Original Article

Frailty Syndrome among oldest old Individuals, aged ≥80 years: Prevalence & Correlates

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Introduction

The number of older people, aged ≥65 years of age is expected to rise up to 1.5 billion by the year 2050 from current 703 million in 2019 in the world. The largest increase is expected to occur in Eastern and South-Eastern Asia, from 261 million (2019) to 573 million by 2050¹. Global increase of oldest old persons, aged ≥80 years of age, will be three times from 137 million in 2017 to 425 million in 2050. India will be the second largest contributor of oldest old population to the world¹. Hence it is crucial to study health problems and correlated factors of older population of India.

Frailty syndrome, a clinical geriatric syndrome, is associated with high risk of adverse health outcomes in older age² like function disabilities, falls, mobility disabilities, frequent hospitalization, cardiovascular diseases, diabetes, and activities of daily living (ADL) as reported from developed countries³. Mortality is reported high in frail elders compared to non-frail elders⁴. Theoretically frailty is defined as a clinically recognizable state of increased vulnerability, resulting from aging-associated decline in reserve and function across multiple physiologic systems such that the ability to cope with every day or acute stressors is compromised⁵. In 2001, Fried and colleagues have defined operational definition of frailty⁶. Age-related changes to various physiological systems, particularly the

Abstract

Objectives: Objectives were to study prevalence of frailty among Indian oldest old population, and to detect its correlates. Methods: A cross sectional community based study was done including 200 healthy participants aged ≥80 years, randomly sampled from Hyderabad city in India. They completed an administered questionnaire and physical function tests including SPPB, grip strength. Cognitive function was assessed using MMSE and depression using GDS. Blood pressure, haemoglobin, and fasting blood sugar were measured for all participants. Frailty was defined using Fried phenotype criteria. Logistic regression was done to identify independently associated correlates. Results: The prevalence of frailty syndrome was 83.4% in our study population. Frailty among men was 80.3% and among women was 84.7%, and it increased with increasing age. The independent correlates which increased the odds of frailty were poor physical performance (SPPB) (OR: 4.21; 95%CI: 1.12-15.83), depression (OR: 3.35; 95%CI:1.29-8.73), chronic joint pains (OR:4.90; 95%CI: 1.97-12.18) and COPD (OR: 3.01; 95%CI:1.03-8.78), while hypertension showed inverse association (OR: 0.33;95%CI:0.11-0.94). Conclusion: The prevalence of frailty among the oldest old is very high. Geriatric medicine protocols must include routine screening for frailty, while also including early detection of poor physical performance, depression, COPD and osteoarthritis.

Keywords: COPD, Depression, Frailty, Hypertension, Oldest old

The authors have no conflict of interest.

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Edited by: Yannis Dionyssiotis

Accepted 26 September 2020

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neuromuscular, neuroendocrine and immunological systems, are fundamental to the development of frailty. Frailty has been considered synonymous with disability, comorbidity, and other characteristics, but it is recognized that it may have a biologic basis and be a distinct clinical syndrome. There are no proven pharmacological interventions yet for treatment of frailty. Only some evidence of improvements have been reported from physical activity intervention studies, but more research is required to establish preventive and therapeutic interventions. It is noteworthy that the lack of a universal definition of frailty, underscores the difficulty in synthesizing the intervention literature for frail adults.

Prevalence of frailty is reported as 7% to 12% in USA in ≥65 year old and 25% in ≥85 year old age; African American 13%; Mexican American 7.8%; wide variations have been observed in European countries from 5.8% Switzerland to 27% in Spain high in southern than northern European countries after adjusting to age and sex; from 5 large Latin American and Caribbean cities the prevalence of frailty was reported as 30% to 48%. All the studies reported prevalence was more in women than men. These wide variations in the geographic prevalence speculates that there may be difference in socio-cultural characteristics influencing frailty.

The data from developing countries are sparse on frailty and its correlates. The dynamics of health changes more rapidly in older ages of life. To our knowledge no population based studies exploring frailty syndrome is available, focussed on oldest old population aged ≥80 years from India. Hence we explored prevalence of frailty syndrome and correlated factors in this analysis. Evaluating the causes and natural history is therefore critical for identifying newer avenues for frailty and treatment.

Method

We enrolled 200 oldest old community-dwelling elders, 76 (38%) men and 124 (62%) women who completed 80 years of age or more, residing in south central part of India, Hyderabad city, Telangana state, in 2017. This cross-sectional research was designed to study frailty syndrome in oldest old urban population of south India. Ethical approval was obtained by institutional review board (IRB) of Mediciti Institute of Medical Sciences, Hyderabad and Indian Council of Medical Research (ICMR), Delhi. The participants were enrolled from twelve residential townships (population ranging from 1000-6000) of Hyderabad city. Data was collected by trained investigator by home visits. Households having at least one age eligible person were enlisted and randomised with random number generator software. All age eligible persons in the selected households were contacted to participate in the study. Total of 218 individuals were contacted to reach required number of 200. The participation rate was 91.7%. Inclusion criteria were: Indian nationality, age >80 years, living in an urban area of Hyderabad city, possessing cognitive ability to understand the investigator’s instructions, and consenting to participate; persons with terminal illness or psychotic conditions were excluded from the study.

We collected data using structured questionnaire and forms prepared by adapting questions and measurement protocols from leading international studies: Mobility and Independent Living in Elders Study and the Lifestyle Interventions and Independence for Elders pilot study, WHO Study of Global AGEing and Adult Health. Our questionnaires included information on age, sex, marital status, education, self-reported health status, medical history, physical functions, chronic diseases, medication inventory and functional disabilities. Other objective measurements included blood pressure, anthropometry (height, weight, waste and hip circumferences), grip strength, cognitive function, depression, haemoglobin and blood sugar.

Definitions and Measurements

Frailty Syndrome: Frailty syndrome was measured by Linda Fried’s Frailty Criteria which includes examining 5 phenotypic criteria: low grip strength, low energy, slowed walking speed, low physical activity, and unintentional weight loss. Participants meeting 3 conditions of the 5 phenotypic criteria indicating compromised energetics were categorised as frail participant.

Cognitive function: Cognitive function was assessed by Mini Mental State Examination scale (MMSE) . MMSE tests orientation, registration, attention and calculation, recall, language and praxis. A hindi (Indian language) version of this tool has been tested earlier in the Indian setting and validated. Single cut-off score <24 on MMSE was defined as cognitively impaired.

Activities of daily living (ADLs) constituted of 6 activities that included walking across the small room, bathing, grooming, dressing eating, getting out of bed and using toilet. If any participant couldn’t do even 1 activity out if above 6 then he was considered having poor activities of daily living.

Depression: The depression was assessed using 15 item Geriatric Depression Scale (GDS = 15) . Of total score from 0 – 15, if participant gets score of >5 he was considered to be suffering from depression.

Blood pressure: Resting blood pressure was measured thrice with a 1 minute interval using an electronic sphygmomanometer (OMRON HEM 7120, OMRON HEALTHCARE Co., Ltd., Japan). Systolic and diastolic blood pressures were recorded on relaxed calm participants in the sitting position with their elbows raised at the level of their heart. They were instructed to abstain from eating, drinking alcohol or caffeinated drinks or exercise at least for 30 min before blood pressure measurement. The average of last two readings were used to define systolic and diastolic blood pressures.

Grip strength: Hand grip strength was measured by JAMAR dynamometer using standard protocol. An
average of the last two readings out of three on the dominant hand was considered as the participant’s grip strength\textsuperscript{20}. It was measured in kgs and expressed in mean and standard deviation.

**Short Physical Performance Battery (SPPB):** The Short physical performance battery (SPPB) consisting of a 4 m walk, repeated chair stands, and three hierarchical standing balance tests, was performed. Each of the three performance measures was assigned a categorical score ranging from 0 to 4, with 4 indicating the highest level of performance and 0 the inability to complete the test. A summary score ranging from 0 (worst performers) to 12 (best performers) was calculated by adding Gait speed, chair stands, and balance scores\textsuperscript{21}.

**Co-morbidities:** Asthma, chronic obstructive pulmonary disease, cardiovascular disease, renal impairment, hypertension, diabetes, osteoarthritis, functional disabilities, vision and hearing were self-reported in the interview. We also measured biomarkers: haemoglobin and blood sugar.

**Statistical analysis**

Data was analyzed using SPSS, version 21 software (SPSS Inc., Chicago, IL, USA). Comparison of characteristics and correlates among frail individuals and non-frail individuals were done by using chi-square test for categorical variables and t-test for continuous variables. The variables those reported statistical significance (P value <0.05) in the univariate analysis were selected for multivariable model. We selected best fit model and checked for collinearity among the variables before running them in the logistic regression model. Specifically we examined Poor vision, osteoarthritis, hypertension, COPD, Body aches and pains, chronic joint pains, pain on standing/sitting down, depression, poor physical performances (SPPB), cognitive and impairment in the model, adjusting for age and sex. We excluded low physical activity, asthma and grip strength variables from the model due to high collinearity. We performed backward elimination logistic regression testing the deletion of each variable using a chosen model comparison criterion, deleting the variable that improves the model the most and repeating this process until no further improvement was possible, to get final set of the independent predictor variables. Variables with P<0.05 were retained in the final model. Results of logistic regression were expressed in odds ratios (OR) and 95% confidence intervals (95% CI). For continuous variables in logistic regression we expressed the OR per 1 standard deviation (SD) increase.

**Results**

**Characteristics of Study population**

In our study population 38.2\% were men and 61.8\% were women. The characteristics of the study population are described in Table 1. The mean ages and BMI of women and men were similar. A significantly higher proportion of women were living single, had no schooling, suffered with depression and impaired cognition, compared with men (p<0.05).

**Prevalence of Frailty syndrome**

The prevalence of frailty syndrome in our study population was 83.4\%, 80.3\% of men and 84.7\% of the women were frail (p=0.26). The prevalence of frailty increased with increasing age and 100\% were frail above the age of 95 years.

**Correlates of frailty**

The frail individuals were older, shorter, lighter, having a lower BMI than their non-frail counterparts, but the differences were not significant (Table 2). A significantly greater proportion of those having frailty had poor vision, osteoarthritis, hypertension, COPD, body pains, chronic joint pains, asthma, low physical activity compared with non-frail (p<0.05). The frail group had more depression, low grip strength, poor SPPB, impaired cognitive function compared with the no frailty group (p<0.01) (Table 2).

Upon logistic regression, the independently associated correlates of frailty were poor SPPB (OR: 4.21; 95\%CI: 1.12-
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15.83), depression (OR: 3.35; 95%CI: 1.29-8.73), chronic joint pains (OR: 4.90; 95%CI: 1.97-12.18) and COPD (OR: 3.01; 95%CI: 1.03- 8.78). Hypertension was negatively associated (OR: 0.33; 95%CI: 0.11-0.94). (Table. 3)

Discussion

We found a prevalence of 83.4% frailty syndrome in our oldest old population; 80% among men and 85% among women. The global prevalence of frailty among

| Characteristics & Correlates | Non – Frail individuals (N=34) (% & mean±sd) | Frail individuals (N=166) (% & mean±sd) | Total (N=200) (% & mean±sd) | P value |
|-----------------------------|---------------------------------------------|----------------------------------------|------------------------------|---------|
| Demographic                 |                                             |                                        |                              |         |
| Age (years) (mean)*         | 82.69±3.46                                 | 83.46±4.01                             | 83.34±3.93                   | 0.31    |
| Height (cm) (mean)*         | 156.72±11.19                               | 153.96±9.56                           | 154.35±9.82                  | 0.71    |
| Weight (kg) (mean)*         | 60.07±4.77                                 | 56.63±35.76                           | 57.12±33.59                  | 0.62    |
| BMI (kg/m²) (mean)*         | 24.19±3.99                                 | 22.67±4.67                            | 22.88±4.60                   | 0.11    |
| Marital status (single) (%) | 54.5                                       | 63.9                                   | 62.3                         | 0.20    |
| No education (%)            | 39.4                                       | 52.1                                   | 50.0                         | 0.12    |

| Medical history & Chronic diseases | | | | |
| Poor self-reported health | 29.4 | 23.5 | 24.5 | 0.29 |
| Smoking (%) | 34.4 | 35.5 | 35.0 | 0.50 |
| Alcohol (%) | 29.4 | 30.7 | 30.5 | 0.54 |
| Poor Vision (%) | 47.1 | 67.5 | 64.0 | 0.02 |
| Osteoarthritis (%) | 26.5 | 46.4 | 43.0 | 0.02 |
| Stroke (%) | 11.8 | 3.6 | 5.0 | 0.06 |
| Hypertension (%) | 79.4 | 61.4 | 64.5 | 0.03 |
| Cardiovascular disease (%) | 85.3 | 90.4 | 89.5 | 0.27 |
| Chronic Obstructive Pulmonary Diseases (COPD) (%) | 17.6 | 36.7 | 33.5 | 0.02 |
| Diabetes (%) | 20.6 | 21.5 | 21.3 | 0.55 |
| Body aches and Pains (muscular) (%) | 60.6 | 80.7 | 77.4 | 0.03 |
| Low physical activity (no exercise/no sports) (%) | 70.6 | 93.4 | 89.5 | <0.001 |
| Asthma (%) | 11.8 | 26.5 | 24.0 | 0.04 |
| Falls (%) | 26.5 | 38.8 | 36.7 | 0.12 |
| Chronic Joint pains (%) | 47.1 | 81.3 | 75.5 | <0.001 |
| Pain on Long standing (%) | 73.5 | 84.3 | 82.5 | 0.10 |
| Pain on standing or sitting down (%) | 58.8 | 77.7 | 74.5 | 0.02 |

| Objective measurements | | | | |
| Depression: >5 (GDS-15 point scale) (%) | 20.6 | 58.4 | 52.0 | <0.001 |
| Grip strength - kg (mean)* | 7.56±10.33 | 4.54±6.45 | 5.06±7.31 | 0.02 |
| Low Grip strength – kg (%) | 70.6 | 98.8 | 94.0 | <0.001 |
| Poor Short Physical Performance Battery (score ≤ 9) (%) | 79.4 | 97.0 | 94.0 | 0.001 |
| Impaired Cognitive function (MMSE <23) (%) | 47.1 | 69.9 | 66.0 | 0.01 |
| Systolic Blood pressure (mmHg)(mean)* | 145.68±24.07 | 142.52±25.05 | 143.05±24.85 | 0.52 |
| Diastolic blood pressure (mmHg)(mean)* | 84.41±14.76 | 82.21±12.21 | 82.15±12.61 | 0.30 |

Table 2. Characteristics and Correlates of Frail and Non – Frail individuals.
octogenarians is reported much lower at 23%22. Overall, the few independent studies on community dwelling oldest old reported lower prevalence of frailty than ours; 20.5% in Spain23, 28% in California (among ages 90+ years)24, 19.5% in Jerusalem25, 21% and 34% (among 90-94 years and 95 years +) in Ireland26, 34.9% in Japan27, and 39.8% in Brazil28. Most of these studies used the frailty phenotype criteria. Most studies on frailty on community dwelling elderly population aged 55 years and older, using varied frailty measurement criteria, reported prevalence rates ranging from 9.9% in developed countries29 to 5.4-44% in developing countries30. A study from Brazil reported higher frailty, 65.2% among individuals aged 80 years and older31.

We attribute our high frailty prevalence to higher levels of low education, low physical activity and lower working status of our population in addition to poor nutrition. A recent study from Thanjavur district of south India also showed that lower education, lower physical activity, and lower working status, higher age increases the odds of frailty in older individuals71. Although their study population was younger than ours i.e. ≥60 years of age, but they also reported higher prevalence of frailty compared to age matched population from other parts of the world. Other studies also reported lower levels of physical activity and working status in our older population16,21. Our high prevalence of frailty may also be explained by varying lifestyles, health statuses, demographic and socioeconomic characteristics across countries as well as lower life expectancy in India.

The prevalence of frailty among women and men was alike in our study. Some others have mirrored this finding showing no difference in frailty prevalence by gender23,32. Global literature, however abounds with findings of women being more commonly frail than men33,34. Alvarado33 and colleagues used a life course design to explain that women had more likelihood of frailty than men due to lack of schooling, a manual occupation, being a housewife, and perceived economic hardship later in life. They further discussed that social and chronic conditions did not totally explain the higher odds of frailty in women, thereby suggesting the presence of unmeasured underlying factors such as differences in biological factors, muscle strength, and other life-course exposures including low food intake and poor nutrition because of lack of social support and networks, low rates of physical activity related to lack of physical activity at younger ages, poorer perception of health, lack of self-sufficiency, and greater exposure to unsafe neighborhoods. Mitnitski et al.24 used a novel theory of accumulated deficits to explain the increasing risk of frailty in community dwelling elders wherein a frailty index was constructed as a proportion of all potential deficits (symptoms, signs, laboratory abnormalities, disabilities) expressed in a given individual. Their model also showed that at given age, women were frailer. Since women live longer and generally have a larger number of comorbidities35 a higher prevalence of frailty is expected among them.

Among functional parameters assessed, SPPB was independently associated with frailty in our population, posing a four folds increase in risk. Frail individuals have lower physical and muscular performances. Previous studies have shown associations between frailty and lower levels of lower limb muscle strength36. Moreover, SPPB is commonly used as a indicator of frailty37; whereby the high prevalence of frailty in our population detected using frailty phenotype criteria explained and justified a strong association with poor SPPB. We could not find any studies that showed this association specifically among the oldest old. Fried et al. theorized the loss of the muscle mass playing an important aetiologic role in the frailty process of elderly subjects8. Sarcopenia is frequently associated with poor endurance, physical inactivity and slow gait speed38,39. It is plausible that the oldest old, as a consequence of ageing, have greater sarcopenia compared with the younger elders, thereby having poorer SPPB scores and higher frailty.

Independently associated clinical parameters included depression, joint pains and COPD. Depression was associated with a 3 folds risk for frailty. Previous literature has also consistently reported this relationship between frailty and depression38,40. It has been earlier suggested that this association might be linked to characteristics present in

| Correlates                                      | Odds Ratio (OR) | 95% Confidence Interval (95% CI) |
|-------------------------------------------------|-----------------|----------------------------------|
| Short Physical Performance Battery (SPPB)***    | 4.21            | 1.12                             |
| Depression (%)**                               | 3.35            | 1.29                             |
| Chronic Joint pains (%)***                     | 4.90            | 1.97                             |
| Hypertension (%)**                             | 0.33            | 0.11                             |
| Chronic Obstructive Pulmonary Disease (COPD)%(**) | 3.01            | 1.03                             |

Backward stepwise logistic regression: **p<0.05; ***p<0.01.
both conditions, such as inactivity, weight loss, low level of physical activity and exhaustion\textsuperscript{40}. Others have suggested a complex and two-way causal nature between frailty and depression, that needs further exploration. While on one hand the presence of depressive symptoms may constitute a risk factor for this syndrome with changes in behavior, activity level or social commitment contributing to the decline of one’s functional state and frailty, often referred to as ‘psychosocial frailty’ \textsuperscript{41}. Depressive symptoms on the other hand, may represent the early manifestation of frailty, worsening one’s mood and depression due to the syndrome\textsuperscript{42}. Researchers have also suggested a considerable overlap between these two conditions\textsuperscript{28,43}. A recent systematic review on co-occurrence of depressive symptoms and frailty among elderly aged 55 years and older, indicated a prospective relationship between depressive symptomatology and increased risk of incident frailty\textsuperscript{44}.

Chronic joint pains were independently associated 4 folds with frailty in our study. Earlier studies on elderly corroborated with this finding of ours. The EPOSA study from six European countries on 2,455 individuals aged 65-85 years showed odds of frailty 2.96 (95 % CI:2.11-4.16) as high among OA individuals than those without. They further found the association to strengthen with increasing number of joints involved than with individual joints\textsuperscript{45}. In another independent study with more than 52% participants aged 80 years and above, Coelho et al. showed that pain predicted physical frailty; through mechanisms that were linked to mobility limitations, fatigue, disturbed sleep and decreased nutritional intake\textsuperscript{46}. Some hypothesized that frailty is associated with physiological changes (in brain, immune system, endocrine system, skeletal system) which could alter pain perception or exacerbate pain in an older person\textsuperscript{47}. Data on chronic pain and frailty among community dwelling elderly are very limited\textsuperscript{48,49} and missing for 80 years and older population. These limited studies showed older people reporting pain to be statistically more likely to be frail. The direction of the relationship however, couldn’t be affirmed due to the lack of prospective data. Additionally, these conditions may overlap considerably, indicating that somatic complaints are symptoms of diseases associated with the frailty syndrome\textsuperscript{50}.

Frailty in our population was also independently associated 3 folds with COPD. Of the very few studies to elaborate on similar association, the Rotterdam study found elderly participants (having mean age 74 years) with COPD showed a more than twofold increased prevalence of frailty (odds ratio 2.2, 95% CI: 1.34-3.54). A recently published meta-analysis on relationship between COPD and frailty among older adults including 27 studies found that patients with COPD had a two-fold increased odds of frailty (pooled OR: 1.97; 95% CI: 1.53-2.53). Three longitudinal studies included in the review suggested a bidirectional association between COPD and frailty\textsuperscript{51}. This association is biologically plausible, since complex age related changes occur in the ageing lung characterized by a decline in FEV1, a reduction in muscular strength and an increase in inflammatory cells in bronchial tissue; these changes are aggravated in frail individuals. Furthermore, the predilection for managing COPDs with steroids predisposes ageing individuals to steroid related multi morbidities and resultant frailty\textsuperscript{52}.

Hypertension emerged as negatively associated with frailty upon logistic regression. The protective effects of hypertension on cardiovascular and all cause mortality has been shown earlier among the oldest old populations\textsuperscript{53,54}. Wong et al. also similarly noted that cross-sectional analysis could not fully exclude the possibility of reverse causation for hypertension and frailty\textsuperscript{55}, with many observational studies indicating weaker associations of blood pressure with CVD in older individuals compared with the middle ages. Our population was however, much older compared with these studies. These earlier findings and the HYVET study recommendations later\textsuperscript{56} questioned the effect of antihypertensive treatment and the ideal blood pressure goal of treatment in the frail elderly\textsuperscript{57}. De Sousa et al., in their frailty prediction model for Brazilian oldest old, failed to find an association with cardiovascular diseases, inspite of CVD being the most commonly reported disease and antihypertensive being the predominant medications\textsuperscript{58}. The mechanisms for negative association of hypertension with frailty, or conversely, positive association of low blood pressure with frailty among the oldest old were well debated\textsuperscript{59}. Few studies proposed that older or frail elders were more likely to have chronic health conditions resulting in low blood pressure\textsuperscript{60}. Others explained this association with increased vascular stiffness resulting from atherosclerosis, arterial calcification, endothelial dysfunction, and smooth muscle cell fibrosis leading to isolated systolic hypertension, more pronounced on the frail old\textsuperscript{61}.

We showed that frailty was significantly associated with cognitive impairment upon univariate analysis. Studies on ageing and frailty have reported this association very often\textsuperscript{62,63}. In a comparative study, Marcucci et al. showed a 5 fold odds (OR=5.15, 95% CI=2.58–10.26) of mortality among the frail oldest old women with cognitive decline compared with the younger elderly (relatively healthy) without cognitive impairment\textsuperscript{64}. The characteristic structural and physiological changes in the brain associated with ageing, which place disproportionate stress on neurons with high metabolic demands, such as the hippocampal pyramidal neurons that are important mediators in pathophysiology of cognitive decline\textsuperscript{65,66}, explain this association. Additionally, several factors that are related to physical frailty also are related to cognitive impairment, including inflammatory markers, diabetes, congestive heart failure, and stroke. In our population, however, most of these factors did not show any association, barring pain on movement which underlines inflammation. Interestingly, stroke showed an inverse relationship with frailty that was nearly significant in this population. These inverse associations with cardiovascular
parameters (hypertension and stroke) lead us to hypothesize that cardiovascular factors may protect the oldest old Indians against frailty. Moreover, it may be assumed that frail elderly who have survived the age of 80 years may have several other compensatory mechanisms in place that mask the risk posed due to adverse cardiovascular events. This remains amenable to testing using more objective criteria and possibly biomarkers, since the phenotypic criteria (based on measures of mobility and motor performance) used in our study were not derived from stroke patients who were originally excluded from the CHS.

We also found an association between frailty and low vision, which has been reported earlier by very few studies. One Chinese study reported low vision to be an independent predictor of frailty among elderly aged 60 years and older. They attributed the association to the increased risk of falls and fractures leading to frailty, consequent to visual impairment. Lang et al. described sensory impairment in relation to and as a manifestation of frailty earlier. This relationship may be independent due to ageing impacting both physical frailty and visual impairment consequent to degenerative conditions including cataract formation.

All the positive associations of risk factors with frailty in our study point to the chronic nature of these diseases which call for early detection and control. Additionally, it is worthwhile to note that most of these conditions are not treated appropriately, and elderly continue to survive in the absence of medical care. The draft National Program for the Health Care of the Elderly (NPHCE) has attempted to identify some of these problems at grass root level but focused interventions on frailty seem missing. Developed countries, on the contrary have already identified frailty as a major problem, with guidelines for preventive interventions instituted. For instance, the revised contract for General Practitioners in the UK for 2017–18 includes advice for frailty screening of older people using electronic frailty questionnaire and advocates strategies for annual review of medication for frail older people. Such screening may include opportunities to review lifestyle advice and medication to optimise control of risk factors, CVD risk factors in particular, for prevention of disability and death in frail older people. Similarly, Arantes P et al. in their systematic review have compared and verified the effect of seven different types of interventions namely, 1) muscle strengthening; 2) exercises for muscle strengthening, balance, coordination, flexibility, reaction time and aerobic training; 3) functional training; 4) physical therapy; 5) at-home physical therapy; 6) environment adaptation and prescription of assistive device; 7) water exercise. de Labra et al. also reported the benefits of exercise interventions in their systematic review that included studies on multi-component exercise interventions (aerobic and resistance training not coexisting in the intervention), physical comprehensive training, and exercises based on strength training, compared with a control group receiving no treatment, maintaining their habitual lifestyle or using a home-based low level exercise program. The benefits reported in the review ranged from positive impact of exercise interventions on falls, enhancements in several measurements of mobility, enhanced balance, and functional ability, increases in muscle strength, improvements in body composition, and improvement in frailty. They however, concluded that though exercise interventions had demonstrated improvement in different outcome measurements in frail older adults, there were large differences between studies with regard to effect sizes, thereby inconclusive regarding an optimal program.

We recommend further studies of similar kind from different regions that can reflect the actual burden and the presumed effect of interventions for frailty prevention. We further recommend that the current geriatric medicine protocols include multidisciplinary group-based rehabilitation interventions in order to reduce the progression and the impact of frailty in this population. The current geriatric medicine protocols of the country should be revisited to address these problems using active ageing and rehabilitation medicine for elderly.

Strengths and limitations

The major strength of this study is the large number of community dwelling participants, aged 80 years and older used to estimate the prevalence of frailty, which provides a stable estimation of prevalence. This is by far, the largest study in India, and in South East Asia, to use the phenotypic definition of frailty to analyze prevalence in this age group, allowing further analysis according to age and sex specific groups. The sample of 200 participants from South India however, may not sufficiently reflect the burden in rural parts of the country, and surrounding states and countries with varying population characteristics and health services. We did not calculate required sample size to state the risk factors due to absence of comparative literature. A post hoc power analysis showed that the included number could detect the prevalence and correlates with sufficient power of more than 90%.

Conclusion

Prevalence of frailty was very high in our oldest old population. Frailty was similar in women and men in our population. The independent positively associated correlates of frailty-poor physical performance, depression, COPD and chronic joint pains were chronic health problems of the oldest old, which suggest the need for early detection and prevention measures in order to control frailty. The current geriatric medicine protocols of the country should be revisited to address these problems using a holistic approach.

Acknowledgements

Research reported in this publication was conducted by scholars, Pawan Kumar Sharma and Enakshi Ganguly, in...
the Fogarty International Center of the National Institutes of Health training program under Award no. D43 TW 009078. The authors sincerely thank the Indian Council of Medical Research for approval to conduct the study under the STS grant, 2017, and SHARE INDIA for providing logistical support.

References

1. United Nations, Department of Economic and Social Affairs. World Population Ageing, 2019.
2. Clegg A, Young J. The frailty syndrome: Clinical medicine 2011;11(1):1-5.
3. Ensrud KE, Ewing SK, Cawthon PM, Fink HA, Taylor BC, Cauley JA, Dam TT, Marshall LM, Orwoll ES, Cummings SR. Osteoporotic Fractures in Men Research Group: A comparison of frailty indexes for the prediction of falls, disability, fractures, and mortality in older men. Journal of the American Geriatrics Society 2009;57(3):492-8.
4. Graham JE, Al Sinh S, Borges IM, Ray LA, Markides KS, Ottenbacher KJ. Frailty and 10-year mortality in community-living Mexican American older adults. Gerontology 2009;55(6):644-51.
5. Sue QL. The frailty syndrome: definition and natural history. Clinics in geriatric medicine 2011;27(1):1-5.
6. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA. Frailty in older adults: evidence for a phenotype. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 2001;56(3):M146-57.
7. Fried L, Walston J Hazzard W, Blass J, Halter J, et al. Frailty and the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 2004;59(3):M255-63.
8. Walston J, Hadley EC, Ferrucci L, Guralnik JM, Newman AB, Studenski SA, Ershler WB, Harris T, Fried LP. Research agenda for frailty in older adults: toward a better understanding of physiology and etiology; summary from the American Geriatrics Society/National Institute on Aging Research Conference on Frailty in Older Adults. Journal of the American Geriatrics Society 2006;54(6):991-1001.
9. Santos-Eggimann B, Cuénot P, Spagnoli J, Junod J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. The Journals of Gerontology: Series A: Biological Sciences and Medical Sciences 2000;59(3):M146-57.
10. Santos-Eggimann B, Cuénot P, Spagnoli J, Junod J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. The Journals of Gerontology: Series A: Biological Sciences and Medical Sciences 2000;59(3):M146-57.
11. Börsch-Supan A, Brugiavini A, Jürges H, Mackenbach J, Sigrist J, Weber G. First results from the Survey of Health, Ageing and Retirement in Europe. MEA, available at www.share-project.org. 2005.
12. Alvarado BE, Zunzunegui MV, Bélard F, Barnvita JM. Life course social and health conditions linked to frailty in Latin American older men and women. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 2008;63(12):1399-406.
13. Singh T, Sharma PK, Jammy GR, Cauley JA, Bunker CH, Reddy PS, Newman AB. Design of the Mobility and Independent Living in Elders Study: An older adult cohort in rural India. Geriatrics & gerontology international 2017;17(1):31-40.
14. Fielding RA, Rejeski WJ, Blair S, Church T, Espeland MA, Gil TM, Guralnik JM, Hsu FC, Katula J, King AC, Kritchevsky SB. The lifestyle interventions and independence for elders study: design and methods. Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences 2011;66(11):1226-37.
15. World Health Organization. SAGE Survey Programme. 2010.
16. Konda PR, Sharma PK, Gandhi AR, Ganguly E. Correlates of cognitive impairment among Indian Urban Elders. Journal of gerontology & geriatric research. 2018;7(6):doi: 10.4172/2167-7182.1000489. Epub 2018 Nov 6. PMID: 31406631; PMCID: PMC6690611.
17. Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. The gerontologist. 1970;10(1_Part_1):230-30.
18. Konda PR, Sharma PK, Gandhi AR, Ganguly E. Geriatric Depression and its Correlates among South Indian Urban. Journal of depression & anxiety 2018;7(4): doi: 10.4172/2167-1044.1000314. Epub 2018 Aug 14. PMID: 31406629; PMCID: PMC6690607.
19. Reddy BM, Ganguly E, Sharma PK. Hypertension and its correlates in the oldest old population aged 80 years and above in urban South India. Journal of gerontology & geriatric research 2018;7(3): doi:10.4172/2167-7182.1000472.
20. Logan S, Thu WP, Lay WK, Wang LY, Cauley JA, Yong EL. Chronic joint pain and handgrip strength correlates with osteoporosis in middle age women: a Singaporean cohort. Osteoporosis International 2017;28(9):2633-43. doi: 10.1007/s00198-017-4095-z.
21. Sharma PK, Bunker CH, Singh T, Ganguly E, Reddy PS, Newman AB, Cauley JA. Burden and correlates of falls among rural elders of South India: Mobility and Independent Living in Elders Study. Current gerontology and genatics research 2017;2017: doi: 10.1155/2017/1290936. Epub 2017 Jun 13. PMID: 28694824; PMCID: PMC5485263.
22. Hamerman D. Toward an understanding of frailty. Ann Intern Med 1999;130(11):945-950. DOI: 10.7326/0003-4819-130-11-199906010-00022.
23. Ferrer A, Badia T, Formiga F, Sanz H, Megido MJ, Pujol R, Octabaz Study Group. Frailty in the oldest old: prevalence and associated factors. Journal of the American Geriatrics Society 2013;61(2):294-6.
24. Lee DR, Kawas CH, Gibbs L, Corrada MM. Prevalence of frailty and factors associated with frailty in individuals aged 90 and older: The 90+ study. Journal of the American Geriatrics Society. 2016 Nov;64(11):2257-62.
25. Jacobs JM, Cohen A, Ein-Mor E, Maaravi Y, Stessman J. Frailty, cognitive impairment and mortality among the oldest old: The 90+ study. Journal of the American Geriatrics Society. 2016 Nov;64(11):2257-62.
26. Santos-Eggimann B, Cuénot P, Spagnoli J, Junod J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. The Journals of Gerontology: Series A: Biological Sciences and Medical Sciences 2000;59(3):M255-63.
27. Shimada H, Makizako H, Doi T, Yoshida D, Tsutsunimoto K, Anan Y, Uiemura K, Ito T, Lee S, Park H, Suzuki T. Combined prevalence of frailty and mild cognitive impairment in a population of elderly Japanese people. Journal of the American Medical Directors Association 2013;14(7):518-24. http://dx.doi.org/10.1016/j.jamda.2013.03.010.
28. Pegoraro MS, Tavares DM. Factors associated with the frailty syndrome in elderly individuals living in the urban area. Revista latino-americana de enfermagem 2014;22(5):874-82.
29. Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: a systematic review. Journal of the American Geriatrics Society 2012;60(8):1487-92.
30. Nguyen T, Cumming RG, Hilmer SN. A review of frailty in developing countries. The journal of nutrition, health & aging 2015;19(9):941-6.
31. Carneiro JA, Cardoso RR, Dùrdes MS, Guedes MC, Santos FL, Costa FM, Caldera AP. Frailty in the elderly: prevalence and associated factors. Revista brasileira de enfermagem 2017;70(4):747-52.
32. Da Mata FA, Pereira PP, Andrade KR, Figueiredo AC, Silva MT, Pereira MG. Prevalence of frailty in Latin America and the Caribbean: a systematic review and meta-analysis. PLoS one 2016; 11(8):e0160019.

33. Alvarado BE, Zununegui MV, Béland F, Barnvita JM. Life course social and health conditions linked to frailty in Latin American older men and women. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 2008;63(12):1399-406.

34. Munttinsi A, Song X, Skogq I, Broe GA, Cox JL, Grunfeld E, Rockwood K. Relative fitness and frailty of elderly men and women in developed countries and their relationship with mortality. Journal of the American Geriatrics Society 2005;53(12):2184-9.

35. Hubbard RE, Rockwood K. Frailty in older women. Maturitas 2011;69(3):203-7.

36. Batista FS, Gomes GA, Neri AL, Guaniento ME, Cintra FA, Sousa MD, D’Elboux LP. A relationship between lower-limb muscle strength and frailty among elderly people. Sao Paulo Medical Journal 2012;1:30(2):102-8.

37. Abizanda P, Romero L, Sanchez-Jurado PM, Atienza-Nunez P, Esquinas-Quenca JL, Garcia-Naguera I. Association between functional assessment instruments and frailty in older adults: the FRADA study. Journal of frailty and aging 2012;1(4):162-8.

38. Roberts HC, Denison HJ, Martin HJ, Patel HP, Syddall H, Cooper C, Sayer AA. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. Age and ageing 2011;40(4):423-9.

39. Landi F, Cruz-Jentoft AJ, Piperoti R, Russo A, Giovannini S, Tosato M, Capuolungo E, Bernabei R, Onder G. Sarcopenia and mortality risk in frail older persons aged 80 years and older: results from iSIRENTE study. Age and ageing 2013;42(2):203-9.

40. Rantanen T, Penninx BW, Masaki K, Lintunen T, Foley D, Guralnik JM. Depressed mood and body mass index as predictors of muscle strength decline in old men. Journal of the American Geriatrics Society 2000;48(6):613-7.

41. de Jonge P, Ormel J, Slaets JP, Kempen GI, Ranchor AV, van Jaarsveld CH, Scal-Klopw WM, Sanderman R. Depressive symptoms in elderly patients predict poor adjustment after somatic events. The American journal of geriatric psychiatry 2004;12(11):57-64.

42. St. John PD, Tyas SL, Montgomery PR. Depressive symptoms and frailty. International journal of geriatric psychiatry 2013;28(6):607-14.

43. Lohman M, Dumenci L, Mezuk B. Depression and frailty in late life: evidence for a common vulnerability. Journals of Gerontology Series B: Psychological Sciences and Social Sciences 2016;71(4):630-40.

44. Vaughn L, Corbin AL, Covejas JS. Depression and frailty in later life: a systematic review. Clinical interventions in aging 2015;10:1947.

45. CastelliMV, VanDerPas S, Otero A, Siviero P, Dennison E, Denikinger M, Pedersen N, Sanchez-Martinez M, Queipo R, Van Schoor N, Zambon S. The relationship between frailty and mental health in elderly individuals across six European countries: results from the European Project on OSteoArthritis (EPOSA). BMC Musculoskeletal Disorders 2015;16(1):359.

46. Coelho T, Lopes C, Gobbens RJ, Fernandes L. Multidimensional frailty and pain in community dwelling elderly. Pain Medicine 2017; 18(4):693-701.

47. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. The lancet 2013;381(9868):752-62.

48. Koponen MP, Bell JS, Karttunen NM, Nyknen IA, Desplenter FA, Hartikainen SA. Analgesic use and frailty among community-dwelling older people. Drugs & aging 2013;30(2):129-36.

49. Miguel CR, Dias RC, Dias JM, Mencuccci PF, Ribeiro TM. Frailty syndrome in the community-dwelling elderly with osteoarthritis. Revista brasileira de reumatologia 2012;52(3):331-47.

50. Theou O, Rockwood MR, Mitnitski A, Rockwood K. Disability and co-morbidity in relation to frailty: how much do they overlap? Archives of gerontology and geriatrics 2012;55(2):e1-8.

51. Marengoni A, Vetrano DL, Manes-Gravina E, Bernabei R, Onder G, Palmieri K. The relationship between COPD and frailty: a systematic review and meta-analysis of observational studies. Chest 2018; 154(1):21-40.

52. Jayadev A, Gill SK. COPD in the elderly: The ageing lung. GM 47, 2017.

53. Poortvliet RK, Blom JW, de Craen AJ, Mooijaart SP, Westendorp RG, Assendelft WJ, Gussekloo J, de Ruijter W. Low blood pressure predicts increased mortality in very old age even without heart failure: the Leiden 85-plus study. European journal of heart failure 2013;15(5):528-33.

54. Satish S, Freeman Jr DH, Ray L, Goodwin JS. The relationship between blood pressure and mortality in the oldest old. Journal of the American Geriatrics Society 2001;49(4):367-74.

55. Wong TY, Massa MS, O’Halloran AM, Kenny RA, Clarke R. Cardiovascular risk factors and frailty in a cross-sectional study of older people: implications for prevention. Age and ageing 2018; 47(5):714-20.

56. Warwick J, Falaschetti E, Rockwood K, Mitnitski A, Thijis L, Beckett N, Buipitt C, Peters R. No evidence that frailty modifies the positive impact of antihypertensive treatment in very elderly people: an investigation of the impact of frailty upon treatment effect in the Hypertension in the Very Elderly Trial (HYVET) study, a double-blind, placebo-controlled study of antihypertensives in people with hypertension aged 80 and over. BMC medicine 2015;13(1):78.

57. Abramov D, Cheng H. Controversy in treating the oldest old with hypertension: is the hypertension in the very elderly trial the final answer? Journal of the American Geriatrics Society 2009; 57(3):570-1.

58. Sousa JA, Lenardt MH, Grden CR, Kusomota L, Deliaroza MS, Bettoli SE. Physical frailty prediction model for the oldest old. Revista latino-americana de enfermagem 2018;26. doi: 10.1590/1518-8345.2016.2346.3023.

59. Odden MC, Belsey PR, Peralta CA. Blood pressure in older adults: the importance of frailty. Current hypertension reports 2015;17(7):55. doi: 10.1007/s11906-015-0564-y.

60. Goodwin JS. Embracing complexity: a consideration of hypertension in the very old. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 2003;58(7):M653-8.

61. Muller M, Smulders YM, de Leeuw PW, Stenhouwer CD. Treatment of hypertension in the oldest old: a critical role for frailty?. Hypertension 2014;63(3):433-41.

62. Boyle PA, Buchman AS, Wilson RS, Urqurgans SE, Bennett DA. Physical frailty is associated with incident mild cognitive impairment in community-based older persons. Journal of the American Geriatrics Society 2010;58(2):248-55. doi:10.1111/j.1532-5415.2009.02671.x

63. Sampner-Tement R, Al Snih S, Raji MA, Markides KS, Ottenbacher KJ. Relationship between frailty and cognitive decline in older Mexican Americans. Journal of the American Geriatrics Society 2008;56(10):1845-52. doi: 10.1111/j.1532-5415.2008.01947.x. Epub 2008 Sep 22.

64. Marucci M, Franchi C, Nobile A, Mannucci PM, Ardoino I. Defining aging phenotypes and related outcomes: clues to recognize frailty in hospitalized older patients. The Journals of Gerontology Series A 2017;72(3):395-402.

65. Bishop NA, Lu T, Yankner BA. Neural mechanisms of ageing and cognitive decline. Nature 2010;464(7288):529-35.

66. Miller DB, O’callaghan JP. Aging, stress and the hippocampus. Aging
research reviews 2005;4(2):123-40.
67. Ferrucci L, Cavazzini C, Corsi A, Bartali B, Russo CR, Lauretani F, Corsi AM, Bandinelli S, Guralnik JM. Biomarkers of frailty in older persons. Journal of endocrinological investigation 2002;25(10 Suppl):1-5.
68. Miu DKY. Visual Impairment Contributes to Frailty among a Group of Healthy Community Dwelling Older Population. J Geriatr Med Gerontol 2018;4:041
69. Lang PO, Michel JP, Zekry D. Frailty syndrome: a transitional state in a dynamic process. Gerontology 2009;55(5):539-49.
70. Indian Ministry of Health and Family Welfare. National Programme for the Health Care of the Elderly (NPHCE): An approach towards active and healthy ageing. https://mohfw.gov.in/sites/default/files/NPHCE.pdf
71. Kendhapedi KK, Devasenapathy N. Prevalence and factors associated with frailty among community-dwelling older people in rural Thanjavur district of South India: a cross-sectional study. BMJ open 2019;9(10):e032904.
72. Arantes PMM, Alencar MA, Dias RC, Dias JMD, Pereira LSM. Physical therapy treatment on frailty syndrome: systematic review. Rev Bras Fisioter 2009;13(5):365-75.
73. de Labra C, Guimaraes-Pinheiro C, Maseda A, Lorenzo T, Millán-Calenti JC. Effects of physical exercise interventions in frail older adults: a systematic review of randomized controlled trials. BMC Geriatr 2015;15:154.
74. Dionyssiotis Y. Active Ageing. Journal of Frailty, Sarcopenia and Falls 2018;3(3):125.
75. Masiero S, Carraro U. Rehabilitation Medicine for Elderly Patients. Springer International Publishing; 2018.
76. Dionyssiotis Y. Analyzing the problem of falls among older people. International Journal of General Medicine 2012;5:805.