Rural-urban and gender differences in metabolic syndrome in the aging population from southern India: Two parallel, prospective cohort studies

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Summary

Background Despite the growing evidence of metabolic syndrome as a major risk factor for cardiovascular and cerebrovascular disease, there are limited studies from India on its prevalence, especially in the aging population. We aimed to estimate the prevalence of metabolic syndrome and associated comorbidities in two prospective, aging cohorts from rural and urban India.

Methods In these two parallel, prospective, aging (≥ 45 years) cohorts, the samples included 2171 people from rural India (Srinivaspura Aging, Neuro Senescence and COGnition, SANSCOG cohort; April 23, 2018 to Sept 25, 2021) and 332 people from urban India (Tata Longitudinal Study on Aging, TLSA cohort; July 8, 2015 to Oct 23, 2021). Using cross-sectional data from baseline clinical and biochemical assessments, we calculated metabolic syndrome prevalence using two well established criteria, namely consensus criteria and National Cholesterol Education Program - Adult Treatment Panel III (NCEP-ATP III) criteria; further, rural-urban, gender, and age-wise differences were compared.

Findings Proportions of metabolic syndrome were 46.2 and 54.8% as per consensus criteria in rural and urban participants, respectively; corresponding numbers using NCEP-ATP III criteria were 40.3 and 45.1%. Rural-dwelling older adults had a significantly lesser prevalence of all individual metabolic syndrome parameters except impaired triglycerides and high-density lipoprotein levels. Rural women had a significantly higher prevalence of metabolic syndrome than rural men, whereas there was no significant difference among urban participants. We did not observe any consistent age-wise trend when comparing both cohorts. There was high burden of comorbidities among both groups, mostly undiagnosed in rural participants.

Interpretation Roughly one in two older adults had metabolic syndrome, urban significantly more than rural, reaching an alarming 63.1% among urban participants aged 65–74 years. The very high prevalence of undiagnosed comorbidities among rural adults is extremely concerning, calling for urgent public health measures in this marginalised and health-disparate population.

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Keywords: Metabolic syndrome; Prevalence; India; Rural; Urban; Aging; Cohort; Gender difference

Introduction

Metabolic syndrome refers to a cluster of related factors, the presence of which confers higher risk of cardiovascular disease and diabetes mellitus. These factors are abdominal obesity, insulin resistance, hypertension, and dyslipidemia. Diagnostic criteria for metabolic syndrome have been provided by different professional bodies, albeit with minor variations.

The first formal criteria was provided by the World Health Organization (WHO) in 1998,[1] which required the presence of diabetes mellitus or impaired glucose regulation (impaired fasting glucose or impaired glucose tolerance) and/or insulin resistance along with any

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Research in context

Evidence before this study

We searched PubMed using keywords "metabolic syndrome", "syndrome x", "insulin resistance", "metabolic syndrome [AND] definition", "metabolic syndrome [AND] diagnostic criteria", "risk", "clinical significance", "metabolic syndrome [AND] prevalence", "metabolic syndrome [AND] India", "metabolic syndrome [AND] rural [OR] urban" and "metabolic syndrome [AND] gender" for literature published during the period Jan 1, 1997 to Dec 31, 2021. There was robust evidence for the association of metabolic syndrome with multiple adverse health incomes. There were wide variations in prevalence globablly as well as within India. A recent meta-analysis of 111 Indian studies by Krisnamoorthy et al. reported a pooled prevalence of 30% among Indian adults.

Added value of this study

Our study adds value to the existing knowledge base since it is one of the few Indian studies on the prevalence of metabolic syndrome among aging adults, from two diverse populations in rural and urban India. We underscore the significant differences in prevalence according to gender, rural-urban status, and varying diagnostic criteria. We recommend using population-specific criteria for increased sensitivity in diagnosis in the Indian population. We also bring to light the alarmingly high prevalence of undiagnosed comorbidities among rural Indians.

Implications of all the available evidence

We propose the need for urgent public health measures including lifestyle-based interventions to prevent or mitigate the adverse consequences of metabolic syndrome in aging Indians. We intend to longitudinally follow-up our participants along with parallel monitoring of cognitive changes to understand how metabolic syndrome contributes to the risk of later life cognitive impairment and dementia.

two of the following risk factors, namely, abdominal obesity (waist/hip ratio >0.9 in men and >0.85 in women and/or body mass index (BMI) >30 kg/m^2), high triglycerides (≥ 150 mg/dl) and/or high HDL (high density lipoprotein) cholesterol (<35 mg/dl in men and 40 mg/dl in women), blood pressure $\geq 140/90$ mmHg and microalbuminuria (urinary albumin >20 μg/min or albumin: creatinine ratio ≥ 30 mg/g). Subsequently, many other professional authorities refined the WHO criteria based on more commonly available metabolic and biochemical parameters in an effort to simplify the criteria and maximize the diagnostic sensitivity. These include the National Cholesterol Education Program - Adult Treatment Panel III (NCEP ATP-III, 2001),[2] International Diabetes Federation (IDF, 2005)[3,4] criteria, National Heart Lung and Blood Institute,[5] American Heart Association,[5] among others. Amidst these variations, a joint scientific statement was published[2] to harmonize criteria from different eminent professional bodies. It is to be taken into account that the term "metabolic syndrome" itself has been put to scrutiny since it has been debated whether this "syndrome" confers any specific risk beyond its individual components.

Despite differences in criteria and cut-offs, several large, prospective studies have established the clinical significance of metabolic syndrome beyond doubt. For example, it increases the risk of cardiovascular disease (CVD), type 2 diabetes mellitus, cancer as well as all-cause mortality, independent of baseline diabetes or CVD status.[3–6] Individuals with metabolic syndrome have also been observed to have an increased risk of stroke.[7,8] Further, a recent meta-analysis[9] of five prospective studies revealed that metabolic syndrome also predicted the risk of recurrent stroke. The association of metabolic syndrome with cerebrovascular dysfunction is indeed highly significant since the role of vascular dysfunction being increasingly recognized in the pathogenesis of dementia.[10] In fact, emerging evidence from longitudinal studies suggests that midlife metabolic syndrome specifically increases the risk of subsequent cognitive decline.[11,12]

It is known that South Asians have higher metabolic risk factors and greater cardiovascular risk than other populations.[13] Previous studies have shown that Indians, in particular, are more prone to abdominal obesity and insulin resistance.[14–20] With this background, the ongoing and rapid epidemiological transition in India[21] could mean that India's burden of diabetes mellitus as well as CVD could reach alarming heights. Therefore, it is important to estimate the proportion of metabolic syndrome in the Indian population. It is also imperative to consider the immense socio-cultural diversity that exists within the Indian population, since this could have a differential effect on the risk of metabolic syndrome. Such differences in culture and lifestyle render a broad categorization of Indians into two distinct populations—urban Indians and rural Indians. Therefore, estimating and comparing the prevalence of metabolic syndrome in these two unique population groups could yield unexplored insights into how lifestyle-related factors differentially influence the risk of metabolic syndrome and its adverse consequences.

We are conducting two parallel, prospective, aging, cohort studies on individuals from rural and urban communities in Karnataka, a southern Indian state. Both these cohort studies are harmonized and are aimed at identifying risk and protective factors of dementia and related disorders. The rural study (Srinivaspura Aging, Neuro Senescence and COGnition, SANSCOG) was conducted in the villages of Srinivaspura, whereas the urban counterpart (Tata Longitudinal Study on Aging,

TLSA) is in the metropolitan city of Bangalore. Both sites are located in the state of Karnataka (approximately 60 miles apart) in southern India. The above studies are aimed at identifying risk and protective factors of dementia, wherein, participants undergo detailed, multimodal assessments (clinical, cognitive, biochemical, genetic and neuroimaging), with periodic follow-up spanning several years. In the current study, we have estimated the prevalence of metabolic syndrome among aging Indians from the above-mentioned rural and urban cohorts, using both the consensus criteria and NCEP-ATP III criteria. We wish to bring to the reader's notice that the term "aging" that we have used in our study refers to the aging process in general, which includes physical, cognitive, biochemical and functional changes that occur as early as the fourth decade itself and the term has not been attributed to a person's age in years.

Methods

Study design and recruitment

Cross-sectional data was used from baseline clinical and biochemical assessments of SANSCOG (rural) study conducted from April 23, 2018 to September 25, 2021 at the project office or mobile assessment unit in Srinivaspura, India, and TLSA (urban) cohort conducted from July 8, 2015 to October 23, 2021 at the project office mobile assessment unit in Bangalore, India. Rural participants were recruited through area sampling strategy from Srinvaspura 'taluk' (equivalent of a sub-district). In India, the primary units of the public-funded healthcare systems are Primary Health Centres (PHCs), with each PHC catering to the primary healthcare needs of around 20,000 to 30,000 people located in its surrounding villages. Srinivaspura taluk has a total of 13 PHCs, out of which, we randomly selected six PHCs for SANSCOG study's recruitment. Our field team works in collaboration with local public health officials as well local community health workers, called ASHAs (Accredited Social Health Activists), to systematically recruit eligible and consenting individuals from the villages attached to each PHC. Awareness programs were conducted in each village, in addition to public announcements and distribution of flyers. By contrast, the urban participants were recruited through convenience sampling, from urban areas in Bangalore city. Study awareness was created through newspaper advertisements, distribution of flyers, social media as well as by conducting awareness programs in large apartment complexes or gated communities.

Participants

Cognitively healthy aging (≥ 45 years) individuals – 2171 (male participants: 1031, female participants: 1140) from the rural cohort and 332 (male participants: 191, female participants: 141) from the urban cohort who had completed their baseline assessments were included in the current study. Individuals were excluded from the study if they had severe or terminal medical illness, severe hearing or visual impairment or locomotor disability that is likely to interfere with study assessments. The population characteristics of the rural and urban participants are distinct. Rural participants are village-dwelling; the majority are agriculture-dependent and belong to a low socio-economic stratum; they typically have low levels of literacy and have not significantly experienced modern lifestyle changes. Contrastingly, urban participants belong to a working, middle-class background. They are typically well educated, have migrated from different parts of India, and have gone through major lifestyle changes in the last few decades.

Ethics clearance and informed consent

Both TLSA and SANSCOG studies have been approved by the Institutional Ethics Committee of the Centre for Brain Research (CBR). Participants provided voluntary, written informed consent for the study procedures including specific consent for clinical assessments and blood collection.

Measurements

Blood biochemistry. Overnight fasting blood samples were collected from both rural and urban participants. In the urban study, samples were collected individually at the participants' homes whereas, in the rural study, we conducted periodic blood collection camps village-wise, wherein samples were collected from groups of participants hailing from the respective villages (due to poor transport facilities in this rural area). Trained phlebotomists collected 15 ml total volume of peripheral venous blood sample using vacutainers, for a detailed panel of biochemical investigations that included glucose, triglycerides and HDL. Glucose estimation was done using hexokinase method, whereas enzymatic method was used for the studied lipid parameters.

Anthropometric and clinical measures. Trained clinicians or nurses conducted the anthropometric and clinical measurements in both rural and urban cohorts. A standard, non-stretchable, measuring tape was used to measure the waist circumference at the level of intersection between the line just above the uppermost lateral border of the right ilium and the midaxillary line of the body, to the nearest 0.1 cm. Systolic and diastolic blood pressure (BP) of all four limbs were measured to the nearest 2 mm Hg using a mercurial sphygmomanometer (Diamond Deluxe BP apparatus, Industrial

Consensus criteria	NCEP-ATP III criteria
3 or more of the below 5 criteria	
Fasting glucose ≥ 100 mg/dl or on drug treatment for diabetes	
Systolic BP ≥ 130 mmHg and/or diastolic BP ≥ 85 mmHg or on drug treatment for hypertension	
Triglycerides ≥ 150 mg/dl or on drug treatment for elevated triglycerides	
HDL cholesterol < 40 mg/dl for men and < 50 mg/dl for women or on drug treatment for low HDL	
WC of ≥ 90 cm in men or ≥ 80 cm in women	WC of ≥ 102 cm in men or ≥ 88 cm in women

***Table 1*: Criteria used for diagnosis of metabolic syndrome.**
*NCEP-ATP III – National Cholesterol Education Program–Adult Treatment Panel III; BP – Blood Pressure; HDL – High Density Lipoprotein; WC – Waist Circumference.

Electronic & Allied Products). BP readings were recorded in all four limbs, in both sitting and supine positions (total of 8 readings, from which the average BP was calculated). For participants who were not comfortable with having multiple BP measurements, the right arm sitting BP was considered). Furthermore, clinical history of previously diagnosed diabetes, hypertension and dyslipidaemia (high triglycerides and low HDL) as well information on drug treatment for any of the above conditions was obtained from baseline clinical assessment data of both cohorts. Using the above information, metabolic syndrome was defined based on the consensus criteria as well as NCEP ATP-III criteria (Table 1).

Prevalence of metabolic syndrome was calculated among rural and urban participants, both overall as well as according to gender (male participant and female participant) and age groups (45–54 years, 55–64 years, 65–74 years, ≥ 75 years). We also measured the proportions of comorbidities (diagnosed and undiagnosed) such as diabetes, hypertension, dyslipidemia as well as cardiovascular and cerebrovascular diseases in both cohorts.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software, version 22. Normality was established using Kolmogorov Smirnov test. Continuous data was expressed as mean and standard deviation. Prevalence of metabolic syndrome, impairment in individual parameters and comorbidities associated with metabolic syndrome was expressed as percentage. Comparison of groups was performed using chi-square test for categorical variables and independent T-test for continuous variables. All test results were interpreted at a significance level of $p < 0.002$ after correction for multiple comparison.

Role of the funding source

The funders had no role in the study design, methods, data collection, analysis or preparation of the paper. All authors (JSS, AS, ALM and VR) had access to the dataset and were responsible for the decision to submit for publication.

Results

Demographic characteristics of the rural and urban cohort are depicted in Table 2. There were significant differences in the mean age, gender distribution, literacy as well as mean years of education between the two cohorts. Rural participants had a lower mean age, lower levels of literacy and very low mean years of education.

Percentages of impairment in individual parameters of metabolic syndrome were compared between the rural and urban cohorts (Table 3). We observed that the rural cohort had significantly lesser percentage of impairment in anthropometric measures such as blood pressure (39.8% vs. 66.2%; $p = 0.0001$) and waist circumference (38.3% vs. 60.9% (consensus), 16.6% vs. 38.2% (NCEP ATP-III); $p = 0.0001$). The urban cohort had lesser percentage of impairment in biochemical measures such as serum triglycerides (45.1% vs. 21.9%; $p = 0.0001$) and HDL (45.1% vs. 25.9%; $p = 0.0001$). There was no significant difference between the cohort with respect to the percentage of impairment in fasting blood glucose (51.3% vs. 50.6%; $p = 0.17$). Overall prevalence of metabolic syndrome using the consensus criteria were 46.2% and 54.8% ($p = 0.002$) in the rural and urban cohorts, respectively. The corresponding numbers applying the NCEP-ATP III criteria were 40.3% and 45.1% ($p = 0.12$). The rural-urban difference was significant with the consensus criteria but not with the NCEP-ATP III criteria (Table 3).

We further gender- and age-stratified the prevalence of metabolic syndrome based on the consensus criteria in both cohorts. We found that women had significantly higher prevalence of metabolic syndrome than men in the rural cohort (57.2 vs. 40.17%, $p = 0.001$; Figure 1). However, there was no significant gender difference in the urban cohort (56.4 vs. 58.3%, $p = 0.2$). Further, urban male participants had significantly higher prevalence than rural male participants (58.3 vs. 40.17%,

Demographic features	Rural cohort	Urban cohort	p value
Total sample	2171	332	-
Age	58.5 ± 10.16	66.6 ± 9.55	0.0001*
Years of education	3.90 ± 4.6	16.6 ± 7.04	0.0001*
Gender distribution			
Males	1031 (47.4%)	191 (57.5%)	0.0006$
Females	1140 (52.5%)	141 (42.4%)	
Literates			
Literate	1185 (54.5%)	332 (100%)	0.0001$
Illiterate	986 (45.5%)	0	
Religion			
Hindu	1689 (77.7%)	207 (62.3%)	–
Others	482 (22.2%)	125 (37.6%)	
Alcohol			
Never used	1830 (84.2%)	270 (81.3%)	–
Currently using	124 (5.7%)	21 (6.3%)	
Currently abstinent	94 (4.3%)	5 (1.5%)	
No response	123 (5.6%)	36 (10.8%)	
Smoking			
Currently using	600 (27.6%)	7 (2.1%)	–
Currently abstinent	339 (15.6%)	1 (0.3%)	
Never used	1200 (55.2%)	285 (85.8%)	
No response	32 (1.4%)	36 (10.8%)	
Marital status			
Married/Cohabiting	1713 (78.9%)	238 (71.6%)	–
Divorced/Separated/ Widowed	378 (17.4%)	90 (27.1%)	
Never married	10 (0.4%)	4 (1.2%)	
No response	70 (3.2%)	0	
Language			
Monolingual	471 (21.6%)	15 (4.5%)	–
Bilingual	1178 (54.2%)	250 (75.3%)	
Multilingual	522 (24.2%)	67 (20.1%)	
Yearly income			
≤ 100,000 rupees	809 (37.3%)	19 (5.7%)	–
> 100,000 rupees	1362 (62.7%)	313 (94.2%)	
Occupation			
Agriculture	1155 (53.2%)	10 (3.0%)	–
Never worked/retired	550 (25.3%)	80 (24.0%)	
Manual laborer	349 (16.0%)	2 (0.6%)	
Professional	52 (2.3%)	151 (45.4%)	
Business	26 (1.1%)	82 (24.6%)	
Skilled jobs	21 (0.9%)	4 (1.2%)	
Semi-skilled labor	18 (0.8%)	3 (0.9%)	

***Table 2*: Demographic characteristics of subjects in rural and urban cohorts.**
The significant *p*-values (corrected $p < 0.002$) are represented by * for independent *t*-test and by $ for Chi-square test after correcting for multiple comparisons.

$p = 0.002$). However, there was no significant difference between urban and rural female participants.

Age-stratification into four age groups (45–54 years, 55–64 years, 65–74 years and ≥ 75 years) revealed an increasing prevalence with age in the first three above-mentioned age groups and a decrease in the age group of ≥ 75 years in the urban cohort; the highest prevalence (63.1%) was found in the urban residents aged 65–74 years (Figure 2). However, there was no consistent age-wise pattern among rural participants.

Additionally, on comparing the prevalence of co-morbidities known to be associated with metabolic syndrome (Table 4), we found that the urban participants had a significantly higher overall prevalence of dyslipidemia (85.2% vs. 80.5%), hypertension (78.3% vs. 25.9%), diabetes mellitus (49.6% vs. 25.7%), cardiovascular diseases (17.7% vs. 1.3%), cerebrovascular diseases (3.3% vs. 0.7%), and cancer (3% vs. 0.3%) compared to rural participants. On comparing the proportion of people with diagnosed and undiagnosed comorbidities, the proportion of undiagnosed comorbidity was higher in rural participants compared to urban cohort with respect to diabetes (62.9% vs. 35.1%), hypertension (71.3% vs. 46.2%) and dyslipidemia (99.1% vs. 71.7%). It should be noted here that the cut-offs used for the diagnosis of comorbidities are different from those used to diagnose metabolic syndrome. Diagnostic cut-offs for comorbidities are fasting glucose ≥ 126 mg/dl for diabetes, BP ≥ 140 / 90 mm Hg for hypertension and abnormality in at least one of the lipid parameters (total cholesterol > 200 mg/dl or triglycerides ≥ 150 mg/dl or HDL: men: < 40 mg/dl, women: < 50 mg/dl or LDL > 100 mg/dl) for dyslipidemia. In comparison, corresponding cut-offs diagnosis of Metabolic syndrome are lower: ≥ 100 mg/dl for diabetes, ≥ 130 / 80 mm Hg for hypertension and abnormality in triglycerides (≥ 150 mg/dl) or HDL (men: < 40 mg/dl, women: < 50 mg/dl) for dyslipidemia.

Discussion

Studies across different parts of the world have shown wide variations in the prevalence of metabolic syndrome.[22–26] This could be due to the differences in diagnostic criteria, population characteristics including the age group studied, geographical regions, etc. A number of studies have been carried out across different parts of India and have shown considerable variations in the prevalence of metabolic syndrome.[27–33] A recent meta-analysis[34] of 111 Indian studies reported a pooled prevalence of 30% among Indian adults (≥ 18 years).

In this study, we estimated the prevalence of metabolic syndrome among aging individuals (≥ 45 years) from rural and urban India, based on two well-established criteria, namely the consensus criteria and the NCEP-ATP III criteria. Both these criteria have four parameters in common: 1. elevated fasting glucose (≥ 100 mg/dl; NCEP ATP-III criterion was originally ≥ 110 mg/dl but was subsequently revised to ≥ 100 mg/dl) or taking medication for diabetes 2. low HDL cholesterol (< 40 mg/dl and < 50 mg/dl in women) or on medication for low HDL 3. high triglycerides

	Rural cohort	Urban cohort	p value
Number of subjects	2171	332	-
Elevated fasting glucose[a] or diagnosis / drug treatment	1116 (51.3%)	168 (50.6%)	NS
Elevated blood pressure[b] or diagnosis / drug treatment	865 (39.8%)	220 (66.2%)	0.0001[$]
Elevated triglycerides[c] or diagnosis / drug treatment	982 (45.1%)	73 (21.9%)	0.0001[$]
Low HDL[d] or diagnosis / drug treatment	982 (45.1%)	86 (25.9%)	0.0001[$]
Higher waist circumference (Consensus criteria[e])	833 (38.3%)	202 (60.9%)	0.0001[$]
Higher waist circumference (NCEP ATP-III criteria[f])	362 (16.6%)	127 (38.2%)	0.0001[$]
Metabolic syndrome (Consensus criteria)	1004 (46.2%)	182 (54.8%)	0.002[$]
Metabolic syndrome (NCEP ATP-III criteria)	877 (40.3%)	150 (45.1%)	NS

***Table 3*: Prevalence of individual parameters of metabolic syndrome in rural and urban cohorts based on the consensus criteria and NCEP-ATP III criteria.**

The statistically significant *p*-values (corrected $p<0.002$) are represented by $.

[$] for Chi-square test after correcting for multiple comparisons.

[a] ≥100 mg/dl.

[b] ≥130 mm Hg systolic and/or ≥ 85 mm Hg diastolic.

[c] ≥150 mg/dl.

[d] <40 mg/dl in men; < 50 mg/dl in women.

[e] ≥90 cm in men; ≥ 80 cm in women.

[f] ≥102 cm in men; ≥88 cm in women.

(≥ 150 mg/dl) or medication for elevated triglycerides 4. high blood pressure (≥ 130/85 mmHg) or on medication for hypertension. However, the fifth parameter, namely, central obesity, differs. The NCEP-ATP III criteria defines a waist circumference of ≥ 102 cm in men or ≥ 88 cm in women as abnormal, whereas the consensus criteria recommend population-specific cut-offs for abnormal waist circumference (≥ 90 cm in men or ≥ 80 cm in women for South Asians).[4] Any three of the five criteria are sufficient according to the NCEP ATP-III and consensus criteria.

In our study, the proportion of metabolic syndrome detected using the consensus criteria was higher than what was picked up using NCEP ATP-III criteria in both our cohorts. This is likely to be due to the use of more appropriate South Asian cut-offs for waist circumference in the consensus criteria rather than the universal cut-offs of NCEP criteria, which are more relevant in Western populations. The above finding is in line with results from a Chinese study[35] in an adult population, which showed higher prevalence of metabolic syndrome using South Asian cut-offs as compared to using universal cut-offs. Furthermore, a large, multi-centric study[31] (n = 6198) across 11 cities in India reported that age-adjusted prevalence of metabolic syndrome was 33.3% (31.7–34.9) and 40.4% (38.6–42.2) in men and women, respectively when the Asian-specific harmonized criteria were used; however, this prevalence was higher when compared to that using the NCEP-ATP-III criteria. A similar trend was also seen in a large rural study[36] among individuals aged ≥ 30 years (n = 4535) across 20 villages in the state of Andhra Pradesh in southern India, wherein the prevalence was higher with use of Asian-specific waist circumference cut-offs (men: 32.5%, women: 23.9%) as compared to the NCEP-ATP-III criteria with universal cut-offs (men: 26.9%, women: 18.4%).

Our urban cohort had a significantly higher prevalence (as per consensus criteria) as compared to the rural (54.8% vs. 46.2%, p = 0.002). This finding was similar to that in the above mentioned Chinese study,[35] wherein, urban-rural difference was seen among both men (urban: 34.3 vs. rural: 2.7%) and women (urban: 24.1 vs. rural: 11.4%). However, in contrast to this, a large study among rural and urban Koreans[37] (age: 40–49 years) study using the same South Asian cut offs for NCEP ATP-III criteria, revealed contrasting results, wherein, rural participants had significantly higher prevalence (age- and sex- adjusted) than urban participants (29.3 vs. 22.3%). Interestingly, the main factor contributing to this difference was in abnormal waist circumference between the rural and urban women (61.1 vs. 41.7%) and not men (23.9 vs. 20.7%). This is possibly due to urban women in Korea having more

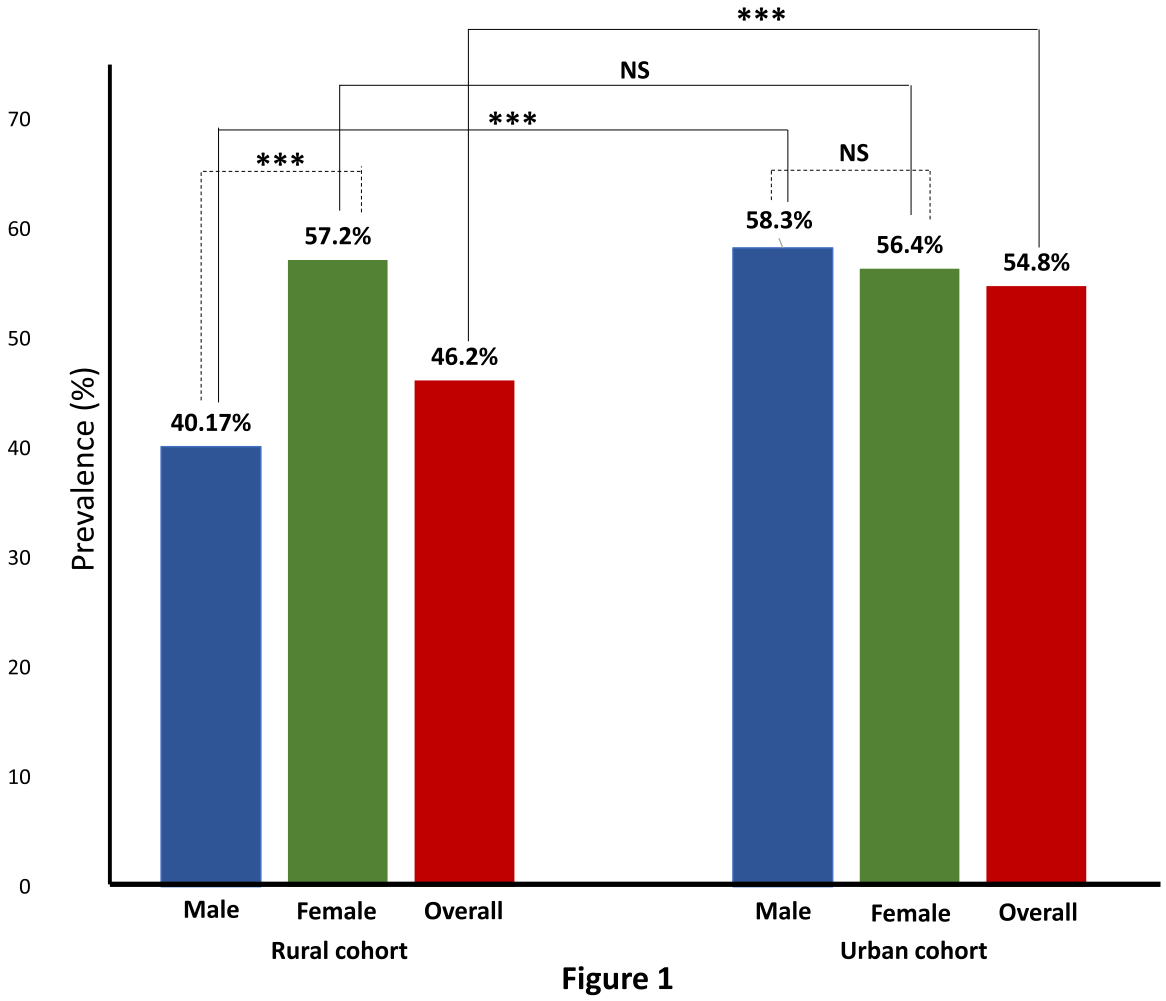

Figure 1. Gender-wise prevalence of metabolic syndrome (%).

Estimated according to the consensus criteria, among aging rural and urban Indians belonging to Srinivaspura Aging, Neuro Senescence and COGnition (SANSCOG) cohort and Tata Longitudinal Study on Aging (TLSA) cohorts. Male participants, female participants and overall participants are represented by blue-, green-, and black-colored bars, respectively). *** Represents significant *p* value <0.002; NS – Not Significant.

body image and weight concerns due to social factors or higher educational attainment influencing their health-related behaviors.[38]

Previous studies in the Indian population[32,39,40] have pointed to urban Indians having higher prevalence of metabolic syndrome than their rural counterparts. A recent large study[32] conducted in the adjoining state of Kerala reported significantly higher prevalence in adult participants living in urban (26%) than in rural areas (22%). Similarly, a study[40] in the national capital region of India reported urban prevalence (NCEP ATP-III) as 21.7% in male participants and 27.8% in female participants, whereas corresponding numbers for rural sites were 13.8% and 18.8%. Kapil et al[27] reported 28.6% prevalence among individuals aged 60 and above from a rural community from a high-altitude region in district of Nainital in northern India, based on the IDF criteria. On the other hand, two studies on older adults in the same age group (≥ 60 years) and using the same (IDF) criteria from an urban setting in central India revealed a much higher prevalence (42.1%).[41] Krishnamoorthy et al[34] reported a significantly higher in urban (32%, pooled prevalence from 49 studies) compared to rural (22%, pooled prevalence from 34 studies) or tribal areas (28%). Thus, several studies, including ours, appear to suggest that urban populations in India have a higher prevalence than rural or tribal populations.

Regarding gender differences, our study revealed that rural women had a significantly higher prevalence of metabolic syndrome than rural men, whereas this gender difference was not significant in the urban population. A considerable number of previous studies from

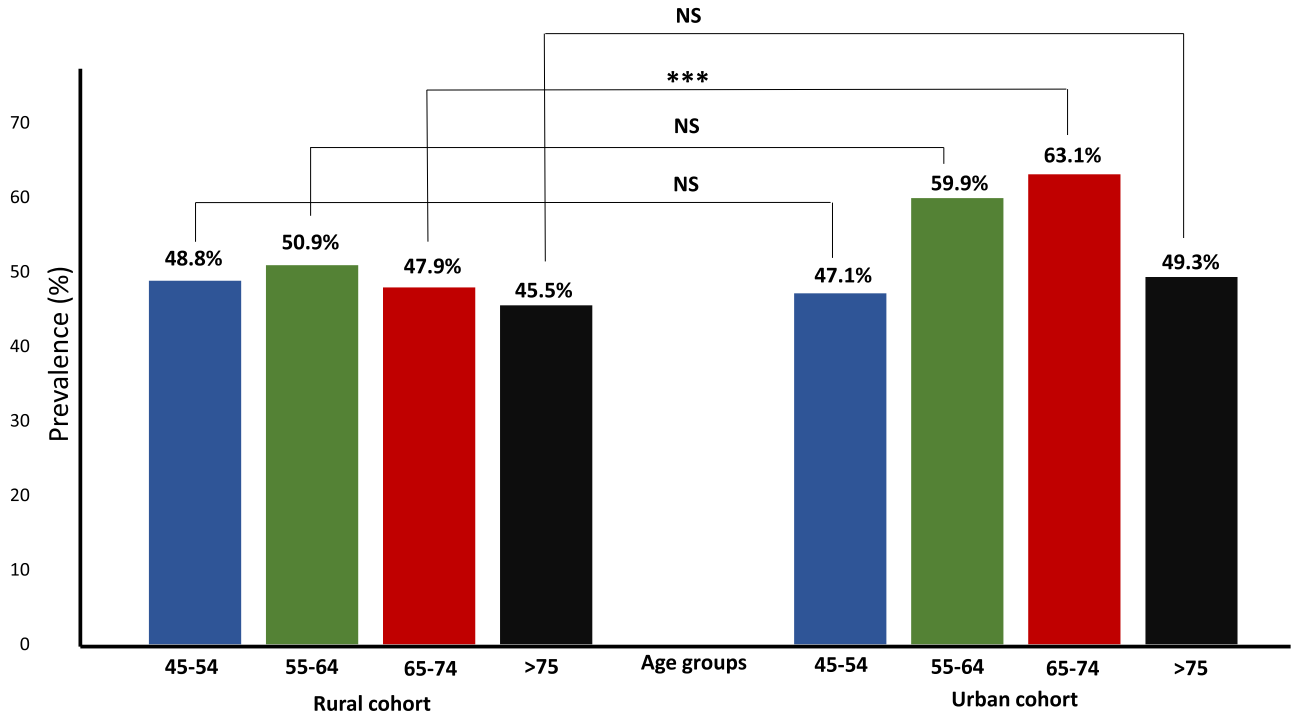

Figure 2. Age-stratified prevalence of metabolic syndrome (%).

Estimated according to the consensus criteria, among aging rural Indians (represented by blue-colored bars) and urban Indians (represented by green-colored bars) belonging to Srinivaspura Aging, Neuro Senescence and COGnition (SANSCOG) cohort and Tata Longitudinal Study on Aging (TLSA) cohorts, respectively. The age groups were categorized as 45−54 years, 55−64 years, 65−74 years and ≥ 75 years, represented by blue-, green-, red-, and black-colored bars, respectively). ***Represents significant *p* value <0.002; NS − Not Significant.

Clinical comorbidities	Rural cohort			Urban cohort			p value
	Overall (%)	Diagnosed (%)	Undiagnosed (%)	Overall (%)	Diagnosed (%)	Undiagnosed (%)	
Dyslipidemia[a]	1748 (80.5%)	16 (0.9%)	1732 (99.1%)	283 (85.2%)	80 (28.2%)	203 (71.7%)	0.002[$]
Hypertension[b]	564 (25.9%)	162 (28.7%)	402 (71.3%)	260 (78.3%)	140 (53.8%)	120 (46.2%)	0.0001[$]
Type 2 diabetes mellitus[c]	559 (25.7%)	207 (37.0%)	352 (62.9%)	165 (49.6%)	107 (64.8%)	58 (35.1%)	0.0001[$]
Cardiovascular disease[d]	29 (1.3%)	29 (100%)	NA	59 (17.7%)	59 (100%)	NA	0.0001[$]
Cerebrovascular disease[e]	16 (0.7%)	16 (100%)	NA	12 (3.3%)	12 (100%)	NA	0.0001[$]
Cancer[f]	8 (0.3%)	8 (100%)	NA	10 (3%)	10 (100%)	NA	0.0001[$]

***Table 4*: Prevalence of co-morbidities in rural and urban populations.**

The statistically significant *p*-values (< 0.002) are represented by $.

[$] for Chi-square test after correcting for multiple comparisons. NA: Not applicable (screening tests not performed).

[a] Dyslipidemia: Self-reported diagnosis / drug treatment and/or any one of total cholesterol ≥ 200 mg/dl or triglycerides ≥150 mg/dl or HDL in men < 40 mg/dl or women < 50 mg/dl or LDL ≥ 100 mg/dl.

[b] Hypertension: Self-reported diagnosis / drug treatment and/or BP ≥ 140 / 90 mm Hg.

[c] Type 2 diabetes mellitus: Self-reported diagnosis / drug treatment and/or fasting glucose ≥ 126 mg/dl and/or HbA1c ≥ 6.5.

[d] Cardiovascular disease: Self-reported diagnosis.

[e] Cerebrovascular disease: Self-reported diagnosis.

[f] Cancer: Self-reported diagnosis.

different parts of India, both in urban[32,40,42] as well as rural[32,33,40,43] settings, have also shown that metabolic syndrome prevalence is higher in female participants than male participants.

Prevalence studies conducted exclusively among the elderly population (> 60 years) are restricted. A study[29] among urban-dwelling elderly participants aged 60 years and above ($n = 295$) from central India revealed a prevalence of 34.58%. Another small study[44] conducted among 106 elderly residents (≥ 60 years) from central India reported a prevalence of 40% in the seventh and eighth decade and slightly higher (46%) prevalence in elderly ≥ 80 years of age. Both the above studies[29,44] reported a higher prevalence in women than men.

Another important finding that our study brings to light is the alarming proportion of rural participants with undiagnosed vascular risk factors such as diabetes, hypertension and dyslipidemia. In particular, our finding that less than 1% of rural older persons who had dyslipidemia had been diagnosed, is alarming. Interestingly, among all the individual metabolic syndrome parameters, the percentage of the two abnormal lipid parameters (triglycerides and HDL) showed the maximum rural versus urban difference (triglycerides 45.1% vs. 21.9% and HDL 45.1% vs. 25.91%). This is concerning since rural Indians are generally perceived to have healthier dietary habits (negligible intake of processed or fast foods, minimal meat intake, high intake of millets and green vegetables, etc.) and higher physical activity (majority engaged in agricultural labor). However, gross under-diagnosis and under-treatment of vascular risk factors could lead to higher burden of cardiovascular and cerebrovascular morbidity. Limitations of our study include an unequal sample size as well as unequal gender distribution between the rural and urban study samples. Further, the study samples may not be representative of the source population, particularly in the urban study since convenience sampling was performed. It is also possible that due to the same reason, sampling bias could have happened with urban participants, wherein participants with pre-existing medical conditions could have been more likely to participate in a study involving clinical assessments and blood investigations. Also, a cross-sectional study design makes it difficult to infer any causal associations. In addition, since the socio-cultural milieu in India is unique, the rural-urban differences observed in our study may not be generalizable to other populations across the world.

With the role of vascular and metabolic risk factors being increasingly recognized in the pathogenesis and progression of dementia,[45] it is essential to longitudinally follow up these individuals while monitoring for cognitive changes. Further, urgent public health measures are necessary to ensure screening and early diagnosis of metabolic syndrome and its components, so that appropriate interventional strategies including lifestyle changes can be initiated. Our finding that more than 57% of aging Indian women in our rural cohort had metabolic syndrome is a cause for concern considering that the prevalence of dementia is higher in women, who also live longer with the disease burden. Therefore, it is essential to strengthen the primary health care system in rural India, especially considering the existing health disparities in rural India where two-thirds of country's population reside.

Contributors

All authors (JSS, AS, ALM and VR) have made a substantial intellectual contribution to the conception, design or conduct of the study. Specific contributions

are as follows: JSS, AS and AML — acquisition of data; JSS, AS, ALM and VR — analysis and interpretation of data; JSS, AS and VR — drafting and reviewing the manuscript. All authors (JSS, AS, ALM and VR) had full access to all the data in the study. All authors (JSS, AS, ALM and VR) approved the final version of the manuscript for publication and accept responsibility to submit for publication.

Data sharing

Data will be shared in conformity with statutory requirements of the government of India, through the Alzheimer's Disease Data Initiative (ADDI) platform.

Declaration of interests

We declare no competing interests.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2022.101395.

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