

# “Metabolic Syndrome and Its Risk Determinants in Sikkim”: A Glimpse from a Hospital Study

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**Abstract** Sikkim has been reported to have the highest percentage of Diabetes Mellitus and Hypertension in the country. The study aimed to focus its precursor termed ‘Metabolic Syndrome’ (MetS) with special attention to its risk determinants as a measure to promote awareness in preventing the rise in number of these non communicable diseases in the state with only 6,10,577 inhabitants. Of 361 participants, 33.5% were diagnosed MetS as per the harmonized MetS criteria, 64.5% deemed non-MetS comprised of participants with “2 Risk”, “1 Risk” and “0 Risk” for MetS, however not enough (3 or more) to be categorized as MetS. A “large WC + elevated BP + raised FBS”; “large WC + elevated BP” and “large WC” were the different types of risk combinations found frequently in the “3 Risk”, “2 Risk” and “1 Risk” category respectively. MetS was most common among the females and highly found in 51–60 years of age. Ethnically “Bhutia/Lepcha/Tamang/Sherpa” were diagnosed with highest percentage of MetS followed by “Nepalese” and “Others”. The chief contributing factor to compose MetS in the female population was a large WC. We conclude, Diabetes and Hypertension are indeed prevailing in Sikkim and that the presence of either an increased waist circumference or an elevated blood pressure mandates a check for the remaining four risk factors for MetS, rendering worthwhile to keep an account of MetS risk types by

stratification to comprehend the influence of socio-cultural and ethno-geographical factors in causing MetS.

**Keywords** Abdominal obesity · Diabetes Mellitus · Hypertension · Metabolic Syndrome · Sikkim

## Introduction

The National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS) has reported Sikkim to have the highest percentage of Diabetes Mellitus (DM) (13.67%) and Hypertension (18.16%) in the country. These non communicable diseases are the leading causes of concern and a significant public health problem in the state of Sikkim, followed closely by alcohol misuse and its related health consequences, accidents, suicides, tuberculosis, respiratory diseases and cancer [1]. According to the 2011 World Health Organization (WHO) report, the total mortality attributed to DM and cardio vascular diseases (CVD) in India is 2 and 26% respectively across all ages and both sexes [2]. In fact, India is considered as the diabetes capital of the world now heading towards Hypertension [3]. The strong correlation between Cardiovascular Disease and Diabetes is an established fact and it has also been stated that adults with DM are two to four times more likely to have a heart disease or stroke than adults without [4]. Moreover, besides the classical complications of both type 1 and type 2 DM, it is also known to double the risk of developing pancreatic cancer [5].

A common precursor of the duo (DM and CVD) has been suggested to be Metabolic Syndrome (MetS) [6]. A person with MetS is twice as likely to die from and three times more likely to have a heart attack or stroke [7] which is indeed an early warning sign.

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The guidelines for the syndrome has been put forward by World Health Organization (WHO) [8], National Cholesterol Education Program—Third Adult Treatment Panel (Revised) (NCEP ATP-III) [9] and International Diabetes Federation (IDF) [10] (Table 1). The 2001 definition for MetS by the ATP-III was updated by the American Heart Association and National Heart Lung and Blood Institute (AHA/NHLBI) in 2005. It requires the presence of any three of increased waist circumference (now ethnic specific), increased fasting blood sugar (FBS; now >100 mg/dl), elevated blood pressure (BP; same as previous >130/85 mmHg), increased triglyceride (TG; same as previous >150 mg/dl) and decreased High Density Lipoprotein-cholesterol (HDL-C; same as previous Male <40 mg/dl; Female <50 mg/dl). Waist circumference values are gender and ethnic specific with cut points of ≥90 cm in males and ≥80 cm in females for South Asian [9]. Thereafter, modification to ATP III definition was soon followed by modification to IDF definition in 2009, undertaken by IDF and AHA/NHLBI. They further reviewed the previous IDF definition for the ‘Syndrome’

and gave a consensus upon abdominal obesity not being a prerequisite but that it is 1 of 5 criteria for diagnosing Metabolic Syndrome. All remaining four risk factors were agreed to remain the same. Special attention was laid on the ethnic specific waist circumference value, and added upon to the previous ethnicity definition for more countries. They proposed in its Joint Interim statement that the risk associated with particular waist circumference measurement will differ in different population and that there should be a single definition with an agreed upon cut points for different ethnic groups and sexes, intended for International comparisons to facilitate etiology. The definition now includes fulfilling any 3 of 5 risk factors of elevated blood pressure, raised triglycerides, raised fasting glucose, and reduced HDL-C and the ethnic specific waist circumference value. Accepting change, IDF and AHA/NHLBI mentions in its statement that it is expected that new expert groups will be formed to assess the evidence with regard to waist circumference thresholds and its associated risk [10]. Nikola Tesla truly said “One of the most gratifying results of intellectual evolution is the continuous opening up of

**Table 1** Metabolic Syndrome definition by IDF, NCEP-ATP III, WHO (*cm* centimeter, *mmHg* millimeter mercury, *mg/dl* milligram/deciliter)

IDF definition for MetS “Harmonized” (2009)	Revised NCEP ATP III definition (2005)	WHO definition (1998)
Any three of the five following features	Any three of the five following features	Diabetes (fasting plasma glucose ≥100 mg/dl) or previously diagnosed type 2 diabetes Plus any two of the following four
<i>Central obesity</i>	<i>Central obesity</i>	Obesity: BMI >30 kg/m <sup>2</sup> , or
Population-specific	Population-specific	Waist–hip ratio >.9 in men and >.85 in women
Asian Indians male ≥90 cm	South male ≥90 cm	
Female ≥80 cm plus any two of the following	Female ≥80 cm plus any two of the following	
<i>Raised triglyceride</i>	<i>Raised triglyceride</i>	Dyslipidemia: triglycerides level >150 mg/dl
≥150 mg/dl	≥150 mg/dl	
Or specific treatment for this lipid abnormality	Or drug treatment for elevated TG	
<i>Reduced HDL-cholesterol</i>	<i>Reduced HDL-cholesterol</i>	HDL-cholesterol <35 mg/dl in men and <39 mg/dl in women
<40 mg/dl in males	<40 mg/dl in males	
<50 mg/dl in females	<50 mg/dl in females	
Or specific treatment for this lipid abnormality	Or drug treatment for reduced HDL	
<i>Raised blood pressure</i>	<i>Raised blood pressure</i>	Raised blood pressure ≥140/90 mmHg or treatment of previously diagnosed hypertension
Systolic: ≥130 mmHg	≥130/85 mmHg	
Or diastolic: ≥85 mmHg	Or drug treatment for hypertension	
Or treatment of previously diagnosed hypertension		
<i>Glucose</i>	<i>Glucose</i>	
≥100 mg/dl	>100 mg/dl (includes Diabetes)	
Or previously diagnosed Type 2 diabetes	Or drug treatment for elevated glucose	

new and greater aspects”. In this study, we followed the latest Harmonized 2009 definition which is similar to the 2005 ATP III definition for MetS.

South Asians are known to have the highest rates of CVD and DM in the globe [11]. Professor Sir George Alberti, co-author of the IDF consensus statement states “whichever definitions is used and whatever the variation in the numbers due to the different criteria, when looking at prevalence data for the Metabolic Syndrome in different countries and across various ethnic groups, one fact is clear universally, Metabolic Syndrome is a huge problem and is one that is growing at an alarming rate”. A check on these growing numbers needs to be critically taken into consideration for an improved lifestyle physically and economically. In this context, we planned to study and assess the occurrence of MetS and its risk determinants in the study population of Sikkim. This was a hospital based study supposed as a pilot for a larger community based prevalence study yet to be undertaken to manage MetS in the state with only 6,10,577 inhabitants [12].

## Methodology

The study was a hospital based cross-sectional design conducted in the department of Biochemistry, Central Referral Hospital, Sikkim Manipal Institute of Medical Sciences. Data were taken from a larger study on ‘Metabolic Syndrome’ (MetS) where non-probability sampling method was adopted after obtaining permission from Institutional Ethical Committee (IEC). A total of 361 outpatients including those who came for annual health checkups  $\geq 20$  years of age visiting the central laboratory with a requisition for biochemical investigations like fasting sugar and lipid profile were enrolled in the study. Willing participants excluding pregnant ladies were informed of the study and a signed consent was obtained. General information on age, sex, anthropometric measurements, ethnicity and history on the past and present diseases were recorded. Blood pressure and waist circumference of all participants were recorded while a 3 ml fasting blood sample was used to measure FBS and Lipid profile using ERBA Kits for a ERBA Manheim EM 200 full auto analyzer. The study subjects were screened for the presence or absence of Metabolic Syndrome by the Harmonized 2009 definition (Table 1).

## Results

Amongst the 361 participants, 121 (33.5%) were diagnosed Metabolic Syndrome (MetS) according to the Harmonized MetS criteria, which requires the presence of any three or

more of the following: larger waist circumference, elevated BP, raised TG, raised FBS and lowered HDL-C (Table 1). The remaining 240 (66.4%) under the non-MetS group consisted of participants with 0, 1 and 2 risk factors of MetS, however not enough (3 or more) to be considered as MetS. For the purpose of risk stratification, the non-MetS group was further sub divided into those with 0 risk factor as “0 Risk, any one risk factor as “1 Risk” and any two risk factors as “2 Risk”. Of the 240 Non-MetS participants, 103 (28.5%) were in the “0 Risk” group, 50 (13.8%) were in the “1 Risk” group and 87 (24.0%) in the “2 Risk” group.

Fifty percent (50%) of the participants under the “1 Risk” group had an increased waist circumference of  $\geq 90$  cm in males and  $\geq 80$  cm in females. Amongst, those in the “2 Risk” group there was a difference in the combination of the risk factors found. The most common 2 Risk amalgamation was the constant appearance of a large waist circumference with an elevated BP (33.3%). This was followed by a large WC and a lowered HDL-C (22.9%); and a raised TG (22.9%); and a raised FBS (10.3%) while the least common were a raised TG + lowered HDL, raised TG + raised FBS, raised TG + elevated BP, raised FBS + elevated BP contributing to only 10.3% altogether. Similarly, of the five risk determinants of Metabolic Syndrome an increased waist circumference and elevated blood pressure were once more present in the study participants of the “3 Risk” group or the “Metabolic Syndrome group”, 107 (87.7%) had an increased waist circumference and 110 (90.9%) had an elevated Blood pressure (Table 2).

Metabolic Syndrome was seen to be increasing with progressing age; highest (31, 47.6%) among those between 51 and 60 years of age but lower (15, 34.8%) among  $>60$  years of age. It was higher among females (78, 48.1%) than in males (43, 21.6%). Sikkim has a unique ethnic population in comparison to rest of India with different ethnic groups like the “Bhutia, Lepcha, Tamang, Sherpa”, “Nepalese”, and “Others” (those that do not belong to the above two ethnic groups). Of the 361 participants enrolled in the study 38% of Nepalese, 48.4% of “Bhutia, Lepcha, Tamang, Sherpa” and 19.0% of those that belong to the “Others” category were diagnosed with MetS with highest rates among the ethnic group of “Bhutia, Lepcha, Tamang, Sherpa” (Table 3).

The Metabolic Syndrome risk factors were further tested for significant differences between those with and without MetS. Continuous variables were normally distributed as inspected by frequency histograms. The waist circumference in males ( $96.9 \pm 7.2$  cm) with MetS were significantly higher than those without MetS ( $88.3 \pm 7.8$  cm) (at  $p = .001$ ). However, there was no significant difference in WC among females with ( $98.1 \pm 8.1$  cm) and without

**Table 2** Frequency percentages of metabolic syndrome and its risk factor types

Metabolic Syndrome by “Harmonized 2009 definition”						
Total participant n (%) = 361 (100)						
Metabolic Syndrome (3 or more Risk)		Non Metabolic Syndrome (2 Risk, 1 Risk, 0 Risk)				
121 (33.5)		240 (66.4)				
Risk type combination for						
Metabolic Syndrome n = 121		Non Metabolic Syndrome n = 240				
3 Risk or more		2 Risk 87 (36.2)		1 Risk 50 (20.8)		0 Risk 103 (42.9)
WC + BP + FBS + TG + HDL	07 (5.7)	WC + BP	29 (33.3)	WC	25 (50)	–
WC + BP + FBS	30 (24.7)	WC + TG	20 (22.9)	TG	13 (26)	–
WC + BP + FBS + HDL	07 (5.7)					
WC + BP + FBS + TG	07 (5.7)					
WC + BP + TG	22 (18.1)	WC + HDL	20 (22.9)	FBS	07 (14)	–
WC + BP + TG + HDL	07 (5.7)					
WC + FBS + TG	04 (3.3)	WC + FBS	09 (10.3)	BP	04 (8)	–
WC + FBS + TG + HDL	10 (8.2)					
WC + HDL + FBS	03 (2.4)	TG + HDL	02 (2.2)	HDL	01 (2)	–
WC + HDL + TG	10 (8.2)	TG + FBS	03 (3.4)	–	–	–
BP + HDL + WC	13 (10.7)	TG + BP	02 (2.2)	–	–	–
BP + HDL + FBS	13 (10.7)	FBS + BP	02 (2.2)	–	–	–
BP + HDL + TG	02 (1.6)	–	–	–	–	–
BP + FBS + TG	02 (1.6)	–	–	–	–	–

**Table 3** Frequency percentages (n %) of metabolic syndrome according to age, sex, and ethnic groups

	n (%)
Metabolic Syndrome according to harmonized Metabolic Syndrome definition	
Gender (n = 361)	
Male (n = 199)	43 (21.6)
Female (n = 162)	78 (48.1)
Ethnicity (n = 361)	
“Bhutia, Lepcha, Tamang and Sherpa” (n = 64)	31 (48.4)
“Nepalese” (n = 176)	67 (38.0)
“Others” (n = 121)	23 (19.0)
Age in years (n = 361)	
20–30 (n = 53)	08 (15.0)
31–40 (n = 106)	23 (21.6)
41–50 (n = 94)	44 (46.8)
51–60 (n = 65)	31 (47.6)
>60 (n = 43)	15 (34.8)

(96.5 ± 11.7 cm) MetS (at  $p = .427$ ). There was a statistically significant difference in levels (higher) of FBS ( $p = .001$ ), TG ( $p = .001$ ), BP both systolic ( $p = .001$ ) and diastolic ( $p = .001$ ) among those with MetS when compared with those without. HDL-C levels in males (42.5 ± 11.2 mg/dl) and females with MetS

(46.0 ± 14.2 mg/dl) was lower than males (48.6 ± 14.6 mg/dl) and females (52.9 ± 15.1 mg/dl) without MetS (males; at  $p < .005$ , females; at  $p < .015$ ) (Table 4).

Irrespective of the MetS status, of the total 361 study population, the percentages of the risk factor noted in

**Table 4** Comparison of risk factors of Metabolic Syndrome in participants with and without Metabolic Syndrome (equal variance *t* test)

	MetS mean $\pm$ SD	Non MetS mean $\pm$ SD	<i>p</i> $\leq$ .05
<i>Waist circumference (cm)</i>			
Male	96.9 $\pm$ 7.2	88.3 $\pm$ 7.8	.001*
Female	98.1 $\pm$ 8.1	96.5 $\pm$ 11.7	.427
FBS (mg/dl)	122.1 $\pm$ 56.9	97.5 $\pm$ 33.66	.001*
TG (mg/dl)	168.2 $\pm$ 94.9	143.7 $\pm$ 110.2	.001*
HDL-male (mg/dl)	42.5 $\pm$ 11.2	48.6 $\pm$ 14.6	.005*
HDL-female (mg/dl)	46.0 $\pm$ 14.2	52.9 $\pm$ 15.1	.015*
BP systolic (mmHg)	135.5 $\pm$ 19.2	125.3 $\pm$ 16.1	.001*
BP diastolic (mmHg)	90.7 $\pm$ 13.3	82.3 $\pm$ 10.0	.001*

\* Significant at *p* < 0.05**Table 5** Frequency percentage (n %) of metabolic syndrome risk determinants

n = 361	Frequency	Percentage (%)
Large Waist circumference (cm)	216	59.8
Elevated blood pressure (mmHg)	143	39.6
Those receiving treatment for Hypertension	119	32.9
Raised triglyceride (mg/dl)	128	35.4
Those receiving treatment for Dyslipidemia	16	4.4
Lowered HDL (mg/dl)	100	27.7
Raised fasting blood sugar (mg/dl)	93	25.7
Those receiving treatment for Diabetes	63	17.4

descending order of occurrence were; a large waist circumference (59.8%, *n* = 216), an elevated BP (39.6%, *n* = 143; 119 of them were known hypertensive), a raised TG (35.4%, *n* = 128), a low HDL (27.7%, *n* = 100) and a raised FBS (25.7%, *n* = 93; 63 were known diabetics) (Table 5).

## Discussions

Metabolic Syndrome (MetS) is on the rise globally [13]. Robert J. Wong and colleagues reported a rise in prevalence of MetS in the United States from 32.9% in 2003–2004 to 34.7% in 2011–2012 based on data from the National Health and Nutrition Examination Survey (NHANES). This was found to be significantly higher in women (35.6%) compared to men (30.3%) with modified NCEP Adult Treatment Panel III guidelines [14]. Data supporting the trend on the rise in the prevalence rate of Indian population remains bare and barren, except for numerous one-time reports on regional prevalence rates which seem alarming. High prevalence of excess body fat, adverse body fat patterning, hyper triglyceridemia and insulin resistance beginning at a young age have been consistently recorded in Indians irrespective of the definitions used and their geographic

locations [15]. Guidelines used in diagnosing MetS vary from study to study and the most frequently used ones are by IDF and NCEP-ATP-III [9, 16]. A recent study conducted (2014) in a rural area of Ambala district, Haryana reports a high MetS prevalence of 66.3% in females and 33.6% of males [17]. Another study from Mumbai, Maharashtra by Ashavaid and colleague reports a MetS prevalence of 19.5% but this time higher in males (25.1%) than in females (12.6%) [18]. Despite the high prevalence of Diabetes and Hypertension in Sikkim, Metabolic Syndrome in the state has earned very little recognition. The only study on MetS in Sikkim was conducted on a single ethnic group namely the Bhutias. Das et al. reported a very high prevalence amongst them, ranging from 30 to 50% using ATP III criteria for MetS [20]. Our study population is a representation of Sikkim's diverse and unique ethnic group and our findings show a 33.5% occurrence of MetS in the study population common amongst the ethnic category of "Bhutia, Lepcha, Tamang and Sherpa" (48.4%) followed by "Nepalese" (38.0%) and "Others" (19%).

Of the remaining 66.4% of the participants who were categorized non-MetS as per the Harmonized Metabolic Syndrome criteria, only 28.5% were free of all the five risks of MetS. Others had a "1 Risk" (13.8%) for example an isolated Hypertension or a "2 Risk" (24.0%), example a combination of large waist circumference and hyper triglyceridemia. It thereby, becomes important to distinguish these individuals in any MetS studies so as to help understand the influence of sociocultural, ethno-geographical factors in causing MetS and to further understand the pathophysiology. These participants with risk factors not amounting to MetS are also at risk for developing CVD or T2DM and require close monitoring, however not as much as people who fit the criteria for MetS [21]. Our findings show, an increased WC ( $\geq 90$  in males and  $\geq 80$  cm in females) as the most frequently occurring risk determinant (50.0%) under the "1 Risk" category. Furthermore, under the "2 Risk" category, a large waist circumference which is ethnic specific was the only component that presented constantly with elevated BP



(33.3%), lowered HDL (22.9%), raised TG (22.9%) and raised FBS (10.3%) with a very few combinations of raised :TG-FBS, raised TG-lowered HDL, raised: TG-BP and raised: FBS-BP (10.3%). Similar observation was also noted in the “3 Risk” or the “MetS” group wherein increased waist circumference and elevated blood pressure maximally contributed to form the MetS. All of this, adds up to how an increased waist circumference or an abdominal obesity could be the driving force for cardio metabolic risk [21]. Lee et al. also reports, accumulation of abdominal fat volume are associated with increased incidence and adverse changes in Cardio Vascular Disease risk factors [22, 23]. Excess subcutaneous and visceral fat deposition in the abdomen increases the risks associated with obesity. Visceral adipocytes are the most metabolically active and have high rates of lipolysis which contribute to increased availability of free fatty acids. The cytokines secreted by the adipose tissue, as well as the free fatty acid from abdominal fat enters the portal vein and therefore have direct access to the liver resulting in insulin resistance and increased synthesis of TG which is released as VLDL particles and contributes to hypertriglyceridemia [24].

There was a significant gender difference of MetS seen mostly in females. Influence of rising age on MetS up to the age of 60 years was also noted by our study in Sikkim with highest rates at 51–60 years of age (47.6%) however decline after 60 years. There was no difference in WC among the female participants because larger waist circumference was seen in both groups with MetS and non MetS. Larger WC was once again the most frequently occurring risk determinant when we tested out, which risk factor of the five was most commonly present amongst the entire study participants (n = 361) Waist circumference (59.8%) was followed by elevated blood pressure (39.6%), raised Triglyceride (35.4%), low HDL-C (27.7%) while FBS (25.7%) was the least frequently occurring risk factor in this study. Prevalence of these individual components of MetS differs from population to population suggestive of an effect of interaction between gene and environment. Roshni et al. [25] reports an increased abdominal girth (76.7%) as the most frequently occurring component of MetS in an Urban South Indian population followed by a low HDL (74.7%), elevated FBS (64.6%), raised BP (60.7%) and a raised TG (55.6%). Similarly, Sawant et al. [19] reports, a 39.9% of impaired blood glucose levels, 38.1% as with hyper triglyceridemia and 47.9% with low HDL-C in Urban Indians. Sikkim is leading in Diabetes and Hypertension prevalence in the country; of the 361 participants 17.4 and 32.9% were known Diabetic and Hypertensive respectively. Careful observation of the study findings, specifically the mode of combination of the five risk factors in those with 3 risks, 2 risks and 1 risk, brings us to the conclusion that, presence of either an increased waist circumference or an elevated blood pressure

in any individual mandates a check for the remaining risk factors of MetS.

## Conclusion

Metabolic Syndrome is indeed prevailing in the North-eastern State of Sikkim. Presence of either an increased waist circumference or an elevated blood pressure mandates a check for the remaining four risk factors for MetS, making it worthwhile to keep an account of MetS risk types by stratification to help understand the influence of socio-cultural and ethno-geographical factors in causing MetS.

## Limitations

There is a sample selection bias as the participants are patients coming for a general health check-up hence the overall percentage of MetS reported in the study may not be a representation of MetS for the general population of Sikkim. Nevertheless, the information contained will definitely set a base for future community based prevalence study which is yet to be undertaken in the state.

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## Compliance with Ethical Standards

**Conflict of interest** There is no conflict of interest.

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