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ASSESSMENT OF METABOLIC SYNDROME AND CLINICAL SIGNIFICANCE OF BRACHIAL-ANKLE PULSE WAVE VELOCITY IN TYPE 2 DIABETES MELLITUS PATIENTS

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Abstract

Background and Aims: *Metabolic syndrome (MS) is a constellation of various CVD risk factors comprised of abdominal obesity, glucose intolerance, hyperinsulinemia, hypertension and dyslipidemia. The present study was aimed to assess the prevalence of MS in type 2 diabetes mellitus (T2DM) patients, and to evaluate the clinical significance of brachial-ankle pulse wave velocity in these patients.* ***Methods:*** *The sample comprised of 251 T2DM patients. MS was evaluated in all the studied subjects according to NCEP-ATP III, IDF and JIS criteria. The subjects were screened for demographic as well as clinical characteristics.* ***Results:*** *Prevalence of MS was estimated to be 65%, 69% and 75% according NCEP-ATP-III, IDF and JIS criteria respectively. JIS criteria was only preceded for further analysis as it explained the highest prevalence and also showed the better level of agreement (0.862) with IDF criteria. Abdominal obesity was the most frequent component of MS in the studied subjects. Moreover, 20.21% of MS subjects were found to have very high risk of cardiovascular disease (CVD) / future mortality according to different combinations of brachial-ankle pulse wave velocity (baPWV) and ankle brachial index (ABI).* ***Conclusions:*** *The study revealed an increased prevalence of MS in the studied subjects. Risk of CVD may be better explained when these subjects were segregated according to different combinations of baPWV and ABI.*

key words: *Pulse wave velocity, Cardiovascular Disease, NCEP-ATP III, IDF, JIS.*

Background and aims

The prevalence and incidence of type 2 diabetes mellitus (T2DM) is increasing at a worrying rate and its inevitable outcomes including cardiovascular diseases (CVD), diabetic retinopathy, nephropathy, and neuropathy adversely affects life quality and longevity of these subjects [1-3]. According to recent reports, more than 65 million people are reported to be suffering from T2DM in India, and the number was expected to be 2-fold increase in the coming 20 years [4]. As CVD is one of the major reasons of impairment of life quality and mortality in patients with diabetes, early identification of individuals at high risk for

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CVD and subsequent rapid intervention is important. Therefore, cardiovascular risk assessment based on conventional risk factors, such as obesity, hypertension and dyslipidemia is recommended for these subjects. However, studies have shown that assessment of these factors in isolation has limited clinical significance [5,6].

Metabolic syndrome (MS) is a constellation of various CVD risk factors comprised of abdominal obesity, glucose intolerance, hyperinsulinemia, hypertension and dyslipidemia [7,8]. Each component of the cluster conveys increased risk of CVD, but as a combination they become much more powerful. Its value as a distinct diagnostic entity is still a matter of debate. Limited studies on MS prevalence were reported from India until now [9-11]. Various criteria for diagnosis for MS have been developed in past years. The first criterion for diagnosis of MS was developed in 1998 by World Health Organization (WHO) [12]. It includes diabetes, impaired glucose intolerance or insulin resistance condition as mandatory factor along with the presence of any two other risk factors out of abdominal obesity, hypertension and dyslipidemia (Supplementary table 1). The other criterion for identification and management of high blood cholesterol in adults was introduced by National Cholesterol Education Program Expert panel (NCEP-ATP III) in 2001. According to this criterion, MS is a condition that includes five major risk factors consisting of elevated blood pressure, increased waist circumference, elevated blood glucose, low HDL cholesterol and high triglycerides [13]. Presence of any three risk factors out of these five, indicates MS. International Diabetes Federation (IDF) developed new definition taking abdominal obesity criteria as mandatory for diagnosis of MS in 2005 [14]. Furthermore, NCEP-ATP III modified the criteria in the same year using revised abdominal obesity cut-offs and lower fasting blood glucose level value of ≥5.6mmol/L as recommended by the IDF for Asians living in United States [13]. The modified NCEP-ATP III retained the same MS diagnosis criteria i.e. presence of any 3 out of 5 risk factors. A Joint Interim statement (JIS) on diagnosis of MS was came into force in 2009 by the National Heart, Lung, and Blood Institute, Task Force on Epidemiology and Prevention, American Heart Association, World Heart Federation, International Association for the Study of Obesity and International Atherosclerosis Society [15]. According to JIS, presence of any three out of five above mentioned risk factors are required for MS diagnosis.

In developed and developing countries, prevention of CVD is an important issue. It is based upon the monitoring of classical risk factors such as Diabetes Mellitus (DM) and hypertension, but it can be difficult to predict future events by linking these factors, thus confirming arterial damage may become important. Many studies have indicated a critical role of arterial stiffness in the pathogenesis of atherosclerosis and CVD [16-18]. Advancing age, as well as various documented CVD risk factors are known to be involved in progression of arterial stiffness [19-21]. Increased arterial stiffness leads to systolic hypertension, left ventricular afterload, and ventricular hypertrophy, which ultimately decrease coronary perfusion [22]. Carotid-femoral pulse wave velocity (cfPWV) and Brachial-ankle pulse wave velocity (baPWV) measurements are commonly used to access arterial stiffness. cfPWV is used to evaluate the central aortic stiffness while baPWV reveals the stiffness in peripheral arteries of arms and legs as well as in both the aorta. Of these, baPWV is considered as more appropriate for common practice as it is automated, uses a separate cuff for all the limbs and easier to operate than cfPWV [23,24]. Furthermore, baPWV was shown to be correlated with cfPWV in several cross-sectional studies, thus could also be a good predictor of CVD [25,26]. Various studies reported baPWV as an independent predictor for the presence MI, CAD, T2DM and future CVD [27-31].

The objective of this study was to assess the prevalence of MS in North Indian T2DM patients using various well-established criteria and to determine the level of agreement among these criteria. The present study also prospectively evaluated the clinical significance of measurement of baPWV along with the conventional cardiovascular risk markers in T2DM patients. Furthermore, association of arterial stiffness with traditional CVD risk factors and 10-year CVD risk in the studied subjects was also evaluated.

Material and methods

The present study enrolled 251 T2DM patients (HbA1c ≥6.5) from Carewell Heart and Superspeciality Hospital, Amritsar, Punjab (PB), India. All the studied subjects belong to North India. The information regarding demographic variables and various disease affecting factors in relation to cardiovascular risk such as familial disease history, age, gender, alcohol consumption, smoking status, total physical activity and dietary pattern were recorded from all the subjects in a pre-designed proforma. Subjects having age 30-80 years and belonging to North Indian states were included in the study. Individuals belonging to east, west and south Indian states, patients having HbA1c less than 6.5, pregnant ladies, having other chronic diseases and age below 30 and above 80 years were excluded from the study. Informed consent was obtained from all the studied subjects and the study protocol was approved by Institutional ethics committee of Guru Nanak Dev University, Amritsar (PB), India, according to declaration of Helsinki.

The various anthropometric measurements consisting of Height, weight, Waist Circumference (WC), Hip Circumference (HC) were performed using standard techniques. Body mass index (BMI), waist hip ratio (WHR) and waist stature ratio (WSR) were calculated using standard formulas [32,33].

Arterial blood pressure (SBP and DBP) was measured using standard mercury sphygmomanometer (Pagoda, New Delhi) with appropriate cuff size and stethoscope. Mean arterial pressure (MAP) and pulse pressure (PP) were calculated using standard formulas [34]. Hypertension was accessed according to the criteria of JNC 7 [35].

Arterial stiffness was measured noninvasively by baPWV test. The measurement of baPWV was performed by using bidirectional automated Doppler ultrasound (VP-2000/1000-Colin Corporation, Hyayashi Komaki, Japan). Subjects were examined in supine position. Electrodes were positioned on both the cuffs and wrists and wrapped around both arms as well as both calves. The pulse volume waveforms in arm and calf were recorded using pressure sensors. Blood pressure in both arms and legs was measured and the mean of left and right values of baPWV was calculated. From this, the values of ankle brachial index (ABI) right and ABI left were also obtained. The stratification of risk of CVD and future mortality was also estimated by combination of baPWV and ABI values [36] (Supplementary table 2).

After completion of various non-invasive measurements, blood sample from all the selected patients was collected in plain vials. For serum separation, blood sample was incubated at 37^{o}C for 30 min and centrifuged at 400×g for 15 min. Isolated serum samples were stored at -

80°C till further use. Serum total cholesterol (TC), triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C) levels were quantified using standard kits (Erba diagnostic Mannheim GmbH, Germany). Low density lipoprotein (LDL) and very low-density lipoproteins (VLDL) were calculated from the above said measurements using standard formulas [37]. HbA1c levels were measured by automated HbA1c levels check instrument (Afinion-AS100, Alera Technologies AS, Norway). Serum high sensitivity C-reactive protein (hs-CRP) levels were determined by sandwich ELISA using commercially available kits (RayBiotech, USA).

All the subjects were accessed for metabolic syndrome (MS) according to NCEP-ATP III (2001), IDF (2005) and JIS (2009) criteria. As modified NCEP-ATP III criteria (2005) has cut-off values almost similar to JIS, thus was excluded from the present analyses.

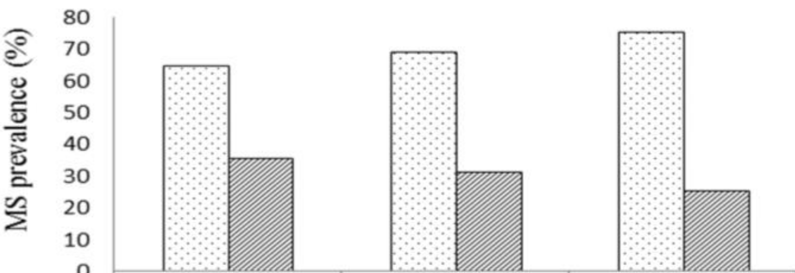
Framingham risk scoring method was used to estimate 10-year risk percentage in the subjects [38]. The main risk factors involved in the Framingham assessment of CVD risk include age, TC, Smoking status, HDL-C, SBP and hypertension treatment. The stepwise procedure was applied for final score calculation. The steps include age-group wise scoring of subjects, TC level scoring according to age groups, Smoking status scoring in different age groups, HDL-C levels scoring and SBP values scoring according to treated/untreated status. After the scores were assigned to each subject, 10-year CVD risk percentage was calculated for each subject.

All the statistical analyses were carried out by Statistical Package for Social science (SPSS) version 16.0. The Continuous variables were presented as mean ± standard deviation (SD) and analyzed by Student's t-test. The level of agreement, sensitivity and specificity using Kappa index were determined by Medcalc software (https://www.medcalc.org/index.php). The logistic regression was done to detect the independent risk factors taking MS as dependent variable. Correlation between baPWV and CVD risk factors was accessed using Pearson correlation analysis. *P* values <0.05 were considered significant.

Results

Out of 251 patients recruited in the present study, 162 were males and 99 were females. The age of the studied subjects ranged from 30 to 80 years. The overall mean age of subjects was found to be 54.23±9.23 years, with 53.73±10.02 in males and 55.02±7.86 years in female subjects.

Prevalence of MS was estimated to be 64.54% (n=162), 68.92% (n=173) and 74.9% (n=187) according to NCEP-ATP III, IDF, JIS criteria respectively (Figure 1).



	NCEP-ATPIII (2001)	IDF (2005)	JIS (2009)
MS	64.54	68.92	74.9
NMS	35.45	31.07	25.1

Figure 1. *Prevalence of MS according to different criteria.*

NCEP-ATP III criteria identified 88.64% of subjects having MS out of total subjects diagnosed for MS by IDF (Table 1).

Table 1. Level of agreement between various MS assessment criteria.

MS definitions	IDF					
	Yes MS	No MS	Sensitivity	Specificity	Kappa Index	*P* value
NCEP-ATP III						
Yes MS	156(88.64%)	8(10.67%)	88.64%	89.33%	0.745	<0.0001***
No MS	20(11.36%)	67(89.33%)				
JIS						
Yes MS	174(100%)	14(18.18%)	100%	81.82%	0.862	<0.0001***
No MS	0 (0.0%)	63(81.82%)				

*** represents *P* value significant at 0.001 level

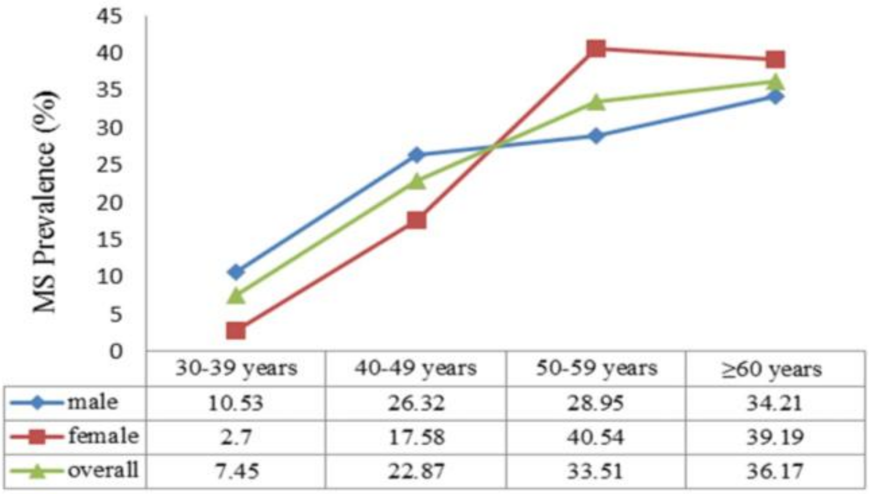


Figure 2. *Gender and age-specific prevalence of MS in T2DM patients.*

Table 2. Association of age and gender with MS.

Factor	OR (95%CI)	*P value*
Age (years)		
30-39	1	1
40-49	3.07 (1.62 to 5.80)	0.0005***
50-49	4.43 (2.40 to 8.18)	< 0.0001***
≥60	4.78 (2.60 to 8.81)	< 0.0001***
Gender		
Male	1	1
Female	0.6491(0.45 to 0.93)	0.0172*

*represents *P* value significant at 0.05 level; *** represents *P* value significant at 0.001 level; OR stands for odds ratio; CI stands for confidence interval

The false negative rate of diagnosis of MS by NCEP-ATP III criteria observed was 11.36%. On the other hand, JIS criteria identified 100% of the subjects that were diagnosed for MS by IDF and the false negative rate was nil. A better level of agreement was observed between IDF and JIS with Kappa index value of 0.862 in contrast to 0.745 for NCEP-ATPIII. As JIS criteria explained the highest prevalence than other criteria and also showed the better level of agreement with IDF criteria, thus only preceded for further analyses.

In overall subjects, the gender- and age-specific prevalence of MS was found to be highest in the age group ≥60 years and lowest in 30-39 years age group (Figure 2).

Male subjects followed the same pattern as in overall subjects while prevalence of MS in female subjects was found to be marginally higher in age group of 50-59 years, along with ≥60 years. This was also higher than the prevalence in overall subjects as well as males of the same age group. Furthermore, the risk of developing MS was found to increase with age being highest in ≥60 years odds ratio (OR) i.e. 4.78 (2.60 to 8.81) (Table 2).

Various demographic, physiometric and serum profile variables were also compared between MS and Non-MS subjects. Overall as well as abdominal obesity, as indicated by BMI, WC, WHR, WSR, was significantly higher (*P* <0.001; *P* =0.026) in MS subjects as compared with Non-MS subjects (Table 3).

Table 3. Demographic and clinical characteristics of subjects with and without metabolic syndrome.

Parameter		Total (251)			Male (152)			Female (99)			*P* value male vs Female
		Number	mean± SD	*P* value	Number	mean± SD	*P* value	Number	mean± SD	*P* value	
Age(years)	Overall	251	54.23±9.23		152	53.73±10.02		99	55.02±7.86		0.256
BMI	MS	188	28.18±4.31	0.000***	114	28.04±4.18	0.000***	74	28.40±4.52	0.345	0.577
	NMS	63	25.93±4.49		38	24.99±3.59		25	27.36±5.35		0.039*
WC(cm)	MS	188	105.22±11.72	0.000***	114	106.53±11.36	0.000***	74	103.20±12.05	0.137	0.057
	NMS	63	97.57±13.60		38	96.84±12.24		25	98.68±15.64		0.604
WHR	MS	188	1.00±0.07	0.026*	114	1.02±0.064	0.014*	74	0.98±0.08	0.414	0.002**
	NMS	63	0.98±0.08		38	0.99±0.07		25	0.96±0.10		0.288
WSR	MS	188	0.63±0.07	0.000***	114	0.62±0.06	0.000***	74	0.64±0.08	0.110	0.025*
	NMS	63	0.58±0.08		38	0.56±0.07		25	0.61±0.10		0.040*
SBP (mm Hg)	MS	188	161.55±23.11	0.942	114	162.65±23.13	0.216	74	159.86±23.15	0.322	0.421
	NMS	63	161.24±31.42		38	157.00±27.38		25	167.68±36.38		0.189
DBP (mm Hg)	MS	188	93.05±12.92	0.039*	114	94.76±13.49	0.018*	74	90.41±11.66	0.813	0.024*
	NMS	63	89.00±14.88		38	88.60±14.49		25	89.60±15.73		0.798
MAP (mm Hg)	MS	188	115.89±15.67	0.305	114	117.39±16.05	0.055	74	113.57±14.89	0.665	0.102
	NMS	63	113.08±19.58		38	111.40±18.01		25	115.63±21.90		0.407
PP (mm Hg)	MS	188	68.49±14.00	0.204	114	67.88±13.64	0.793	74	69.43±14.59	0.098	0.461
	NMS	63	71.44±20.62		38	67.07±17.14		25	78.08±23.87		0.037*
TG(mg/dl)	MS	188	248.95±112.25	0.000***	114	250.19±112.51	0.000***	74	247.04±112.59	0.000***	0.851
	NMS	63	109.96±32.20		38	109.45±35.21		25	110.74±27.67		0.877
HDL(mg/dl)	MS	188	37.11±11.83	0.000***	114	35.76±11.18	0.000***	74	39.19±12.58	0.000***	0.052
	NMS	63	56.32±16.39		38	54.06±16.65		25	59.74±15.68		0.181
CHL(mg/dl)	MS	188	200.87±65.61	0.182	114	193.46±63.13	0.312	74	212.29±68.11	0.374	0.054
	NMS	63	188.28±61.73		38	181.40±64.21		25	198.73±57.43		0.279
LDL(mg/dl)	MS	188	113.39±78.56	0.174	114	106.38±74.26	0.410	74	124.19±84.14	0.265	0.129
	NMS	63	98.69±58.59		38	95.60±53.58		25	103.40±66.35		0.609
VLDL(mg/dl)	MS	188	49.79±22.45	0.000***	114	50.03±22.50	0.000***	74	49.40±22.51	0.000***	0.851
	NMS	63	21.99±6.44		38	21.89±7.04		25	22.14±5.53		0.877
HbA1c (%)	MS	188	9.45±2.11	0.403	114	9.47±2.28	0.411	74	9.40±1.86	0.759	0.886
	NMS	63	9.18±2.17		38	9.14 ±2.13		25	9.24 ±2.25		0.754
hs-CRP(mg/dl)	MS	184	13.84±12.74	0.000***	113	10.42±7.55	0.014*	71	19.28±16.87	0.000***	0.000***
	NMS	59	7.75±5.62		35	7.04±5.00		24	8.79±6.37		0.243
Framingham Point Score	MS	188	13.93±5.76	0.025*	114	12.07±5.80	0.180	74	16.79±4.38	0.018	0.000***
	NMS	63	12.11±4.76		38	10.71±3.89		25	14.24± 5.23		0.003**
baPWV (m/s)	MS	188	19.31±3.63	0.706	114	18.76±3.66	0.554	74	20.17±3.44	0.331	0.003**
	NMS	63	19.56±4.70		38	18.36±3.37		25	21.38±5.81		0.024*

*represents *P* value significant at 0.05 level; ** represents *P* value significant at 0.01 level *** represents *P* value significant at 0.001 level; MS-metabolic syndrome; NMS- Non metabolic syndrome

Overall as well as abdominal obesity was also significantly high (*P* <0.001) in males with MS compared to males without MS. However, no significant difference was observed between females with and without MS. Furthermore, no significant difference was observed for physiometric variables in any of the studied groups except DBP which was found to be significantly high in all MS subjects as compared to Non-MS subjects. Same trend was found between MS and Non-MS males while no significant difference was observed between females.

The MS subjects were also found to have significantly elevated levels of triglycerides, VLDL and reduced levels of HDL-C (*P* <0.001

each) as compared to Non-MS subjects in each category (Table 3). Furthermore, hs-CRP levels were found to be significantly high in each MS group as compared to respective Non-MS group (*P* <0.001). When compared according to gender, the female MS subjects were found to have significantly high hs-CRP levels (*P* <0.001) as compared to MS males. The MS subjects were found to have significantly high Framingham risk score than Non-MS subjects (*P=0.025*). When compared according to gender, female subjects with as well as without MS were found to have significantly higher CVD risk (*P<0.001* and *P* =0.003 respectively) than male subjects in the respective groups.

The logistic regression was performed using various demographic and clinical characteristics as independent and MS as dependent variable (Table 4). The regression analysis revealed that WC (OR =3.16, CI =1.24–8.05, *P* =0.016) and WSR (OR =0.107, CI =0.035–0.330, *P* =0.000) are the major predictors of MS in the studied subjects. The various established biochemical parameter (TC, TG, HDL-C, LDL, VLDL) were not found to have any significant contribution towards CVD risk in the studied subjects.

Table 4. Logistic Regression analysis of having MS among the studied subjects

Parameters	B	S.E.	Wald	Df	*P* value	OR	95% CI for EXP(B)	
							Lower	Upper
Age	-0.194	0.354	0.299	1	0.584	0.824	0.411	1.650
Gender	0.325	0.529	0.378	1	0.539	1.384	0.491	3.900
PWVr	-0.371	0.471	0.619	1	0.432	0.690	0.274	1.738
PWVl	0.253	0.486	0.270	1	0.604	1.287	0.496	3.339
WC	1.152	0.476	5.857	1	0.016*	3.165	1.245	8.047
Height	-0.189	0.521	0.131	1	0.717	0.828	0.298	2.301
Weight	-0.205	0.468	0.193	1	0.661	0.814	0.325	2.038
BMI	0.833	0.500	2.773	1	0.096	2.299	0.863	6.126
WHR	0.792	0.407	3.780	1	0.052	2.208	0.994	4.907
WSR	-2.233	0.574	15.121	1	0.000***	0.107	0.035	.330
SBP	0.378	0.527	0.513	1	0.474	1.459	0.519	4.100
DBP	-0.407	0.419	0.943	1	0.331	0.666	0.293	1.513
MAP	0.230	0.454	0.256	1	0.613	1.258	0.517	3.061
PP	-0.629	0.456	1.900	1	0.168	0.533	0.218	1.304
TG	-0.564	0.457	1.526	1	0.217	0.569	0.232	1.392
HDL-C	-0.161	0.349	0.213	1	0.645	0.851	0.430	1.686
TC	0.802	0.487	2.710	1	0.100	2.230	0.858	5.792
LDL	-0.662	0.469	1.994	1	0.158	0.516	0.206	1.293
VLDL	-0.340	0.439	0.600	1	0.439	0.712	0.301	1.683
hs-CRP	-0.365	0.337	1.178	1	0.278	0.694	0.359	1.342
HbA1c	-.074	0.294	0.063	1	0.801	0.929	0.522	1.651
Constant	-0.418	0.709	0.347	1	0.556	0.659		

*represents *P* value significant at 0.05 level; *** represents *P* value significant at 0.001 level; OR stands for odds ratio; CI stands for confidence interval

MS subjects were also assessed for the risk of future mortality and CVD. Out of total, 20.21% (n =38) of subjects were found to have very high risk, 47.87% (n =90) subjects have high risk, 31.38% (n =59) subjects have moderate risk and only 1 subject was found with lower risk (Figure 3). Similarly, 25.4% (n =16) of Non-MS subjects were detected with very high risk of CVD, while 31.75% (n =20) and 42.86% (n =27) of Non-MS subjects were found to have high and moderate risk respectively. None of the Non-MS subjects were found in lower risk category.

No significant difference was observed in mean baPWV between MS and Non-MS subjects (Table 3). The same pattern was found in MS male/Non-MS males as well as MS females/NMS females. However, mean baPWV of MS females was found to be significantly high (*P =0.003*) as compared to MS males. Furthermore, when subjects were segregated according to age, the mean baPWV was found to be significantly different between males and females with age below 60 years (Table 5).

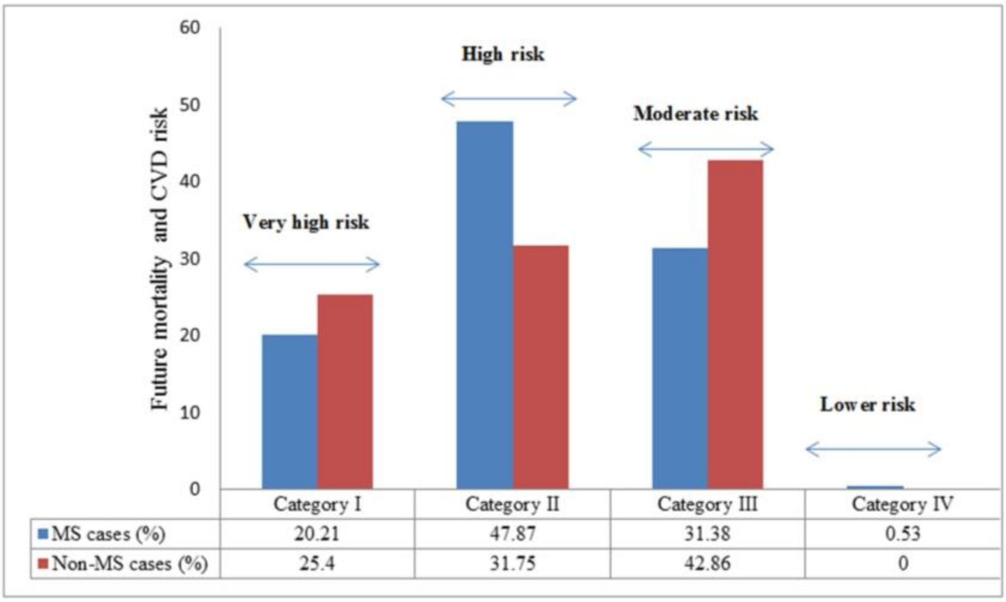


Figure 3. *Mortality and CVD risk stratification in studied subjects according to combination of baPWV and ABI values.*

Table 5. Comparison of baPWV according to age in overall subjects (n=251).

Age Groups	Overall subjects	*P* value	Males	*P* value male	Females	*P* value female	*P* value male & female
Group I (<60 years)	18.73±3.55	0.001**	17.98±2.98	0.003**	19.98±4.06	0.121	0.001**
Group II (≥60years)	20.58±4.30		20.03±4.28		21.32±4.27		0.169

** represents *P* value significant at 0.01 level

Table 6. Pearson Correlation Coefficient between mean baPWV and cardiovascular risk factors.

Factor	**R**	***P* value**
BMI	-0.016	0.805
WC(cm)	0.009	0.881
WSR	-0.019	0.765
WHR	0.112	0.078
SBP	0.452	0.000***
DBP	0.314	0.000***
MAP	0.400	0.000***
PP	0.439	0.000***
TC	0.025	0.691
TG	-0.047	0.455
HDL	0.089	0.159
LDL	0.013	0.841
VLDL	-0.047	0.455
hs-CRP	-0.083	0.195
HbA1c	-0.095	0.135

*** represents *P* value significant at 0.001 level

However, no significant difference in baPWV was observed in subjects with age ≥ 60 years. In addition, when overall subjects of both the age groups were compared for arterial stiffness, subjects with age ≥60 years were found to have higher mean baPWV. Furthermore, physiometric parameters i.e. SBP, DBP, MAP and PP were found to be positively associated with baPWV (*P* <0.001 each) (Table 6). However, no significant correlation was observed with any of the other studied variables (*P* >0.05).

Discussions

Asian Indians are at alarming stage of diabetes as well as CVD risk, and number of those having these risks is growing consistently. This is a first report on assessment of MS and clinical significance of baPWV along with conventional cardiovascular risk markers in North Indian Diabetic patients.

In this study, JIS criteria gave the highest prevalence of MS in studied subjects. This criterion gave advantage over the other criteria to identify larger group of population with MS, due to presence of any three risk factors with modified cut-off values. This study clearly demonstrates that irrespective of the type of the definition used, a high prevalence of MS was observed in the studied subjects. Furthermore, females were found to have higher prevalence than males according to both NCEP-ATP III as well as IDF criteria. On the other hand, the prevalence of MS was found to be almost same in case of males (75%) and female (74.74%) according to JIS. The reason behind this may be that JIS criterion diagnosed higher number of males, even with WC value <90 cm (not in MS category according to IDF criteria). This finding is in consonance with a previous study, involving 1349 European subjects, in which men has shown to have higher prevalence of MS women by JIS criteria [39]. Another prospective study on mortality in men reported that CVD mortality was found to be high in men because of presence of several risk factors, even in the absence of abdominal obesity [40]. Various reports suggested higher risk of CVD may better be identified by JIS as compared to NCEP ATP-III and IDF [39,41].

To evaluate the level of agreement between these three criteria, the most widely accepted criteria IDF was used as a reference. JIS and IDF showed the higher level of agreement with the Kappa index value of 0.862. This finding can be attributed to the similar cut-off values for WC, TG and HDL used in both diagnosis criteria. On the other hand, NCEP-ATP III and IDF definitions shared a lower level of agreement with the Kappa index value of 0.745. It was expected in the view that both the criteria involve different reference cut off values. A similar trend of agreement among these criteria was also observed in a previous study [41].

Various studies have suggested association of MS with T2DM as well as arterial stiffness separately. A recent study has indicated high prevalence of MS and positive association with its different components with high risk of CVD in North Indian diabetic patients [11]. In another report, MS was found to increase the relative CVD risk in males and for T2DM in both genders of middle age [42]. Furthermore, in several studies MS was also found to be associated with arterial stiffness in healthy individuals of different age groups. Kim and associates (2010) have reported that arterial stiffness was associated with age and metabolic syndrome in Korean adults [27]. In another report, baPWV was found to be strongly associated with MS in middle aged Taiwan Chinese [43]. In previous report, components of MS were found to be allied with arterial stiffness in younger population [44]. These findings suggested that elasticity of arteries can be better retained in persons without MS. Furthermore, advancing age was suggested as a detrimental factor for affecting elasticity of arteries [45]. In the present analyses, subjects with age ≥60 years were found to have higher baPWV values, showing that age is positively correlated with arterial stiffness. Furthermore, significant difference in mean baPWV value was found between males and females of age less than 60 years. On the other hand, no difference was observed in older subjects (≥60 years). This finding is in consonance with a previous study indicating that gender difference in baPWV disappears with increasing age [45]. The increase in arterial stiffness linked with age may be attributed to change in estrogen levels after attaining menopausal state. In concordance with other studies, present study also showed increased incidence of MS with advancing age, which can be attributed to increased hypertension, obesity and dyslipidemia with age [11, 39,41,42].

The various metabolic syndrome components are well known to be associated with CVD mortality and morbidity [8]. This was assessed by regression analysis and among various risk factors of MS, abdominal obesity was found to be the most significant contributor for MS. On the other hand, the established risk factors like hypertension and dyslipidemia were not contributing towards the risk of CVD. Although, hypertension and dyslipidemia were found to be high in subjects with MS as compared subjects without MS, but not found to be contributing towards MS risk. The reason behind this may be the use of anti-hypertensive and lipid lowering drugs by most of the patients of the present study. There was a previous report on the reduction of CVD risk in T2DM patients using statin therapy [46]. Furthermore, when classic CVD risk factors were compared with baPWV values, only physiometric variables were found to be positively correlated with arterial stiffness. Lipid lowering drugs might contribute to non-significant contribution of dyslipidemia in the development of arterial stiffness.

In addition to this, when 10-year risk of CVD was estimated using Framingham risk scoring method and MS subjects were found to have higher risk than Non-MS subjects. Furthermore, females were found to be at higher risk of CVD than males. Moreover, a meta – analysis showed that females with diabetes have higher risk of CVD mortality than male diabetic patients [47]. The probable explanation for such gender related difference in CVD risk could be due to distinct biological as well as gender-related acculturation, difference in physical activity and dietary patterns among males and females. Furthermore, subjects were also segregated based on various combinations of baPWV and ABI values to determine the risk of future mortality and CVEs. It was observed that more NMS patients belong to very high-risk category than patients with MS. This may be attributed to comparatively high mean SBP value in NMS patients as compared to patients with MS.

Various reports suggested C-Reactive Protein (CRP) as an important predictor of vascular inflammation [48]. CRP produced by arterial wall or in liver that is induced by IL-6 that produced by atheroma [49]. These inflammatory cytokines are the essential components to facilitate the development of atherosclerosis plaques. In this study, no significant association of hsCRP level was found with metabolic syndrome as well as with baPWV. This finding is in consonance with a previous study [50]. However, limited studies have shown significant association of hsCRP levels with arterial stiffness [45,51]. Thus, the exact mechanism and relationship of hsCRP levels with arterial stiffness has not been fully explained and remain unclear. These evidences may support the prospective that both the factors are independent predictors of CVD.

Furthermore, smoking is an important CVD risk marker, reported to be significantly associated with MS [52]. Furthermore, it has been reported to be associated with increased arterial stiffness [53]. But in the present study, we were unable to collect information regarding the amount smoked and time period for past smokers. Hence, we were unable to find any correlation between smoking and metabolic syndrome.

The strengths of the present study include presence of wide age range of T2DM patients from different areas of North India. The prevalence of the MS was estimated by extensively used and most recent definitions. As arterial stiffness and T2DM are suggested as a predictive factor for cardiovascular risks, thus early detection and control of arterial stiffness is essential to reduce the future mortality and CVD risk.

Conclusions

This study indicated an increased prevalence of MS in the studied subjects. The JIS definition was more efficient to detect the larger group of population with MS, thus considered to be ideal diagnostic criteria. The abdominal obesity may be an independent predictor for occurrence of MS. Subjects having MS were found to have higher 10-year CVD risk than Non-MS subjects. Furthermore, baPWV is significantly correlated with age and physiometric variables. Risk of CVD may be better explained when these subjects were segregated according to different combinations of baPWV and ABI. Thus, screening of arterial stiffness, along with conventional CVD risk factors, may be helpful in more effective identification of individuals at high risk of CVD and future mortality.

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