Title: Prevalence and predictors of osteosarcopenia and relationship with physical functionality in rural and urban Indian women

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Mini Abstract:

Age-related bone and muscle impairments lead to osteoporosis and sarcopenia, and their coexistence, osteosarcopenia, causes functional decline but is less studied. We found higher prevalence of osteosarcopenia in rural (13.9%) vs urban women (1.6%), with risk factors including older age, low BMI, tobacco use, low protein, and low socioeconomic status.

Abstract:

Background: With ageing, bone and muscle impairment leading to osteoporosis and sarcopenia often co-exist, increasing risk of falls/fractures, physical disability, and premature mortality. Osteosarcopenia, where osteoporosis and sarcopenia co-exist, and its relationship with physical functionality in older adults is relatively less explored. Hence, we aimed to assess the prevalence, predictors, and physical functionality in urban and rural women with osteosarcopenia.

Methods: We included 397 women >40 years (182 urban, 215 rural, mean age 52±7) from Pune and nearby villages. Height, weight, BMI, bone density (lumbar spine, femur via DXA), grip strength (JAMAR dynamometer), and muscle function (SPPB) were assessed. Sarcopenia and osteoporosis were diagnosed using AWGS and WHO guidelines, with osteosarcopenia defined as both conditions. Lifestyle factors (diet, physical activity, tobacco use, socioeconomic status) were evaluated by validated questionnaire.

Results: Rural women had higher rates of osteoporosis (42%), sarcopenia (19%), and osteosarcopenia (13.9%) compared to urban women (18%, 3.8%, and 1.6%, respectively). Sarcopenic women had nearly 6 times higher risk (OR=6.2, 95%CI=3.2-11.9, p=0.001) of developing osteoporosis, with the risk remaining significant after adjusting for age and location. Osteosarcopenic women showed impaired physical function and lower bone density, with older age and low BMI as key risk factors.

Conclusion: Rural Indian women showed high rates of osteosarcopenia, osteoporosis, and sarcopenia, with older, low-BMI, postmenopausal women at higher risk. Contributing factors included low socioeconomic status, tobacco use, and poor protein intake. Addressing modifiable risks is important to reduce frailty-related outcomes in rural population.

Keywords: ***Osteosarcopenia, Physical Function, Urban-rural, Prevalence***

Introduction:

Ageing affects musculoskeletal health, leading to osteoporosis and sarcopenia; rising prevalence of which impose significant economic, societal and social burden on older adults and healthcare system [1,2]. While osteoporosis is a disease characterized by decreased bone mineral density (BMD), sarcopenia is an age-related loss of skeletal muscle mass, leading to a decline in muscle strength and function [3,4]. The co-existence of both these conditions called as osteosarcopenia, coined by Duque et a [5], is a serious concern among older adults. This 'hazardous duet' combines the increased fall risk from sarcopenia, with the bone fragility from osteoporosis and increases risk of falls and fractures as compared to osteoporosis and sarcopenia alone [6,7,8]. The growing interest in osteosarcopenia over recent years has led to publication of few studies on its prevalence. Neilsen et al in their systematic review reported 5-37% of prevalence depending on the classification used. [9]. However, there still lack of studies on global prevalence and contributing risk factors of osteosarcopenia.

The global burden of disease study highlighted significant impact of musculoskeletal conditions on ageing population and identifying it as a second leading cause of disability globally [10]. The development of osteosarcopenia is influenced by various genetic, hormonal, and lifestyle factors (nutrition and physical activity). Genetics affects peak muscle and bone mass impacting musculoskeletal health across adulthood [11], while physical activity supports bone density through muscle loading (Frost's mechanostat hypothesis) [12]. Adequate protein intake supports muscle and bone health, whereas poor nutrition and inactivity cause their atrophy [11]. Menopause-related estrogen decline in women reduces lean mass and bone density, contributing to higher rates of sarcopenia (10%-40%) and osteoporosis (around 30%) in postmenopausal women [13,14]. Hence, identifying the various risk factors in this group is crucial.

Global life expectancy is expected to increase, with the individuals over 60 years projected to increase from 600 million to 2 billion by 2050 [15], thus also leading to a rise in osteosarcopenia prevalence [2]. In 2011, 8.6% of India's population was above 60 years, and this percentage is expected to reach 20% by 2050, presenting a substantial challenge to the country's healthcare system. Around 71% of older adults in India live in rural areas, where factors like nutrition, physical activity and sunlight exposure which influence the risk of sarcopenia and osteoporosis are different from those in urban settings. [16,17]. Also, our previous study reports higher prevalence of sarcopenia in men and women from rural areas. [18]

The increasing prevalence of sarcopenia and osteoporosis in the elderly can significantly affect mobility and quality of life. However, research on osteosarcopenia and its impact on physical function and well-being remains limited. Few studies have explored its association with physical functionality and disabilities. A Japanese study by Kobayashi et al. found osteosarcopenia was strongly associated with muscle weakness [1], while a Mexican study identified its connection to functional disabilities in older adults over 50 years [19].

Few studies have explored the prevalence of osteosarcopenia in women. Hamad et al reported around 64% prevalence of osteosarcopenia among post-menopausal women above 60 years of age. [20]. A study by Wang et al in Chinese population showed higher prevalence of osteosarcopenia in women than men (15% vs 10%) [4]. Also, a study by Huo et al showed higher odds of osteosarcopenia in women. This could lead to a hip fracture potentially resulting in around 13 years of life lost for women aged 65 to 69 years [7].

Studying sarcopenia and osteoporosis in younger post-menopausal women is crucial for early detection and intervention, as risk factors like low bone mineral density and muscle loss often begin early. Hormonal changes and lifestyle factors, such as nutrition and physical activity, may increase the risk of osteosarcopenia. Hence, our study aims to assess the prevalence and determinants of osteosarcopenia and examine its relationship with physical functionality in middle-aged pre- and post-menopausal women from urban and rural areas of Pune, India.

Methods:

Study participants, design, and approvals:

This cross-sectional, observational study was conducted in Pune city (Western Maharashtra, India) and nearby villages from June 2020 until February 2022. Based on available data from a previous study on bone health among Indian men and women (Kadam et al,2010), sample size was calculated (175 from urban and 175 from rural women) by considering attrition rate. All women above age 40 years were approached for the study. Urban women were screened from a tertiary care hospital attending regular health check-up and rural women were screen from the health camps arranged in different villages near Ranjangaon, from Shirur district. Total 565 women were screened from both the places. While screening, women were asked if they are taking any regular medicine to ascertain regarding any medical conditions. Rural women who met the inclusion criteria were enrolled in study. At the time of screening, women were asked if they are taking any medications. As a part of their routine health check, hemogram, fasting blood sugar concentrations and lipid profile tests were performed. Women with high fasting blood sugar levels were advised to undergo post-prandial and HbA1c testing. Based on the results, participants were diagnosed with or without diabetes. Women diagnosed with diabetes were excluded from the study.

Among total screened, 168 women were excluded due to conditions such as diabetes, thyroid disorders, heart disease (n=35), arthritis/other severe bone diseases (n=07), hysterectomy (n=102) and other reasons such as age criteria, metallic implants in bones, presence of any acute illness/ liver/kidney disease etc (n=24).

Women who met the inclusion criteria and who gave written informed consent were included in the study. A total of 397 women, with 182 from urban and 215 from rural areas were enrolled in the study.

Ethics approval was obtained from the Institutional Ethics committee (Jehangir Clinical Development Centre) before enrolment of participants (Approval dated 02/03/2020).
A post-hoc power analysis using G-power confirmed sufficient power (>0.80) for assessing osteoporosis and sarcopenia prevalence ($\alpha = 0.05$, two-tailed).

Anthropometry:

Height was measured using a Seca Portable stadiometer (Hamburg, Germany) to the nearest 0.1 cm and weight was measured using a digital scale of a bioelectrical impedance analyzer (BIA) (Tanita Body Composition Analyzer (Model BC-420MA)) to the nearest 0.1Kg. Body mass index (BMI) was calculated by dividing weight in kg by height in metres squared. Waist circumference (in cm) was measured at the midpoint between the lowest rib and the iliac crest with the help of a SECA tape as per WHO guidelines [21].

Questionnaires about socio-demography and general health status:

Demographic data including age, location (urban or rural), and reproductive history including age at menarche, age at marriage, number of children, age at menopause and general health status were recorded. Urban and rural settings were defined by Census directorate based on administrative units such as municipal corporations, population density, socio-cultural aspects, and occupation such as agriculture. We conducted this community-based study by collecting data from participants visiting rural and urban healthcare centres [22,23]. Socio-economic status was assessed with the help of a questionnaire [24]. Data on other lifestyle related factors including smoking/tobacco habits and sunlight exposure [25], were assessed using validated questionnaires.

Dietary assessment:

Nutrient intake was assessed using a 24-hr diet recall method (one working day) in which women were asked what they had consumed the day before assessment. Total energy, carbohydrate, protein, fat and calcium intake were estimated using C-diet software [26].

Physical activity:

Physical activity was assessed using the Global Physical Activity Questionnaire (GPAQ) [27,28]. This questionnaire was adapted for activities reported from urban and rural areas. The reliability of the questionnaire was tested which showed good internal consistency with Cronbach's alpha of 0.80, while test-retest reliability was assessed by administering the questionnaire to the same participants two weeks apart for which the correlation coefficient was 0.80. The activities were classified as occupational, household, and recreational activities and further categorized into heavy, moderate, and light activities. Activities were recorded as minutes per week.

Biochemical parameters:

A fasting blood sample (5 ml) was collected between 7-9 am in a plain vacutainer (BD-Plymouth, PL6 7BP, UK) by a trained phlebotomist. After centrifugation (2500 rpm for 15 min) serum was separated and stored at -80ºC until analysis. Serum 25 hydroxyvitamin D and serum parathyroid hormone (PTH) was measured by enzyme-linked immunosorbent assay using standard kits (Beckman Coulter, intra-assay coefficient of variation, CV<10%).

Measurement of Bone density and Lean body mass:

Dual Energy X-ray Absorptiometry (DXA) scans (Lunar iDXA-GE Healthcare, Wisconsin, USA, fan beam scanner, Encore software version-16) measured parameters including lean mass, fat mass, bone mass, and BMD at lumbar spine, femur neck and total femur were measured. The machine was calibrated daily using the phantom provided by the manufacturer and was regularly reviewed by the engineers. Scans were performed and analysed by the same operator to reduce variation. The coefficient of variation for lumbar spine and femur BMD was 1%, for lumbar spine BMC 2.8% and total body composition was 1% [29,30]. Lean mass was measured by DXA to calculate total and appendicular skeletal muscle mass (ASM), with ASMI derived as ASM/ (height in m^2). The coefficient of variation (CV) for total lean mass was <1% [29,30].

Measurement of physical functionality

1. Measurement of Handgrip (muscle) strength:

Handgrip strength was measured using a hydraulic type hand dynamometer (JAMAR-Plus Hand dynamometer, Warrenville, IL, USA) with the participant seated in the upright position with 90-degree elbow flexion as the standard position. The dynamometer handle was adjusted to accommodate the participants' hand size and grip strength was measured for both hands [31,32]. Three readings with a rest of 30-seconds were recorded and the average was considered for the assessment.

2. Measurement of muscle function by Short Physical Performance Battery (SPPB)

Muscle function was assessed using the Short Physical Performance Battery (SPPB) [33]. This includes three simple tests: 1) Standing balance test, 2) The 4-m Gait speed test and 3) 5-times chair stand test. Standing balance was assessed by asking the participant to balance for ten seconds with feet side-by-side, then in semi-tandem and tandem positions. Gait speed was assessed at normal walking pace over a four-metre course, and the time taken to rise from a standard chair five times as quickly as possible was recorded. All the tests were scored from 0 to 4 and total score ranging from 0 to 12; higher scores indicate better muscle function [33].

Definitions of sarcopenia, osteoporosis and osteosarcopenia

Sarcopenia was defined as per the Asian Working Group for Sarcopenia (AWGS)-2019 guidelines, as presence of low muscle mass, low muscle strength and low muscle function, with cutoff values for appendicular skeletal muscle index (ASMI) of 7.0kg/m^2 for men and 5.4 kg/m^2 for women by using DXA, handgrip strength <28kg for men and <18kg for women and SPPB score ≤ 9 [31]. Sarcopenia was classified by AWGS into four levels: "No Sarcopenia," "Possible Sarcopenia" (low grip strength, normal muscle mass), "Sarcopenia" (low muscle mass with low grip strength or function), and "Severe Sarcopenia" (low muscle mass, grip strength, and function) [31].

Diagnosis of osteoporosis was based on the WHO classification. [34]. Based on the BMD T-score obtained from DXA scans in healthy young adults of the same sex, women were characterized as having normal bone (T-score < -1 SD), osteopenia (T-score observed between -1 to -2.5 SD) or osteoporosis (T-score ≤ - 2.5 SD).

Osteosarcopenia was defined as presence of both osteoporosis and sarcopenia defined by WHO and AWGS criteria respectively.

Statistical Analysis:

Data were analysed using the IBM SPSS Statistics for Windows, Version 21. Continuous variables were expressed as means and standard deviation or median and IQR and categorical variables were expressed as numbers and percentages. The normality of the variables was tested with Kolmogorov-Smirnov (K-S) test. Independent sample T-test was used for comparison of basic characteristics and bone and muscle parameters between urban and rural pre- and post-menopausal women. We categorized participants into four groups as neither osteoporosis/sarcopenia, osteoporosis alone, sarcopenia alone and osteosarcopenia. Body composition, muscle and bone parameters and biomarkers were compared using one way analysis of variance (ANOVA) or the Kruskal-Wallis test depending on normality of variables. Post-hoc analysis used Dunnet T3 test. Univariate analysis determined factors associated with sarcopenia, osteoporosis and osteosarcopenia. Multivariate analysis adjusted for confounders including significant variables *($p<0.05$)* from univariate analysis to determine independent risk factors in urban and rural population.

<u>Results:</u>

Table 1 summarizes the key characteristics of the study population.

The mean age and height of women studied was similar (urban 51.8 vs rural 50.8yrs and 153.3 vs 152.0cm respectively).The mean age at menopause was 46.9 ± 4 years for rural women and 47.8 ± 4 years for urban women ($p>0.05$). Rural women (both pre- and post-menopausal) had significantly lower intakes of energy, carbohydrates, protein, fat, and calcium compared to their urban counterparts (p <0.05). Tobacco use and adequate sunlight exposure were significantly higher among rural post-menopausal women (p < 0.05), and heavy physical activity was also more prevalent in the rural group (p < 0.05).

Figure 1: Prevalence of osteoporosis, sarcopenia and osteosarcopenia

Prevalence of osteoporosis, sarcopenia and osteosarcopenia in pre- and post-menopausal women is illustrated in **Fig 1.** Overall prevalence of osteoporosis was 31.4% (Urban= 18.1%, Rural=42.6%), sarcopenia was 12.1% (U=3.8%, R= 19%) and osteosarcopenia was 8.3% (U=1.6%, R= 13.9%); all were higher in rural women. Prevalence of osteoporosis was higher in post-menopausal (45.7%) women than pre-menopausal women (4.3%) and was higher in rural post-menopausal women (57.5%) than urban post-menopausal women (28.6%) (p<0.05).

Table 2 compares the physical function, bone health and lifestyle factors between women across four groups: neither osteoporosis nor sarcopenia, osteoporosis alone, sarcopenia alone, and osteosarcopenia. Women with osteosarcopenia were older, shorter, and had the lowest weight, BMI, ASMI, and grip strength (all p<0.05. They also had the slowest gait speed, longest 5T-chair stand time, and lowest SPPB scores, indicating poor physical function. Their bone mineral density (BMD) and T-scores were significantly lower at the spine and femur compared to the other groups (p<0.05). Women with osteosarcopenia showed lower dietary protein and calcium intake, more heavy activity time and higher percentage of tobacco use as compared to women in the other groups (all p <0.05),

Table 3 shows that women with sarcopenia had almost 6 times higher risk (OR= 6.2, 95%CI= 3.2-11.9, $p=0.001$) of developing osteoporosis and the risk remained significant even after adjusting the model for age, location.

Table 4 shows factors determining risk of osteoporosis, sarcopenia and osteosarcopenia among post-menopausal women. Older age, rural residence, lower BMI, menopause, low socioeconomic status, tobacco consumption and inadequate protein intake were all positively associated with risk of osteoporosis, sarcopenia and osteosarcopenia. In multivariate analyses, older age was associated with risk of sarcopenia, and older age and lower BMI were associated with risk of osteoporosis and osteosarcopenia (all $p < 0.05$).

Discussion:

In the present study, we assessed prevalence and risk factors for sarcopenia, osteoporosis and osteosarcopenia in Indian urban and rural, pre- and post-menopausal women. Older rural women showed an alarmingly higher prevalence of osteoporosis (42%), sarcopenia (19%) and osteosarcopenia (13.9%) as compared to urban women (18.1%, 3.8%, 1.6% respectively). Osteosarcopenia was observed only in postmenopausal women, with higher prevalence in rural areas than urban (19.6% vs 2.9%). Women with osteosarcopenia showed poor muscle function indicated by lower grip strength and lower SPPB score. While comparing with osteoporosis / sarcopenia alone, women with osteosarcopenia showed significantly lower ASMI and bone mineral density at the spine and femur. We also found that osteoporosis and sarcopenia were strongly related as women with sarcopenia had six times higher odds for developing osteoporosis. On comparing lifestyle factors, women with osteosarcopenia showed lower protein and calcium intake and a higher percentage used tobacco and were involved in heavy physical activity. Age and lower BMI were found to be significant predictors for osteosarcopenia.

This is the first Indian study on osteosarcopenia. Most studies focus on older adults, with only a handful of studies addressing younger or middle-aged groups, especially in South Asia. In a review by Belchior et al, the prevalence of osteosarcopenia ranged from 5-40% depending on the criteria used for diagnosis, with a greater prevalence in women and consistently higher in old age [35]. A study by Yoshimura et al reported co-existence of osteoporosis and sarcopenia (≥60 years of age) and found 4.7% prevalence of osteosarcopenia with higher prevalence in women than men [36]. Similar findings have been reported in a study by Drey et al from Germany [37]. We found higher rates of osteoporosis (rural-57% urban-28%) than that of sarcopenia (rural- 17%, urban-2.6%) among post-menopausal women. Similar findings were described by Inoue et al., where individuals with the lowest BMD were more likely to have osteosarcopenia [3]. Using the WHO and AWGS criteria, we report an alarming 19.6% prevalence of osteosarcopenia in rural postmenopausal women. Yoshimura et al. reported 4.7% in a four-year study with the same criteria [36]. The difference in the prevalence rates could be due to ethnic differences, non-rural population and differences in techniques used as their study has used bioimpedance analysis to measure mass. Okamura et al. (19.6%) and Inoue et al. (11%) used Japan Osteoporosis Society and AWGS criteria, with Inoue measuring muscle mass via calf circumference. Wang et al. termed it as "sarco-osteoporosis," with a 15% prevalence using bioelectrical impedance analysis [4].

There is a paucity of studies examining urban-rural differences in prevalence of sarcopenia and osteoporosis. Similar to the findings of our study, studies from Korea and China report higher prevalence of sarcopenia in rural [38,39] as compared to urban areas [40]. A systematic review revealed that in lower- and middle-income countries, BMD was lower in rural than urban areas [41]. These rural-urban differences may be explained by differences in body composition i.e. low BMI, lower lean mass and fat mass in rural women than their urban counterparts. This in turn could be mediated by other lifestyle factors such as malnutrition and poor access to food including lower protein and calcium intake, more tobacco use, lower education, and socio-economic status in rural areas as compared to their urban counterparts. Similar exposures such as higher tobacco use and lower protein intake in rural population were found to be associated with sarcopenia in our study. Protein is essential for muscle and bone health, aiding collagen synthesis, calcium absorption, and muscle maintenance. Inadequate intake can reduce muscle mass and function, decreasing mechanical loading on bones, leading to lower bone density and a higher risk of osteoporosis and fractures.

We found a higher prevalence of osteosarcopenia in postmenopausal women from both urban and rural areas, partly due to the decline in estrogen, which is vital for maintaining muscle mass and bone density. Studies by Sipila et al. and Hamad et al. also highlight the linear decline in muscle and bone parameters and the higher prevalence of osteosarcopenia in this group [42,20].

There are very limited studies assessing physical functionality in people with osteosarcopenia. A study by Kobayashi et al from Japan assessed the effect of osteosarcopenia on physical function in a healthy cohort and found 8% prevalence of osteosarcopenia with reduced weight, BMI, grip strength and back muscle strength indicating adversely affected physical function. [1]. Lopez et al also studied the association of osteosarcopenia with functional disability among community dwelling Mexican middle-aged and older adults. They found 8.9% prevalence of osteosarcopenia and found greater association of functional disability with osteosarcopenia than sarcopenia alone [19]. Our findings are in line with both above studies; grip strength and gait speed were significantly reduced in women with osteosarcopenia than in women with sarcopenia or osteoporosis alone [1,19]. The impact on physical function in women with osteosarcopenia could be explained by low ASMI, low BMI, low BMD, lower nutrient intake and higher tobacco intake. In the study by Hamad et al, the authors also found that the group with osteosarcopenia had the lowest body mass index, skeletal mass index, handgrip strength values, and physical performance test results [20].

In the current study, prevalence of sarcopenia was associated with osteoporosis, in line with other reports [13,43]. The six-fold and fourteen-fold greater prevalence of osteoporosis and sarcopenia respectively in individuals with the opposing condition are also in line with previous studies [14,36,]. We found that women with osteosarcopenia had a broad range of musculoskeletal deficits including lower ASMI, grip strength, muscle function and BMD at spine and femur as compared to women with osteoporosis or sarcopenia alone. Similar findings were obtained by Inoue et al and Wang et al [3,4].

Increasing age and lower BMI were significant predictors of osteosarcopenia in our population. A lower BMI in rural women may indicate undernutrition which compromises bone and muscle health. Inadequate caloric intake with low protein intake may lead to frailty which increases risk of falls and fractures. On the other hand, higher BMI of urban women (within healthy range) may have a protective effect on bones as it provides mechanical loading. A systematic review and meta-analysis on osteosarcopenia has identified various environmental factors in addition to some of genetic factors contributing to the etiology of osteosarcopenia [35]. However, there is a paucity of studies that have investigated the influence of lifestyle factors such as nutrition, physical activity, socio-economic status and tobacco consumption on osteoporosis and sarcopenia and none of them have explored their impact on the development of osteosarcopenia. Hamad et al, in their study on post-menopausal women found that insufficient protein and calcium intake and low physical activity were significant risk factors for osteosarcopenia [20]. These findings are in line with our study. Urban women from higher economic status have better access to food, especially protein and calcium rich food which may explain their better musculoskeletal health in our study. However, higher BMI in urban women caused due to unhealthy food habits may lead to an increase in obesity and other related metabolic issues like insulin resistance which may negatively affect bone health.

Though physical activity was one of the important lifestyle factors and determinant of muscle and bone health, it was not found to be significantly associated with osteosarcopenia in our study. We found significant difference in physical activity between urban and rural women. Also, we observed significant difference in physical activity between pre- and post-menopausal rural women. In rural settings, post-menopausal women engage in heavy physical activities such as farming and also some household work, while pre-menopausal women were mainly engaged in childbearing and family care, limiting their outdoor activities. Physical activity influences bone and muscle health, but excessive labour with inadequate nutrition (especially low protein and calcium) increases the risk of fragility, frailty, and fractures in post-menopausal women. Our finding underscores the need to study lifestyle differences across age groups and rural-urban populations. While physical activity benefits musculoskeletal health, adequate nutrition is crucial for its maintenance. Similar findings were reported in a South Indian study by Jayamani et al and a study from North India by Tripathi et al in which rural women were engaged in more vigorous physical activity than urban women. [44,45]

Additionally, in post-menopausal women, declining estrogen levels may contribute to muscle loss and reduced muscle strength and function. Thus, physical activity, hormonal changes, chronic undernutrition and age-related muscle and bone loss may all contribute to these findings. The rural women had poor bone health than their urban counterparts which is in line with study by Zheng et al from China [40]. This probably was due to nutritional deficiencies in protein, calcium and micronutrients and limiyed access to healthcare. Urban women had better bone health in this study possibly due to better nutrition and healthcare access rather than urbanization.

This is the first Indian study on osteosarcopenia prevalence and determinants, also assessing its impact on physical function. The high prevalence of osteosarcopenia in relatively young rural post-menopausal women highlights urgent public health concerns. Unlike most studies on older adults (≥65 years), we included women over age 40 years for early detection and intervention. Strengths include standardized definitions (WHO, AWGS) and DXA assessments. However, as a cross-sectional, single-centre study, causality and generalizability are limited. We assessed limited biochemical markers and did not report fracture data. Larger multicentre studies are needed for deeper insights.

Conclusion:

In the context of ageing of the global and the Indian population, prevalence of osteoporosis, sarcopenia and osteosarcopenia are projected to rise. Alarmingly higher prevalence of osteoporosis, sarcopenia and osteosarcopenia in rural and especially postmenopausal women is a matter of serious concern. Identifying individuals at risk and focussing on modifiable risk factors identified in this study such as nutrition and tobacco consumption is critical for reducing frailty related health outcomes, especially in undernourished, rural, post-menopausal women.

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Conflict of interest: Gauri Bhat, Alex Ireland, Nikhil Shah, Ketan Gondhalekar, Anuradha Khadilkar declare that they have no conflict of interest.

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Table 1: Basic characteristics of women from urban and rural areas categorized as pre- and post-menopausal.

Variables	Urban (182)		Rural (215)	
	Pre-menopausal (n=77)	Post-menopausal (n=105)	Pre-menopausal (n=62)	Post-menopausal (n=153)
Demographic characteristics				
Age (years) [a, b]	45.8 ± 3.6	57.7 ± 5.7	45.1 ± 4.1	56.5 ± 5.9
Age at menarche (years)	13.7 ± 1.6	14.0 ± 1.7	14.1 ± 1.4	14.1 ± 1.6
Age at marriage (years) [b, c, d]	22.5 ± 4.2	21.9 ± 4.3	17.2 ± 3.0	16.0 ± 2.5
Socio-economic status				
Lower/Middle n (%) [c, d]	5 (6.5%)	6 (5.7%)	34 (54.8%)	90 (58.8%)
Higher n (%) [c, d]	72 (93.5%)	99 (94.3%)	28 (45.2%)	63 (41.2%)
Dietary intake				
Energy (kcal) [b, c, d]	1550 ± 350	1483 ± 337	1285 ± 406	1068 ± 314
Protein (gm/day) [b, c, d]	37 ± 10	35 ±15	30 ± 14	24 ± 8.3
Carbohydrate (gm/day) [b, c, d]	251 ± 61	245 ± 53	208 ± 59	183 ± 52
Fat (gm/day) [b, c, d]	42 ± 16	39 ± 15	35 ± 17	25 ± 12
Calcium (gm/day) [b, c, d]	416 ±158	434 ± 357	320 ± 138	278 ± 117
Other lifestyle factors				
Tobacco intake n (%) [b, c, d]	4 (5.2%)	8 (7.6%)	11 (17.7%)	71 (46.4%)
Adequate Sunlight exposure n (%) [c, d]	1 (1.3%)	2 (1.9%)	19 (30.6%)	57 (37.3%)
Physical Activity				
Heavy Activity(min/week) [c, d] (mean ± SD)	72 ± 433	37 ± 284	756 ± 1271	1165 ± 1396
Moderate Activity (min/week) (mean ± SD)	1758 ± 1398	1158 ± 1130	1372 ± 1198	968 ± 910
Light Activity (min/week) [d] (mean ± SD)	2014 ± 1361	1607 ± 957	1537 ± 811	1064 ± 777
Anthropometry				
Height (cm)	153.4 ± 5.8	153.3 ± 5.3	152.7 ± 5.8	151.2 ± 5.9
Weight (kg) [b]	64.7 ± 10.2	65.0 ± 10.8	62.6 ± 9.9	54.5 ± 11.2
BMI (kg/m^2) [b]	27.5 ± 4.2	27.6 ± 4.2	26.9 ± 4.4	23.8 ± 4.6
Waist circumference(cm) [b, c]	85.8 ± 8.9	87.6 ± 9.7	82.2 ± 8.9	76.7 ± 11.0
Muscle and Bone health parameters				
Muscle mass (kg)	35.1 ± 4.4	34.6 ± 4.1	34.3 ± 4.0	30.7 ± 4.0
ASMI (kg/m^2)	6.9 ± 0.8	6.7 ± 0.8	6.7 ± 0.8	5.9 ± 0.8
Grip strength (kg)	19.6 ± 4.9	18.4 ± 4.6	17.1 ± 4.0	14.9 ± 3.7
Muscle function score	11.5 ± 0.9	10.8 ± 1.2	10.6 ± 1.7	9.8 ± 2.1
BMD at Spine (g/cm^2)	1.12 ± 0.14	0.96 ± 0.14	1.09 ± 0.12	0.88 ± 0.15
BMD at total femur (g/cm^2)	0.98 ± 0.11	0.89 ± 0.12	0.99 ± 0.10	0.83 ± 0.13

Data represented as mean ± SD, n (%), and as median (IQR) BMI-Body Mass Index
Physical activity presented as mean ± SD and median (IQR)
a Statistically significant difference between pre- and post-menopausal urban women
b Statistically significant difference between pre- and post-menopausal rural women
c Statistically significant difference between pre-menopausal urban and pre-menopausal rural women
d Statistically significant difference between post-menopausal urban and post-menopausal rural women

Table 2: Comparison of physical function (Grip strength, Gait speed and 5T-chair stand test), bone health and lifestyle factors between women with osteosarcopenia, osteoporosis alone, sarcopenia alone and neither (n=398)

Characteristics	**Neither Osteoporosis / Sarcopenia (n= 258)**	**Osteoporosis alone (n=92)**	**Sarcopenia alone (n=15)**	**Osteosarcopenia (n=33)**	**P value**
Age (Years)	50.4 ± 7.0	57.7 ± 6.0[*a]	54.1±6.8	59.8 ± 5.4[*a]	<0.001
Height (cm)	153.2 ± 5.5	150.6 ± 5.5[*a]	154.3 ± 6.1	150.5 ± 7.2	<0.001
Weight (kg)	64.7 ± 10.7	56.4 ± 8.2[*a]	50.2 ± 7.6[*a]	44.0 ± 6.1[*a b]	<0.001
BMI (kg/m^2)	27.6 ± 4.4	24.8 ± 3.5[*a c]	20.9 ± 2.2[*a b]	19.4 ± 2.1[*a b]	<0.001
ASMI (kg/m^2)	6.7 ± 0.8	6.2 ± 0.6[*a]	5.1 ± 0.2[*a b]	4.9 ± 0.3[*a b]	<0.001
Grip strength (kg)	18.1 ± 4.7	16.1 ± 4.0[*a]	13.9 ± 2.3[*a]	13.2 ± 2.9[*a b]	<0.001
Gait speed (min)	4.2 ± 0.6	4.6 ± 1.2[*a]	4.6 ± 0.7	4.7 ± 1.1[*a]	<0.001
5T-chair stand time (min)	11.4 ± 2.6	12.4 ± 3.2[*a]	13.6 ± 4.7[*a]	13.0 ± 4.2[*a]	0.001
SPPB score	10.9 ± 1.4	10.0 ± 2.2[*a]	9.8 ± 2.0	9.5 ± 2.0[*a]	<0.001
Spine L1-L4 BMD (g/cm^2)	1.08 ± 0.12	0.79 ± 0.07[*a c]	0.99 ± 0.09[*a b]	0.75 ± 0.08[*a b c]	<0.001
Femur total BMD (g/cm^2)	0.97 ± 0.11	0.80 ± 0.10[*a]	0.86 ± 0.08[*a]	0.71 ± 0.08[*a b c]	<0.001
Spine L1-L4 T-score	-0.92 ± 0.99	-3.24 ± 0.57[*a c]	-1.58 ± 0.74[*a b]	-3.57 ± 0.67[*a b c]	<0.001
Femur total T-score	-0.29 ± 0.89	-1.62 ± 0.82[*a]	-1.14 ± 0.70[*a]	-2.29 ± 0.65[*a b c]	<0.001
Vitamin D (ng/ml)	27.2±10.2	27.5±11.6	26.4±7.8	24.6±9.9	0.828
PTH (pg/ml)	52.5±23.9	54.2±23.9	48.1±20.7	52.6±23.7	0.928
Lifestyle factors					
Dietary protein intake (gm/day)	33 ± 13	27 ± 9	25 ± 8	23 ± 13	<0.001
Dietary calcium intake (mg/day)	378 ± 257	314 ± 138	300 ± 111	280 ± 168	0.016
Heavy physical activity (min /week)	0 (0) 449 ± 1044	0 (2100) 831 ± 1279	0 (1440) 796 ± 1322	0 (2730) 1018 ± 1366	0.050
Sunlight exposure (min/day)	58 ± 81	80 ± 90	80 ± 78	90 ±103	0.061
Tobacco use (%)	12.8%	39.1%	40%	60.6%	0.050

BMI- Body Mass Index, ASMI- Appendicular Skeletal Muscle Index, 5T-5-times, SPPB- Short Physical Performance Battery, BMD- Bone Mineral Density

Significant differences between the groups are indicated by asterisks, comparing against women without either condition, osteoporosis alone, and sarcopenia alone.

***a compared with neither osteoporosis nor sarcopenia**

***b compared with osteoporosis alone**

***c compared with sarcopenia alone**

Table 3: Relationship of sarcopenia with osteoporosis

Variables	Dependent Variable- Osteoporosis			
	Unadjusted model OR (95%CI)	Adjusted Model 1 OR (95%CI)	Adjusted Model 2 OR (95%CI)	Adjusted Model 3 OR (95%CI)
Sarcopenia	6.2 (3.204-11.878) ***	3.9(1.886-7.954) ***	2.4 (1.134-5.216) **	1.0 (0.441-2.491)
*** $p<0.001$, **$p<0.05$ Model 1: adjusted for age, Model 2: adjusted for age, location Model 3: adjusted for age, location, fat mass				

Table 4:

Factors determining risk of osteoporosis, sarcopenia and Osteosarcopenia among urban and rural women.

	Univariate analysis				Multivariate analysis			
Sarcopenia		95%CI				95%CI		
Parameter	OR	LOWER	UPPER	P value	OR	LOWER	UPPER	P value
Age	1.1	1.06	1.15	0.001	1.1	0.98	1.15	0.134
Rural residence	5.9	2.55	13.41	0.001	1.3	0.34	4.66	0.738
Low BMI	0.5	0.43	0.61	0.001	0.5	0.44	0.65	0.001
Menopause	9.6	2.91	31.43	0.001	2.2	0.42	11.08	0.358
Low SES	3.8	2.05	7.18	0.001	0.9	0.34	2.44	0.859
Tobacco intake	4.8	2.57	8.99	0.001	1.4	0.59	3.44	0.426
Inadequate protein	0.4	0.17	0.93	0.001	0.9	0.25	2.99	0.826
Osteoporosis								
Age	1.2	1.13	1.22	0.001	1.1	1.07	1.19	0.001
Rural residence	3.4	2.17	5.32	0.001	1.8	0.86	3.78	0.113
Low BMI	0.8	0.76	0.85	0.001	0.8	0.81	0.93	0.001
Menopause	18.7	8.0	43.9	0.001	3.8	1.3	11.1	0.014
Low SES	2.6	1.70	4.11	0.001	1.4	0.74	2.71	0.286
Tobacco intake	4.8	2.98	7.94	0.001	2.1	1.09	3.88	0.025
Inadequate protein	2.1	1.25	3.54	0.001	0.8	0.44	1.79	0.743
Osteosarcopenia								
Age	1.2	1.08	1.21	0.001	1.2	1.06	1.25	0.001
Rural residence	9.6	2.9	32.1	0.001	1.2	0.19	7.58	0.836
Low BMI	0.5	0.41	0.62	0.001	0.6	0.44	0.69	0.001
Low SES	0.2	0.07	0.36	0.001	1.7	0.50	5.53	0.395
Tobacco intake	5.9	2.83	12.50	0.001	1.6	0.59	4.56	0.342
Inadequate protein	3.0	1.03	8.76	0.001	0.9	0.19	4.85	0.972

Figure 1: Prevalence of osteoporosis, sarcopenia and osteosarcopenia

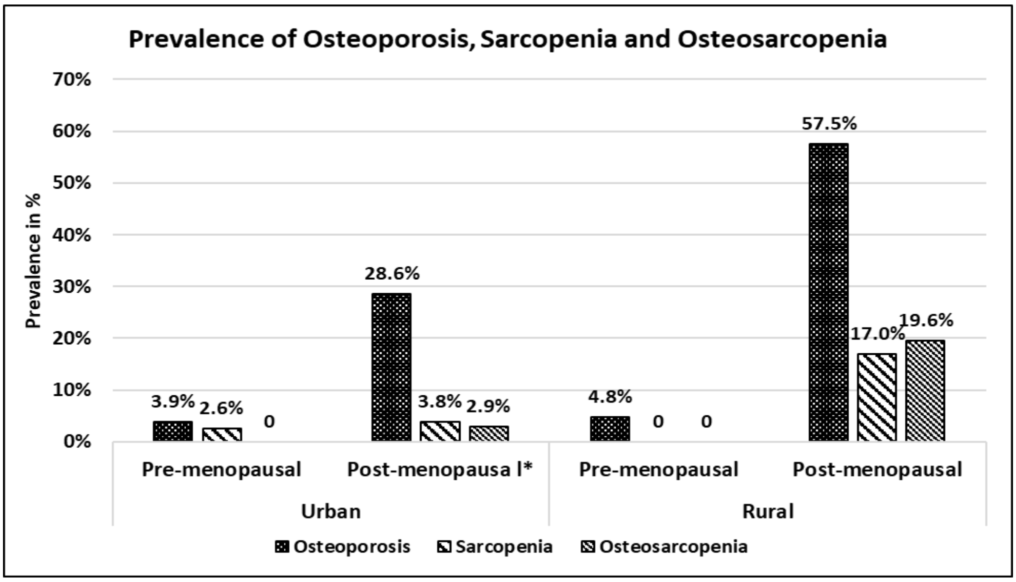

Figure 1Prevalence of osteoporosis, sarcopenia and osteosarcopenia among urban and rural pre- and post-menopausal women.
*Indicated significant differences among subgroups (p<0.05)