



Original Article

Assessment of frailty syndrome with coexisting hypertension and depression among older individuals, aged >80 years of age

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Abstract

Objectives: The objective was to determine odds of frailty syndrome with coexistence of hypertension and depression among oldest-old adults. **Methods:** We analysed secondary data from 167 community-dwelling hypertensive participants aged 80 years and older from a cross-sectional study of frailty conducted in India. Data included sociodemographic, medical history, physical performance, functional limitations, mobility-disability, cognition, depression, sleep, frailty syndrome and chronic diseases. Odds of frailty syndrome was compared among individuals having only hypertension, and individuals having hypertension and depression. Chi-square test, t-test and logistic regression were performed to determine odds of frailty. **Results:** Frailty was significantly higher (OR:4.93;95%CI: 1.89–12.84) among individuals having hypertension and coexisting depression, compared to individuals having only hypertension. Men (OR:5.07;95%CI:1.02-25.17) and women (OR: 4.58;95%CI:1.36-15.40) with hypertension and depression showed a higher risk of frailty, compared with hypertension alone. Logistic regression models were adjusted for age, sex, cognitive impairment, chronic obstructive pulmonary disease, cardiovascular diseases, anaemia, diabetes, obesity, physical performance, activities of daily living and 4-meter walking speed. **Conclusion:** Coexistence of hypertension and depression increased risk of frailty syndrome among men and women above 80 years of age by almost 5 folds. Treating depression in hypertensive older individuals may reduce the risk of frailty among them.

Keywords: Depression, Frailty, Hypertension, India, Oldest-old

Introduction

The world's oldest old population, aged 80 years and older, is increasing rapidly, more in developing countries than developed, mostly due to declining birth rates and increasing longevity. The octogenarians are expected to increase by three times from the current number of 137 million to 425 million by the year 2050, hence their health priorities are of great concern¹. Hypertension and depression are highly prevalent in this age and are leading cause of morbidity and mortality. Blood pressure rises with age, and approximately 80% of the people in western countries, aged ≥80 years have hypertension². India also reported 83% of hypertension in oldest old, 81% among men and 85% among women, with 53% having uncontrolled hypertension³. The severity of hypertension increases more in women than in men above the age of 80 years, with 63% women reporting stage II hypertension⁴. Some however, reported no significant difference among sexes at this age⁵. Studies on prevalence

of depression in octogenarians reported wide variations in different populations, such as 12% in USA, 25% in Netherlands⁶, 31% to 45.19% in Chinese^{7,8}, and among men in Finn, it was 27% and women reported 24%⁹. In India, geriatric depression was reported 23%, higher in women

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than men, in elderly cohort of ≥ 60 years of age¹⁰.

The relationship between hypertension and depression has been studied by many researchers. Increased prevalence of depression was seen in hypertensive patients by Rabkin et al., they found a three times increased frequency of major depression in patients with hypertension¹¹. A prospective study from Finland found that "hopelessness" was associated with three times increased incidence of hypertension in previously normotensive men, after adjusting for confounders including age, education, body mass index, resting blood pressure, parental history of hypertension, physical activity, smoking and alcohol consumption¹². Meng et al., too suggested that individuals experiencing depression were at high risk of developing hypertension¹³. Conversely some studies reported association of depression with low blood pressure^{14,15}. The exact mechanism of relation of hypertension and depression is not yet established, but sympathetic nervous system hyper-reactivity and genetic influences are hypothesised as underlying mechanisms in the relationship between depression and hypertension¹⁶⁻¹⁸. Recent theories regarding depression revolve around the biogenic amine pathway, and suggested that the disease is related to a deficiency in monoamines (serotonin, dopamine and norepinephrine) in the central nervous system. The compounds that inhibit monoamine reuptake, leading to an increased concentration of monoamines in the synaptic cleft, have been proven to be clinically effective antidepressants^{19,20}. Monoamine oxidase inhibitors therefore have anti-hypertensive effect on individuals²¹.

Although evidence of an association between depression and development of hypertension is not clear, but, that depression can impair the management and prognosis of hypertension, is proven^{22,23}. Moreover, hypertension and depression follow the same biological pathway independently influencing several morbidities, however there is no information on their combined effect on other chronic conditions among older individuals.

Frailty syndrome is a clinical geriatric syndrome which is responsible for high risk of adverse health outcomes, compromises physical functions of an individual at older age and leads to high risk of mortality²⁴. It is described as loss of body reserves and difficulty in coping up with day to day stressors of everyday life. Frailty increases exponentially with increasing age, in the Cardiovascular Health Study (CHS), a population-based, longitudinal study of coronary heart disease and stroke with 1250 participants aged 65 year old, the prevalence of frailty increased with age, from 3.9% in the 65-74 age group to 25% in the 85+ group and was greater in women than men²⁵. Our earlier paper reported prevalence of frailty of around 80% among Indian individuals aged ≥ 80 years of age with no significant difference in sexes²⁶.

We believe that there is link between hypertension, depression and frailty syndrome because all three conditions are associated with high inflammation in the body. To the best of our knowledge, there is no study that determined risk

of frailty syndrome with coexistent effect of hypertension and depression, more so in oldest old individuals ≥ 80 years of age. The objective of this study was to determine the combined effect of hypertension and depression in relation to odds of frailty syndrome in oldest old individuals (≥ 80 years of age) in India.

Materials and Methods

This analysis was done using data collected from a cross-sectional study conducted on frailty syndrome and associated factors among community dwelling octogenarians, aged 80 years and older, residing in Hyderabad city of Telangana, India, in the year 2017. The detailed methodology is described elsewhere³, briefly 200 participants (38% men) were randomly enrolled from 12 large residential gated communities. The data was collected by trained investigators upon home visits, after written informed consent was obtained from all the participants. Ethical approval was obtained from Institutional Review Board (IRB) of Medciti Institute of Medical Sciences (MIMS), Ghanpur, Hyderabad and Indian Council of Medical Research (ICMR), Delhi. Out of 200 participants, 167 participants (62 men and 105 women) were hypertensive. In this analysis we included these 167 hypertensive participants and divided them into two groups: Individuals having *Hypertension Coexisting with Depression* and individuals having *Hypertension but no Depression*.

Measurement of blood pressure

Three readings of resting blood pressure were measured with interval of 1 minute, using an electronic sphygmomanometer (OMRON HEM 7120, Omron Healthcare Co., Ltd., Japan). Systolic and diastolic blood pressures were recorded on relaxed calm participant in the sitting position, with knees flexed at 90 degrees with heel and foot touching the ground, elbows raised at the level of their heart. They were instructed to abstain from eating, drinking alcohol/caffeinated drinks or exercise at least for 30 min before blood pressure measurement. The average of last two readings was considered to define systolic and diastolic blood pressure of the individual²⁷.

Ascertainment of Hypertension

Individuals were categorised as hypertensive when their systolic blood pressure (SBP) ≥ 140 mmHg, diastolic blood pressure (DBP) ≥ 90 mmHg²⁸, and/or self-reported hypertension and /or taking anti-hypertensive medicine, prior diagnosed hypertensive by the doctor. Controlled hypertension was defined as individuals having a current SBP < 140 mmHg and DBP < 90 mmHg and taking anti-hypertensive medicines, or diagnosed hypertensive by the doctor and having a current SBP < 140 mmHg and DBP < 90 mmHg. Uncontrolled hypertension was defined as individuals with SBP ≥ 140 mmHg and DBP ≥ 90 mmHg and taking anti-hypertensive medicines or individuals diagnosed with

hypertension by the doctor and not taking pharmacological treatment and SBP ≥ 140 mmHg, and DBP ≥ 90 mmHg.

Measurement of Depression

The depression was ascertained using Geriatric Depression Scale (GDS) 15 – points. The total score ranges from 0–15. Higher scores suggest increase in depressive symptoms; scores ≥ 5 indicated presence of depression; scores 9 to 11 were described as moderate and 12 to 15 was described as severe depression. The Geriatric Depression Scale (GDS) is a valid tool for detecting depression among elderly persons residing in community settings²⁹.

Measurement of Frailty syndrome

Frailty phenotype was measured by Linda Fried's Frailty Criteria^{25,30} which includes examining 5 phenotypic criteria i.e. 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.

Measurements of each component of Frailty

Slow walking was defined by, walk time taken to complete 4-meter walk, stratified by gender and height (gender-specific cut-off a medium height) (Table 1).

Table 1. Gender-specific cut-off time to walk.

Men	Cut-off Time to Walk
Height ≤ 173 cm	≥ 7 seconds
Height > 173 cm	≥ 6 seconds
Women	
Height ≤ 159 cm	≥ 7 seconds
Height > 159 cm	≥ 6 seconds

Low grip strength was defined based on BMI, separately among men and women (Table 2).

Table 2. Cut-off for grip strength based on BMI, among men and women.

Men	Cut-off for grip strength
BMI ≤ 24	≤ 29
BMI 24.1 – 26	≤ 30
BMI 26.1 – 28	≤ 30
BMI > 28	≤ 32
Women	
BMI ≤ 23	≤ 17
BMI 23.1 – 26	≤ 17.3
BMI 26.1 – 29	≤ 18
BMI > 29	≤ 21

Low energy (exhaustion) was ascertained upon interview. A question was asked whether the person feels low energy and exhausted, if the person answered “Yes” affirmatively then the participant was considered having low physical activity.

Unintentional weight loss was asked to the participants using a question whether they were losing significant weight in past 12 months, followed by the question whether they are trying to lose their weight. If a participant answered the first question as “Yes” and second question as “No”, then the participant was categorised as having unintentional weight loss.

Low Physical activity was measured by asking question whether the participant does any physical activity like playing sports, going to the gym, walking, gardening, hiking, jogging, biking, exercise cycling, dancing, aerobics, swimming (moderately strenuous chores excluding normal daily routine work). If the participant said “No” then he was considered as having low physical activity

Other measurements

Socio demographic data included age, sex, schooling and status of living single was collected by interviewing using a structured questionnaire; Anthropometric measurements were done by standard protocol using seca measuring scales, weighing machine and stationmaster; Medical history i.e. chronic obstructive pulmonary disease (COPD), cardio vascular diseases (CVD), was measured upon interview using structured questionnaire; Anaemia was ascertained upon haemoglobin examination and using cut offs of WHO classification; Diabetes was ascertain on previous history of diabetes and/or fasting blood sugar examination; Obesity was measured by BMI, Asian Indian classification.

Cognitive impairment was measured by using Mini Mental State Examination (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.

Physical performance was measured by Short Physical Performance Battery (SPPB). The SPPB consists of a 4-meter walk, 5 times repeated chair stands, and 3 hierarchical standing balance tests. 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 which is a score of three tests.

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 of above 6 then he was considered having poor activities of daily living.

Variables	Hypertensive (mean or %) (n=85)	Hypertensive & Depression (mean or %) (n=82)	P Value	Odds Ratio (OR) Or Mean difference	95% Confidence Interval (CI)
Demographic Characteristics					
Age (%)*	82.35 ± 3.11	84.35 ± 4.46	0.001	2.00 ^a	0.82 – 3.17 ^b
Men (%)	44.7	29.3	0.02	1.95	1.03 – 3.07
Women (%)*	55.3	70.7			
No Schooling (%)*	26.2	72.8	<0.001	7.22	3.64 – 14.33
Living single (%)*	49.4	75.3	<0.001	3.12	1.61 – 6.04
Anthropometric measurements					
Hip Circumference (cm) (mean ± SD)*	100.73 ± 11.20	93.85 ± 10.51	<0.001	6.88 ^a	3.55 – 10.20 ^b
Waist Circumference (cm)(mean ± SD)*	93.85 ± 10.51	90.35 ± 16.60	0.01	3.5 ^a	-0.7294 – 7.72 ^b
Body Mass Index (kg/m ²) (mean ± SD)*	24.32 ± 4.37	22.21 ± 4.63	0.004	2.10 ^a	0.69 – 3.51 ^b
Obesity (%)*	62.7	29.9	<0.001	0.25	0.13 – 0.49
Frailty syndrome					
Frailty syndrome (scores) (mean ± SD)*	3.02 ± 0.87	3.79 ± 0.78	<0.001	- 0.77 ^a	- 1.02 – (- 0.52) ^b
Frailty syndrome (score ≥3) (%)*	70.6	92.7	0.001	5.27	2.03 – 13.69

*p<0.05 considered significant, **t test, ***chi sq. test, ^a mean difference, ^b 95%Confidence Interval of mean difference.

Table 3. Characteristics and Odds of Frailty among Individuals having Only Hypertension and Hypertension coexisting Depression.

Statistics

Data was analysed using SPSS, version 25 software (SPSS Inc., Chicago, IL, USA). Comparison of characteristics and outcome variable – Frailty phenotype, was done among “individuals having hypertension and depression” and “individuals with only hypertension”, using chi square (χ^2) test for categorical variables and t test for continuous variables in univariate analysis. Odds ratio (OR) and 95% confidence interval (95%CI) were calculated by backward logistic regression analysis to determine association of coexisting hypertension and depression with frailty syndrome, $p < 0.05$ was considered significant. To determine the association we created three logistic regression models namely for total study population, men and women and calculated OR and 95%CI for each separately. Following variables were adjusted in Logistic regression models: age, sex, cognitive impairment, chronic obstructive pulmonary disease (COPD), cardio vascular diseases (CVD), anaemia, diabetes, obesity, physical performance (SPPB), activities of daily living (ADLs) and 4 - meter walking speed. The data was projected in Odds ratio, 95% confidence interval, proportions and means. Post-hoc analysis showed at least 96.4% power for prevalence of Frailty

Results

Total 167 hypertensive participants were considered for this analysis, out of which 37.1% were men. The mean age of

the study participants was 83.34 ± 3.95 years and there was no significant difference in mean age of men (83.52 ± 4.10) and women (83.23 ± 3.88). 62% participants were living single; more women were living single (80%) than men (37.1%). 48.1% participants did not attend school; illiteracy was higher among women (52%). Body Mass Index was 23.31 ± 4.67 kg/m² for our study participants, with no significant difference in men (22.8 ± 4.40 kg/m²) and women (23.56 ± 4.72 kg/m²). 49.1% participants had Depression, it was significantly higher in women hypertensives (55.2%) than men hypertensives (61.1%).

Table 3 describes the characteristics of the individuals having hypertension and individuals having hypertension and depression coexisting upon univariate analysis. In demographic characteristics, hypertensive with depression group were older, had more women, less individuals attended formal schooling and more participants were living single ($p < 0.05$). Individuals in only hypertensive group were taller, heavier, had higher waist and hip circumference, had higher BMI and more obesity compared to hypertensive with depression group ($p < 0.05$). Prevalence of frailty syndrome was significantly higher ($p < 0.05$) in hypertensive individuals who had depression coexisting. Age wise stratification of frailty with Hypertension, and with Hypertension plus Depression is shown in Table 4.

Table 5 shows Frailty syndrome stratified with stages of Hypertension (according to Joint National Committee – 7 guidelines) using current blood pressure measurement.

Age group	Hypertension without depression (%) n = 85	Hypertension with depression (%) n = 82	P value	OR (95%CI)
80 to 84	67.7	97.7	<0.001	20.47 (2.62 – 159.51)
85 to 89	77.8	90.9	0.24	2.85 (0.42 – 17.80)
90 and above	100.00	86.7	0.44	1.30 (1.05 – 1.70)

Table 4. Age wise stratification of Frailty with Hypertension and with Hypertension plus Depression.

Stages of Hypertension	Systolic blood pressure without depression	Systolic blood pressure with depression	P value	Diastolic blood pressure without depression	Diastolic blood pressure with depression	P value
	% Frailty	% Frailty		% Frailty	% Frailty	
Prehypertension	69.2	92.1	0.02	70.8	88.9	0.07
Stage 1	69.2	90.6	0.04	83.3	100.00	0.16
Stage 2	72.4	100.00	0.03	61.5	80.0	0.43

Table 5. Frailty syndrome stratified with stages of Hypertension (Joint National Committee - 7) using current blood pressure measurement.

Variables	Men (n=62)				Women (n=105)			
	Hypertensive (mean or %)	Hypertensive & Depression (mean or %)	P Value	Odds Ratio (OR) 95% Confidence Interval (CI)	Hypertensive (mean or %)	Hypertensive & Depression (mean or %)	P Value	Odds Ratio (OR) (95% Confidence Interval (CI))
Age (%)	81.93 ± 2.48	84.26 ± 4.26	0.002	-	82.84 ± 3.71	84.58 ± 4.53	0.10	-
No Schooling (%)	25.5	74.1	<0.001	8.36 (3.46 – 23.16)	27.0	66.7	0.003	5.40 (1.76 – 16.49)
Living single (%)	72.3	86.2	0.06	2.39 (0.89 – 6.39)	21.1	47.8	0.02	3.43 (1.11 – 10.64)
Height (cm) (mean±SD)	152.11 ± 4.85	148.63 ± 7.48	0.007	-	164.74 ± 8.57	159.35 ± 8.92	0.02	-
Weight (kg) (mean±SD)	58.59 ± 12.76	50.26 ± 12.19	0.001	-	63.40 ± 14.53	54.10 ± 13.63	0.005	-
Body Mass Index (kg/m ²) (mean±SD)	24.59 ± 4.32	22.88 ± 4.91	0.03	-	23.96 ± 4.47	21.05 ± 3.72	0.01	-
Obesity (%)	66.7	22.7	0.001	0.14 (0.04 – 0.49)	59.6	32.7	0.006	0.33 (0.14 – 0.74)
Frailty syndrome (scores) (mean±SD)	2.84	3.79	<0.001	-	3.17	3.79	<0.001	-
Frailty syndrome (%) (score ≥3)	68.4	91.7	0.03	5.07 (1.02 – 25.17)	72.3	93.1	0.004	5.16 (1.55 – 17.13)

p<0.05 considered significant.

Table 6. Characteristics and Odds of Frailty among Men and Women having Only Hypertension and Hypertension coexisting Depression.

Variable	Model 1	Model 2	Model 3	Model 4	Model 5
	OR (95%CI)				
Coexisting Hypertension with Depression	5.06 (1.94, 13.18)	4.33 (1.62, 11.60)	4.25 (1.06, 11.29)	4.14 (1.55, 11.02)	4.93 (1.89, 12.84)

Model 1: Adjusted with, Age and Sex.

Model 2: Adjusted with, Model 1 + COPD, CVD, Diabetes, Cognitive Impairment.

Model 3: Adjusted with, Model 1 + SPPB, ADLs.

Model 4: Adjusted with, Model 2 + Poor SPPB, ADLs.

Model 5: Adjusted with, (fully adjusted) age, sex, cognitive impairment, chronic obstructive pulmonary disease (COPD), cardio vascular diseases (CVD), diabetes, anaemia, obesity, physical performance (SPPB), activities of daily living (ADLs) and 4-meter walk speed.

Table 7. Logistic Regression Models showing Odds of Frailty syndrome with Coexisting Hypertension and Depression.

Variables	Total		Men		Women	
	Odds ratio (OR)	95% Confidence Interval (CI) (Lower – Upper)	Odds ratio (OR)	95% Confidence Interval (CI) (Lower – Upper)	Odds ratio (OR)	95% Confidence Interval (CI) (Lower – Upper)
Coexisting Hypertension with Depression	4.93***	1.89 – 12.84	5.07*	1.02 – 25.17	4.58**	1.36 – 15.40
Only Hypertension [#]	0.67	0.12 – 3.63	-	-	-	-
Only Depression [#]	4.66	0.37 – 58.24	-	-	-	-

Backward stepwise logistic regression: * $p < 0.05$; ** $p = 0.01$; *** $p = 0.001$. [#]Analyses with 'only hypertension' and 'only depression' was not performed stratified by gender due to low numbers in these variables.

Table 8. Logistic regression predicting Odds of Frailty syndrome in total population, Men and Women.

Comparison of Systolic blood pressure without and with depression showed a significantly higher proportion of frailty across all stages in the latter group, while for diastolic blood pressure no statistically difference for frailty prevalence was observed. Upon stratification by gender, frailty syndrome was significantly higher ($p < 0.05$) among individuals with hypertension coexisting with depression in both men and women (Table 6). Characteristics of hypertensive and hypertensive with depression in men and women are described in Table 6.

Logistic regression was performed while adjusting for different variables and confounders. Multiple models showing Odds of Frailty syndrome with Coexisting Hypertension and Depression are presented in Table 7. Odds of frailty was assessed by backward logistic regression separately among total study population, men and women. Odds of frailty syndrome significantly increased when hypertension coexisted with depression. If only hypertension or only depression existed among older individuals, our study populations showed no significant associations with frailty syndrome. However, when hypertension and depression existed together in older individuals there was

significant association with frailty (Table 8). Among men and women coexistence of hypertension and depression was independently associated with odds of frailty syndrome (Table 8).

We also compared individuals having controlled and uncontrolled hypertension. In controlled hypertensive with depression group, frailty was 94.0% compared to 71.1% in only controlled hypertensive group ($p = 0.003$), and in uncontrolled hypertension with depression, frailty was 90.6% compared to only uncontrolled hypertension group where it was 70.0% ($p = 0.03$).

We further did trend analysis by checking interaction between hypertension and depression for odds of frailty. We found frailty significantly increased by about 4 folds upon interaction ($p < 0.004$) (OR: 3.94; 95%CI 1.55 – 10.01).

Discussion

Depression in hypertensive individuals

In our cohort of hypertensive octogenarians, 49% individuals reported having coexisting depression. Proportion of coexisting depression was more in women

than men. A study from China, with participants' mean age of 69 years, reported similar prevalence of 42% depression in hypertensive cohort³¹. A study from Mexico reported 57% prevalence of depression in hypertensive patients in a younger population of mean age 60 years³². We could not find age matched population study for comparison of our prevalence of depression in hypertensive individuals, although it is clear that depression is highly prevalent in hypertensive elders with variations across age and ethnic groups³¹.

Sympathetic nervous system hyper-reactivity and genetic influences are hypothesised as underlying mechanisms in the relationship between depression and hypertension^{16,17}. More recently, the biogenic amine pathway has been implicated for depression¹⁹, as well as the anti-hypertensive effects of anti-depressants. Also, research widely indicates that depression can impair the management and prognosis of hypertension^{22,23}, even though the association between depression and hypertension development is unclear.

Odds of Frailty

In the present paper, we report that hypertension that shows weak association with frailty, becomes strongly associated when depression is a co-existent condition, among the oldest old. Also, the present study found a high prevalence of frailty syndrome among persons aged 80 years and older having depression co-existent with hypertension, irrespective of hypertension being controlled or uncontrolled. Though there were sufficient reports to suggest independent associations of either hypertension or depression with frailty amongst the older adults, we however, did not find any population studies to compare our finding of increased frailty associated with coexistence of depression and hypertension.

Few studies among the oldest old population have concluded that hypertension may show a strong association with frailty. There are ample population based studies, on the contrary, to suggest that hypertension, specifically high systolic blood pressure, plays a rather protective role against most co-morbid conditions resulting from hypo perfusion of tissues, thereby advocating not controlling hypertension within acceptable limits of blood pressure. We found similar relationship of frailty with hypertension in our population earlier³³.

The present study brought out significant difference in the presence of frailty among hypertensive, and hypertensive individuals having depression and the status of hypertension control also did not apparently change this relationship, thereby leading us to assume that preventing or treating depression among hypertensive individuals may reduce the odds of acquiring frailty.

The plausibility of a neurological pathway connecting the three entities seems most probable, in the absence of polypharmacy and social isolation in our population. The high prevalence of frailty among the hypertensive depressive

group in our study is explained by the vascular depression model described by Alexopoulos et al. that provided the basis for development of depression in later life among those having cerebrovascular disease^{34,35}. Depression is a common condition encountered in late life and has been variously attributed to adverse life events and loss of socialization by many. Some neuro-radiological studies described the development of late life depression symptoms consequent to prefrontal subcortical white matter hyperintensities typically attributed to CVB studies³⁶, whereas few others favoured the relationship using clinical perspective, wherein it was found that presence of multiple cerebrovascular risk factors including hypertension, led to development of depression symptoms in late life³⁷.

The same model has also not only been suggested as prodromal to frailty development³⁸, but also a predictor for mortality among older women. Depression and frailty have been shown to be strongly associated among Indian oldest old earlier³³. The vascular depression model may suggest that Indian population having hypertension as younger adults may develop late life depression as they enter the geriatric age group due to continued microvascular insults³⁶ to the network of fronto-striatal projections responsible for affective functioning³⁹, and such long standing hypertension and depression directly contributes to development of frailty among the oldest old hypertensive depressives.

Few researchers attempted to describe relationship between hypertension and frailty employing a theory of greater arterial stiffness among pre-frail and frail older adults, possibly describing the association between frailty, hypertension and cardiovascular disease⁴⁰. Others showed the association of frailty with hypertensive target organ damage in older adults, thereby hypothesizing that the common mechanism leading to frailty, hypertension, and target organ damage was arteriosclerosis⁴¹. Recent research points to inflammation and oxidative stress as common mechanisms underlying both hypertension and frailty, with specific markers including C-reactive protein, TN-factor- α , IL-6, leukocytes and fibrinogen elevated in frail elders compared with non-frail⁴². Moreover, oxidative stress markers are also elevated in frailty⁴³.

Depression and frailty are also being studied for common biological pathways. Brown et al.⁴⁴ described the depressed frail phenotype wherein they proposed potential common biological substrates such as decreased mitochondrial functioning, reduced dopaminergic neurotransmission, and inflammatory processes interfering with activity and mobility as well as causing neurodegenerative disorders including depression, and therefore linking frailty with depression among older adults. Some role of insulin resistance has also been identified. It may therefore, be seen that biological processes that mark old age namely, arteriosclerosis, inflammatory processes, endocrine, and immune changes compound individual's vulnerability to depression⁴⁵. We too, believe that frailty, hypertension and depression

share a common underlying biology involving changes in endocrine, hematologic, and immunologic systems^{46,47} and, that presence of hypertension and depression together enhances the deterioration in these systems and leads to frailty. We also believe that the relationship may be tri-directional, implying the presence of any two entities out of hypertension, depression and frailty in combination, may cause the third. Further longitudinal researches in these direction may generate clear evidences.

Conclusion

In a community based study upon oldest old community dwelling individuals having hypertension, we studied the coexistence effect of hypertension and depression on development of frailty. It was found that the coexistence of depression among hypertensive older adults was strongly associated with frailty syndrome among them, whereas both hypertension and depression in isolation were not. Early depression screening along with routine blood pressure control among hypertensives is needed among oldest old and would help to reduce frailty and improve their quality of life. It will be important to explore further that hypertension influences depression or depression influences hypertension for the enhanced negative outcomes in terms of frailty.

Strength and Limitations

The limitations of the present study are its cross sectional design wherein we could not ascertain whether hypertension or depression developed earlier. Further, the element of recall bias in reporting duration of either condition can also not be ruled out. We used geriatric depression scale (GDS-15) which is used for screening and not for diagnosis in clinics, although epidemiological studies use this scale for measure depression. Our strength is a robust population based sample of oldest old individuals, coupled with high response rates, that provided diverse opportunities to study various associations paired with commonly existing co-morbidities. Training of the investigators was done by certified faculty from university of Pittsburgh and NIH, USA, who also followed quality of the data closely.

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Authors' contributions

Study design: AA, PKS and EG. Data collection and processing: BMR and PKS. Data analysis: BMR and PKS. Data interpretation: AA, PKS and EG. Drafting manuscript: AA.

Revising manuscript content: AA, EG and PKS. Approving final version of manuscript: AA, BMR, PKS and EG. PKS takes responsibility for the integrity of the data analysis.

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