like age, gender, duration of DM and HbA1c in the logistic regression model.

Statistical methods: The data on demographic, anthropometric and metabolic parameters were obtained and summarized in terms of frequencies and percentages. The parameters on continuous scale were expressed in terms of mean and standard deviation. The risk of diabetic nephropathy associated with different factors was obtained in terms of crude odds ratio. The adjusted odds ratios were obtained using multivariate logistic regression analysis. All the analyses were performed using SPSS version 20.0 (IBM Corp., Armonk USA) and statistical significance was evaluated at 5%.

Results:

Out of 1037 patients included in the study, 657 (63.36%) were males and 380 (36.64%) were females as shown in Table 1. The mean age of patients was 50.46±9.901 years and the mean duration of diabetes was 5.69±5.68 years. 78.8% of studied population had generalized obesity with BMI > 23 kg/m^2. Overall, patients were obese as indicated by mean BMI of 26.56±4.43 kg/m^2. Majority, i.e. 1001 (96.53%) cases had abnormal (high) WHR; while 83.67% had high waist circumference. 837 (80.71%) cases had HbA1c more than 7.0. and 973 (93.83%) cases had dyslipidemia. Metabolic syndrome (MetS) was found in 902 (86.98%) subjects. The prevalence of MetS in female (91.3%) was higher than in male subjects (84.5%). Waist circumference and low HDL-cholesterol were found to be the major contributors towards this high prevalence of metabolic syndrome in our population as shown in Table 2. The prevalence of DKD in studied group was 6.85% and of CAD was 13.5%

The association between diabetic kidney disease (DKD) with the levels of different risk factors were evaluated by using unadjusted (univariate analysis) and adjusted (multivariate analysis) odds ratio and shown in Table 3. DKD was treated as dependent variable and age, gender, duration of DM, BMI, diet, and family history of DM, waist hip ratio, HbA1C, hemoglobin, hypothyroidism and metabolic syndrome as independent variables. Independent variable age showed highly significant association with the disease as indicated by p-value < 0.0001, where the odds of having DKD was 4.1446 [95% CI: 2.1235, 8.0894] times higher in group with age > 50 years, as compared to those with ≤ 50 years of age. As compared to patients having duration of type 2 diabetes (T2DM) ≤ 10 years, the odds ratio was 3.2212 [95% CI: 1.7075, 6.0765] times higher in the patients whose duration of T2DM was > 10 years. The difference was statistically significant with p value of 0.0003. Further, the odds of DKD in subjects with low hemoglobin was 2.2078 [95% CI: 1.1909, 4.0930] times significantly higher as compared to patients with normal hemoglobin (p-value = 0.0119)

In multivariate logistic regression analysis, only those independent variables (risk factors) which were found significant in univariate analysis were included in the model. The adjusted odds ratio associated with subjects having age > 50 years was 3.2894 [95% CI: 1.6468, 6.5698] times higher as compared to subjects with ≤ 50 years of age; which was statistically significant as indicated by p-value of 0.0007. Subjects suffering with T2DM for more than 10 years showed adjusted odds ratio of 2.1058 [95% CI: 1.0804, 4.1041] times higher as compared to those having ≤ 10 years duration of DM (p-value=0.0287). Further, the adjusted odds ratio for patient group with low hemoglobin level was 1.654 [0.8720, 3.1372] times higher as compared to those having normal hemoglobin level, however the effect was statistically insignificant (p-value = 0.1234). The OR associated with metabolic syndrome to develop diabetic nephropathy was high in univariate as well as multivariate analysis, though it was statistically insignificant. Although, metabolic syndrome was insignificant in univariate model due to higher OR, it was retained in the multivariate model to understand its effect on diabetic nephropathy. The effect in multivariate model was found statistically insignificant (p-value = 0.1372) with

adjusted odds ratio of 2.4831 [95% CI: 0.7485, 8.2372] as compared to patients without metabolic syndrome. High waist circumference was found to be the highest contributing factor to MetS with 91.69%, followed by HDL-C with 71.73% and TG with 63.08% (Table 1, 2). Table 4 shows the unadjusted and adjusted odds ratio associated with four factors of metabolic syndrome with diabetic kidney disease (DKD) as dependent variable. The crude odds ratio associated with abnormal waist circumference was 1.4018 [95% CI: 0.5423, 3.6234] times higher in subjects as compared to those having it in normal range although insignificant (p-value = 0.4857). Similarly, subjects with abnormal triglycerides and HDL-C levels were found at higher risk of DKD, although statistically insignificant. However, hypertension was strongly associated with DKD as indicated by crude odds ratio of 2.4146 [95% CI: 1.2906, 4.5176] and the effect was statistically significant with p value of 0.0058**.** In the adjusted analysis, the factors found significant in univariate analysis were included in the multivariate analysis model. The adjusted odds ratio associated with abnormal waist circumference was 1.1404 [95% CI: 0.4352, 2.9883] times higher as compare to normal waist circumference. The effect was statistically insignificant with p-value of 0.7892. The risk of DKD associated among patients having hypertension was 2.1957 [95% CI: 1.1618, 4.1496] times higher as compared to patients without hypertension and the effect was also statistically significant as indicated by p-value of 0.0154.

Discussion:

The prevalence of obesity and metabolic syndrome amongst people with type 2 diabetes is high. M Deepa et al [18] have shown in CURES: 47 study that, in Asian Indians, the age standardized prevalence of generalized obesity was 45.9% [95% CI: 43.9–47.9%], (women: 47.4%; men: 43.2%, p = 0.210), while that of abdominal obesity was 46.6% [95% CI: 44.6–48.6%], (women: 56.2%4 men: 35.1%, P<0.001). Our study has shown the higher prevalence of generalized obesity including overweight (78.8%), central obesity (83.7%) and metabolic syndrome (86.98%). This is because all our studied subjects have known type 2 diabetes, with mean age of 50.457 ± 9.901 years and the mean duration of diabetes of 5.69 ± 5.69 years. Waist circumference and low HDL-cholesterol were found to be the major contributors towards this high prevalence of metabolic syndrome in our population. Pooled data from 54 countries shows that at least 80% of cases of end-stage renal disease (ESRD) are caused by diabetes, hypertension or a combination of the two. The incidence of ESRD is up to 10 times as high in adults with diabetes as those without. [19] In CURE 45 study [20], the prevalence of overt nephropathy was found to be 2.2% in urban citizen with diabetes. We considered e-GFR of less than 60 ml/min/1.73 m^2 to define renal impairment as cut off point for DKD. Our data has shown the prevalence of DKD as 6.85%. We observed that people with long duration of diabetes and higher age, are significantly at higher risk to have diabetic nephropathy. There are scanty Indian papers available for the association of diabetic nephropathy with metabolic syndrome. Mohan Vinoth et al [14] in his study on 241 diabetic from Goa has shown that 17.4% of people had diabetic nephropathy. He also observed that DKD was higher in people with MetS (21.22%) versus people without MetS (6.45%). Our data of 1037 T2DM subjects have also observed that people with MetS have higher prevalence of DKD (6.4%) compared to those without MetS (2.52%). Thus, people with metabolic syndrome are 2.5 times higher risk to develop diabetic nephropathy versus those without MetS, though statistically insignificant. CURE 45 study [20] has shown that hypertension is positively associated with overt diabetic nephropathy. We have evaluated the impact of various components of MetS on DKD. High waist circumference, low HDL-C and high triglyceride have shown to insignificantly increase risk of DKD, while hypertension has shown highly significant association with DKD in people with T2DM having MetS.

Conclusion:

Prevalence of metabolic syndrome is high amongst people with type 2 diabetes mellitus. Central obesity and low HDL-cholesterol were observed to be the major contributors towards this high prevalence. Though, metabolic syndrome is traditionally known for its association with macro-angiopathy, the risk of diabetic nephropathy was found to be higher in our studied population of T2 DM having metabolic syndrome. Amongst all components of metabolic syndrome, hypertension plays the most significant role towards occurrence of diabetic kidney disease in people with type 2 diabetes mellitus with metabolic syndrome.

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Table 1: Demographic profile of studied people with type 2 DM

Characteristics	Levels	No.	%	Mean ± SD
Age (years)	≤ 50	531	51.21	50.457 ± 9.901
	> 50	506	48.79	
Gender	Female	380	36.64	
	Male	657	63.36	
Duration of DM (years)	≤ 10	854	82.35	5.692 ± 5.688
	> 10	183	17.65	
BMI (kg/m2)	≤ 23	220	21.22	26.565 ± 4.431
	> 23	817	78.78	
Diet	Veg	458	44.17	
	Mixed	579	55.83	
Family history of DM	No	369	35.58	
	Yes	668	64.42	
Waist hip ratio	Normal	36	3.47	0.993 ± 0.064
	Abnormal	1001	96.53	
HbA_1C (%)	≤ 7	200	19.29	8.969 ± 2.192
	> 7	837	80.71	
HB (g/dL)	Normal	803	77.43	13.261 ± 1.766
	Low	234	22.57	
Dyslipidemia	No	64	6.17	
	Yes	973	93.83	
Hypertension	No	500	48.22	
	Yes	537	51.78	
Hypothyroidism	No	911	87.85	
	Yes	126	12.15	
Metabolic syndrome	No	135	13.02	
	Yes	902	86.98	

Table 2: Contribution of various components towards metabolic syndrome

Characteristics	Levels	Metabolic Syndrome present [No. (%)]
Waist circumference	Normal	73 (8.09)
	Abnormal	827 (91.69)
Triglycerides (mg/dL)	≤ 150	329 (36.47)
	> 150	569 (63.08)
HDL-C (mg/dL)	Normal	248 (27.49)
	Abnormal	647 (71.73)
Hypertension	No	376 (41.69)
	Yes	526 (58.31)

Table 3: Unadjusted and adjusted risk of diabetic kidney disease (DKD) associated with the levels of different risk factors

Characteristics	Levels	Diabetic Nephropathy patients/Total (%)	Prevalence odds ratio [95% CI]; P-value	
			Unadjusted	Adjusted
Age (years)	≤ 50	12/461 (2.6)	1	1
	> 50	36/361 (9.97)	4.1446 [2.1235 , 8.0894]; < **0.0001**	3.2894 [1.6468 , 6.5698]; **0.0007**
Gender	Female	21/291 (7.22)	1	
	Male	27/531 (5.08)	0.6888 [0.3821 , 1.2415]; 0.2148	
Duration of DM (years)	≤ 10	32/702 (4.56)	1	1
	> 10	16/120 (13.33)	3.2212 [1.7075 , 6.0765]; **0.0003**	2.1058 [1.0804 , 4.1041]; **0.0287**
BMI (kg/m2)	≤ 23	7/170 (4.12)	1	
	> 23	41/652 (6.29)	1.5625 [0.6882 , 3.5477]; 0.2860	
Diet	Veg	22/457 (4.81)	1	
	Mixed	26/365 (7.12)	1.5165 [0.8446 , 2.7228]; 0.1632	
Family history of DM	No	17/291 (5.84)	1	
	Yes	31/531(5.84)	1.0007 [0.5440 , 1.8410]; 0.9982	
Waist-Hip-Ratio	Normal	4/33 (12.12)	1	
	Abnormal	44/789 (5.58)	0.4282 [0.1441 , 1.2719]; 0.1268	
HbA_1C (%)	≤ 7	6/173 (3.47)	1	
	> 7	42/649 (6.47)	1.9259 [0.8049 , 4.6079]; 0.1409	
HB (g/dL)	Normal	31/651 (4.76)	1	1
	Abnormal	17/171 (9.94)	2.2078 [1.1909 , 4.0930]; **0.0119**	1.654 [0.8720 , 3.1372]; 0.1234
Thyroid	No	39/725 (5.38)	1	
	Yes	9/97 (9.28)	1.7990 [0.8430 , 3.8391]; 0.1289	
Metabolic syndrome	No	3/119 (2.52)	1	1
	Yes	45/703 (6.4)	2.6444 [0.8083 , 8.6512]; 0.1078	2.4831 [0.7485 , 8.2372]; 0.1372

Table 4: Effect of various components of Metabolic Syndrome on Diabetic Kidney Disease

Characteristics	Levels	* *DKD Total (%)	Odds ratio [95% CI]; P-value	
			Unadjusted	Adjusted
Waist circumference	Normal	5/118 (4.24)	1.00*	1.00*
	Abnormal	41/702 (5.84)	1.4018 [0.5423, 3.6234]; 0.4857	1.1404 [0.4352, 2.9883]; 0.7892
Triglycerides (mg/dl)	≤ 150	18/356 (5.06)	1.00*	1.00*
	> 150	30/454 (6.61)	1.3286 [0.7280, 2.4247]; 0.3546	1.4551 [0.7712, 2.7460]; 0.2469
HDL-C (mg/dl)	Normal	15/275 (5.45)	1.00*	1.00*
	Abnormal	33/528 (6.25)	1.1556 [0.6163, 2.1665]; 0.6521	1.1367 [0.5881, 2.1970]; 0.7033
Hypertension	No	15/420 (3.57)	1.00*	1.00*
	Yes	33/402 (8.21)	2.4146 [1.2906, 4.5176]; **0.0058**	2.1957 [1.1618, 4.1496]; **0.0154**

*Reference level, **DKD: e-GFR cut off: 60 ml/min/1.73 m^2

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