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Prevalence of Metabolic Syndrome in Rural Premenopausal and Postmenopausal females of Amritsar (Punjab) using threeInternational definitions: ATP-III, IDF and mATP-III

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Abstract

Background: Metabolic Syndrome (MS) is one of the major cause of morbidity and mortality across the globe. Therefore, this study was aimed to assess the prevalence of MS and its components using three international diagnostic criteria in the pre- and postmenopausal rural females of Amritsar (Punjab). *Methods:* This cross-sectional study was conducted among 300 rural females (186 premenopausal and 114 postmenopausal) of Amritsar (Punjab) during the period from June 2013 to June 2014. The age range of females was 25-55 years. WC and blood pressure of each participant was also measured. Fasting blood samples were analysed to estimate TC, TGL, HDL-C and FBG. LDL-C and VLDL-C were also calculated. The prevalence of MS was assessed using three international criteria ATP-III, IDF and mATP-III, respectively. For data analysis mean and standard deviation were calculated. Further Student's t-test, chi-square test and kappa statistic were also applied. *Results:* The postmenopausal women had significantly higher values of WC, SBP and DBP. In context to lipid profile variables, the values were again significantly higher among postmenopausal females except LDL-C. The prevalence of MS was 21.66 %, 24.33% and 25.66 % using ATP-III, IDF and mATP-III criterion, respectively. The postmenopausal females were observed to have significantly higher prevalence of MS. The degree of agreement (kappa statistic) was more (0.87) between mATP-III and IDF criteria as compared to between ATP-III and IDF (0.85) and between mATP-III and ATP-III (0.76) which shows that mATP-III has more concordance with IDF and less with ATP-III . Among 300 rural females, 18.3% (55) females were screened positive for MS by all the three criteria. The most prevalent component of MS was reduced levels of HDL-C whereas the least common was elevated levels of FBG. *Conclusion:* MS is quite prevalent in rural women of Amritsar using all the three criteria.

Introduction

The Metabolic Syndrome (MS) is a major, widely prevalent and escalating public health challenge in both developed and developing countries *(Ford, 2004; Kraja et al, 2005; Allal-Elasmi et al, 2010; Sidorenkov et al, 2010; Mozumdar & Liguori, 2011; Okafor, 2012; Shen et al, 2012; Kaur, 2014).* The term MS is a web of interconnected physiological, biochemical, clinical and metabolic risk factors like abdominal obesity, insulin resistance, elevated levels of triglycerides (TGL), reduced levels of High Density Lipoproteins-Cholesterol (HDL-C) and hypertension. *Stern et al. (2004); Enas et al.(2010), Sidorenkov et al. (2010)* reported that individuals with MS have two-fold risk of developing Cardiovascular Diseases (CVDs), three-fold risk of heart attack and five-fold risk of developing Type-2 Diabetes Mellitus (T2DM).

MS was first observed and described by the anatomist Morgagniin 1765 *(Enzi et al, 2003).* He manifested the link of abdominal obesity to the metabolic factors like hypertension, atherosclerosis, dyslipidemia, sleep apnea-hyponea and hyperuricemia. Later in 1920, *Kylin (1923),* a Swedish physician described the clustering of hypertension, hyperglycemia and gout. Some decades later, *Vague (1947)* found that abdominal obesity was a determinant factor in predisposing individuals to diabetes, atherosclerosis, gout and uric calculi. Following this, in 1965, an abstract was presented at the European Association for the Study of Diabetes *(Avogaro & Crepaldi, 1965)* which again described this syndrome comprising of hypertension, hyperglycemia and obesity. In 1988, *Reaven (1988)* reintroduced the concept of syndrome 'X' for the clustering of cardiovascular risk factors like hypertension, glucose intolerance, and high TGL and LDL-C concentration. His main contribution was an introduction of the concept of the insulin resistance. Unfortunately, he missed abdominal obesity from the definition which was added later as a crucial abnormality. Later on, *Kaplan (1989)* introduced the term "The Deadly Quartet" to describe the joint presence of upper body obesity, hypertriglyceridemia, glucose intolerance and hypertension. Over the years, the syndrome has been given several names including Insulin Resistance Syndrome X, Reaven Syndrome X, Metabolic Cardiovascular Syndrome and Dysmetabolic Syndrome.

Different diagnostic criteria have been proposed by various agencies for the assessment of MS during the past three decades. For the first time, in the year 1998, World Health Organisation *(Alberti & Zimmet, 1998)* provided a criterion for the assessment of MS. Then European Group for the Study of Insulin Resistance (EGIR) *(Balkau and Charles, 1999)* countered with a modification of the WHO criterion in 1999. In 2001, the National

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Cholesterol Education Program Adult Treatment Panel-III (NCEP-ATP III) introduced an alternative clinical criterion for defining the MS with the aim to identify people at long term risk for ischemic heart disease. The ATP-III criterion did not mandate the requirement of any single risk factor for diagnosis. With the formulation of these guidelines, some uniformity and standardization has occurred in the definition and criterion of MS which has been very useful for epidemiological purposes. Then, later on, International Diabetes Federation *(IDF, 2005),* proposed a new criterion in April, 2005 suggesting that abdominal obesity assessed with the help of waist circumference (WC) is mandatory for the diagnosis of MS. Once this essential condition was present, at least two additional risk factors out of four were necessary for the diagnosis. Later on, in the year 2005, NCEP ATP-III *(Grundy et al, 2005)* proposed a modified criterion for the assessment of MS with modification in the cut-off values of WC.

Table: Diagnostic criteria for the assessment of Metabolic Syndrome among females

Variables	NCEP ATP-III (2001)	IDF (2005)	mNCEP ATP-III (2005)
WC (cm)	≥ 88	≥ 80	≥ 80
BP (mm Hg)	≥ 130/85	≥ 130/85	≥ 130/85
TGL (mg/dl)	≥ 150	≥ 150	≥ 150
HDL-C (mg/dl)	<50	<50	<50
FBG (mg/dl)	≥ 110	≥ 100	≥ 110

Many studies from developed countries *(Kawamoto et al, 2011; Arthur et al, 2012; Marjani et al, 2012; Liu et al, 2013; Shahbazian et al, 2013; Ali et al, 2014; Xu et al, 2014)* have reported that MS and CVDs are more common in postmenopausal women when compared with premenopausal women, which may be related to hormonal changes during menopausal transition. There is a paucity of studies on MS and menopausal status in the developing countries especially in India using different definitions. Therefore, in the present study, an attempt has been made to assess the prevalence of MS among the rural premenopausal and postmenopausal women of Amritsar (Punjab).

Materials &Methods

The data for the present cross-sectional study was collected from various rural areas of Amritsar during the period from June 2013 to June 2014. The study group included 300 rural females, of which 186 were premenopausal women (those who were regularly menstruating and non-pregnant) and 114 postmenopausal women (those who had reached natural menopause and had their last menstrual bleeding at least 12 months previously) ranging in age between 25 to 55 years. Those women who experienced cessation of menstruation due to hysterectomy or any other surgical cause were excluded from the study. Ethical clearance from the Institutional Ethical Review Committee of Guru Nanak Dev

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University was obtained prior to carrying out the study. After fully explaining the nature, procedures, aims and objectives of the study to all the females in a language they understood, verbal as well as written informed consent was obtained. The participation of women was voluntary. First of all, the women were taken into confidence. All the females were interviewed in person at their homes to collect information regarding age, menopausal status, reproductive history as well as family history using a well designed and structured proforma. The WC is the best tool for the assessment of abdominal obesity, it was measured with the help of a non-stretch fibre glass measuring tape at a point midway between the inferior margin of the ribs and the superior border of the iliac crest on each subject single handedly by the investigator herself *(Weiner and Lourie, 1981)*. Blood pressure of each participant was measured using auscultatory method with the mercury sphygmomanometer and a stethoscope after rest of 15 minutes as per recommendation of the American Heart Association *(Ataman et al, 2005)*. Three readings each of Systolic Blood pressure (SBP) and Diastolic Blood Pressure (DBP) were recorded at an interval of 5 minutes at least and the mean values were used in the data for analysis. A certified technician assisted in the withdrawl of 2 ml venous blood from all the subjects in the morning after a twelve hour overnight fast. The blood samples were centrifuged for 10 minutes at 3000 rpm. Lipid levels were determined using commercially available Erba kits and levels of Total Serum Cholesterol (TC), Triglycerides (TGL), High Density Lipoproteins-Cholesterol (HDL-C) and Fasting Blood Glucose (FBG) were estimated from the absorbance values obtained on semi-automated biochemical analyser. Very Low Density Lipoproteins-Cholesterol (VLDL-C) was calculated by indirect method as VLDL-C is one fifth of TGL. Low Density Lipoproteins-Cholesterol (LDL-C) was calculated by subtracting VLDL-C and HDL-C from TC. Following three diagnostic criteria were utilized for the assessment of MS.

Data was analysed using the Statistical Package for Social Sciences (SPSS inc, Chicago, IL, USA; version 15). The mean and standard deviation were calculated for continuous variables and percentage for categorical variables. The baseline characteristics were compared between premenopausal and postmenopausal women by Student's t-test. The chi- square (χ^2) test was applied to compare differences between proportions. All analyses were two-tailed and a p-value <0.05 was considered statistically significant. The prevalence of MS was assessed among premenopausal and postmenopausal females. For estimation of agreement between different definitions kappa statistic was also used.

Results

The baseline characteristics of the studied females stratified with respect to the menopausal status are presented in Table 1. Out of the 300 rural females, 186 were premenopausal and 114 were postmenopausal. The mean age of postmenopausal (52.66±7.45 years) women was significantly higher ($p<0.01$) than the mean age of premenopausal (32.68±5.86 years) women. In the pooled sample, the mean values of WC, SBP and DBP were significantly ($p<0.05$) higher among postmenopausal women than premenopausal women. Similarly, the postmenopausal women had significantly ($p<0.05$) higher values of all the biochemical parameters as compared to their premenopausal counterparts except LDL-C.

Table 1. Baseline Characteristics of Premenopausal and Postmenopausal Women

VARIABLES	Premenopausal Women (N=186)		Postmenopausal Women (N=114)		Total Number Of Women (N=300)		't' value
	MEAN	SD	MEAN	SD	MEAN	SD	
Age (years)	32.68	5.86	55.66	7.45	41.41	12.92	28.038***
WC (cm)	78.64	10.78	81.68	12.02	79.80	11.34	3.667***
SBP (mm Hg)	122.28	13.94	140.64	20.51	129.26	18.94	8.436***
DBP (mm Hg)	81.15	11.05	87.68	12.36	83.63	11.98	4.626***
TC (mg/dl)	143.37	42.69	158.08	60.00	148.96	50.39	2.287*
TGL (mg/dl)	103.49	45.84	160.97	68.05	125.33	61.90	7.978***
HDL-C (mg/dl)	41.70	16.89	47.56	17.36	45.33	17.39	2.888**
LDL-C (mg/dl)	83.93	54.65	75.11	41.59	78.46	47.10	1.524
VLDL (mg/dl)	20.70	9.17	32.19	13.61	25.02	12.38	7.978***
FBG (mg/dl)	83.25	7.93	89.45	13.86	85.61	10.98	4.356***

Significant at p<0.05; **Significant at p<0.01, ***Significant at p<0.001

Table 2 shows the prevalence of MS and metabolic risk factors in the premenopausal women, postmenopausal women and pooled sample. The prevalence of MS was 21.66%, 24.33% and 25.66% according to ATP-III, IDF and mATP-III criteria, respectively. The postmenopausal women were found to have significantly ($p<0.05$) higher prevalence of MS as compared to premenopausal women using all the three criteria. The prevalence of metabolic risk factors like high WC, raised blood pressure, reduced levels of HDL-C, elevated levels of TGL and FBG was also significantly ($p<0.05$) higher in postmenopausal women than their premenopausal counterparts. In the pooled sample, according to ATP-III criterion, the most prevalent component was reduced levels of HDL-C followed by raised blood pressure, high WC, elevated levels of TGL and elevated levels of FBG. Based on IDF and mATP-III criteria, the most frequent component was reduced levels of HDL-C

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followed by high WC, raised blood pressure, elevated levels of TGL and elevated levels of FBG. It is apparent from this table that the most prevalent component of MS among both premenopausal and postmenopausal rural females was reduced levels of HDL-C and the least prevalent was elevated levels of FBG.

Table 2. Prevalence of Components of Metabolic Syndrome among Participants

NCEP ATP-III (2001)	*Total(N=300)*	*Premenopausal(N=186)*	*Postmenopausal(N=114)*
WC (cm)	28.33(85)	25.80(48)	32.45(37)
BP (mm Hg)	34.33(103)	21.50(40)	55.26(63)
TGL (mg/dl)	28.00(84)	15.05(28)	49.12(56)
HDL-C (mg/dl)	59.66(179)	56.98(106)	64.03(73)
FBG (mg/dl)	4.00(12)	-----	10.52(12)
Metabolic Syndrome	21.33(65)	6.98 (14)	44.73(51)
IDF (2005)	*Total(N=300)*	*Premenopausal(N=186)*	*Postmenopausal(N=114)*
WC (cm)	49.00(147)	43.54(81)	57.89(66)
BP (mm Hg)	34.33(103)	21.50(40)	55.26(63)
TGL (mg/dl)	28.00(84)	15.05(28)	49.12(56)
HDL-C (mg/dl)	59.66(179)	56.98(106)	64.03(73)
FBG (mg/dl)	16.33(49)	15.05(28)	18.42(21)
Metabolic Syndrome	24.33(73)	11.82(22)	44.73(51)
mNCEP ATP-III (2005)	*Total(N=300)*	*Premenopausal(N=186)*	*Postmenopausal(N=114)*
WC (cm)	49.00(147)	43.54(81)	57.89(66)
BP (mm Hg)	34.33(103)	21.50(40)	55.26(63)
TGL (mg/dl)	28.00(84)	15.05(28)	49.12(56)
HDL-C (mg/dl)	59.66(179)	56.98(106)	64.03(73)
FBG (mg/dl)	4.00(12)	-----	10.52(12)
Metabolic Syndrome	25.66(77)	10.75(20)	50.00(57)

Figures in parenthesis indicate the number of subjects

NCEP ATP-III (National Cholesterol Education Program Adult Treatment Panel- III)

mNCEP ATP-III (modified National Cholesterol Education Program Adult Treatment Panel- III)

IDF (International Diabetes Federation)

Waist Circumference (WC); Blood Pressure (BP);Triglycerides (TGL); High Density Llipoprotein-Cholesterol (HDL-C); Fasting Blood Glucose (FBG)

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Table 3. Clustering Of Components of Metabolic Syndrome among Studied Participants

Components of Metabolic Syndrome	NCEP ATP-III (2001)		
	Premenopausal (N=186)	*Postmenopausal (N=114)*	*Total (N=300)*
0	21.50(40)	13.15(15)	18.3(55)
1	45.69(85)	22.80(26)	36.66(110)
2	25.80(48)	19.29(22)	23.33(70)
3	6.98(13)	26.31(30)	14.33(43)
4	0.53(1)	17.54(20)	7.0(21)
5	00	0.88(1)	0.3(1)
Components of Metabolic Syndrome	**mNCEP ATP-III (2005)**		
	Premenopausal (N=186)	*Postmenopausal (N=114)*	*Total (N=300)*
0	16.66(31)	9.64(11)	14(42)
1	40.32(75)	20.17(23)	32.66(98)
2	32.25(60)	19.29(22)	27.33(82)
3	9.67(18)	24.56(28)	15.33(46))
4	1.07(2)	21.92(25)	9.0(27)
5	00	3.50(4)	1.3(4)
Components of Metabolic Syndrome	**IDF (2005)**		
	Premenopausal (N=186)	*Postmenopausal (N=114)*	*Total (N=300)*
0	19.89(37)	12.28(14)	17(51)
1	43.01(80)	21.92(25)	35(105)
2	23.65(44)	14.91(17)	20.33(61)
3	10.75(20)	20.17(23)	14.3(43)
4	1.07(2)	17.54(20)	7.3(22)
5	00	7.01(8)	2.7(8)

Figures in parenthesis indicate the number of subjects

NCEP ATP-III (National Cholesterol Education Program Adult Treatment Panel- III)

mNCEP ATP-III (modified National Cholesterol Education Program Adult Treatment Panel-III)

IDF (International Diabetes Federation)

Table 3 manifests the clustering of the number of components of MS in the studied females. According to ATP-III criterion, 45.69% of premenopausal and 22.80% of postmenopausal women had at least one risk factor, 25.80% of premenopausal and 19.29% of postmenopausal had atleast two risk factors, 6.98% of premenopausal and 26.31% of postmenopausal had at least three risk factors, 0.53% of premenopausal and 17.54% of postmenopausal had any four risk factors. None of the

premenopausal had all the five risk factors whereas 0.88% of postmenopausal women had all the five risk factors of MS. This shows that about half of the postmenopausal females had two and three risk factors. Almost similar results were observed while applying IDF and mATP-III criteria.

Discussion

In developed and developing countries, now these days, CVD is the leading cause of mortality in the postmenopausal women *(Matthews et al, 1989; Carr, 2003, Mesch et al, 2006; Lejskova et al, 2011).* Various scientists *(Kannel, et al, 1976; Kannel, 1987; Carr, 2003, Cameron et al, 2004, Eshtiaghi et al, 2010)* observed that menopause is a risk factor for CVD which may be due to estrogen hormone deficiency. According to *Gohlke-Barwolf (2009)* and *Spadafranca et al. (2013)* estrogen deficiency play an important role as a determinant of MS in postmenopausal women which makes these females susceptible to CVD. Estrogen has protective effects on the cardiovascular system due to which there is an increase in the prevalence of CVDs in the postmenopausal women. In India, few studies *(Pandey et al, 2010, Tandon et al, 2010, Chhabra et al, 2014)* have investigated the prevalence of MS in premenopausal and postmenopausal women but not much information is available regarding MS among rural women from Punjab. Therefore, in the present study, the prevalence of MS was estimated in rural premenopausal and postmenopausal women of Amritsar (Punjab).

The overall prevalence of MS in the pooled sample was 21.66%, 24.33% and 25.66% using ATP-III, IDF and mATP-III criteria, respectively. The postmenopausal females were observed to have significantly higher prevalence of MS than premenopausal females (Table 1). Slightly higher prevalence of MS by using mATP-III and IDF criteria can be explained by lower cut-off points of WC than used by original ATP-III criterion. It is also observed that the difference in the percentage prevalence estimated by these three criteria was small and statistically non-significant. Further kappa statistics was applied for finding agreement between the three definitions. The degree of agreement between mATP-III and IDF was 0.87, between IDF and ATP-III was 0.85 while it was 0.76 between mATP-III and ATP-III which shows that mATP-III has more concordance with IDF and less concordance with ATP-III criterion. It can be concluded from the present results that we can use mATP-III or IDF criterion in future studies for detection of MS even though all these criteria have significant agreement but the maximum agreement was observed between mATP-III and IDF criteria. It is interesting to observe that out of 300 rural females, (18.3%) 55 females

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were screened positive for MS by using all these three criteria despite the fact that these three criteria share most of the components but still misclassify a number of subjects as having MS.

Table 4: Percentage Prevalence of Metabolic Syndrome among Rural Indian Females

Area	Age	Number of females	Criteria used	Percentage prevalence	Investigator
Mandur /Goa	**>25**	**176**	**ATP-III**	**39.80**	***Peixoto and Shah (2014)***
North Indian population	**Pre-M=25-40 Post-M=45-60**	**200**	**ATP-III**	**Pre-M=20.00 Post-M=41.00**	***Chhabra et al. (2014)***
Tumkur/Karnataka	**≥18**	**433**	**mATP-III**	**55.19**	***Shalini et al. (2013)***
Ambala/Haryana	**≥20**	**627**	**IDF**	**11.64**	***Pathania et al. (2013)***
Thiruvallur /TamilNadu	**30-50**	**150**	**ATP-III mATP-III**	**30.70 36.00**	***Selvaraj et al. (2012)***
Jammu & Kashmir	**Mean age=49.35 (Post-M women)**	**500**	**ATP-III**	**13.00**	***Tandon et al. (2010)***
Chandigarh	**≥18**	**315**	**ATP-III IDF**	**34.90 41.30**	***Mangat et al. (2010)***
Wardha/Mumbai	**≥18**	**131**	**ATP-III**	**7.60**	***Kamble et al. (2010)***
Amritsar females	**25-55**	**300 Pre-M=186 Post-M=114**	**ATP-III IDF mATP-III**	**21.66 24.33 25.66**	***Present study***

The magnitude of the MS in rural females of Punjab can be best judged via comparison with the prevalence of MS in other rural populations of India. The data on the prevalence of MS in some rural Indian populations is shown in Table 4. It is evident from this table that most of the studies have used ATP-III criterion for screening of MS whereas very few studies have used IDF and mATP-III criteria. The prevalence rate of MS among rural Indian females varies considerably from one region to another region. The present study presents one of the first report on the comparison of the prevalence of MS among rural premenopausal and postmenopausal Punjabi females using three international criteria namely ATP, IDF and mATP-III. No study from Punjab is available till date in literature which has compared these three criteria to assess the prevalence of MS. While *Deepa et al. (2007)* compared the prevalence of MS in South Indian population by using three criteria in which again mATP-III was not used for screening of MS. The results of the premenopausal and postmenopausal women of the present study regarding the prevalence of MS were compared with general women population studies conducted in India because only one study is available in literature on premenopausal and postmenopausal women.

Chhabra et al. (2014) studied North Indian premenopausal and postmenopausal females and reported higher prevalence of MS using ATP-III criterion as compared to the rural females of Amritsar. This study highlights the high prevalence of MS among rural women which could increase the burden of diabetes and CVDs in near present future in Punjabi population. If the present trend continues, the situation can get worse even within a decade and MS and its associated diseases can emerge as important public health problem in rural adults of Punjab.

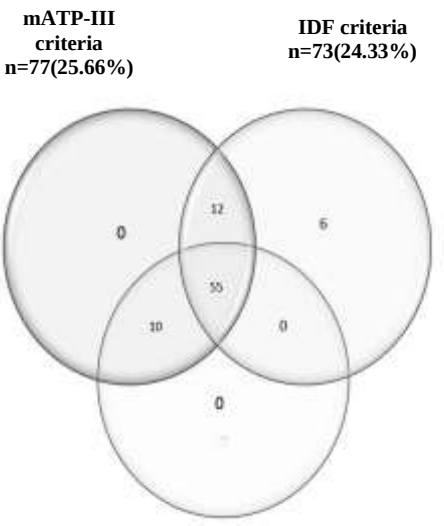

Fig: Showing the Overlapping of Subjects withMetabolic Syndrome Based on ThreeCriteria

The economic cost attributable to MS is so high that country like India can ill-afford to spend its meagre resources on the co-morbidities which are strongly influenced by MS. There is an urgent need to establish magnitude of the problem and the risk estimates for various NCDs and incorporate management prevention strategies within the existing health infrastructure.

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Author Disclosure Statement

No conflicts of interest. The authors have no disclosures to make in relation to the content of this manuscript.

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