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Original Research Article

Assessing frailty index and correlation with crp and serum albumin and clinical outcome in terms of length of hospital stay

Akash Durgakar[1], Pratibha Pereira[1], Shilpa Avarebeel[1,*], Tandure Varsha[1], Mahesh Poojari[1], S Meenakshi[1]

[1] *Dept. of Geriatric Medicine, JSS Hospital, Mysuru, Karnataka, India*

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ABSTRACT

Background : Frailty is defined as "a clinically recognizable state of increased vulnerability, resulting from aging associated decline in reserve and function across multiple
Materials and Methods: A Hospital based descriptive cross-sectional study in tertiary care hospital. A total of 294 patients admitted in the Medicine/Geriatric Ward, were included in stressors is compromised". It is a robust and powerful risk factor for disability. With this background, study was conducted at a tertiary centre with objectives to assess the frailty in elderly patients and to assess the correlation of frailty with Serum Albumin and CRP physiologic systems, such that the ability to cope with every day or acute and evaluate the clinical outcome in terms of length of hospital stay. The study. Demographic details and details of known comorbidities were recorded. Cognition score of all patients were assessed using mini mental scale examination. Investigations like Serum Albumin and CRP were done. The data was analyzed using statistical software.
Results: Our results show that in hospitalized patients frailty is seen in both gender. The presence of co-morbidities worsens the frailty. 30 second chair test is very good indicator for frailty and risk of fall and we observed reduced duration in the Pre-Frail group. The cognition score decreased along with the increase in age groups. When compared with the Frailty index, it was more in the Pre-Frail group. The duration of hospital stay was more in Frail group. The mean serum albumin level is important marker to identify early frailty.
Conclusion: Assessment of frailty in elderly patients is necessary and identifying Pre-Frailgroup is very important. 30 second chair stand test and serum albumin are very important early markers in the assessment of frailty. Cognitive function is also very important to identify early frailty. Our study shows that the length of hospital stay is more in the Frail group. Frailty is important aspect of elderly. It should be included in routine clinical assessment of all elderly patients.

1. Introduction

Frailty is defined as the syndrome characterized by a decreased ability of individuals to restore homeostasis in response to stress. It is clinically identifiable syndrome found in old age group which consists of features like an increased susceptibility to stressors due to impaired multiple, inter-connected systems, reduced physiological reserves and a decreased ability to maintain homeostasis.[1]

Frailty index helps to measure the health condition of older population-as proxy measure of ageing and exposed to poor outcomes. It is the proportion of deficits found in a subject out of total number of age associated health variables considered.[2] Frail means physically weak and delicate.

A cross-sectional study of 250 older adults (65 years) was done in Pune, Maharashtra. The study showed 26% of prevalence of frailty.63.6% of population accounted

* *Corresponding author*.
E-mail address: shilpaavarebeel@gmail.com (S. Avarebeel).

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for pre frail and 10.4% were non-frail. Low education, functional impairment, polypharmacy and reduced access to instrumental support increased the probability of being frail as compared to non-frail population.[2]

The importance of frailty is brought out by consistent associations with increased mortality from all causes and adverse aging outcome such as institutionalization, physical limitations, disability, recurrent hospitalization and falls. Frailty provides a high predictive value for adverse outcomes in the elderly population, especially those suffering from chronic diseases and those undergoing major surgeries, like cardiac surgery.[3]

Low grade chronic inflammation in the geriatric population is considered as risk factor for developing age related disorders and frailty. Increased levels of acute phase reactants were found in frail individuals hence it infers frailty is associated with marked inflammatory activity. C-reactive protein takes a major part in several disease processes and increased CRP levels have been found to have increased vulnerability for disease and mortality in older subjects.[4] Serum albumin is another independent risk factor for frailty in elderly patients.

Some studies have been conducted in this regard. One such example is the English Longitudinal Study of Ageing. It studied the association of inflammatory markers causing the incident frailty in men and women. This study was done among subjects of 60years to over 90 years. It was observed that the higher baseline values of CRP and fibrinogen levels were separately related to an increased risk of incident frailty in women.[5]

The first index for the measurement of frailty was developed by Fried.[6] Since then many scales and indexes have been developed. But in spite of increasing population of geriatric with multiple comorbidities and frailty[7], which implies need of geriatric assessment routinely by health care providers during routine health checkup. Complete comprehensive geriatric assessment and/or FIs remain ignored in many settings.[8] The root cause for this lack of widespread acceptance, mainly in the context of acute care clinical setups,[9,10] could be the amount of time required to provide these instruments.[11–15]

Though some studies have been conducted in this regard, however, the importance of predictive value of frailty in elderly population remains largely unrealized and the underlying pathogenic mechanisms remain unexplored. There is an urgent need to achieve a uniform definition and develop an internationally acceptable criteria for the diagnosis of frailty to enable its optimal utilization clinically and to decrease the burden on the already scarce health resources.

So, our study was done to assess the frailty index in the elderly, along with its major determinants and to find its correlation with the markers of inflammation and nutritional status.

2. Aims and Objectives

1. To assess Frailty index in elderly patients
2. To assess the incidence of Pre frail
3. To correlate the frailty index with CRP and Serum Albumin
4. To evaluate the clinical outcome in terms of length of hospital stay

3. Materials and Methods

3.1. Inclusion criteria

1. Patients of more than 70 years of age, getting admitted under the Department of Medicine/Geriatrics.

3.2. Exclusion criteria

1. Very ill patients where Frailty cannot be assessed.
2. Patients with CPS score of more than 7.
3. Patients who do not give consent to participate in the study.

3.3. Sample size estimation and sampling procedure

Considering Type I error at 5%, margin of error/precision at 5%, power of the study at 80% and based on a prevalence of Frailty is 26% as per previous studies, a sample size of 294 was calculated and purposive sampling technique is adopted to enroll the subjects into study

3.4. Ethical considerations

Prior approval of the Institutional Ethics Committee was taken before conducting the study.

3.5. Method of data collection

All patients who were (aged more than 70 years) admitted in the Medicine/Geriatric ward during the study period were included in the study after screening for inclusion and exclusion criteria. They were explained the purpose and methodology of the study and the importance of this study. They were assured about the maintenance of confidentiality and the nature of voluntary participation after taking written informed consent.

The demographic parameters were recorded. Detailed past and personal history were recorded. Details of known comorbidities were recorded.

Assessment of the CPS Score:

The number of pre-hospital medications were noted. Each comorbidity and each pre-hospital medication was assigned a score of 1. The CPS Score was calculated by adding the number of comorbidities and the number of pre-hospital medications for each patient. Severity of the CPS Score was stratified as:

1. Mild (0-7)

2. Moderate (8-14)
3. Severe (15-21)
4. Morbid (>22)

Patients having CPS Score of more than 7 were excluded from the study as per the exclusion criteria.

1. Assessment of the Cognition Score:
2. Mini mental scale examination.
3. Assessment of the Physical Activity:

Patients were asked 3 questions regarding the frequency of which they perform vigorous, moderate or mild physical activity. The rank combinations of feedback to these questions were analyzed as:

1. Amount of exercise
2. Intensity of exercise

These parameters provided an estimate of physical activity. Frequency, duration, intensity of usual activities were analyzed. Frequency of exercise of less than 5 times a week was considered positive. Based on this, the presence of low physical activity was determined and the response was recorded as "Yes/No".

3.6. Assessment of self-reported parameters

Unintentional Weight loss: 4.5 kg or 5 percent of weight loss in previous year (Self-reported, "Yes/No") or BMI =18.5

Exhaustion: Patients were further asked about self-reported exhaustion/tiredness. The response was recorded as "Yes/No".

3.7. Assessment of the physical attributes:

Weight was measured by the standard weighing machine. Height was measured by the portable Stadiometer. BMI was calculated by the Quetlet Index (Weight (kg)/Height $(m)^2$).

Using a hand dynamometer the Maximum handgrip strength was recorded three times on both hands. The average of the readings was recorded in kg.

Gait speed was measured by stopwatch by assessing time required to walk a distance of 8 feet at their normal pace and it was repeated twice and its mean was recorded in seconds.

Second chair stand test: It was conducted to test leg strength and endurance

The number of times patient came to full standing position in 30 seconds were counted and recorded.

3.8. Scoring

3.9. Assessment of frailty

For the assessment of Frailty, the Fried Frailty Phenotype method was used. It is a five criteria scale as follows:

1. Self-reported exhaustion

Table 1:

Age	Males	Females
70-74	<12	<10
75-79	<11	<10
80-84	<10	<9
85-89	<8	<8
90-94	<7	<4

2. Low physical activity
3. Hand grip strength
4. Unintentional weight loss
5. Gait speed/Walking time

3.10. These criteria were operationalized as follows:

1. For the first three criteria:

- a. Yes = 1
- b. No = 0

2. Hand grip strength(Muscle strength measured by hand dynamometer): Cut-offs according to gender and BMI:

- a. For Men

1. BMI >28 kg/m^2; grip strength ≤ 32 kg
2. BMI ≥ 24.1 kg/m^2; grip strength ≤ 30 kg
3. BMI < 24.1 kg/m^2; grip strength ≤ 29 kg

- b. For Women

1. BMI >29 kg/m^2; grip strength ≤ 21 kg
2. BMI ≥ 26.1 kg/m^2; grip strength ≤ 18 kg
3. BMI < 26.1 kg/m^2; grip strength ≤ 17 kg

Patients whose attributes were above the cut-offs, were assigned a score of 1 and those below the cut-offs were assigned a score of 0.

3. Gait speed: Cut-offs according to gender and height:

- a. For Men

1. Height ≤ 173 cm; gait speed ≥ 7 seconds
2. Height > 173 cm; gait speed ≥ 6 seconds

- b. For Women

1. Height ≤ 159 cm; gait speed ≥ 7 seconds
2. Height > 159 cm; gait speed ≥ 6 seconds

Patients whose attributes were above the cut-offs, were assigned a score of 1 and those below the cut-offs were assigned a score of 0.

All the scores were added to calculate the Fried Frailty index for each patient. The patients were further categorized as:

1. Robust/Non-Frail: Score 0
2. Pre-Frail: Scores 1 and 2
3. Frail: Scores 3 to 5

3.11. Laboratory investigations

10 ml of the blood sample was collected and the volume was divided into Fluoride (for albumin) and Plain bulb (for CRP) for further analysis. All samples were stored at 2 to 8º C until processing.

The serum albumin level was assessed by Colorimetric method. At a pH of 4.1, albumin displays cationic character, which can bind with an anionic dye bromcresol green (BCG), to form a blue-green complex.

Albumin + BCG → Albumin – BCG complex

The color intensity of the blue-green color is directly proportional to the albumin concentration in the sample and is measured photometrically. The albumin level was recorded as g/dL.

The serum CRP level was assessed by Particle enhanced Immunoturbidimetric assay. Monoclonal anti-CRP antibodies were used to coat Human CRP agglutinates with latex particles. The aggregates are determined turbid metrically. The CRP level was recorded as mg/L.

The duration of hospital stay was also recorded. All the data was recorded in excel and analysis done using appropriate software.

3.12. Statistical analysis

The data was analyzed using statistical software (IBM SPSS, IBM Corporation, Armonk, NY, USA). Descriptive statistics: The Numerical data were expressed as Mean ± Standard Deviation and the Categorical data was analyzed as Percentages. Analytical statistics: The Numerical data was analyzed by the 'Unpaired t test' and the Categorical data was assessed by the Chi square test (Fischer's exact test was used when more than 20% of the cells had value less than 5). Bar charts, Pie diagrams and Scatter plots were used for the presentation of the data as applicable. P value of less than 0.05 was considered as "statistically significant"

4. Results

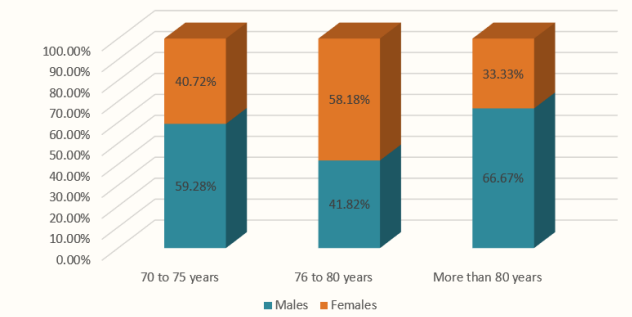

Fig. 1: Distribution of the study population according to age and gender

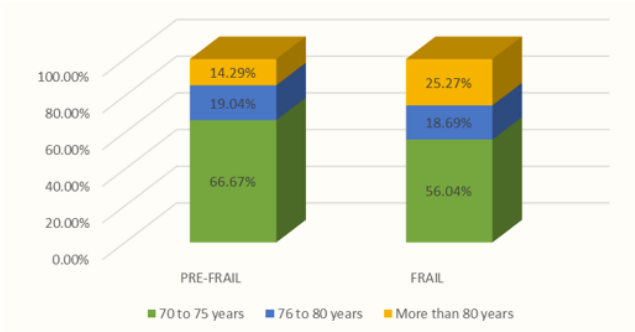

Fig. 2: Distribution of the study population according to age and Frailty Index

1. The prevalence of Frail (92.86%) is more than the Pre-Frail (7.14%).
2. There is a slight male preponderance (57.82%).
3. The CPS score is more in the Pre-Frail group than in the Frail group; P value: <0.001.
4. The 30 second stand test shows decreasing duration alongwith the increase in age groups; P value: 0.002. It is also less in females as compared to males; P value: 0.009. When compared with the Frailty index, it is more in the Pre-Frail group than in the Frail group; P value: <0.001.
5. The cognition score decreases alongwith the increase in age groups; P value: <0.001. When compared with the Frailty index, it is more in the Pre-Frail group than in the Frail group; P value: 0.031.
6. The mean duration of hospital stay is almost similar in the Pre-Frail and Frail groups (P value: 0.827).
7. The BMI is less is females than in males; P value: <0.001. The difference according to the Frailty groups is statistically insignificant (P value: 0.272).
8. The mean serum albumin level is more in the Pre-Frail group than in the Frail group; P value: 0.027.

Our study was done to assess the frailty index in the elderly, along with its major determinants and to find its correlation with the markers of inflammation and nutritional status.

1. *Demographics:* In our study, the average age group of the study population was 76.35 ± 5.88 years (range: 70 to 95 years). There was a male preponderance (57.82%). The mean age of the two genders was almost similar, as the difference was statistically insignificant (P value: 0.624). It was also observed that the age and gender wise differences between the two categories: Pre-Frail and Frail, were statistically insignificant (P value: 0.174 and 0.326, respectively). In the study by da Silva Alves B. et al[120], they compared cognitive functions among Frail and Pre-Frail older adults. They included a total of 51 participants. They observed that the average age was 84 ± 7 years. This was almost similar to the present study. They found that there was

no age wise difference between the two groups; similar to our study. In another study by Pritchard J. et al[121], conducted to compare the physical frailty assessment methods, they included a total of 120 participants. They compared the Fried's Phenotype method (weight loss, exhaustion, physical activity, walk time for 15ft walk and grip strength) with Short Performance Physical Battery method/SPPB (repeated chair stands, balance tests and 8 foot walk test). They found that the average age group of the study population was 80.6 ± 6.3 years. This was almost similar to our study. Hong X. et al[122] have done a study to assess the relation between nutritional status and Frailty in hospitalized older patients. They included a total of 380 patients. They found that the mean age was 86.75 ± 5.80 years. They found a male preponderance, similar to our study.

2. *Frailty Index:* In our study, it was found that majority of the patients under to the "Frail" category (92.86%), followed by "Pre-Frail" (7.14%). The age and gender wise difference between the two groups was statistically insignificant (P value: 0.174 and 0.326, respectively). In the study by da Silva Alves B. et al[120], conducted to compare the cognitive functions among Frail and Pre-Frail older adults, they found that majority of the cases (54.90%) belonged to the Frail category. This was almost similar to our study. In another study by Hong X. et al[122], showed the relationship between nutritional status and Frailty in hospitalized older patients, it was found that 41.8% cases were Frail, 21.3% were Pre-Frail and 36.9% cases were Non-Frail, according to the Fried's Frailty Phenotype. This was similar to the present study.
3. *BMI:* In our study, it was found that the mean BMI was 26.26 ± 2.91 kg/m^2. The mean BMI was more in males than in females; P value: <0.001. When compared according to Frailty, there was no statistically significant difference between the Pre-Frail and the Frail groups (P value: 0.272). In the study by da Silva Alves B. et al[120], they compared cognitive functions among Frail and Pre-Frail older adults. They found no difference in the BMI in the Pre-Frail and Frail groups (P value: >0.05). This was similar to our study. In another study by Hong X. et al[122], conducted a study to compare the association between nutritional status and Frailty in hospitalized older patients, they included a total of 380 cases. They found that the mean BMI was 23.39 ± 4.11 kg/m^2. They found that there was no significant association of BMI between the Frailty groups; P value: >0.05. This was similar to our study. In the study by Pritchard J. et al[121], conducted to compare the physical frailty assessment methods, they found that the mean BMI of the study population was 26.9 ± 4.9 kg/m^2. This was almost similar to our study. Thus, it can be concluded that there is no difference in the BMI in the Pre-frail and Frail groups.
4. *CRP:* In our study, it was found that the mean CRP level in the study population was 23.80 ± 23.88 mg/L. The gender wise difference in the mean CRP level was statistically insignificant; P value: 0.741. When compared according to Frailty, no significant difference in the CRP level in the Pre-Frail and the Frail groups (P value: 0.156).
5. *Albumin:* In our study, it was found that the mean albumin level in the study population was 3.29 ± 0.50 g/dl. The gender wise difference in the mean albumin level was statistically insignificant; P value: 0.925. When compared according to Frailty, the mean albumin level was more in the Pre-Frail group (3.52 ± 0.40 g/dl) than the Frail group (3.27 ± 0.50 g/dl) and the difference was statistically significant (P value: 0.027). Hong X. et al[122], has done a study to evaluate the relationship between nutritional status and Frailty, it was observed that the highest mean albumin levels were recorded in the Non-Frail group (41.71 ± 3.27 g/L), followed by Pre-Frail group (38.10 ± 4.44 g/L) and the Frail group (38.07 ± 3.87 g/L). They found statistically significant difference between the three groups (P value: <0.001). This was almost similar to our study. Thus, it can be effectively concluded that the mean albumin levels are lower in the Frail group than in the Pre-Frail group.
6. *Length of Hospital Stay:* In the present study, it was found that the mean duration of hospital stay was 5.44 ± 5.02 days. The length of stay was more in Frail groups although P value is statistically insignificant (P value: 0.827).
7. *CPS Score:* In our study, it was observed that the mean CPS score of the study population was 3.95 ± 1.77. There was no difference in CPS scores when compared amongst the age categories and gender (P value: 0.848 and 0.722, respectively). However, when compared according to Frailty, it was observed that the CPS score was more in the patients who were Frail (4.05 ± 1.76) than the patients who were Pre-Frail (2.62 ± 1.28); the difference was statistically significant (P value: <0.001). Saum K. et al[79] conducted a study to find association between the polypharmacy score and Frailty. They included a total of 3058 cases. They used the Fried's Phenotype method for the assessment of Frailty. They defined polypharmacy as the use of 5 or more drugs and hyper pharmacy as 10 or more drugs. They observed that polypharmacy/hyper pharmacy was present in 78.23% of the cases in the Frail group, 49.5% in the Pre-Frail group and 37.09% in the Non-Frail group; P value: <0.001. Thus, polypharmacy was associated with increased Frailty. This was almost similar to the present study.

8. *30 second chair Stand Test:* In the present study, it was observed that the mean duration of the test was 9.35 ± 2.13 seconds. There were significant age and gender wise differences in the test duration (P value: 0.002 and 0.009, respectively). A decrease in the test duration was noted along with an increase in the age categories. The test duration was also less in males than in females. Furthermore, when compared according to the Frailty, it was observed that the test duration was more in the patients who were Pre-Frail (10.95 ± 1.83 seconds) than the patients who were Frail (9.23 ± 2.10 seconds); the difference was statistically significant (P value: <0.001).
9. *Cognition Score:* In our study, it was observed that the mean cognition score of the study population was 24.64 ± 2.68. There was no difference in the cognition scores when compared according to gender (P value: 0.411). Statistically significant differences were noted when compared according to age categories (P value: <0.001). A decrease in the cognition score was noted along with an increase in the age categories. Furthermore, when compared according to the Frailty, it was observed that the cognition score was more in the patients who were Pre-Frail (25.86 ± 2.69) than the patients who were Frail (24.55 ± 2.66); the difference was statistically significant (P value: 0.031). In the study by da Silva Alves B. et al[120], they assessed the cognitive score by MMSE scale, Digit Span Forward, Digit Span Backward and Verbal Fluency. They found that all the four scores were higher in patients who were Pre-Frail than the patients who were Frail. There was statistically significant difference in the 2 groups for each parameter (P value: <0.05). Thus, they concluded that Frailty was more commonly associated to poor global cognition and short-term memory scores compared to those with Pre-Frailty. This was similar to our study. In another study by Pritchard J. et al[121], conducted to compare the physical frailty assessment methods, they included a total of 120 participants. They compared the Fried's Phenotype method with the Short Performance Physical Battery method/SPPB method. They assessed the cognitive impairment by the Standardized Mini-Mental State Exam score; with cognitive impairment being defined as SMMSE less than 24. They found that when assessed with the Fried's Phenotype method, 59% of the patients of the Frail category had cognitive impairment, compared to 52% in the Pre-Frail category. Thus, more patients in the Frail category had cognitive impairment compared with the Pre-Frail category. This was similar to our study. Thus, it can be effectively concluded that the decline increased Frailty is associated with decline in cognitive function.

5. Conclusion

Co-morbidities and acute illness in hospitalized patients worsens the Frailty.30 second chair test is a very good indicator for Frailty and risk of fall even in the Pre Frail group has decreased performance. Cognition score must be evaluated even in pre frail group as our study shows that cognition score are decreased in pre frail group. The duration of hospital stay is more in frail group although p value is statically insignificant. The BMI doesn't correlate with frailty index. The mean serum albumin level is another important marker to identify early Frailty.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Author biography

Akash Durgakar, Post Graduate

Pratibha Pereira, Professor & HOD

Shilpa Avarebeel, Assistant Professor

Tandure Varsha, Assistant Professor

Mahesh Poojari, Post Graduate

S Meenakshi, Clinical Research Assistant

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