

Prevalence of Metabolic Syndrome in Newly Diagnosed Type 2 Diabetes Mellitus

Tamrakar R,¹ Shrestha A¹, Tamrakar D²

¹Department of Internal Medicine

²Department of Community Medicine

Kathmandu University School of Medical Sciences

Dhulikhel, Nepal.

Corresponding Author

Rajendra Tamrakar

Department of Internal Medicine

Kathmandu University School of Medical Sciences

Dhulikhel, Nepal.

E-mail: tamrakaraj@gmail.com

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ABSTRACT

Background

The clustering of risk factors in metabolic syndrome increases the risk of atherosclerotic cardiovascular disease and all-cause mortality. The prevalence of coronary heart disease is high in diabetic patients with metabolic syndrome than non diabetic patients with metabolic syndrome.

Objective

To determine the prevalence of metabolic syndrome in new onset Type 2 Diabetes Mellitus (T2DM) and to study the risk components of metabolic syndrome.

Method

This is a hospital based cross sectional study conducted in 132 newly diagnosed T2DM patients at Dhulikhel Hospital, Kathmandu University Hospital in Nepal in 2018. The socio-demographic profile, clinical characteristics, and biochemical parameters were analyzed to study the prevalence, risk factors, and concordance between various definitions of metabolic syndrome. Statistical analysis was done using Student's t-test, Chi-square test and Kappa statistics.

Result

One hundred and thirty two newly diagnosed T2DM patients were included in the study. Majority of the patients (58.9%) were in the age group of 40-60 years with the mean age of 49.72±12.44 years. The prevalence of metabolic syndrome was 111 (84.1%), 106 (80.3%), 94 (71.2%) and 82 (62.1%) using World Health Organization(WHO), Harmonized, National Cholesterol Education Program-Adult Treatment Panel III (NCEP ATP III) and International Diabetes Federation (IDF) definitions respectively. One hundred and six patients (80.3%) had 3 or more individual components of metabolic syndrome. There was substantial agreement between NCEP ATP III-Harmonized ($k=0.714$, $p<0.001$) and Harmonized-WHO ($k=0.716$, $p<0.001$) definitions for diagnosing metabolic syndrome. The increased prevalence of metabolic syndrome in females than males is due to increased prevalence of abdominal obesity ($p<0.05$), dyslipidemia (low HDL cholesterol ($p<0.05$)) and presence of diabetes.

Conclusion

The prevalence of metabolic syndrome in newly diagnosed T2DM is high in the Nepalese population. The central obesity and low HDL cholesterol were significant risk factors in female diabetic patients predisposing to metabolic syndrome.

KEY WORDS

Metabolic syndrome, Prevalence, Type 2 diabetes mellitus

INTRODUCTION

Studies have shown that patients diagnosed with metabolic syndrome, by either the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), or World Health Organization (WHO) definition, are at increased cardiovascular disease (CVD) risk.¹ Metabolic syndrome is defined by a constellation of an interconnected physiological, biochemical, clinical, and metabolic factors that directly increases the risk of atherosclerotic cardiovascular disease (ASCVD), (T2DM), and all-cause mortality.² The clustering of risk factors like dyslipidemia, hypertension, and hyperglycemia, and its association with insulin resistance led investigators to propose the existence of a unique pathophysiological condition, called the “metabolic” or “insulin resistance” syndrome.¹ World Health Organization (WHO), the European Group for the study of Insulin Resistance (EGIR), the NCEP ATP III, American Association of Clinical Endocrinologists (AACE), and the International Diabetes Federation (IDF) have given criteria for defining metabolic syndrome.³ Of these various definitions, only the IDF considers ethnicity in their criteria in which waist circumference is an essential component for defining metabolic syndrome and for South Asians based Chinese, Malay and Asian Indian population waist circumference ≥ 90 cm in males, ≥ 80 cm in females is considered increased waist circumference.²

The prevalence of metabolic syndrome was very high among individuals with diabetes. The prevalence of coronary heart disease was increased in diabetes patients having metabolic syndrome than non diabetic patients with metabolic syndrome.⁴ The prevalence of metabolic syndrome in type 2 diabetes mellitus is 45.8%, 57.7% and 28% following NCEP-ATPIII Criteria, IDF and WHO definitions, respectively in Central India.⁵ A study done in Nepal showed the total age adjusted prevalence rates of metabolic syndrome were 80.3%, 73.9%, 69.9% and 66.8% according to Harmonized, NCEP ATP III, WHO and IDF definitions, respectively and there was highest overall agreement between Harmonized and NCEP ATP III definitions and the lowest between WHO and IDF definitions.⁶

Most individuals who develop CVD, which is viewed as primary clinical outcome of metabolic syndrome have been linked with multiple risk factors like dyslipidemia, hypertension, and hyperglycemia. ATP III identified six components of the metabolic syndrome as “underlying,” “major,” and “emerging” CVD risk factors namely abdominal obesity, atherogenic dyslipidemia, hypertension, insulin resistance, proinflammatory state and prothrombotic state.^{1,7} A study conducted at Kathmandu, Nepal showed strong association with obesity in diabetic patients with metabolic syndrome.⁸ Dyslipidemia and abdominal obesity could be the major contributors to metabolic syndrome in Nepal.⁹

The studies done in longstanding or ongoing T2DM had

shown the prevalence of metabolic syndrome among Nepalese type 2 diabetic patients is very high suggesting that these patients are at increased risk of strokes, cardiovascular diseases and premature death. However the prevalence of metabolic syndrome in new onset T2DM is obscured. The early recognition of metabolic syndrome in T2DM will help to initiate appropriate preventive and therapeutic approaches in such patients. This study is therefore aimed at determining the prevalence of metabolic syndrome in newly diagnosed T2DM patients attending Dhulikhel Hospital, Kathmandu University Hospital and determining their level of agreement in the diagnosis of metabolic syndrome.

METHODS

This is hospital based descriptive Cross sectional study including type T2DM patients diagnosed within 3 months. Patients with type 1 Diabetes, pregnant ladies, established serious metabolic disorders, established cardiovascular diseases and thyroid disorders and patients taking psychiatric treatment were excluded from the study. The study was conducted at Dhulikhel Hospital, Kathmandu University Hospital from January to August, in 2018. Dhulikhel Hospital is the tertiary level hospital in central Nepal. Patients attending the outpatient and inpatient department of Internal Medicine department were enrolled in the study.

Data was taken from newly diagnosed T2DM patients meeting the American Diabetes Association criteria.¹⁰ Information regarding demographic profile including age, sex, ethnicity, residence was recorded according to the proforma. Anthropometric measurement like height, weight, waist circumference and body mass index were measured with the subject barefooted and lightly dressed. Recent WHO guideline for South Asian population (18.5 - 22.9 kg/m²) was followed to classify their BMI status.¹¹ Waist circumference (WC) was measured at the midpoint between the lower margin of the least palpable rib and the top of the iliac crest, using a stretch resistant tape. Blood pressure was measured by standardized protocols using a sphygmomanometer. Serum triglycerides (TG), total cholesterol (TC), HDL-cholesterol and LDL-cholesterol value were recorded. Dyslipidemia was defined by the presence of one or more abnormal serum lipid concentration. Patients were classified as metabolic syndrome meeting criteria for metabolic syndrome using WHO, NCEP ATP III, Harmonized and IDF criteria.^{2,12}

This study was approved by the institutional review committee of Kathmandu University School of Medical Sciences and informed consent was obtained from all the enrolled study patients. A total of 132 newly diagnosed T2DM were enrolled in the study. Non probability consecutive sampling technique was used. Statistical analysis was performed using Statistical Package for the

Social Sciences (SPSS) 20.0 software for windows. Data for categorical variables were expressed either in number and percentage. Numerical data for continuous variables were expressed in the form of mean ± standard deviation. The agreements among the definitions of WHO, NCEP ATP III, IDF and harmonized criteria were assessed with kappa statistics. Pearson’s Chi-square test and Independent sample test (p values, 2 tailed) were used for statistical significance of difference between the proportion and mean values of two or more groups of variables respectively. The tests were considered statistically significant when p <0.05.

RESULTS

There were 132 newly diagnosed T2DM patients included in the study among which 77 (58.3%) were male and 55(41.7%) were female. Majority of the patients (58.9%) were in the age group of 40-60 years with the mean age of 49.72±12.44 years. Majority of the patients were from Newar ethnicity (40.2%) followed by Bramhin (23.5%), Chhetri (13.6%), Tamang (11.4%), Dalit (4.5%) and others (6.8%). Hypertension was present in 52 patients (39.4%). Out of 132 patients, 4 (3.0%) were underweight, 35 (26.5%) had normal BMI, 30 (22.7%) were overweight, 48 (36.4%) had Grade I obesity, and 15 (11.4%) had Grade II obesity. The prevalence of metabolic syndrome was 111 (84.1%), 106 (80.3%), 94 (71.2%) and 82 (62.1%) using WHO, Harmonized, NCEP ATP III, and IDF definition respectively. Metabolic syndrome was more prevalent in females using IDF criteria (p < 0.05) while the prevalence of metabolic syndrome was not statistically different in males and females using other definitions.

The mean values of various anthropometric and biochemical parameters of the male and female study patients are presented in Table 2. Waist to hip ratio (WHR) and Triglycerides was significantly higher in males (p < 0.05). Though the mean BMI, HbA1C, LDL cholesterol, HDL cholesterol of females were higher than males, there was no statistical significance. One hundred and six patients (80.3%) had 3 or more individual components of metabolic syndrome with no significant difference between males and females using IDF definition.

The most prevalent component was the central obesity according to WHO definition (93.2%). Decreased HDL-cholesterol was the most prevalent component according to IDF, NCEP ATP III and Harmonized definitions (75.8%). Raised triglycerides was prevalent in 60.6% of patients. Increased BMI (≥ 30 kg/m²) was the least prevalent component (11.4%) according to WHO definition. Hypertension was prevalent in 39.4% of patients. Abdominal obesity and low HDL were more prevalent in females using IDF, NCEP ATP III and Harmonized definitions (p < 0.05).

There was substantial agreement between NCEP ATP III-

Table 1. Frequency analysis of socio-demographic and anthropometric parameters of the study subjects

Characteristic variable	Male n(%)	Female n(%)	Total n(%)
	77(58.3)	55(41.7)	132(100)
Age group			
<30	2(2.6)	2(3.6)	4(3.0)
30-40	14(18.2)	11(20.0)	25(18.9)
40-50	23(29.9)	14(25.5)	37(28.0)
50-60	23(29.9)	19(34.5)	42(31.8)
>60	15(19.5)	9(16.4)	20(18.2)
Ethnicity			
Newars	31(40.3)	22(40.0)	53(40.2)
Bramhin	18(23.4)	13(23.6)	31(23.5)
Chhetri	11(14.3)	7(12.7)	18(13.6)
Tamang	7(9.1)	8(14.5)	15(11.4)
Dalit	3(3.9)	3(5.5)	6(4.5)
Others	7(9.1)	2(3.6)	9(6.8)
Address			
Kavre	55(71.4)	42(76.4)	97(73.5)
Bhaktapur	11(14.3)	5(9.1)	16(12.1)
Sindhupalchok	5(6.5)	3(5.5)	8(6.1)
Sindhuli	1(1.3)	3(5.5)	4(3.0)
Others	5(6.5)	2(3.6)	7(5.3)
BMI			
<18.5 (Underweight)	1(1.3)	3(5.5)	4(3.0)
18.5-22.9 (Normal range)	18(23.4)	17(30.9)	35(26.5)
23-24.9 (Overweight)	22(28.6)	8(14.5)	30(22.7)
25-29.9 (Obese I)	30(39.0)	18(32.7)	48(36.4)
>30 (Obese II)	6(7.8)	9(16.4)	15(11.4)

Table 2. Anthropometric and biochemical parameters of the type 2 diabetic patients

Variable	Male (n=77)	Female (n=55)	p-value	Total
	Mean±SD	Mean±SD		Mean±SD
Age	49.87±12.34	49.51±12.69	0.870	49.72±12.44
WC	92.06±8.83	88.07±13.07	0.052	90.40±10.93
WHR	0.98±0.06	0.93±0.07	0.001	0.96±0.07
BMI	25.02±3.26	25.19±4.39	0.812	25.09±3.76
FBS	212.31±84.50	234.67±88.49	0.144	221.63±86.56
PPBS	339.91±134.55	390.16±158.18	0.051	360.85±146.40
HbA1c	10.18±3.11	10.79±2.99	0.261	10.43±3.06
Total Cholesterol	190.52±62.42	193.49±45.05	0.764	191.76±55.67
LDL Cholesterol	105.17±36.72	106.89±30.15	0.776	105.89±34.02
HDL Cholesterol	35.88±10.73	36.85±10.80	0.610	36.29±10.73
Triglycerides	241.00±205.18	186.04±89.46	0.039	218.10±168.71

Table 3. Prevalence of Metabolic Syndrome using different criteria in diabetic patients

	Male n=77	Female n=55	Total	p-value
WHO criteria	67(87.0)	44(80.0)	111(84.1)	0.227
Harmonized criteria	59(76.6)	47(85.5)	106(80.3)	0.208
NCEP ATP III criteria	51(66.2)	43(78.2)	94(71.2)	0.135
IDF criteria	42(54.5)	40(72.7)	82(62.1)	0.034

Table 4. Prevalence of the various components of metabolic syndrome among the study population stratified by gender

Parameter	Total	Male (n=77)	Female (n=55)	p-value
IDF				
Abdominal obesity	88 (66.7)	46 (59.7)	42 (76.4)	0.046
Raised TG	80 (60.6)	48 (62.3)	32 (58.2)	0.630
Decreased HDL	100 (75.8)	52 (67.5)	48 (87.3)	0.009
High blood pressure	52 (39.4)	33 (42.9)	19 (34.5)	0.335
NCEP ATP III				
Abdominal obesity	36 (27.3)	10 (13.0)	26 (47.3)	0.001
Raised TG	80 (60.6)	48 (62.3)	32 (58.2)	0.630
Decreased HDL	100 (75.8)	52 (67.5)	48 (87.3)	0.009
High blood pressure	52 (39.4)	33 (42.9)	19 (34.5)	0.335
Harmonized				
Abdominal obesity	88 (66.7)	46 (59.7)	42 (76.4)	0.046
Raised TG	80 (60.6)	48 (62.3)	32 (58.2)	0.630
Decreased HDL	100 (75.8)	52 (67.5)	48 (87.3)	0.009
High blood pressure	52 (39.4)	33 (42.9)	19 (34.5)	0.335
WHO				
Obesity	123 (93.2)	73 (94.8)	50 (90.9)	0.381
Raised TG	80 (60.6)	48 (62.3)	32 (58.2)	0.630
Decreased HDL	61 (46.2)	33 (42.9)	28 (50.9)	0.360
High blood pressure	52 (39.4)	33 (42.9)	19 (34.5)	0.335

Harmonized ($k=0.714$, $p < 0.001$) and Harmonized-WHO ($k=0.716$, $p < 0.001$) definitions for diagnosing metabolic syndrome. The agreement was moderate between NCEP ATP III-WHO ($k=0.510$, $p < 0.001$) and IDF-Harmonized ($k=0.574$, $p < 0.001$) definitions while the agreement was fair between NCEP ATP III-IDF ($k=0.392$, $p < 0.001$) and IDF-WHO ($k=0.365$, $p < 0.001$) definitions.

Table 5. The agreement between various definitions for identifying metabolic syndrome in type 2 diabetic patients

Definitions	k value (95% CI)	p value	Agreement
NCEP ATP III vs IDF	0.392	<0.001	Fair
NCEP ATP III vs Harmonized	0.714	<0.001	Substantial
NCEP ATP III vs WHO	0.510	<0.001	Moderate
IDF vs Harmonized	0.574	<0.001	Moderate
IDF vs WHO	0.365	<0.001	Fair
Harmonized vs WHO	0.716	<0.001	Substantial

DISCUSSION

The prevalence of metabolic syndrome ranges from <10% to 84% depending upon the population studied and definition used for defining metabolic syndrome.² The prevalence of metabolic syndrome in general population in India was found to be 23.2% by WHO criteria, 18.3% by ATP III criteria and 25.8% by IDF criteria.¹³ The prevalence of metabolic syndrome is higher in diabetics than the general population. A study done in Srilanka had shown the prevalence of metabolic syndrome in T2DM patients varied from 28.9%, 43.8% and 70.6% using NCEP-ATP III, IDF, and WHO criteria, respectively.¹⁴ Similarly, a study done in central India had shown the prevalence of metabolic syndrome in T2DM patients ranged from 28% to 58% using different definitions.⁵ The prevalence of metabolic syndrome in T2DM was found to be higher in Nepal than reported in other countries in South Asia. The total crude prevalence was 81.1%, 83.0%, 80.5% and 91.6% according to WHO, NCEP ATP III, IDF and Harmonized criteria, respectively as shown in the study done by Pokharel et al.⁶ In our study, majority of the patients (58.9%) were in the age group of 40-60 years with the mean age of 49.72 ± 12.44 years. The prevalence of metabolic syndrome in newly diagnosed T2DM was 111 (84.1%), 106 (80.3%), 94 (71.2%) and 82 (62.1%) using WHO, Harmonized, NCEP ATP III, and IDF definition respectively. The high prevalence of metabolic syndrome in the study is comparable to the study done in Nepal.⁶ The prevalence of metabolic syndrome was high using Harmonized definitions because of low cut off point used for waist circumference and requirement of at least any three of the five criteria present. Similarly the prevalence of metabolic syndrome was high using WHO criteria because presence of diabetes mellitus is one of the prerequisite criteria and the use of WHR for defining central obesity. Despite the lower BMI in South Asians, they tend to have larger waist measurement and WHR indicating more abdominal fat which predispose them to insulin resistance, low HDL levels, high triglycerides and increased susceptibility to T2DM and coronary artery disease.¹⁵

In our study, there was substantial agreement between NCEP ATP III-Harmonized and Harmonized-WHO definitions for diagnosing metabolic syndrome. The agreement was moderate between NCEP ATP III-WHO and IDF-Harmonized definitions while the agreement was fair between NCEP ATP III-IDF and IDF-WHO definitions. A study done by Herath et al. in Srilanka had shown the concordance of individuals with metabolic syndrome between IDF-WHO definitions was 0.37 which was similar to our study and between NCEP ATP III-IDF definitions was 0.53 which was comparatively higher whereas it was 0.24 between NCEP-ATP III-WHO definitions which was comparatively lower than our study.¹⁴ A study done in Nepal showed substantial agreement between NCEP ATP III- Harmonized ($k = 0.62$), moderate between WHO-NCEP ATP III ($k = 0.51$) and IDF-Harmonized ($k = 0.51$), fair between NCEP ATP III-IDF ($k = 0.33$) which was similar to our study.⁶ Another study done

in India in general population had shown that IDF had a higher agreement with NCEP ATP III ($k = 0.58$) and WHO ($k = 0.44$) in comparison to our study.¹³ The substantial agreement between NCEP ATP III and Harmonized definition for diagnosing metabolic syndrome in this study is due to the requirement of any three of five criteria present despite different cut off point used for waist circumference. Similarly the presence of increased WHR in the study population resulted in substantial agreement between Harmonized and WHO definition despite different cut off values for HDL cholesterol. The fair agreement between IDF and NCEP ATP III/ WHO definition is due to inclusion of ethnicity based waist circumference as an essential component for diagnosing metabolic syndrome. The disparity in concordance between various definitions in South Asian population may be due to variability of obesity in different ethnic groups. Hence the agreement between different definitions for metabolic syndrome depends on various factors as ethnicity, ethnic origins, abdominal obesity, and presence of diabetes. Despite lower WC and hip circumference in Asian Indians, various studies had shown they have a higher WHR and there is correlation of BMI with WC but not with WHR. Thus WC and BMI are better predictors of metabolic syndrome than WHR in Asian Indians. The WHO has not lowered BMI cut-offs for Asian population while defining metabolic syndrome despite considerable evidence. However, lower WC cut offs (≥ 90 cm in males and ≥ 80 cm in females) in South Asians has been adopted in the modified NCEP ATP III and IDF definitions.¹⁶ Central obesity should be included as an optional component rather than essential component while defining metabolic syndrome as high risk individuals for cardiovascular disease will be identified. The modified ethnicity based NCEP ATP III criteria may be better than the IDF criteria in diagnosing metabolic syndrome among Asians as central obesity is an optional component in revised NCEP ATP III definition.^{17,18} Thus ethnicity based definition requiring any three out of five criteria can be used for diagnosing metabolic syndrome in the Nepalese population as this can identify patients with high CVD risk.

The percentage of patients with metabolic syndrome was higher in females using Harmonized, NCEP ATP III and IDF definitions. The high prevalence of central obesity and low HDL cholesterol in diabetic females have resulted in higher percentage of metabolic syndrome in females. The Third National Health and Nutrition Survey (NHANES III, 1998-1994, NCEP criteria) in the United States demonstrated that, the increased triglycerides, low HDL cholesterol, and central obesity were the most common risk components in younger women. While the combination of increased triglycerides, low HDL cholesterol, and hypertension were common in younger males. When comparing data from NHANES during 1988-1994 to NHANES 1999-2000, the age-adjusted prevalence of the metabolic syndrome increased by 23.5% among women ($p = 0.021$) and 2.2% among men ($p = 0.831$).^{19,20} There are several factors unique to women

like pregnancy-related weight gain, hormonal contraceptive use, polycystic ovary syndrome, gestational diabetes, pre-eclampsia, menopause that can impact the prevalence and characteristics of metabolic syndrome in women.²¹

In 106 patients (80.3%), there was clustering of 3 or more individual components of metabolic syndrome in our study. The most prevalent components in diabetic patients were central obesity, reduced HDL-cholesterol and raised triglycerides using various definitions. Increased BMI (≥ 30 kg/m²) was the least prevalent component (11.4%) according to WHO definition. Various definitions of metabolic syndrome incorporate risk components as hyperglycemia, hypertension, and dyslipidemia, with the main difference being whether abdominal obesity (IDF definition) is obligatory and whether national or regional waist circumference cut points should be used (IDF and harmonizing definitions). The measurement of waist circumference rather than BMI reflects growing evidence for a critical role of central obesity as an alternate unifying mechanism.²⁰ In Nepal, the most prevalent component was the central obesity (WHO, 98.8% and IDF, 99.9%) followed by decreased HDL cholesterol in more than 90% of patients. Obesity as defined by increased BMI (≥ 30 kg/m²) was the least prevalent component (4.0%).⁵ The findings are comparable to our study. Similarly, obesity, hypertension, low HDL cholesterol and elevated triglycerides were highly prevalent in diabetic population with metabolic syndrome in Malaysians.²² The difference in prevalence of central obesity, low HDL cholesterol is due to use of gender and ethnicity specific cut off values for waist circumference, WHR, HDL cholesterol in various definitions for defining metabolic syndrome.

The study is not without limitations. This study is a cross sectional study conducted in newly diagnosed T2DM patients. Since this study included diabetic patients diagnosed within 3 months, the number of patients enrolled in this study is less. The presence of urine albumin on routine urinalysis was taken into consideration rather than urine microalbumin as one of the criteria according to WHO definition. The study is done in a single center therefore the findings of the study can't be generalized to the whole diabetic population in Nepal. Despite these limitations, this type of study is one of few studies carried out in newly diagnosed T2DM patients to study the prevalence of metabolic syndrome.

CONCLUSION

The prevalence of metabolic syndrome in newly diagnosed T2DM was high ranging from 62% to 84% in the Nepalese population using various definitions. The highest prevalence was observed with WHO and the least prevalence was observed with IDF definition. The central obesity and low HDL cholesterol were significant risk factors in female diabetic patients predisposing to metabolic syndrome.

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