



# The combined role of diabetes and obesity in susceptibility to musculoskeletal disorders and its subtypes in older men and women in India

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## Abstract

**Background and aims** In later life, diabetes and obesity can cause a change in musculoskeletal systems that can lead to aching joints and a myriad of other musculoskeletal disorders such as arthritis, osteoporosis, rheumatism, bone fractures etc., resulting in significant morbidity including pain and disability. There is a paucity of research to know how comorbidity of diabetes and obesity increase musculoskeletal disorders among older people. Therefore, the present study used nationally representative data to examine the interaction of diabetes and obesity on musculoskeletal disorders and its subtypes including arthritis, osteoporosis, and rheumatism among older men and women in India.

**Methods** Data were extracted from the first wave of the nationally representative survey Longitudinal Aging Study in India (LASI) conducted in 2017-18. The final sample includes 31,464 people aged 60 years or above. Primary outcome variable was any listed musculoskeletal disorders and secondary outcomes were its subtypes including arthritis, osteoporosis, and rheumatism based on self-reported questions. Diabetes and obesity based on anthropometric index of weight and height (i.e., body mass index (BMI) with a standard cut-off of 30 kg/m<sup>2</sup> or over) were considered as explanatory variables of interest. Logistic regression was used to assess the relationship between diabetes and musculoskeletal disorders. Interaction analysis was performed by both additive and multiplicative scales.

**Results** Comparing older people without diabetes, the prevalence of musculoskeletal disorders and its subtypes were higher among those with diabetes, particularly arthritis disorders in older women. Diabetes was significantly correlated with the risk of musculoskeletal disorders and its subtypes including arthritis and osteoporosis even after controlling potential factors. The combination of diabetes and obesity was significantly and positively associated with musculoskeletal disorders (aOR: 4.14; p-value < 0.0001; 95% CI: 1.96 to 8.74) and its subtype only arthritis (aOR: 4.36; p-value < 0.0001; 95% CI: 1.76 to 10.8) comparing to those without both the conditions. However, the association was strong for older women as compared to older men. Notwithstanding, multiplicative scale interaction showed statistically significant for musculoskeletal disorders and its three subtypes among older women, however it was not significant for osteoporosis and rheumatism disorders among older men. When we analyzed interaction on additive scale, we found it only for arthritis disorder among older women suggesting the risk from obesity (relative excess risk due to interaction (RERI): -0.83, 95% CI: -1.44 to -0.22, attributable proportion due to interaction (AP): -0.54, 95% CI: -1.05 to -0.03, synergy index (S): 0.39, 95% CI: 0.16 to 0.93) was additive to the risk from diabetes.

**Conclusions** This study suggests an elevated risk of musculoskeletal disorders among Indian older adults with diabetes. The result of this study also suggests an interactive association of diabetes and obesity with musculoskeletal disorders, particularly with arthritis disorder. There is a need to pay attention to the BMI level while treating diabetes in Indian older population.

**Keywords** Diabetes · Musculoskeletal disorders · Obesity · Older people · India

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## Introduction

Diabetes has been one of the major global health emergencies of the 21st century across the globe in general and low- and middle-income countries in particular. In India, the burden of diabetes has been increasing over the three decades (from 5.5% to 1990 to 8.9% in 2019), however, the speed of rate become faster since the year 2000 [1]. India is a major contributor to the global burden of diabetes and is considered the diabetic capital of the world because of a dramatic change in demographic structure and a shift in disease pattern over two decades [1, 2]. In India, the increased aging population is contributing a greater share of the country's burden of diabetes with a higher prevalence among older people compared to the middle-aged or younger age group [3]. The main causes of rising diabetes prevalence are changes in behavioral and lifestyle factors, such as physical inactivity, unhealthy diets, smoking, and excessive alcohol consumption. A well-known fact is that diabetes can lead to health complications in later life if it is not adequately managed.

Diabetes is a chronic metabolic disease that includes both type 1 diabetes (T1D) and type 2 diabetes (T2D). It is characterized by hyperglycemia and high glycated hemoglobin with or without glycosuria and is recognized as an important cause of premature death and disability [4]. Diabetes has appeared as one of the key risk factors not only for metabolic abnormalities but also for a wide range of other disabling and life-threatening problems that can result in disability and lower quality of life. Higher blood glucose level increases the risk of both chronic and acute microvascular and macrovascular complications, dysfunction, higher mortality, and higher institutionalization, particularly in the older population [5, 6]. The likelihood of diabetes and its related complications and mortality is more likely to occur in older ages than in younger counterparts [7]. Therefore, the management of diabetes in the older population always requires special care and attention.

Furthermore, diabetes can cause changes in musculoskeletal system including muscles, bones, joints, and ligaments. Diabetes can cause musculoskeletal systems in a variety of ways. For instance, hyperglycaemia which is a central disorder in diabetes or a disturbance in insulin metabolism may cause neuropathic changes by harming or damaging the nerves and bones [8]. Also, diabetic amyotrophy, a different form of neuropathy is characterized frequently by weakness followed by wasting of muscles, and excruciating pain in the muscles of the lower extremities including the thigh, hip, and buttocks making them weak [9, 10]. Similarly, diabetic cheiroarthropathy, a disorder to limit joint mobility in the upper extremities is a cutaneous condition characterized by the thickening of the skin resulting in a contracture of the

fingers as a result of vascular insufficiency [10–12]. Growing studies revealed that there is a range from very rare to more common muscle and skeletal problems in the individual with diabetes including hand abnormalities (carpal tunnel syndrome or dupuytren's contracture), shoulder pain, osteoarthritis, limited joint ability and other bone diseases [9, 13, 14]. In low- and middle-income countries, the burden from musculoskeletal disorders that may pose a significant concern for the health system owing to rapidly aging populations and rising diabetes prevalence, which are two of the major risk factors for dysfunctional musculoskeletal system [15].

Elevated body mass index (BMI) has emerged with diabetes as the pandemic and most prevalent health risk in developing nations, and both chronic diseases with multifactorial etiology contribute to health problems. Subsequently, it has also a number of implications in terms of the musculoskeletal system [16]. A number of research indicated that BMI has a positive association with bone mineral density (BMD) [17–19]. Sarcopenic obesity, a disorder characterized by excess of adiposity can induce oxidative stress, systematic inflammation, and insulin resistance, all of which may have contributed to the loss of skeletal muscle mass and function [20]. It is evident that being obese (BMI  $\geq 30$ ) could affect chronic musculoskeletal conditions in a rapidly aging population and may provide a significant barrier to their physical and social well-being [21].

Above discussed chronic conditions including diabetes and obesity share common pathophysiological pathways of insulin resistance that include chronic inflammatory responses and hyperglycemia, which leads to the systematic changes in body organs [22, 23]. Therefore, there might be a possible underlying mechanism in which obesity and diabetes may mutually contribute to the development of musculoskeletal disorders. These conditions are expected to increase in developing countries particularly due to rapidly aging populations which makes the importance of the present study. India has been experiencing increasing prevalence of diabetes and obesity over the period, it may be speculated that these conditions may mutually significantly increase the morbidity, mortality and poor quality of life.

To date, there is a paucity of large-population based study to understand the underlying mechanism of action of obesity and diabetes mellitus on musculoskeletal disorders in an older population. To fill this resource gap in India, the Longitudinal Aging Study in India (LASI) focused on middle-aged to older adults, a sister study of the global family of longitudinal health and aging studies in more than 30 countries, is an initiative [24]. Therefore, the present study used data from the LASI survey and aimed to examine the interaction of diabetes and obesity on musculoskeletal disorders and its subtypes among older people in India. Gender

or sex becomes a significant factor in analyzing the health of individuals. Numerous studies have pointed out gender-related differences in diabetes in recent years and it is discussed that women are disproportionately affected by T2D [25–27]. Therefore, all the analyses were also gender-stratified. A conceptual framework has been given in Fig. 1.

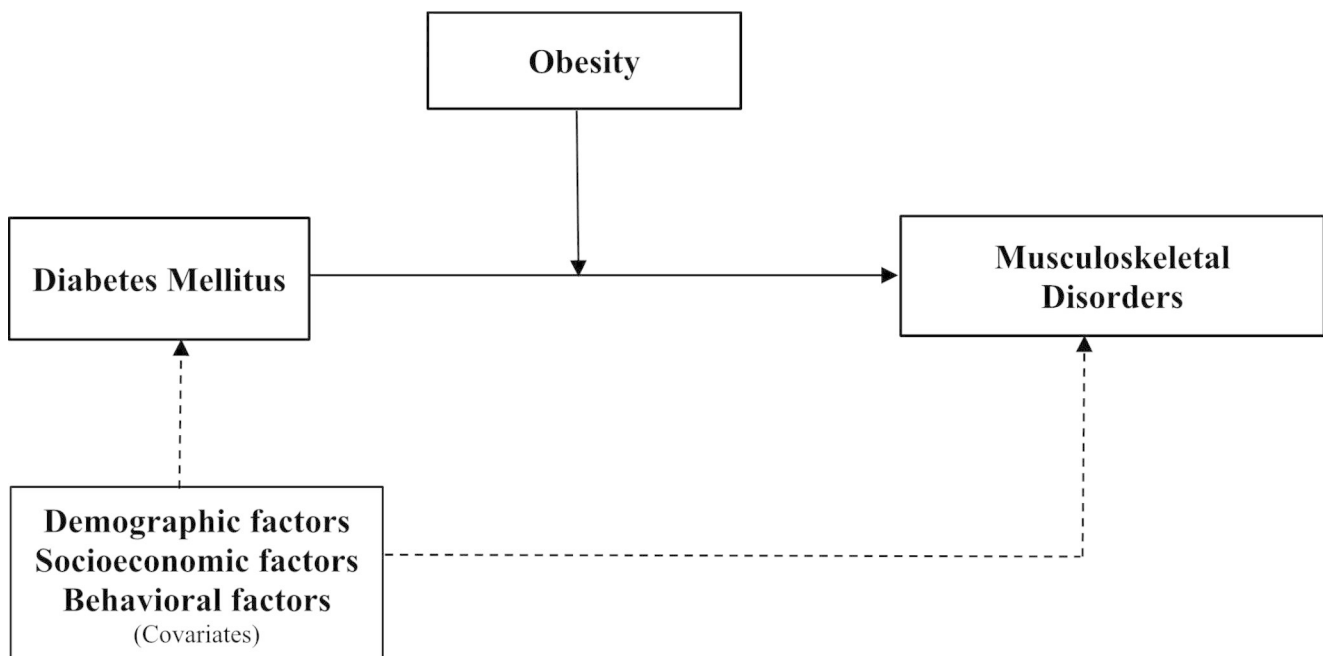
## Material & methods

### Study design and participants

This study utilized the data from the first wave of the nationally representative survey Longitudinal Aging Study in India (LASI) conducted in 2017–18. LASI is a large-scale nationally representative data covering people aged 45 and above. The prime objective of this survey is to provide information on the health, economic, social, and psychological behaviors of older adults in India. In the first wave, LASI adopted a multistage stratified area probability cluster sampling design, and a final sample of 72,250 individuals aged  $\geq 45$  years and their spouses (irrespective of age) from all States (except Sikkim) and Union Territories (UTs) were included in the survey. Informed consent was taken from all eligible participants to ensure anonymity and to inform them about the goals of the survey. The ethical guidelines for data collection in LASI were approved by the Indian Council of Medical Research (ICMR). The present study included 31,464 older people aged 60 years or above in the final analytical sample.

### Sampling procedure

LASI wave 1 survey adopted a three-stage sampling design in rural areas and a four-stage sampling design in urban areas. In each state/UT, the first stage involved the selection of Primary Sampling Units (PSUs), that is, sub-districts (Tehsils/Talukas), and the second stage involved the selection of villages in rural areas and wards in urban areas in the selected PSUs. In rural areas, households were selected from selected villages in the third stage. However, sampling in urban areas involved an additional stage. Specifically, in the third stage, one Census Enumeration Block (CEB) was randomly selected in each urban area. In the fourth stage, households were selected from this CEB. The goal was to select a representative sample in each stage of sample selection. The major objective of the LASI is to estimate the prevalence of chronic diseases among the middle-aged and older population across the socioeconomic spectrum in India and its states and union territories. Therefore, the minimum necessary estimated sample size is 1,000 age-eligible persons to obtain reliable estimates of disease prevalence by state or union territory and by social and economic stratum for the smallest states or union territories. Further, an individual survey schedule was administered to each consenting respondent age 45 and above and their spouses (irrespective of age) in the sampled households. In addition, the LASI included an individual module on biomarkers and direct health examination. Detailed information on ethical protocols, survey design, and sampling procedure data collection is available in the LASI India report [28].



**Fig. 1** Conceptual framework

## Variables of interest

### Outcome variable: musculoskeletal disorders outcomes

Primary outcome of the present study was musculoskeletal disorders and it was coded as 1 “Yes” if one of our prespecified secondary outcome (arthritis, osteoporosis, and rheumatism) occurred and 0 “No” otherwise. Secondary outcomes were assessed using the following question: “*Has any health professional ever diagnosed you with the Arthritis/Osteoporosis/rheumatism?*” These three listed musculoskeletal disorders were considered as three different outcome variables for secondary outcome. All three variables were coded as 1 “Yes” and 0 “No”.

### Explanatory variable: diabetes

Information regarding diabetes mellitus was based on the self-reported question: “*Has any health professional ever diagnosed you with the Diabetes or high blood sugar?*”. In the epidemiological study, either self-reported or medical records of chronic diseases were applied to estimate their incidence and prevalence [29]. Self-reported diabetes was found to be the most accurate with a higher level of agreement among all the chronic diseases. Therefore, this self-reported diabetes was taken as an exposure variable in the present study. An individual with self-reported diabetes was coded as 1 “Yes” and without condition was coded as 0 “No”.

### Explanatory variable: obesity

The LASI survey included several internationally validated, relatively inexpensive, and logistically feasible

biomarker tests. There were some anthropometric measurements including height, weight, waist circumference, and hip circumference taken at the participant’s home by trained staff. Therefore, body mass index (BMI) was calculated by dividing an individual’s weight (in kilograms) by the square of their height (in meters). Obesity was considered based on a standard cut-off ( $BMI \geq 30 \text{ kg/m}^2$ ) according to World Health Organization (WHO) classification. A dichotomous variable was created to measure obesity status in older people and coded as 1 “Yes” and 0 “No”.

### Covariates

Several covariates were taken in the present study. Age was categorized into three age groups 60–69 years, 70–79 years, and 80 or more years. Marital status was classified as currently in union and currently not in the union. Educational attainment was categorized into no education, primary,

secondary, and higher. Religion was coded as Hindu, Muslim, and others. Place of residence was given as rural and urban. Living arrangement was categorized as living alone and living with somebody (living with spouse and/or others, living with spouse and children, living with children and others, and living with others only).

Information on the monthly per capita expenditure (MPCE) of the households was used to determine the wealth status of the respondents. MPCE is defined as the total monthly household consumption expenditure divided by household size and coded as poor, middle, rich. Includes household’s per capita spending on food and non-food items including spending on health, education, utilities etc. It was assessed using household consumption data. A set of 11 questions on the expenditures on food items and 29 questions on expenditures on non-food items were used to canvass the sampled households [28].

Social groups were classified as Scheduled Caste (SC), Scheduled Tribe (ST), Other Backward Class (OBC), and others. It is worth mentioning that social groups are legally designated groupings of individuals who are among India’s most disadvantaged socioeconomic groups. The SC, ST, and OBC are structurally discriminated members of groups experiencing stigma, limited access to education, lower asset holding and reduced access to health and healthcare. Additionally, these disadvantaged groups face various barriers due to their multiple identities, such as age and gender, which exacerbates disadvantages in the social-economic sphere affecting their nutrition and health. Among these social groups, SC and ST people are entitled to more government benefits because they are more deprived and backward than OBC people.

Pain was coded as Yes (if any individual troubled with pain Rarely/Occasionally/Frequently) and No (never troubled with pain). Alcohol consumption was categorized as frequent (weekly and several times a week) and non-frequent (occasionally and never). Smoking was classified as current smoker and not current smoker. Physical activity was coded as frequent (every day), rare (more than once a week, once a week, and 1–3 times a month), and never (hardly ever or never).

### Statistical analysis

Descriptive statistics was performed for study participants. A chi-square test was utilized to determine whether there is a statistically significant between gender and study variables. Bivariate analysis was used to examine the prevalence of musculoskeletal disorders and its subtypes (arthritis, osteoporosis, and rheumatism). Further, binary logistic regression models were used to assess the relationship of diabetes with musculoskeletal disorders outcomes. Model 1 was adjusted

for demographic and socioeconomic variables (for age, education, religion, caste, marital status, monthly per capita expenditure, living arrangement, and place of residence), whereas Model 2 was adjusted for the variables adjusted in Model 1, behavioral factors (alcohol consumption, smoking status, and physical activity) and pain. We also performed subgroup analysis and four different combinations were created after categorizing the respondents according to the presence of diabetes with or without obesity. Unadjusted odds ratios (uOR) and adjusted odds ratios (aOR) along with 95% confidence intervals (95% CI) were calculated.

In the clinical perspective, there is an importance of the way that how joint effects and interactions between risk factors should be evaluated. The Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines suggested that authors should perform interaction analysis in both additive and multiplicative scales when examining the combined effect of two or more risk factors [30]. Therefore, we performed interaction analysis (i.e., interaction of diabetes and obesity) on both additive and multiplicative measures simultaneously. To determine the interactive effect on multiplicative scale, an interaction term of diabetes and obesity was included in the logistic regression and models were controlled for the potential covariates including individual demographic, socioeconomic, and behavioral factors. If interaction term was found significant, we considered joint effect of diabetes and obesity on respective musculoskeletal disorders. Additive interaction or synergic effects of diabetes and obesity on musculoskeletal disorders were estimated using the relative excess risk due to interaction (RERI), attributable proportion due to interaction (AP) and synergy index (S). Formulas for these measures are as follow:

$$RERI = RR_{Diabetes+Obesity+} - RR_{Diabetes+Obesity-} - RR_{Diabetes-Obesity+} + 1$$

$$AP = \frac{RERI}{RR_{Diabetes+Obesity+}}$$

$$S = \frac{RR_{Diabetes+Obesity+} - 1}{(RR_{Diabetes+Obesity-} - 1) + (RR_{Diabetes-Obesity+} - 1)}$$

Where  $RR_{Diabetes+Obesity+}$ ,  $RR_{Diabetes+Obesity-}$ , and  $RR_{Diabetes-Obesity+}$  represents the logistic regression adjusted estimated RR of the covariates of diabetes and obesity, diabetes but not obesity, and obesity but not diabetes, respectively. RERI and AP greater than 0 and value of S greater than 1 indicated an additive interaction or synergic effect between diabetes and obesity. Multiplicative interaction was examined using the following formula:

$$Multiplicative\ interaction = \frac{OR_{Diabetes+Obesity+}}{(OR_{Diabetes+Obesity-} \times OR_{Diabetes-Obesity+})}$$

A two-tailed P value < 0.05 was regarded as statistically significant. Also, individual weights were used to make the estimates nationally representative. For all the analyses, STATA version 16 has been used [31].

## Results

Of 31,464 individuals aged 60 years or above, there were 47% older men and 53% older women. About 58% of the older men and nearly 59% of older women were in the age group 60–69 years. Among older men, almost 72% resided in rural areas, nearly 18% were not in marital union, and about 11% have had family history of diabetes. For older women, approximately 56% were not in their marital union, nearly 15% had family history of diabetes, and about 73% were without education. In the study sample, 25.05% of older men and only 3.37% of older women were currently smoker, whereas 9.25% of older men and 1.15% of older women were consuming alcohol frequently. The prevalence of diabetes was nearly 15% and 14% among older men and women, respectively. The prevalence of musculoskeletal disorders was 22.6% and 15.9% among older men and women, respectively. Whereas, the prevalence of arthritis (8.6%: men vs. 13%: women), osteoporosis (4.2% vs. 5.2%), rheumatism (6.3% vs. 9.2%) was higher among older women as compared to older men (Table 1).

The prevalence of musculoskeletal disorders and its subtypes was higher among individuals with diabetes compared to their counterparts without diabetes and it was relatively higher for older women. The prevalence of musculoskeletal disorders among individual with diabetes was 18.8% and 35.49% for older men and women, respectively (Fig. 2). Among including musculoskeletal disorders, the prevalence of arthritis was higher among older people with diabetes and older women in particular.

Diabetes was significantly and positively associated with the risk of musculoskeletal disorders and its subtypes including arthritis and osteoporosis based on crude odds ratios (uOR) and 95% confidence intervals (CIs) for diabetes in both gender-stratified models. After adjusting demographic and socioeconomic variables (Model 1) and behavioral factors (Model 2), the association was similar to those of the crude model. However, the association between diabetes and arthritis disorder was strong for older women whereas association between diabetes and osteoporosis disorder was stronger for older men. Musculoskeletal disorders were 1.28 times prevalent among older men reporting diabetes as older men with no diabetes (aOR: 1.25; p-value < 0.0001; 95% CI: 1.02 to 1.59), whereas it was 1.79 times as prevalent among older women reporting diabetes as women with no diabetes even after controlling potential covariates (aOR:

**Table 1** Characteristics of study participants by gender

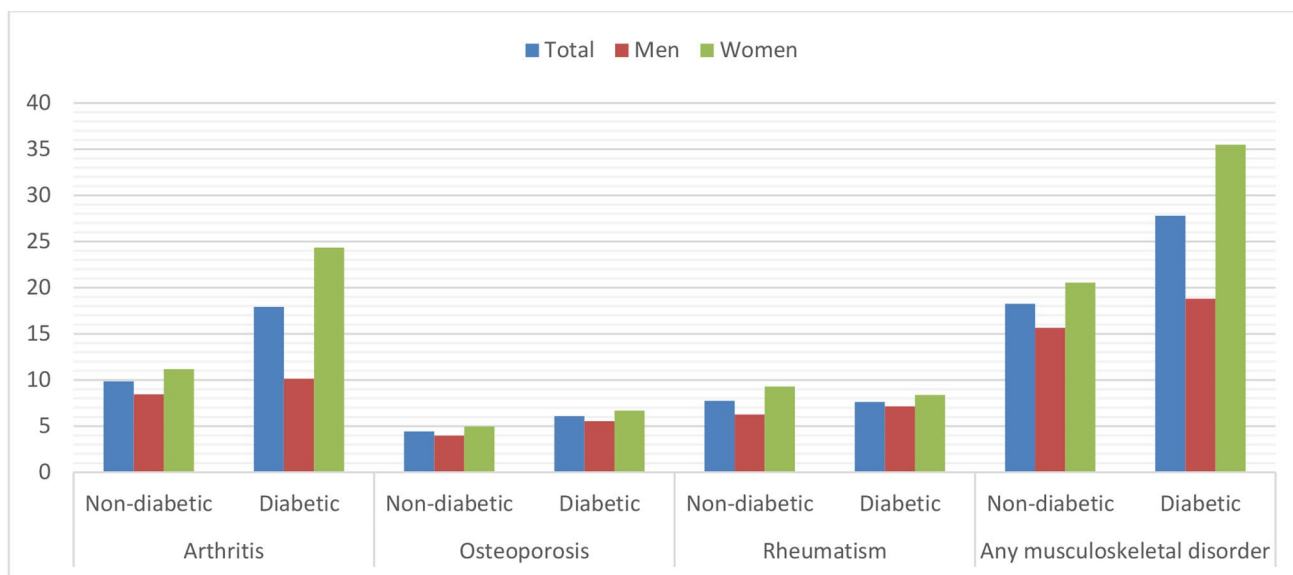
Characteristics	Men (n = 15,098) n (%)	Women (n = 16,366) n (%)	P-Value
<i>Outcome variables</i>			
<b>Musculoskeletal disorders</b>			
No	12,694 (84.08)	12,673 (77.43)	< 0.0001
Yes	2,403 (15.92)	3,693 (22.57)	
<b>Arthritis</b>			
No	13,811 (91.51)	14,190 (86.71)	< 0.0001
Yes	1,281 (8.49)	2,175 (13.29)	
<b>Osteoporosis</b>			
No	14,443 (95.66)	15,507 (94.77)	< 0.0001
Yes	655 (4.34)	859 (5.23)	
<b>Rheumatism</b>			
No	14,137 (93.64)	14,853 (90.75)	< 0.0001
Yes	960 (6.36)	1,513 (9.25)	
<i>Explanatory variables</i>			
<b>Diabetes</b>			
No	12,594 (85.39)	13,927 (86.06)	< 0.0001
Yes	2,444 (14.61)	2,416 (13.94)	
<b>Obesity (BMI <math>\geq</math> 30 kg/m<sup>2</sup>)</b>			
No	13,065 (97.21)	13,352 (92.09)	< 0.0001
Yes	444 (2.79)	1,189 (7.91)	
<i>Covariates</i>			
<b>Demographic Factors</b>			
<b>Age (in years)</b>			
60–69	8,961 (57.82)	10,013 (59.13)	< 0.0001
70–79	4,545 (31.14)	4,556 (29.13)	
80	1,592 (11.04)	1,797 (11.52)	
<b>Residence</b>			
Urban	5,021 (27.95)	5,718 (30.82)	0.002
Rural	10,077 (72.05)	10,648 (69.18)	
<b>Marital Status</b>			
Currently in union	12,506 (81.72)	7,584 (44.36)	< 0.0001
Not in union	2,592 (18.28)	8,782 (55.64)	
<b>Social group</b>			
SC	2,448 (19.26)	2,692 (19.56)	0.15
ST	2,436 (7.92)	2,737 (8.73)	
OBC	5,781 (47.03)	6,105 (45.93)	
Others	3,970 (25.8)	4,248 (25.78)	
<b>Religion</b>			
Hindu	11,078 (82.12)	11,959 (82.48)	0.496
Muslim	1,804 (11.73)	1,927 (10.89)	
Others	2,186 (6.14)	2,444 (6.63)	
<b>Family history of diabetes</b>			
No	12,952 (88.35)	13,751 (85.41)	< 0.0001
Yes	2,007 (11.65)	2,450 (15.12)	
<i>Socioeconomic factors</i>			
<b>Education</b>			
No Education	5,479 (38.6)	11,410 (72.7)	< 0.0001
less than 5 years	2,184 (14.52)	1,597 (8.65)	
5–9 years	3,850 (24.11)	2,167 (12.16)	
10 or more years	3,585 (22.78)	1,192 (6.48)	
<b>MPCE Quintile</b>			
Poor	6,103 (42.15)	6,858 (44.56)	0.007



**Table 1** (continued)

Characteristics	Men (n = 15,098) n (%)	Women (n = 16,366) n (%)	P-Value
Middle	3,064 (21.6)	3,352 (20.35)	
Rich	5,931 (36.24)	6,156 (35.09)	
<b>Behavioral factors</b>			
<b>Smoking status</b>			
Currently not smoking	11,273 (74.95)	15,660 (96.63)	< 0.0001
Currently smoking	3,668 (25.05)	706 (3.37)	
<b>Alcohol consumption</b>			
Not Frequently	13,417 (90.75)	16,103 (98.85)	< 0.0001
Frequently	1,681 (9.25)	263 (1.15)	
<b>Physical activity</b>			
Frequent	3,543 (24.55)	1,990 (12.01)	
Ever	2,310 (15.63)	1,702 (10.21)	< 0.0001
Never	9,245 (59.82)	12,674 (77.77)	

BMI: Body mass index; SC: Scheduled caste; ST: Scheduled tribe; OBC: Other backward class; MPCE: Monthly per capita expenditure; n: frequency; %: Percentages; Weighted percentages and unweighted frequencies were given

**Fig. 2** Prevalence (%) of musculoskeletal disorders and its subtypes by diabetes status among older people in India

1.79; p-value < 0.0001; 95% CI: 1.29 to 2.51). When comparing older men with diabetes to their counterparts without diabetes, the risk of osteoporosis was 1.51 times higher (aOR: 1.51; p-value < 0.0001; 95% CI: 1.31 to 2.35), and when comparing older women with diabetes to women without diabetes, the risk was 1.18 times higher (aOR: 1.18; p-value < 0.0001; 95% CI: 1.06 to 1.43). However, diabetes was found to be insignificantly positively associated with rheumatism among older men (aOR: 1.21; p-value = 0.234; 95% CI: 0.88 to 1.66), while for older women it was insignificantly negatively associated even after controlling potential covariates (aOR: 0.83; p-value = 0.651; 95% CI: 0.62 to 1.13) (Table 2).

In the total population, the combination of diabetes and obesity was more likely to have musculoskeletal disorders (aOR: 4.28; p-value < 0.0001; 95% CI: 1.84 to 9.96) and its subtype arthritis (aOR: 4.48; p-value < 0.0001; 95% CI: 1.67 to 12.07) as compared to those without both conditions. However, the risk of osteoporosis and rheumatism disorders were 1.80 and 1.87 times more likely among those had only obesity compared to the reference group. Compared to older men with both diabetes and obesity, the odds ratios for musculoskeletal disorder were significantly higher among older women with both diabetes and obesity (Table 3).

Results from interaction analysis on multiplicative scale showed statistically significant for musculoskeletal

**Table 2** Association of musculoskeletal disorders and its subtypes with diabetes mellitus among older people in India

Outcomes	Crude model	Model 1	Model 2
	uOR [95% CI]	aOR [95% CI]	aOR [95% CI]
<b>Overall analysis</b>			
Musculoskeletal disorders	1.72* [1.24 to 2.40]	1.62* [1.26 to 2.06]	1.72* [1.23 to 2.41]
<i>Arthritis</i>	2.01* [1.22 to 3.27]	1.77* [1.27 to 2.47]	1.71* [1.22 to 2.39]
<i>Osteoporosis</i>	1.39* [1.08 to 1.80]	1.34* [1.01 to 1.77]	1.33* [1.01 to 1.76]
<i>Rheumatism</i>	0.98 [0.80 to 1.21]	1.01 [0.81 to 1.26]	0.96 [0.77 to 1.20]
<b>Gender stratified analysis</b>			
<b>Men</b>			
Musculoskeletal disorders	1.25* [1.04 to 1.51]	1.35* [1.10 to 1.66]	1.25* [1.02 to 1.59]
<i>Arthritis</i>	1.22* [1.01 to 1.51]	1.29* [1.03 to 1.62]	1.22* [1.03 to 1.49]
<i>Osteoporosis</i>	1.41* [1.16 to 2.08]	1.65* [1.08 to 2.52]	1.51* [1.31 to 2.35]
<i>Rheumatism</i>	1.15 [0.87 to 1.51]	1.25 [0.92 to 1.70]	1.21 [0.88 to 1.66]
<b>Women</b>			
Musculoskeletal disorders	2.11* [1.34 to 3.3]	1.81* [1.30 to 2.51]	1.79* [1.29 to 2.51]
<i>Arthritis</i>	2.56* [1.35 to 4.84]	2.08* [1.36 to 3.19]	2.03* [1.35 to 3.04]
<i>Osteoporosis</i>	1.37* [1.01 to 1.89]	1.20* [1.04 to 1.65]	1.18* [1.06 to 1.43]
<i>Rheumatism</i>	0.89 [0.67 to 1.19]	0.88 [0.66 to 1.17]	0.83 [0.62 to 1.13]

OR: Odds ratio; aOR: adjusted odds ratio; CI: Confidence interval; Reference category is "No" for each exposure variables in the models; \* $p < 0.05$ ;

Model 1 is adjusted for age, education, religion, caste, marital status, monthly per capita expenditure, living arrangement, and place of residence

Model 2 is adjusted for Model 1, pain, smoking, alcohol consumption, and physical activity

**Table 3** Estimated odds ratios (ORs) from binary logistic regression for musculoskeletal disorders and its subtypes among older people in India

Combinations of diabetes & obesity	Musculoskeletal disorders	<i>Arthritis</i>	<i>Osteoporosis</i>	<i>Rheumatism</i>
	aOR [95% CI]	aOR [95% CI]	aOR [95% CI]	aOR [95% CI]
<b>Overall analysis</b>				
<i>Obesity-</i> & <i>Diabetes-</i> (Ref.)	1	1	1	1
<i>Obesity-</i> & <i>Diabetes+</i>	1.45* [1.09 to 1.92]	1.53* [1.03 to 2.26]	1.37* [1.01 to 1.87]	0.98 [0.77 to 1.23]
<i>Obesity+</i> & <i>Diabetes-</i>	1.87* [1.43 to 2.45]	1.65* [1.22 to 2.22]	1.80* [1.24 to 2.59]	1.87* [1.35 to 2.58]
<i>Obesity+</i> & <i>Diabetes+</i>	4.28* [1.84 to 9.96]	4.48* [1.67 to 12.07]	1.71 [0.94 to 3.11]	1.41 [0.78 to 2.54]
<b>Gender stratified analysis</b>				
<b>Men</b>				
<i>Obesity-</i> & <i>Diabetes-</i> (Ref.)	1	1	1	1
<i>Obesity-</i> & <i>Diabetes+</i>	1.28* [1.01 to 1.61]	1.19 [0.92 to 1.54]	1.54 [0.95 to 2.50]	1.24 [0.89 to 1.73]
<i>Obesity+</i> & <i>Diabetes-</i>	1.72* [1.08 to 2.74]	2.45* [1.48 to 4.07]	0.64 [0.28 to 1.47]	0.94 [0.43 to 2.06]
<i>Obesity+</i> & <i>Diabetes+</i>	1.75* [1.03 to 3.20]	2.49* [1.23 to 5.06]	1.05 [0.39 to 2.34]	1.06 [0.36 to 2.57]
<b>Women</b>				
<i>Obesity-</i> & <i>Diabetes-</i> (Ref.)	1	1	1	1
<i>Obesity-</i> & <i>Diabetes+</i>	1.62* [1.08 to 2.41]	1.83* [1.10 to 3.04]	1.24 [0.85 to 1.81]	0.80 [0.57 to 1.11]
<i>Obesity+</i> & <i>Diabetes-</i>	1.89* [1.39 to 2.56]	1.46* [1.04 to 2.06]	2.08* [1.40 to 3.11]	2.13* [1.48 to 3.06]
<i>Obesity+</i> & <i>Diabetes+</i>	4.37* [2.00 to 9.56]	3.98* [1.62 to 9.81]	1.62 [0.76 to 3.47]	1.52 [0.79 to 2.94]

aOR: adjusted odds ratio; CI: Confidence interval; Ref: Reference category; \* $p < 0.05$ ;

Models are adjusted for age, education, religion, caste, marital status, monthly per capita expenditure, living arrangement, place of residence, pain, smoking, alcohol consumption, and physical activity



disorders and its three subtypes among older women, however it was not significant for osteoporosis and rheumatism disorders among older men. When we analyzed interaction on additive scale, we found it only for arthritis disorder among older women suggesting the risk from obesity (RERI: -0.83; p-value < 0.0001; 95% CI: -1.44 to -0.22, AP: -0.54; p-value < 0.0001; 95% CI: -1.05 to -0.03], S: 0.39; p-value < 0.0001; 95% CI: 0.16 to 0.93) was additive to the risk from diabetes. (Table 4).

## Discussion

In this study, we used a nationally representative sample of 31,464 respondents aged 60 years or more from the first wave of LASI survey in India. This study found that the prevalence of musculoskeletal disorders and its subtypes was higher among individuals with diabetes compared to their counterparts without diabetes and it was relatively higher for older women. The prevalence of arthritis was higher among included musculoskeletal disorders in the study. Moreover, subgroup analysis according to the combinations of diabetes and obesity (BMI  $\geq$  30) indicated that individuals with the presence of both conditions were associated with an increased risk of musculoskeletal disorders than individual without both conditions. Furthermore, interaction analysis observed the interactive association of

diabetes and obesity with musculoskeletal disorders and its subtypes in total sample. In a gender-specific analysis, it was found that the interactive association was significant for all three subtypes in women but only for arthritis in older men. These findings implied that obesity could be a moderating factor, altering the strength of the association between diabetes and musculoskeletal disorders in older people.

Existing evidences implied that older people may have greater risk of diabetes-related complications particularly musculoskeletal disorders because of a progressive and generalized loss of strength and toughness of skeletal and muscle mass in later life [32, 33]. It is also reported that high blood glucose levels may add to the list of risk factors of poor musculoskeletal systems by causing nerve damage, vascular diseases, arterial disease, declined bone mineral density, or obesity [34]. In accordance with these explanations, present study suggested that older people with diabetes are at increased risk of complications related to musculoskeletal systems. Likewise, people with diabetes are at higher risk of other serious muscle and skeletal-related complications including rheumatoid arthritis, osteoarthritis, frozen shoulder, and flexor tenosynovitis [23]. Gender stratified analysis implied that older women living with diabetes showed a slightly higher risk of musculoskeletal disorders compared to older men. This may be because of women have a disadvantage in biochemical and functional impairments associated with diabetes, putting them at risk for aberrant

**Table 4** Estimates from interaction analysis of diabetes and obesity on musculoskeletal disorders and its subtypes among older people in India

Interaction of diabetes & obesity	Musculoskeletal disorders	Arthritis	Osteoporosis	Rheumatism
	Estimate [95% CI]	Estimate [95% CI]	Estimate [95% CI]	Estimate [95% CI]
<b>Overall analysis</b>				
<b>Additive scale</b>				
RERI	-0.38 [-0.87 to 0.12]	-0.69* [-1.23 to -0.16]	-0.23 [-0.92 to 0.47]	-0.18 [-0.81 to 0.45]
AP	-0.19 [-0.46 to 0.09]	-0.43* [-0.85 to -0.02]	-0.12 [-0.54 to 0.29]	-0.11 [-0.51 to 0.29]
S	0.73 [0.47 to 1.13]	0.47* [0.23 to 0.95]	0.78 [0.36 to 1.72]	0.79 [0.33 to 1.89]
<b>Multiplicative scale</b>				
	2.01* [1.64 to 2.46]	1.61* [1.25 to 2.09]	1.82* [1.32 to 2.49]	1.66* [1.22 to 2.26]
<b>Gender stratified analysis</b>				
<b>Men</b>				
<b>Additive scale</b>				
RERI	-0.26 [-0.16 to 0.63]	-0.57 [-1.72 to 0.58]	0.03 [-1.24 to 1.29]	-0.23 [-1.44 to 0.97]
AP	-0.15 [-0.71 to 0.41]	-0.33 [-1.14 to 0.47]	0.02 [-0.86 to 0.89]	-0.17 [-1.17 to 0.82]
S	0.74 [0.25 to 2.19]	0.56 [0.15 to 2.12]	1.06 [0.05 to 2.98]	0.60 [0.03 to 1.29]
<b>Multiplicative scale</b>				
	1.75* [1.16 to 2.65]	1.72* [1.03 to 2.87]	1.43 [0.68 to 2.98]	1.35 [0.65 to 2.82]
<b>Women</b>				
<b>Additive scale</b>				
RERI	-0.47 [-1.04 to 0.11]	-0.83* [-1.44 to -0.22]	-0.29 [-1.08 to 0.49]	-0.04 to -0.72 to 0.64]
AP	-0.24 [-0.57 to 0.09]	-0.54* [-1.05 to -0.03]	-0.17 [-0.65 to 0.31]	-0.02 [-0.46 to 0.41]
S	0.68 [0.41 to 1.13]	0.39* [0.16 to 0.93]	0.73 [0.30 to 1.76]	0.94 [0.31 to 2.80]
<b>Multiplicative scale</b>				
	1.98* [1.57 to 2.51]	1.54* [1.14 to 2.07]	1.79* [1.25 to 2.56]	1.61* [1.14 to 2.28]

RERI: relative excess risk due to interaction; AP: attributable proportion due to interaction; S: synergy index; CI: Confidence interval; \*p < 0.05

Models are adjusted for age, education, religion, caste, marital status, monthly per capita expenditure, living arrangement, place of residence, pain, smoking, alcohol consumption, and physical activity

blood sugar fluctuations leading to muscle cells atrophy (dying) and therefore loss of muscle mass [35–37]. Another explanation can be drawn out in a way that the process of skeletal aging occurs in women after menopause, with the changes in hormone levels including loss of calcium in the bones due to inconsistent blood glucose levels [38]. Furthermore, prevalence of arthritis was relatively higher for older women living with diabetes compared to older men. This could be explained by the fact that older women are no longer protected by the estrogen hormone in order to keep the inflammation levels under check. Given that women have a better and more reactive immune system, they are also at increased risk for auto-immune arthritis and its subtypes [39]. These findings suggested that better control of blood glucose level early in life may have more long-term health benefits of musculoskeletal system in later life. Although diabetes was not significantly associated with rheumatism disorder even after controlling the potential covariates but prevalence of rheumatism disorders was relatively higher among older people with diabetes mellitus.

In addition, it has been observed that the presence of concurrent diabetes and obesity had the greater risk of musculoskeletal disorders and its subtype arthritis. Also, these factors had significant multiplicative interaction in the study. It may be speculated that endothelial dysfunction is accompanied with insulin resistance due to obesity in the diabetic conditions might contribute to dysregulation of protein for muscle anabolism in the elderly [40]. It is also reported that diabetes and obesity are frequently accompanied by a dysfunction of  $\beta$  cells that is responsible for facilitating glucose disposal in insulin-sensitive tissues (or peripheral tissues) including skeletal muscle and functions, increasing the risk of musculoskeletal conditions in older people [41, 42]. This could be the possible mechanism of the comorbidity of diabetes and obesity for increasing the risk of musculoskeletal disorders and have been discussed in depth elsewhere [43, 44]. When sample was stratified into men and women, this trend still existed, however, the association was stronger for older women. It may be explained by the fact that women are more insulin sensitive than men due to enhanced glucose uptake by skeletal muscle in women [45]. Predefined gender differences in glucose homeostasis and energy balance are again pointing to the substantial role played by the various hormonal pathways in a woman's physiology and how they drastically change with the emergence of menopause [46]. Culturally, women are also prone to poorer nutrition during childhood, adolescence and child bearing ages, suggesting a role of chronic nutritional deficiencies and its implications on musculoskeletal health which subsequently puts them at greater risk for non-communicable diseases.

After further performing additive interaction which only existed in older women with obesity for arthritis disorder,

indicating risk from obesity was additive to the risk from diabetes. It may be suggested that there should be given pay attention on the BMI level when treating diabetes of older women reduce the risk of arthritis disorder.

This study had several strengths. We used a recently released nationally representative dataset to make our results more scientific and included and controlled several potential covariates. In addition, we analyzed the combined role of diabetes and obesity on three different musculoskeletal disorders. We carried out interaction analysis on both additive and multiplicative scales in order to produce findings that are relevant to clinical epidemiology and public health [30]. A theoretical foundation is presented by this study for prospective longitudinal studies, cohort studies, and clinical trials. However, this study also met with some limitations which should be considered while interpreting results. Firstly, the cross-sectional nature of data does not infer causality or linkages between diabetes and musculoskeletal disorders. Secondly, only the information of obesity contained anthropometric criteria, whereas diabetes and musculoskeletal disorders is based on self-reporting and this might create some bias in estimates due to recall bias. Although a series of confounding were taken into consideration for the adjustment purpose of the estimates, other potential covariates including family history and medication were not considered in the analysis. Thus, our analysis may partially influence the validity and accuracy of the findings.

## Conclusion

This cross-sectional study suggests an elevated risk of musculoskeletal disorders among Indian older adults with diabetes. However, the risk was found to be higher among older women as compared to older men. In order to reduce the diabetes related complications, it is implied to have a more focus on musculoskeletal system when treating diabetes in clinical practice. The result of this study also suggest that the co-occurrence of diabetes and obesity may increase the risk of musculoskeletal disorders in later life. Therefore, clinicians should be aware of the pathophysiological relationship between diabetes and musculoskeletal problems that result from obesity-related metabolic dysregulation when treating diabetes in the elderly population. Further longitudinal studies are required to define better mechanism by which obesity makes stronger the association of diabetes and musculoskeletal disorders in later life.

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**Author Contribution** Salmaan Ansari (SA) and Shazina Saeed (SS) contributed to the conceptualization and study design. SA carried out data curation and statistical analysis. SA interpreted the results and

discussed the findings. SA and SS drafted and finalized the manuscript. Both the authors have read and approved the final manuscript.

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**Data Availability** The datasets generated and/or analyzed during the current study are available in the International Institute for Population Sciences (IIPS), Mumbai repository. The reasonable request for data access can be made at <https://www.iipsindia.ac.in/content/LASI-data>.

## Declarations

**Ethics approval and consent to participate** The study was performed as per the Helsinki Declaration and the national and international guidelines. The necessary guidance and ethical guidelines in LASI survey were approved by Indian Council of Medical Research (ICMR), India. More details on the guidelines and protocols are available in LASI India report. [https://www.iipsindia.ac.in/sites/default/files/LASI\\_India\\_Report\\_2020\\_compressed.pdf](https://www.iipsindia.ac.in/sites/default/files/LASI_India_Report_2020_compressed.pdf).

**Consent for publication** Not applicable.

**Competing interests** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References

- Tandon N, Anjana RM, Mohan V, Kaur T, Afshin A, Ong K, et al. The increasing burden of diabetes and variations among the states of India: the global burden of Disease Study 1990–2016. *Lancet Glob Health*. 2018;6(12):e1352–62.
- Joshi SR, Parikh RM. India - Diabetes capital of the world: now heading towards hypertension. *J Assoc Physicians India*. 2007;55(MAY):323–4.
- Kutty VR, Dilip T, Archana A, Gopinathan S, Ramanathan M. Shifting pattern of diabetes among the elderly in India: evidence from the National Sample Survey Organization's data, 2004–2014. *Int J Non-Commun Dis*. 2018;2(3):45–8.
- Alqahtani N, Khan WAG, Alhumaidi MH, Ahmed YAAR. Use of glycosylated hemoglobin in the diagnosis of diabetes mellitus and pre-diabetes and role of fasting plasma glucose, oral glucose tolerance test. *Int J Prev Med*. 2013;4(9):1025–9.
- American Diabetes Association (ADA). Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2013;36(SUPPL1):67–74.
- Nieves-Plaza M, Castro-Santana LE, Font YM, Mayor AM, Vilá LM. Association of hand or knee osteoarthritis with diabetes mellitus in a population of Hispanics from Puerto Rico. *J Clin Rheumatol*. 2013;19(1):1–6.
- Sloan F, Bethel A, Ruiz DJ, Shea A, Feinglos M. The growing burden of diabetes mellitus in the US elderly population (Archives of Internal Medicine (2008) 168 (2) (192–199)). *Arch Intern Med*. 2008;168(8):860.
- Schreiber AK. Diabetic neuropathic pain: Physiopathology and treatment. *World J Diabetes*. 2015;6(3):432.
- Sozen T, Calik Basaran N, Tinazli M, Ozisik L. Musculoskeletal problems in diabetes mellitus. *Eur J Rheumatol*. 2018;5(4):258–65.
- Lichtenstein A, Tiosano S, Comaneshter D, Amital H, Cohen AD, Amital D. Cross-sectional analysis of the associations between fibromyalgia and diabetes mellitus. *Reumatologia*. 2018;56(5):275–8.
- Jelinek JE. The skin in diabetes. *Diabet Med J Br Diabet Assoc*. 1993 Apr;10(3):201–13.
- Kapoor A, Sibbitt WLJ. Contractures in diabetes mellitus: the syndrome of limited joint mobility. *Semin Arthritis Rheum*. 1989 Feb;18(3):168–80.
- Majjad A, Errahali Y, Toufik H, Djossou JH, Ghassem MA, Kasouati J et al. Musculoskeletal Disorders in Patients with Diabetes Mellitus: A Cross-Sectional Study. *Int J Rheumatol*. 2018;2018(January 2015).
- Bianchi L, Volpato S. Muscle dysfunction in type 2 diabetes: a major threat to patient's mobility and independence. *Acta Diabetol*. 2016;53.
- Hoy D, Geere JA, Davatchi F, Meggitt B, Barrero LH. A time for action: Opportunities for preventing the growing burden and disability from musculoskeletal conditions in low- and middle-income countries. *Best Pract Res Clin Rheumatol*. 2014;28(3):377–93.
- Kelly T, Yang W, Chen CS, Reynolds K, He J. Global burden of obesity in 2005 and projections to 2030. *Int J Obes*. 2008 Sep;32(9):1431–7.
- Nguyen TV, Kelly PJ, Sambrook PN, Gilbert C, Pocock NA, Eisman JA. Lifestyle factors and bone density in the elderly: Implications for osteoporosis prevention. *J Bone Miner Res*. 2009 Dec3;9(9):1339–46.
- Barrera G, Bunout D, Gattás V, de la Maza MP, Leiva L, Hirsch S. A high body mass index protects against femoral neck osteoporosis in healthy elderly subjects. *Nutrition*. 2004 Sep;20(9):769–71.
- Bauer DC, Browner WS, Cauley JA, Orwoll ES, Scott JC, Black DM et al. Factors Associated with Appendicular Bone Mass in Older Women. 9.
- Hong S, Choi KM. Sarcopenic Obesity, Insulin Resistance, and Their Implications in Cardiovascular and Metabolic Consequences. *Int J Mol Sci*. 2020 Jan 13;21(2):494.
- Anandacoomarasamy A, Catterson I, Sambrook P, Fransen M, March L. The impact of obesity on the musculoskeletal system. *Int J Obes*. 2008;32(2):211–22.
- Karvonen-Gutierrez CA, Sowers MFR, Heeringa SG. Sex dimorphism in the association of cardiometabolic characteristics and osteophytes-defined radiographic knee osteoarthritis among obese and non-obese adults: NHANES III. *Osteoarthritis Cartilage*. 2012 Jul;20(7):614–21.
- Ghosal S, Ghosal A. Diabetes and musculoskeletal disorders-a review. *J Diabetes Metab Disord Control*. 2020;7(2):63–71.
- Arokiasamy P, Bloom D, Lee J, Feeney K, Ozolins M. Longitudinal Aging Study in India: Vision, Design, Implementation, and Some Early Results. 2011 Jan 1
- Arnetz L, Ekberg NR, Alvarsson M. Sex differences in type 2 diabetes: focus on disease course and outcomes. *Diabetes Metab Syndr Obes Targets Ther*. 2014;7:409–20.
- Lee DS, Kim YJ, Han HR. Sex differences in the association between socio-economic status and type 2 diabetes: data from the 2005 Korean National Health and Nutritional Examination Survey (KNHANES). *Public Health*. 2013;127(6):554–60.
- Annandale E, Riska E. New connections: towards a gender-inclusive approach to women's and men's health. *Curr Sociol*. 2009;57(2):123–33.
- International Institute for Population Sciences (IIPS), MoHFW NPHCE, Harvard TH. Chan School of Public Health (HSPH), The University of Southern California (USC). Longitudinal Ageing Study in India (LASI) Wave 1. India Report. Mumbai, India; 2020.
- Okura Y, Urban LH, Mahoney DW, Jacobsen SJ, Rodeheffer RJ. Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension, myocardial

- infarction and stroke but not for heart failure. *J Clin Epidemiol*. 2004;57(10):1096–103.
30. Vandembroucke JP, Poole C, Schlesselman JJ, Egger M. Strengthening the reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *PLoS Med*. 2007;4(10):27.
  31. StataCorp, Stata. Release 14. Statistical Software. College Station, TX: StataCorp LP; 2015.
  32. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing*. 2010 Jul 1;39(4):412–23.
  33. Colón CJP, Molina-Vicenty IL, Frontera-Rodríguez M, García-Ferré A, Rivera BP, Cintrón-Vélez G, et al. Muscle and bone Mass loss in the Elderly Population: advances in diagnosis and treatment. *J Biomed*. 2018;3:40–9.
  34. Wyatt LH, Ferrance RJ. The musculoskeletal effects of diabetes mellitus. *Diabetes Mellit*:8.
  35. Chiu CJ, Wray LA. Gender differences in functional limitations in adults living with type 2 diabetes: biobehavioral and psychosocial mediators. *Ann Behav Med Publ Soc Behav Med*. 2011 Feb;41(1):71–82.
  36. Tramunt B, Smati S, Grandgeorge N, Lenfant F, Arnal JF, Montagner A, et al. Sex differences in metabolic regulation and diabetes susceptibility. *Diabetologia*. 2020 Mar;63(3):453–61.
  37. Wu CH, Chen CY, Wu YC, Weng LJ, Baai-Shyun H. Diabetes mellitus and functional impairment in Taiwanese older men and women. *Arch Gerontol Geriatr*. 2010 Feb;50(Suppl 1):6–10.
  38. Sirola J, Kröger H. Similarities in acquired factors related to postmenopausal osteoporosis and Sarcopenia. *J Osteoporos*. 2011;2011:1–14.
  39. Fairweather D, Rose NR. Women and Autoimmune Diseases I. *Emerg Infect Dis*. 2004 Nov;10(11):2005–11.
  40. Matsuzawa Y, Sugiyama S, Sugamura K, Nozaki T, Ohba K, Konishi M, et al. Digital Assessment of endothelial function and ischemic heart disease in women. *J Am Coll Cardiol*. 2010 Apr;55(16):1688–96.
  41. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB et al. Pathophysiology of Type 2 Diabetes Mellitus. *Int J Mol Sci*. 2020 Aug 30;21(17):6275.
  42. Inaishi J, Saisho Y. Beta-Cell Mass in Obesity and Type 2 Diabetes, and Its Relation to Pancreas Fat: A Mini-Review. *Nutrients*. 2020 Dec 16;12(12):3846.
  43. Teng S, Huang P. The effect of type 2 diabetes mellitus and obesity on muscle progenitor cell function. *Stem Cell Res Ther*. 2019 Dec;10(1):103.
  44. Eshima H. Influence of obesity and type 2 diabetes on Calcium handling by skeletal muscle: spotlight on the Sarcoplasmic Reticulum and Mitochondria. *Front Physiol*. 2021 Nov;2:12:758316.
  45. Geer EB, Shen W. Gender differences in insulin resistance, body composition, and energy balance. *Gend Med*. 2009 Jan;6:60–75.
  46. Mauvais-Jarvis F. Gender differences in glucose homeostasis and diabetes. *Physiol Behav*. 2018 Apr;187:20–3.

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