CME LIVE OPEN ACCESS

Journal of
Epidemiology and Public Health

Research Article

"Association of Multimorbidity And Frailty Among Middle Aged and Older Population: Evidence from Longitudinal Aging Study in India (Lasi-1st Wave)."

Pritam Halder*[1], Anamika Soni[2], Saumyarup Pal[3], Anshul Mamgai[1], Amartya Dutta[4], and Arpan Das[5], Shivani Rathor[6]

[1]*Department of Community Medicine and School of Public Health, Post Graduate Institute of Medical research, Chandigarh in India.*
[2]*Gandhi Medical College, Bhopal Madhya Pradesh in India.*
[3]*Department of Geriatric Medicine, AIIMS, New Delhi in India.*
[4]*Desun Hospital and Heart Research Institute, 60/8 Hari pada Dutta Lane, Golf Gardens, Kolkata in India.*
[5]*BP Poddar Hospital, 104, Ramkrishna Nagar, Garia, Kolkata, pin-700084*
[6]*University of Delhi, Delhi, pin-110007*

Corresponding Author: Pritam Halder, Department of Community Medicine and School of Public Health, Postgraduate Institute of Medical Education and Research, Chandigarh in India.

Running title- Association of Multimorbidity And Frailty Among Middle Aged and Older Indian Population.

Received: 2024 Jan 26 **Accepted:** 2024 Feb 08 **Published:** 2024 Feb 25

Abstract

Introduction: Frailty is associated with older age and multimorbidity (two or more long-term conditions); We aimed to investigate frailty among the >=45 years population, and its association with multimorbidity. This paper aims to examine the association between frailty and multimorbidity in middle aged and older population.

Methods: The analysis used data from the first wave of LASI, a longitudinal survey from 35 Indian states and union territories intended to collect detailed information on the psychological, social, economic, and health aspects of ageing in India. Self-reported exhaustion, unintentional weight loss, weak grip strength, self-reported low physical activity, and slow walking time. Participants were categorised as having 'no frailty' (score 0 to 2 and 'frailty' (score >3).

Findings: 56492 participants aged 45 years or more were included in the study, of whom 8802 (15.58% were considered frail. Frailty was significantly associated with multimorbidity [prevalence 67.41% (at least one morbidity)]; odds ratio [OR] 1.65, 95% CI 1.52-1.79). Socioeconomic deprivation, living area, occupation, obesity, smoking, and infrequent alcohol consumption seems to play an important role in deciding frailty status. The top five conditions associated with frailty were hypertension, diabetes, cancer, chronic lung disease and chronic heart disease. Female gender was significantly associated with frailty.

Conclusion: Our emphasis on inclusive efforts for identifying, managing, and preventing frailty among older adults with multimorbidity is crucial. Shifting the focus from single conditions to the complexity of patient populations aligns with the multifactorial nature of frailty. This holistic approach, encompassing research, clinical guidelines, and healthcare services, is pivotal for providing comprehensive care to a growing demographic facing intricate health challenges.

Keywords: Multimorbidity, Frailty, Middle aged, Older, LASI

1. Introduction

It's fascinating to see how the ageing population is reshaping the landscape of healthcare and bringing to light the intricate relationship between frailty and multimorbidity. In India, the population increased from 3.7 % in 1973 to 6.9 % in 2022 growing at an average annual rate of 1.27%. According to the estimates of WHO, by 2050 about 22% of the world's population will be above 60 years of age and 80 of them will be living in middle and low-income countries

Frailty is a multidimensional syndrome characterised by physical, psychological, and social vulnerability with decrease in resiliency and adaptive capacity predisposing to unfavourable outcomes including reduction in survival time [1,2].

Frail individuals struggle to maintain balance during stress due to multiple organ deficiencies and neuroendocrine dysregulation, highlighting the interconnected nature of frailty.

This emphasizes the need for holistic care, considering both specific medical conditions and overall physiological well-being. Addressing frailty is to be emphasized for improving overall health outcomes, especially in older adults and other adverse outcomes, such as the need for home care or nursing home admission. The frailty index, driven by accumulation of deficits model and encompassing medical, functional along with psychosocial factors aids to understand the vulnerability of older individuals and hence can guide comprehensive care [3-6].

The presence of two or more chronic diseases is known as multi-morbidity. Chronic multimorbidity is common in the older people, posing a significant challenge for healthcare professionals. It has also become a crucial indicator for monitoring the health of older individuals. The bidirectional relationship between frailty and multimorbidity is a newly developed area of interest [7-10].

Multimorbidity and frailty are associated. Chronic diseases contribute to the development of frailty. Conversely, frailty-related health deterioration in health status may lead to the development of comorbidities, thus multimorbidity. Both are linked to reduced quality of life, functional decline, and increased healthcare use A systematic review examined nine studies, pooling data from 14704 community-dwellers. Out of 1271 frail patients, 868 had multi-morbidity. These 868 patients with both multi-morbidity and frailty comprised 42% of those who had multi-morbidity. Multimorbidity and frailty are risk factors for adverse outcomes in hospitalized older patients. Scarcity of data on frailty, multimorbidity, and healthcare use in developing countries, particularly in Indian primary care settings, revealing a critical gap in knowledge [11-17].

Objective

- To determine the association between frailty and multimorbidity-
- Among the male and female Indian population.
- Among middle aged (45-59 years and older (>60 years population in India.

2. Methods

The current analysis used LASI-1st wave data from 35 Indian states and union territories (UTs), except Sikkim. It is a longitudinal survey with a national representation that intends to collect detailed information on the psychological, social, economic, and health aspects of ageing in India. It was created to close the knowledge gap about comprehensive and globally comparable survey data on ageing in India. The National Institute on Ageing, the Government of India's Ministry of Health and Family Welfare, and the United Nations Population Fund all provided funding for the study. The University of Southern California, the International Institute for Population Sciences, and the Harvard T.H. Chan School of Public Health are working together on it. The demography, health, economy, and social factors are just a few of the important topics it focuses on. There were 73,000 adult Indians in LASI. 66,606 Indian volunteers above the age of 45 were included in the current study.

The study, which is the biggest of its kind in the world and the first of its kind in India, evaluates the scientific evidence in the context of variables like demographics, household economic status, chronic health conditions, symptom-based health conditions, functional health, mental health (cognition and depression), biomarkers, healthcare utilisation, family and social networks, social welfare programmes, employment, retirement, satisfaction, and life expectations. The survey intends to follow a representative sample of the older adult population every two years for the following 25 years, with a revised sample size to account for attrition due to death, migration, non-reachable, and non-response [18].

2.1 Ethics

Ethical approval was granted by the Indian Council of Medical Research [19].

2.2 Outcome Variable

The outcome variable of interest was frailty, Consisting of five following components- 1 self-reported exhaustion, 2 unintentional weight loss, 3 weak grip strength, 4 self-reported low physical activity, and 5 slow walking time. Thus, the range was 0 to 5. Participants were categorised as having 'no frailty' (score 0 to 2 and 'frailty' (score >3 [20]. (Table 1)

Table 1: Components of frailty

Component		Criteria
1) Self-reported exhaustion		"During the past week, how often did you feel: (i) tired or low in energy; (ii) that everything you did was an effort." <3days=0; >3 days =1
2) Unintentional weight loss		"Do you think that you have lost weight in the last 12months because there was not enough food at your household?" No=0, Yes=1
3) Weak grip strength		Grip strength score (average) in dominant hand (trials 2) using Smedley's handheld dynamometer (adjusted for gender and body mass index (BMI))
Gender	BMI	Current grip strength (kilogram)
Male	<=24.0	<=29
	24.1-26.0	<=30
	26.1-28.0	<=30
	>28.0	<=32
Female	<=23.0	<=17
	23.1-26.0	<=17.3
	26.1-29.0	<=18
	>29.0	<=21
4) Self-reported low physical activity		"How often do you take part in sports or vigorous activities, such as running or jogging, swimming, going to a health center or gym, cycling, or digging with a spade or shovel, heavy lifting, chopping, farm work, fast bicycling, cycling with loads?" • Once/ week or more than once a week=0 • 1 to 3 times/ month or hardly ever or never=1
5) Slow walking time		Participants were asked to walk 4 meters twice. The time taken to complete walk was documented in seconds each time, and the average time taken in both trials was calculated. (Adjusted for gender and height (gender and height -specific cut-off)
Gender	Height (centimeter)	Walking (4meter) time (seconds) cut-off
Men	<=173	>=7
	>173	>=6
Female	<=159	>=7
	>159	>=6

2.3 Explanatory Variables

The explanatory variable of interest is multimorbidity. Following chronic health conditions were considered while accounting for multimorbidity- hypertension, diabetes, cancer, chronic lung diseases (e.g.- chronic obstructive pulmonary disease, asthma, chronic bronchitis, other chronic lung problems), chronic heart disease (e.g.- congestive heart failure, myocardial infarction, heart attack, other chronic heart diseases), stroke, musculoskeletal disorder (MSD e.g.- rheumatism, arthritis, osteoporosis, other chronic joint or bone disorders), dyslipidaemia (high cholesterol), thyroid disorders, chronic renal failure, visual impairment and hearing impairment. The interviewer asked proper questions related to chronic health conditions with dichotomous answers (no/ yes)- "Has any health professional ever diagnosed you with the following chronic conditions or diseases?" Participants having at least two chronic health conditions were described as multimorbidity.

Age (years 45-59, >60), gender (male, female), minimum education (illiterate, less than primary. primary completed, middle completed, secondary school, higher secondary, and Diploma/ graduate), residence (rural, urban), marital status (unmarried, married/ in live-in, Widow/ separated/ divorced), MPCE (monthly per capita expenditure- poorest, poorer, middle, richer, richest quintile, health insurance (no, yes), occupation (unemployed, professional and semi-professional- 'legislators and senior officials, professionals, technicians and associate professionals'. clerical and skilled- 'clerks, service workers and shopkeepers, skilled agriculture and fishery workers, craft and related trade worker, plant and machine operator', unskilled), living arrangement (living alone, with spouse and/ or family, with spouse and children, with children and others, with others only), self-rated health (excellent, very good, good, fair, poor,), tobacco abuse (no, yes and alcohol abuse (no, yes were taken as other explanatory variables.

To conduct this study, we have removed data from participants below the age of 45 years. After adjusting missing data by row-wise deletion and excluding BMI outliers, we have included participants for this study. Details are provided in

Figure 1. Thus, this secondary study of LASI-first wave data included information from 56492 participants.

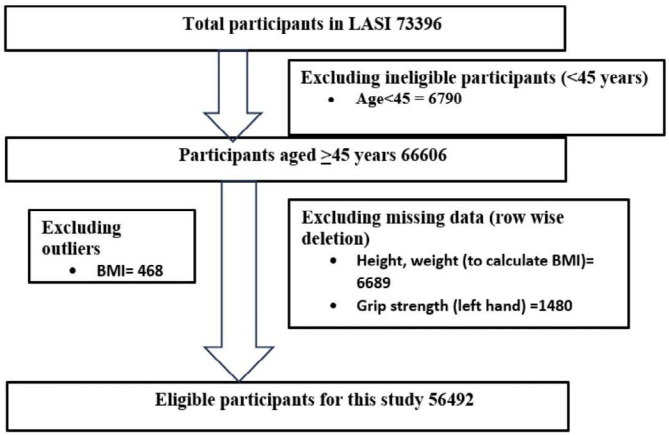

Figure 1

2.4 Statistical Analysis

Univariate logistic regression was conducted between the outcome variable and each explanatory variable. To avoid multicollinearity among explanatory variables P-values <0.05 were considered as statistically significant. P-value <0.2 was taken for further multivariable logistic regression. The association was calculated in the overall population and was further categorised as per gender and age groups [20].

3. Results

A total of 56492 participants were included in the study and the following results were seen in the analysis. Table 2 describes that Among the total participants, 15.58% of the study participants were frail. Females showed statistically significant higher frailty (17.97%, p<0.001 [Table 5]. Frailty was seen more in the age group 60 years and above (25.5%, p<0.001). As per the other sociodemographic factors and various other characteristics, frailty was seen more in Illiterate (19.42%), poorest participants (16.64%), unemployed (23.31%), participants without health insurance (15.68%), malnourished (22.41%)> obese (18.68% and alcohol users (11.98% with significant p<0.001. These findings highlight the diverse sociodemographic factors associated with frailty in the study population. Similar consistent findings were also illustrated in Figure 2.

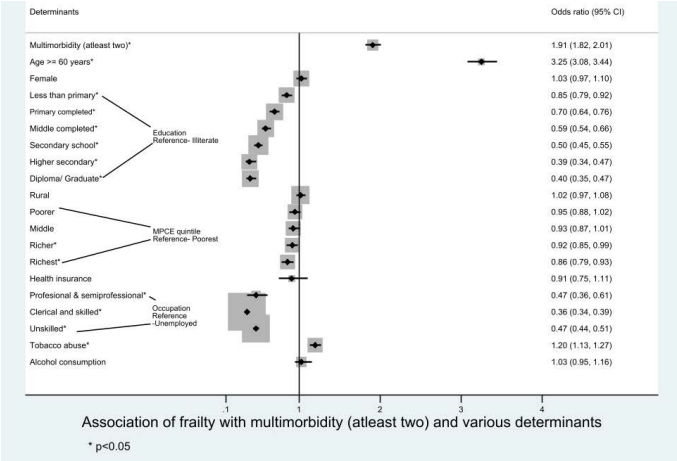

Figure 2

Table 2: Various characteristics of the Indian population aged >45 years, 45-59 years and >60 years.

Variable	Overall population (>45 years)			Middle aged population (45-59 years)			Older population (>60 years)		
	Total (N=56492) N (%)	Frailty (N=8802) (15.58%) N (%)	p-value	Total (N= 30112) N (%)	Frailty (N=2074) (6.89) N (%)	p-value	Total (N=26380) N (%)	Frailty (N=6728) (25.50) N (%)	p-value
Sex									
Male	26315 (46.58)	3378 (12.84)	<0.001	13453 (44.68)	663 (4.93)	<0.001	12862 (48.76)	27115 (21.11)	<0.001
Female	30177 (53.42)	5424 (17.97)		16659 (55.32)	1411 (8.47)		13518 (51.24)	4013 (29.69)	
Age (years)									
45-59	30112 (53.30)	2074 (6.89)	<0.001	-	-	-	-	-	-
>60	26380 (46.70)	6728 (25.50)		-	-	-	-	-	-
Education (minimum)									
Illiterate	26,472 (46.86)	5,140 (19.42)	<0.001	12,415 (41.23)	1,041 (8.39)	<0.001	14,057 (53.29)	4,099 (29.26)	<0.001
Less than primary	6,604 (11.69)	1,109 (16.79)		3,347 (11.12)	245 (7.32)		3,257 (12.35)	864 (26.53)	
Primary completed	7,565 (13.39)	1,024 (13.54)		4,359 (14.48)	302 (6.93)		3,206 (12.15)	722 (22.52)	
Middle completed	5,456 (9.66)	583 (10.69)		3,538 (11.75)	186 (5.26)		1,918 (7.27)	397 (20.70)	
Secondary school	4,981 (8.82)	507 (10.18)		3,010 (10.00)	175 (5.81)		1,971 (2.47)	332 (16.84)	
Higher secondary	2378 (4.21)	184 (7.74)		1,583 (5.26)	53 (3.35)		795 (3.01)	131 (16.48)	

Ciatation: Halder, P., Soni, A., Pal, S., Mamgai, A., Dutta, A., Das, A., Rathor, S. et al (2024). "Association of Multimorbidity And Frailty Among Middle Aged and Older Population: Evidences from Longitudinal Aging Study in India (Lasi-1st Wave)." Journal of Epidemiology and public health, 2(1), 1-11.

Diploma/ Graduate	3036 (5.37)	255 (8.40)		1,860 (6.18)	72 (3.87)		1,176 (4.46)	183 (15.56)	
Residence									
Rural	37243 (65.93)	5815 (15.61)	0.766	19574 (65.00)	1311 (6.70)	0.076	17669 (66.98)	4504 (25.49)	0.944
Urban	19249 (34.07)	2987 (15.52)		10538 (35.00)	763 (7.24)		8711 (33.02)	2224 (25.53)	
MPCE quintile									
Poorest	11,214 (19.85)	1,866 (16.64)	<0.001	5,802 (19.27)	424 (7.31)	0.215	5,412 (20.52)	1,442 (26.64)	0.017
Poorer	11,430 (20.23)	1,828 (15.99)		5,974 (19.84)	392 (6.56)		5,456 (20.68)	1,436 (26.32)	
Middle	11,447 (20.26)	1,808 (15.79)		6,005 (19.94)	424 (7.06)		5,442 (20.63)	1,384 (25.43)	
Richer	11,394 (20.17)	1,741 (15.28)		6,168 (20.48)	440 (7.13)		5,226 (19.81)	1,301 (24.89)	
Richest	11,007 (19.48)	1,559 (14.16)		6,163 (20.47)	394 (6.39)		4,844 (18.36)	1,165 (24.05)	
Health insurance									
No	55240 (97.78)	8662 (15.68)	<0.001	29414 (97.68)	2003 (6.91)	0.285	25826 (97.90)	6629 (25.67)	<0.001
Yes	1252 (2.22)	140 (11.18)		698 (2.32)	41 (5.87)		554 (2.10)	99 (17.87)	
Occupation									
Unemployed	28,175 (49.87)	6,569 (23.31)	<0.001	11,122 (36.94)	1,157 (10.40)	<0.001	17,053 (64.64)	5,412 (31.74)	<0.001
Professional and semi-professional	1,304 (2.31)	66 (5.06)		1,075 (3.57)	38 (3.53)		229 (0.87)	28 (12.23)	
Clerical and skilled	14,622 (25.88)	1,066 (7.29)		9,445 (31.37)	403 (4.27)		5,177 (19.62)	663 (12.81)	
unskilled	12,391 (21.93)	1,101 (8.89)		8,470 (28.13)	476 (5.62)		3,921 (14.86)	625 (15.94)	
BMI									
<18.5	10691 (18.92)	2,396 (22.41)	<0.001	4,449 (14.77)	392 (8.81)	<0.001	6,242 (23.66)	2,004 (32.11)	<0.001
18.5-22.9	20769 (36.76)	2,965 (14.28)		10,724 (35.61)	641 (5.98)		10,045 (38.08)	2,324 (23.14)	
23-24.9	8694 (15.39)	1,075 (12.36)		4,950 (16.44)	271 (5.47)		3,744 (14.19)	804 (21.47)	
25-29.9	12473 (22.08)	1,644 (13.18)		7,531 (25.01)	497 (6.60)		4,942 (18.73)	1,147 (23.21)	
>30	3865 (6.84)	722 (18.68)		2,458 (8.16)	273 (11.11)		1,407 (5.33)	449 (31.91)	
Tobacco abuse									
No	35601 (63.02)	5518 (15.50)	0.486	19664 (65.30)	1433 (7.29)	<0.001	15937 (60.41)	4085 (25.63)	0.556
Yes	20891 (36.98)	3284 (15.72)		10448 (34.70)	641 (6.14)		10443 (39.59)	2643 (25.31)	
Alcohol abuse									
No	46314 (81.98)	7583 (16.37)	<0.001	24534 (81.48)	1788 (7.29)	<0.001	21778 (82.55)	5795 (26.61)	<0.001
Yes	10178 (18.02)	1219 (11.98)		5576 (18.52)	286 (5.13)		4602 (17.45)	933 (20.27)	

Ciatation: Halder, P., Soni, A., Pal, S., Mamgai, A., Dutta, A., Das, A., Rathor, S. et al (2024). "Association of Multimorbidity And Frailty Among Middle Aged and Older Population: Evidences from Longitudinal Aging Study in India (Lasi-1st Wave)." Journal of Epidemiology and public health, 2(1), 1-11.

Table 3 describes the distribution of frailty across the age groups along with the prevalence of multimorbidity. The proportion of people being frail increases with age, sharply after the age of 60 years. Using multivariate logistic regression, there was a significant association of these comorbidities (Stroke, Chronic lung disease, chronic heart disease, chronic renal failure, cancer, hypertension, MSD, hearing impairment, Neuropsychiatric disease, diabetes, dyslipidaemia, thyroid disease F/b Visual impairment with being frail was observed.

Table 3: Prevalence of morbidity/ multimorbidity among the Indian population aged >45 years, 45-59 years and >60 years.

Variable	Overall population (>45 years)			Middle aged population (45-59 years)			Older population (>60 years)		
	Total (N=56492) N (%)	Frailty (N=8802) (15.58%) N (%)	p-value	Total (N= 30112) N (%)	Frailty (N=2074) (6.89) N (%)	p-value	Total (N=26380) N (%)	Frailty (N=6728) (25.50) N (%)	p-value
Hypertension	15883 (28.12)	3460 (21.78)	<0.001	6848 (22.74)	721 (10.53)	<0.001	9035 (34.25)	2739 (30.32)	<0.001
Diabetes	7004 (12.40)	1424 (20.33)	<0.001	3041 (10.10)	337 (11.08)	<0.001	3963 (15.02)	1087 (27.43)	0.003
Cancer	341 (0.60)	76 (22.29)	0.001	165 (0.55)	16 (9.70)	0.153	176 (0.67)	60 (34.09)	0.009
Chronic lung disease	3160 (5.59)	902 (28.54)	<0.001	1192 (3.96)	177 (14.85)	<0.001	1968 (7.46)	725 (36.84)	<0.001
Chronic heart disease	1992 (3.53)	498 (25.00)	<0.001	695 (2.13)	84 (12.09)	<0.001	1297 (4.92)	414 (31.92)	<0.001
Stroke	739 (1.31)	239 (32.34)	<0.001	247 (0.82)	27 (10.93)	0.012	492 (1.87)	212 (43.09)	<0.001
MSD	8084 (14.31)	2047 (25.32)	<0.001	3502 (11.63)	43 (12.31)	<0.001	4582 (17.37)	1616 (35.27)	<0.001
Neuropsychiatric disease	1102 (1.95)	307 (27.86)	<0.001	518 (1.72)	75 (14.48)	<0.001	584 (2.21)	232 (39.73)	<0.001
Dyslipidemia	1910 (3.38)	391 (20.47)	<0.001	954 (3.17)	107 (11.22)	<0.001	956 (3.62)	284 (29.71)	0.002
Thyroid disease	1639 (2.90)	337 (20.56)	<0.001	1026 (3.41)	125 (12.18)	<0.001	613 (2.32)	212 (34.58)	<0.001
Chronic renal failure	399 (0.71)	99 (24.81)	<0.001	177 (0.59)	20 (11.30)	0.020	222 (0.84)	79 (35.59)	0.001
Visual impairment	27213 (48.17)	5136 (18.87)	<0.001	12716 (42.23)	1012 (7.96)	<0.001	14497 (54.95)	4124 (28.45)	<0.001
Hearing impairment	3799 (6.72)	1060 (27.90)	<0.001	1287 (4.27)	138 (10.72)	<0.001	2512 (9.52)	922 (36.70)	<0.001
Atleast one morbidity	38084 (67.41)	7039 (18.48)	<0.001	18353 (60.95)	1551 (8.45)	<0.001	19731 (74.80)	5488 (27.81)	<0.001
Multimorbidity (atleast 2)	20668 (36.59)	4694 (22.71)	<0.001	8812 (29.26)	948 (10.76)	<0.001	11856 (44.94)	3746 (31.60)	<0.001
Multimorbidity (atleast 3)	4257 (7.54)	1098 (25.79)	<0.001	1550 (5.15)	199 (12.84)	<0.001	2707 (10.26)	899 (33.21)	<0.001
Multimorbidity (atleast 4)	123 (0.22)	50 (40.65)	<0.001	38 (0.13)	6 (15.79)	0.030	85 (0.32)	44 (51.76)	<0.001

Table 4 data suggested, that, there is a significant association of comorbidities with frailty. The adjusted odds ratio of 3.02 [2.06-4.44], p<0.001 (with 95% Confidence interval indicates that the odds of frailty are about double higher in individuals with multiple comorbidities compared to participants with single morbidity (1.65 [1.52-1.79] p<0.001).

Table 4: Univariate and multivariable logistic regression of frailty and morbidity /multimorbidity

Characteristics	Univariate		Multivariable			
	Crude odds ratio (95% Confidence interval)	p-value	Adjusted odds ratio (95% Confidence interval) Model-1	p-value	Adjusted odds ratio (95% Confidence interval) Model-2	p-value
No morbidity	Reference	-	Reference	-	Reference	-
Atleast one morbidity	2.01 (1.87-2.16)	<0.001	1.62 (1.50-1.75)	<0.001	1.65 (1.52-1.79)	<0.001
Multimorbidity (atleast 2)	2.14 (2.03-2.26)	<0.001	1.75 (1.65-1.85)	<0.001	1.77 (1.66-1.87)	<0.001
Multimorbidity (atleast 3)	2.27 (2.17-2.38)	<0.001	1.85 (1.77-1.94)	<0.001	1.91 (1.82-2.01)	<0.001
Multimorbidity (atleast 4)	3.73 (2.60-5.34)	<0.001	3.03 (2.07-4.43)	<0.001	3.02 (2.06-4.44)	<0.001
*Model 1= adjusted for age, gender Model 2= adjusted for age, gender, education, residence, mpce quintile, health insurance, occupation, alcohol abuse, tobacco abuse Classification accuracy= 84.42% Pseudo R^2= 0.1298						

Table 5 showed that taking no morbidity as reference, with gradual increase in the number of morbidities the adjusted odds were increasing gradually which was almost similar irrespective of gender except for atleast 4 multimorbidity, where adjusted odds were much higher among male (5.12 than female (2.01).

Table 5: Association of frailty and morbidity/ multimorbidity concerning gender

Gender	Univariate		Multivariable	
	Crude odds ratio (95% Confidence interval)	p-value	Adjusted odds ratio (95% Confidence interval)	p-value
Male (N=26315)				
No morbidity	Reference	-	Reference	-
Atleast one morbidity	2.05 (1.82-2.30)	<0.001	1.65 (1.45-1.87)	<0.001
Multimorbidity (atleast 2)	2.11 (1.93-2.30)	<0.001	1.70 (1.54-1.86)	<0.001
Multimorbidity (atleast 3)	2.35 (2.18-2.53)	<0.001	1.92 (1.77-2.08)	<0.001
Multimorbidity (atleast 4)	6.84 (4.01-11.67)	<0.001	5.12 (2.88-9.13)	<0.001
Female (N=30177)				
No morbidity	Reference	-	Reference	-
Atleast one morbidity	1.96 (1.78-2.15)	<0.001	1.66 (1.50-1.83)	<0.001
Multimorbidity (atleast 2)	2.12 (1.97-2.28)	<0.001	1.82 (1.68-1.97)	<0.001
Multimorbidity (atleast 3)	2.16 (2.03-2.29)	<0.001	1.91 (1.79-2.04)	<0.001
Multimorbidity (atleast 4)	2.29 (1.39-3.78)	0.001	2.01 (1.19-3.41)	<0.001
Adjusted for age, gender, education, residence, mpce quintile, health insurance, occupation, alcohol abuse, tobacco abuse Classification accuracy= 82.03% Pseudo R2= 0.1108				

Table 6 showed that frailty tends to increase with the number of comorbidities, the strongest association observed in the 45-59 years age group. The adjusted odds ratio was 3.49 [2.24-5.43], p<0.001 for participants with a single morbidity being almost more than double compared to those with at least one morbidity (OR-1.59, [1.45-1.74] p<0.001). Interestingly, in the age group of 60 years and above, there's a slightly increased frailty (OR-2.00 [0.83-4.85], p<0.001 with multiple morbidities compared to participants with single morbidity of the same age group (OR-1.95 [1.65-2.28], p<0.001).

Table 6: Association of frailty and comorbidity/ multimorbidity concerning age group

Age group	Univariate		Multivariable	
	Crude odds ratio (95% Confidence interval)	p-value	Adjusted odds ratio (95% Confidence interval)	p-value
45-59 years (N=30112)				
No morbidity	Reference	-	Reference	-
Atleast one morbidity	1.52 (1.39-1.66)	<0.001	1.59 (1.45-1.74)	<0.001
Multimorbidity (atleast 2)	1.68 (1.57-1.80)	<0.001	1.65 (1.53-1.78)	<0.001
Multimorbidity (atleast 3)	1.79 (1.69-1.89)	<0.001	1.83 (1.72-1.95)	<0.001
Multimorbidity (atleast 4)	3.15 (1.06-4.82)	<0.001	3.49 (2.24-5.43)	<0.001
>60 years (N=26380)				
No morbidity	Reference	-	Reference	-
Atleast one morbidity	1.98 (1.79-2.20)	<0.001	1.95 (1.65-2.28)	<0.001
Multimorbidity (atleast 2)	2.10 (1.97-2.36)	<0.001	2.01 (1.81-2.40)	<0.001
Multimorbidity (atleast 3)	2.16 (1.79-2.45)	<0.001	2.14 (1.95-2.35)	<0.001
Multimorbidity (atleast 4)	2.54 (1.06-6.07)	0.036	2.00 (0.83-4.85)	0.126
Adjusted for age, gender, education, residence, mpce quintile, health insurance, occupation, alcohol abuse, tobacco abuse Classification accuracy= 74.05% Pseudo R2= 0.0623				

4. Discussion

The present study sheds light on a significant relationship between multi-morbidity and frailty. As the number of co-morbidities increases, so do the odds of frailty. This aligns with the hypothesis that chronic diseases are crucial in determining frailty. A recent systematic review on community-dwelling older individuals reported a pooled prevalence of approximately 70% for multi-morbidity and 20% for frailty. Our cohort study encompassed a total population of 56,492 individuals aged 45 years and older. Within this group, the prevalence of frailty was 6.89% (Adjusted OR 1.59 among those aged 45-59 years and notably higher at 25.50% (Adjusted OR 1.95 among individuals aged 60 years and above. These findings highlight a substantial increase in frailty with advancing age within the study population. Similar results were shown in previous studies as well. Our study supports the independent association of old age and female gender with frailty. This is congruent with preexisting data indicating a higher prevalence of frailty in females (Adjusted OR 1.66 even when age is taken into account It reinforces the consensus that both factors play distinct roles in the manifestation of frailty, However, non-modifiable factors, underscore their role primarily in screening for vulnerability rather than offering direct intervention points [21-25].

It's interesting to note that our study identified an association between frailty and several modifiable factors such as education. The inverse relationship, where higher education generally leads to awareness and knowledge about various preventive strategies for different diseases besides healthy lifestyle practices corresponds to a lower likelihood of frailty is supported by the collective evidence from various studies. Emphasis on education and public health campaigns could be a valuable strategy in mitigating the risk of frailty in future. The study did not uncover any significant findings concerning the living area (rural/urban and its association with frailty. The percentages of frail individuals were similar to the findings of Rodriguez et al where 16.3% of older individuals above 65 years living in urban and 15.4% in rural areas had frailty [25-30].

Our observation aligns harmoniously with prior research pointing towards a correlation between higher per capita income and a diminished risk of frailty. The coherence across studies fortifies the comprehension that economic factors, particularly elevated income levels, might play a role in reducing the likelihood of frailty. This can be explained by the financial limitations hindering the use of health care resources whereas, having adequate monetary resources may help in better health-seeking behaviour and early detection of age-related physical limitations [5-32].

The recognition of health insurance as a crucial modifiable factor linked to a reduced likelihood of developing frailty, particularly in the age group over 60 years. Similar results were observed in a few previous studies as well [33–36].

The resonance between our study's findings and previous research. underscores the significant link between employment status and frailty risk. The heightened likelihood of frailty in unemployed and unskilled workers contrasted with a lower prevalence in skilled/professional workers, underscores the influence of occupational factors on frailty. Late-career unemployment is associated with the risk of decreased personal and household income, loss of health insurance, and inability to rack up valuable assets. Previous studies have shown that late-career unemployment could cause poor mental health, heavy smoking, myocardial infarction, stroke, and even disability and mortality [37-40].

Our study's findings regarding BMI and frailty align with previous research, highlighting a notable association. The escalated vulnerability to frailty observed in underweight and obese participants, as opposed to those within the normal weight range, underscores the pivotal significance of delving into Body Mass Index (BMI for a comprehensive understanding of frailty outcomes. The correlation unearthed by this study, linking heightened tobacco use with an elevated risk of frailty, resonates with the outcomes of prior research endeavours [25-46].

Our study's observation that alcohol abuse contributes to frailty development aligns with prior research but conflicts with the results from a meta-analysis by Kojima et al which may also be due to demographic differences or ethnicity. Higher blood alcohol concentration due to age-related decreased proportion of water compartment to total body mass in older, alcohol drug interactions alongside increased falls and hospital admissions. Conversely, improvement of insulin sensitivity with light-to-moderate alcohol intake, increased high-density lipoprotein cholesterol, decrease inflammation, and increase adiponectin have been proposed but these protective effects are controversial. Based on this study de-addiction and abstinence can be emphasized upon and clinical trials may provide further information [25-48].

As indicated by longitudinal studies, the bidirectional association between multi-morbidity and frailty (Adjusted OR-3.02 adds depth to our understanding of the complex relationship between these two. The intricate characterisation of frailty in our study not only advances our comprehension of the condition but also provides insights into potential causative factors [49,50].

The robust associations identified between frailty and major chronic diseases—such as chronic heart diseases, stroke, chronic lung disease, musculoskeletal disorders, thyroid diseases, visual and hearing impairment, hypertension, and diabetes—suggest plausible etiological links with these specific health conditions. Particularly noteworthy is the heightened probability of frailty when two or more diseases coexist, underscoring multimorbidity cumulative impact and complexity in contributing to frailty. This nuanced understanding holds the potential to inform targeted interventions tailored to individuals with specific combinations of chronic diseases. The consistency of our findings with those of a previous study further strengthens the evidence for the associations between frailty and major chronic diseases [30-50].

5. Conclusion

Our study has succinctly identified a cluster of factors associated with frailty, such as age, gender, low income, low educational level, physical inactivity, obesity etc, and most importantly multiple comorbidities paints a comprehensive picture of the multifaceted influences on frailty occurrence. Among all participants, 15.58% showed frailty. The cautious stance on establishing a clear causal association between frailty and multimorbidity is well-founded, considering the bidirectional possibilities at play. The correlation between frailty and multimorbidity, as highlighted in our findings, opens a gateway for future research endeavours. The emphasis on prediction, prevention, and intervention strategies underscores the importance of proactive healthcare approaches.

Funding

Nil

Acknowledgement

We want to convey our sincere gratitude towards the participants and the Indian Council of Medical Research.

References

1. Beard, J. R., Officer, A., De Carvalho, I. A., Sadana, R., Pot, A. M., Michel, J. P., ... et al (2016). The World report on ageing and health: a policy framework for healthy ageing. The lancet, 387(10033), 2145-2154.
2. Rockwood, K., Mitnitski, A., Song, X., Steen, B., Skoog, I. (2006). Long-term risks of death and institutionalization of elderly people in relation to deficit accumulation at age 70. Journal of the American Geriatrics Society, 54(6), 975-979.
3. Fried, L. (2003). Frailty and failure to thrive. Principles of geriatric medicine and gerontology, 1387-1402.
4. Griffiths, R., Mehta, M. (2014). Frailty and anaesthesia: what we need to know. Continuing Education in Anaesthesia, Critical Care Pain, 14(6), 273-277.
5. Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., et al (2001). Frailty in older adults: evidence for a phenotype. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 56(3), M146-M157.
6. Middleton, R., Poveda, J. L., Orfila Pernas, F., Martinez Laguna, D., Diez Perez, A., Nogués, X., ... Prieto-Alhambra, D. (2022). Mortality, falls, and fracture risk are positively associated with frailty: a SIDIAP cohort study of 890 000 patients. The Journals of Gerontology: Series A, 77(1), 148-154.
7. Hewitt, J., McCormack, C., Tay, H. S., Greig, M., Law, J., et al (2016). Prevalence of multimorbidity and its association with outcomes in older emergency general surgical patients: an observational study. BMJ open, 6(3).
8. Le Cossec, C., Perrine, A. L., Beltzer, N., Fuhrman, C., Carcaillon-Bentata, L. (2016). Pre-frailty, frailty, and multimorbidity: prevalences and associated characteristics from two French national surveys. The journal of nutrition, health aging, 20, 860-869.
9. Lee, H., Lee, E., Jang, I. Y. (2020). Frailty and comprehensive geriatric assessment. Journal of Korean medical science, 35(3).
10. Salive, M. E. (2013). Multimorbidity in older adults. Epidemiologic reviews, 35(1), 75-83.
11. Chen, C., Park, J., Wu, C., Xue, Q., Agogo, G., et al (2020). Cognitive frailty in relation to adverse health outcomes independent of multimorbidity: results from the China health and retirement longitudinal study. Aging (Albany NY), 12(22), 23129.
12. Nicholson, K., Griffith, L. E., Sohel, N., Raina, P. (2021). Examining early and late onset of multimorbidity in the Canadian Longitudinal Study on Aging. Journal of the

American Geriatrics Society, 69(6), 1579-1591.
13. Clegg, A., Young, J., Iliffe, S., Rikkert, M. O., et al (2013). Frailty in elderly people. The lancet, 381(9868), 752-762.
14. Villacampa-Fernandez, P., Navarro-Pardo, E., Tarin, J. J., Cano, A. (2017). Frailty and multimorbidity: two related yet different concepts. Maturitas, 95, 31-35.
15. Guaraldi, G., Brothers, T. D., Zona, S., Stentarelli, C., Carli, F., Malagoli, A., et al (2015). A frailty index predicts survival and incident multimorbidity independent of markers of HIV disease severity. Aids, 29(13), 1633-1641.
16. Vetrano, D. L., Palmer, K., Marengoni, A., Marzetti, E., Lattanzio, F., et al Joint Action ADVANTAGE WP4 Group. (2019). Frailty and multimorbidity: a systematic review and meta-analysis. The Journals of Gerontology: Series A, 74(5), 659-666.
17. Turner, G., Clegg, A. (2014). Best practice guidelines for the management of frailty: a British Geriatrics Society, Age UK and Royal College of General Practitioners report. Age and ageing, 43(6), 744-747.
18. Iips, I. (2017). National family health survey (NFHS-4), 2015–16. International Institute for Population Sciences (IIPS), Mumbai, India, 791-846.
19. https://main.icmr.nic.in/content/icmr-central-ethics-committee-human-research-icmr-cechr.
20. https://en.wikipedia.org/wiki/Frailty_syndrome.
21. Pai, M., Muhammad, T., Das, S., Chaudhary, M., Srivastava, S. (2023). Gender differences in the association between physical frailty and life satisfaction among older adults in India. Psychogeriatrics, 23(6), 930-943.
22. Stolz, E., Mayerl, H., Waxenegger, A., Freidl, W. (2017). Explaining the impact of poverty on old-age frailty in Europe: material, psychosocial and behavioural factors. The European Journal of Public Health, 27(6), 1003-1009.
23. Mielke, N., Schneider, A., Huscher, D., Ebert, N., Schaeffner, E. (2022). Gender differences in frailty transition and its prediction in community-dwelling old adults. Scientific reports, 12(1), 7341.
24. Das, S., Prasad, J. (2023). Gender Differences in Determinants of the Components of the Frailty Phenotype among Older Adults in India: Findings from LASI Wave-1. International Journal of Environmental Research and Public Health, 20(4), 3055.
25. Avila-Funes, J. A., Helmer, C., Amieva, H., Barberger-Gateau, P., Goff, M. L., Ritchie, K., et al (2008). Frailty among community-dwelling elderly people in France: the three-city study. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 63(10), 1089-1096.
26. Zazzara, M. B., Vetrano, D. L., Carfì, A., Onder, G. (2019). Frailty and chronic disease. Panminerva Medica, 61(4), 486-492.
27. Soysal, P., Arik, F., Smith, L., Jackson, S. E., et al (2020). Inflammation, frailty and cardiovascular disease. Frailty and cardiovascular diseases: Research into an elderly population, 55-64.
28. Uchmanowicz, I. (2020). Oxidative stress, frailty and cardiovascular diseases: current evidence. Frailty and Cardiovascular Diseases: Research into an Elderly Population, 65-77.
29. Xu, R., Li, Q., Guo, F., Zhao, M., Zhang, L. (2021). Prevalence and risk factors of frailty among people in rural areas: a systematic review and meta-analysis. BMJ open, 11(4), e043494.
30. Rodriguez, J. J. L., Prina, A. M., Acosta, D., Guerra, M., Huang, Y., et alPrince, M. J. (2018). The prevalence and correlates of frailty in urban and rural populations in Latin America, China, and India: a 10/66 population-based survey. Journal of the American Medical Directors Association, 19(4), 287-295.
31. Szanton, S. L., Seplaki, C. L., Thorpe, R. J., Allen, J. K., et al (2009). Socioeconomic status is associated with frailty: the Women's Health and Aging Studies. Journal of Epidemiology Community Health.
32. Tan, V., Chen, C., Merchant, R. A. (2022). Association of social determinants of health with frailty, cognitive impairment, and self-rated health among older adults. Plos one, 17(11), e0277290.
33. Bock, J. O., König, H. H., Brenner, H., Haefeli, W. E., Quinzler, R., et al (2016). Associations of frailty with health care costs–results of the ESTHER cohort study. BMC health services research, 16(1), 1-11.
34. Li, J., Wu, D., Li, H., Chen, J. (2023). Unmet healthcare needs predict frailty onset in the middle-aged and older population in China: A prospective cohort analysis. Frontiers in Public Health, 11, 1064846.
35. Lavado, À., Serra-Colomer, J., Serra-Prat, M., Burdoy, E., Cabré, M. (2023). Relationship of frailty status with health resource use and healthcare costs in the population aged 65 and over in Catalonia. European Journal of Ageing, 20(1), 20.
36. Palladino, R. (2023). Voluntary private health insurance and management of frailty in European Health Systems: a longitudinal analysis. European Journal of Public Health, 33(Supplement_2), ckad160-105.
37. Matsugaki, R., Matsuzaki, H., Saeki, S., Fujino, Y.,Matsuda, S. (2023). Frailty and occupational falls among older Japanese workers: An Internet-based cross-sectional study. Journal of Occupational Health, 65(1), e12424.
38. Iavicoli, I., Leso, V., Cesari, M. (2018). The contribution of occupational factors on frailty. Archives of gerontology and geriatrics, 75, 51-58.
39. Johansson, M. M., Nätt, M., Peolsson, A., Öhman, A. (2023). Frail community-dwelling older persons' everyday lives and their experiences of rehabilitation–a qualitative study. Scandinavian Journal of Occupational Therapy, 30(1), 65-75.
40. Couch, K. A. (1998). Late life job displacement. The Gerontologist, 38(1), 7-17.
41. Chu, W. M., Ho, H. E., Yeh, C. J., Tsan, Y. T., Lee, S. H., et al (2021). Late-career unemployment and risk of frailty among older adults in Taiwan: An 8-year population-based cohort study. Geriatrics Gerontology International, 21(4), 353-358.
42. Helman, R., Copeland, C., VanDerhei, J. (2010). The 2010 retirement confidence survey: Confidence stabilizing, but preparations continue to erode. EBRI issue brief, (340).
43. Zhang, Q., Guo, H., Gu, H., Zhao, X. (2018). Gender-associated factors for frailty and their impact on hospital-

ization and mortality among community-dwelling older adults: a cross-sectional population-based study. PeerJ, 6, e4326.
44. Llano, P. M. P. D., Lange, C., Sequeira, C. A. D. C., Jardim, V. M. D. R., Castro, D. S. P., Santos, F. (2019). Factors associated with frailty syndrome in the rural elderly. Revista Brasileira de Enfermagem, 72, 14-21.
45. Rietman, M. L., Spijkerman, A. M., Wong, A., van Steeg, H., Bürkle, A., et al (2019). Antioxidants linked with physical, cognitive and psychological frailty: analysis of candidate biomarkers and markers derived from the MARK-AGE study. Mechanisms of ageing and development, 177, 135-143.
46. Syddall, H., Roberts, H. C., Evandrou, M., Cooper, C., Bergman, H.,et al (2010). Prevalence and correlates of frailty among community-dwelling older men and women: findings from the Hertfordshire Cohort Study. Age and ageing, 39(2), 197-203.
47. Kojima, G., Liljas, A., Iliffe, S., Jivraj, S., Walters, K. (2018). A systematic review and meta-analysis of prospective associations between alcohol consumption and incident frailty. Age and ageing, 47(1), 26-34.
48. Bye, E. K., Bogstrand, S. T., Rossow, I. (2022). The importance of alcohol in elderly's hospital admissions for fall injuries: a population case-control study. Nordic studies on alcohol and drugs, 39(1), 38-49.
49. Heuberger, R. A. (2009). Alcohol and the older adult: a comprehensive review. Journal of Nutrition for the Elderly, 28(3), 203-235.
50. O'Keefe, J. H., Bhatti, S. K., Bajwa, A., DiNicolantonio, J. J., Lavie, C. J. (2014, March). Alcohol and cardiovascular health: the dose makes the poison… or the remedy. In Mayo Clinic Proceedings (Vol. 89, No. 3, pp. 382-393). Elsevier.