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Factors Affecting Frailty Scores in Elderly with Chronic Kidney Disease Undergoing Regular Haemodialysis at Haji Adam Malik Hospital

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ABSTRACT

Background: The prevalence of frailty in the elderly population is reported to be >60% in haemodialysis-dependent CKD patients. According to the Comprehensive Geriatric Assessment, several factors can influence frailty score. Identification of these risk factors is essential to improve and enhance the quality of care for CKD patients with frailty.
Method: This is a cross sectional study done on elderly CKD patients undergoing routine haemodialysis at Haji Adam Malik Hospital Medan. Bivariate and multivariate data analysis was done to analyze correlations of factors towards frailty score.
Results: From 62 samples, there was a correlation of age (p=0.019; R 0.298); nutritional factors (p<0.001; R -0.666); comorbidities (p<0.001; R 0.556); functional status (p<0.001; R -0.875); mental status (p<0.001; R -0.711); depression (p<0.001; R 0.557) with frailty and no correlation of gender with frailty (p=0.962). Multivariate analysis of all factors toward frailty showed significant p values in CCI, MMSE and ADL respectively 0.006; 0.004; 0.000 with R2 value of 80.1%.
Conclusion: There were strong correlations on better geriatric nutritional, functional and mental status on a lower frailty score. Comorbidity severity and depression increased frailty scores moderately. Increasing age may increase frailty scores with a weak correlation magnitude. There was no significant correlation between gender and frailty. Multivariate analysis showed CCI, MMSE and ADL as the variables influencing frailty most.

Keywords: Frailty, chronic kidney disease, haemodialysis.

INTRODUCTION

The elderly population is rapidly growing, and by 2050, it is estimated to reach 2 billion individuals aged 65 and above. With this demographic shift, attention is drawn to frailty, a condition characterized by increased vulnerability to poor haemostasis resolution after stress, leading to adverse outcomes such as falls, delirium, and disability.[1] Frailty is a complex set of symptoms associated with decreased organ function due to factors like sarcopenia, nutritional deficiencies, hormonal changes, and increased inflammation. While not a disease itself, frailty is closely linked to coexisting health issues.[2] Fried et al.'s definition, known as the Phenotype Model, includes clinical manifestations like unintentional weight loss, fatigue, weak grip strength, slow walking speed, and low physical activity. A person is considered frail if they meet at least 3 out of 5 criteria and pre-frail if they meet 1 or 2 out of 5

criteria.[3,4] Two commonly used scoring systems for frailty are Fried's scoring and the Frailty Index (FI) by Mitnitski et al., with the latter providing a more comprehensive assessment.[3,5] Although FI may not be the most popular model, it is a sensitive predictor of adverse health outcomes due to its nuanced risk scale and clinical relevance concerning the quantity and composition of items in the index.[5]

The prevalence of frailty among the elderly varies globally, with studies reporting rates between 4% and 59.1%.[6] In Indonesia, studies have reported frailty prevalence ranging from 8.1% to 25.2%, with factors like age, functional status, and nutritional status identified as risk factors.[7] Additionally, frailty is prevalent in elderly individuals with chronic kidney disease (CKD), with implications for adverse clinical outcomes. Interestingly, the prevalence of frailty is reported to be over 60% in CKD patients on haemodialysis, independently associated with adverse clinical outcomes in all CKD stages, including increased risk of mortality and hospitalization. Studies also associate frailty with progressive kidney damage.[8]

Various factors influence frailty scores in elderly individuals with CKD, including age, body mass index (BMI), estimated glomerular filtration rate (eGFR), haemoglobin levels, oral diadochokinetic, and swallowing ability.[9] Other factors related to frailty in CKD patients include depression, fall history, hospitalization, and polypharmacy.[10] Gender differences in frailty prevalence are also noted, with higher rates among elderly women awaiting kidney transplantation compared to men.[11]

According to the Comprehensive Geriatric Assessment (CGA), there are a few factors that affect frailty.[12] The CGA consists of important elements which include (1) physical health including nutritional status assessed using the Mini Nutritional Assessment (MNA) scale as well as comorbidities assessed using the Charlson Comorbidity Index (CCI) scale, (2) functional efficiency as assessed by the Barthel Index Of Activities of Daily Living (ADL) scale, (3) mental health as assessed by a cognitive assessment test with the Mini Mental State scale Examination (MMSE) and assessment of mood disorders using the Geriatric Depression Scale (GDS), and (4) social conditions include age and gender.[12,13] Identification of risk factors is essential to improve and improve the quality of care for vulnerable CKD patients. The researcher aims to conduct a study analysing CGA-related factors influencing frailty scores diagnosed with FI-40 in elderly individuals with chronic kidney disease at Haji Adam Malik Hospital Medan.

MATERIALS & METHODS

This is an analytical study utilizing a cross-sectional research design to analyse factors influencing frailty in elderly individuals with CKD undergoing regular haemodialysis at Haji Adam Malik Hospital Medan in Indonesia. The research commenced in May 2023.

Consecutive sampling technique was conducted, including all eligible elderly subjects with CKD undergoing routine haemodialysis at Haji Adam Malik Hospital Medan within the study period. The total sample size for the study is 62 research subjects. Data collection involves both primary and secondary data, incorporating patient questionnaire results and medical records from RSUP Haji Adam Malik Medan. The inclusion criteria for respondents are elderly individuals with CKD aged over 60, undergoing regular haemodialysis at Haji Adam Malik Hospital Medan, capable of effective communication, and willing to participate by signing an informed consent. Respondents must also have a frailty score $\geq$ 0.25. Exclusion criteria involve elderly individuals unable to participate or complete the questionnaire for any reason.

Data collection was done by instructing respondents to complete the FI-40 questionnaire, and the researcher performed scoring using the MNA questionnaire, CCI questionnaire, ADL questionnaire, MMSE

questionnaire, and GDS questionnaire. Additionally, the researcher conducted a review of medical records. Lastly, the scoring was calculated by the researcher.

STATISTICAL ANALYSIS

The obtained data will undergo bivariate analysis using Spearman's test as an alternative for analysing factors associated with frailty in the elderly population with chronic kidney disease undergoing regular haemodialysis, aged over 60 years, at Haji Adam Malik Hospital Medan. Gender analysis will utilize an independent T-test, and mental status will be assessed using Pearson correlation with frailty. Significance will be determined by a P-value < 0.05, and the strength of correlation will be evaluated based on the R-value. Multivariate analysis will be employed to examine the simultaneous relationship between all factors and frailty using linear regression analysis.

RESULT

The study comprises 62 patient data as research subjects. Subjects were selected based on inclusion and exclusion criteria, with all meeting a frailty index above 0.25, indicating frailty. Factors analyzed include age, gender, comorbidities, nutritional status, functional status, mental health, and depression status in relation to frailty score, which are presented on table 1.

Bivariate analysis was done to assess the relationship between each of the factor characteristics and the frailty score of research subjects as shown on table 2.

Table 1: Sample Characteristics

Parameters	N = 62
Gender	
Male	43 (69.4%)
Female	19 (30.6%)
Age	
60 – 69	49 (79.0%)
70 – 79	12 (19.4%)
80 – 89	1 (1.6%)
Length of Haemodialysis	
< 1 year	14 (22.6%)
1-3 years	36 (58.0%)
4-6 years	10 (19.4%)
Comorbidities	
Moderate or severe liver disease	2 (3.2%)
Cerebrovascular disease	4 (6.5%)
Peripheral vascular disease	3 (4.8%)
Diabetes with end organ damage	18 (29%)
Lymphoma	2 (3.2%)
Chronic pulmonary disease	10 (16.1%)
Leukaemia	2 (3.2%)
Tumour	7 (11.3%)
Metastatic solid tumour	5 (8.1%)
Congestive heart failure	9 (14.5%)
Nutritional Status	
Normal	13 (20.9%)
At risk of malnutrition	15 (24.2%)
Malnutrition	34 (54.8%)
Functional Status	
Independent	11 (17.7%)
Mild dependency	25 (40.3%)
Moderate dependency	21 (33.9%)
Severe dependency	5 (8.0%)
Total dependency	0 (0%)
Mental Status	
Normal cognitive function	38 (61.3%)
Probable cognitive dysfunction	20 (32.2%)
Definite cognitive dysfunction	4 (6.4%)
Depression	
Suggestive of depression	19 (30.6%)
Depression	43 (69.3%)

Table 2: Relationship between frailty score and sample characteristic scores on elderly CKD patients undergoing haemodialysis

Parameters	Frailty Score	
	R	*p.*
Age	0.298	0.019
Gender*	-	0.962
Nutritional Status (MNA score)	-0.666	< 0.001
Comorbidities (CCI score)	0.556	< 0.001
Functional Status (ADL score)	-0.875	< 0.001
Mental Status (MMSE score) **	-0.711	< 0.001
Depression (GDS score)	0.557	< 0.001

*Independent sample T-test
**Pearson correlation test

Analysis of all variables was also carried out on the frailty score value. The results of the analysis of all factors with the strength of the relationship between each factor is shown on table 3. Based on table 3, the results of the analysis of variables in the study on frailty scores are presented. The table indicates that the factors CCI, MMSE, and ADL have the most significant simultaneous impact on frailty, with a combined influence of 80.1%.

Table 3: Multivariable analysis of the strength of the relationship between frailty score and each characteristic factors on elderly CKD patients undergoing haemodialysis

	Variable	R	*p.*
1	*(Constant)*		0.000
	Age	0.054	0.408
	MNA	-0.057	0.487
	CCI	0.196	0.009
	MMSE	-0.198	0.023
	GDS	-0.042	0.603
	ADL	-0.600	0.000
2	*(Constant)*		0.000
	Age	0.054	0.405
	MNA	-0.054	0.507
	CCI	0.192	0.009
	MMSE	-0.210	0.012
	ADL	-0.569	0.000
3	*(Constant)*		0.000
	Age	0.054	0.403
	CCI	0.202	0.005
	MMSE	-0.208	0.012
	ADL	-0.602	0.000
4	*(Constant)*		0.000
	CCI	0.195	0.006
	MMSE	-0.231	0.004
	ADL	-0.608	0.000

R^2=80.1%

DISCUSSION

Frailty is a multi-system symptom group caused by the accumulation of vascular disorders, inflammatory processes, nutritional status, and influenced by age, resulting in accelerated aging, increased vulnerability, and long-term functional impairment.[14] It leads to body reserve depletion, rendering individuals unable to cope with environmental stressors and impacting survival.[15] Frailty is often associated with the geriatric population to identify patients with increased mortality and institutionalization, validated, even in CKD patients undergoing haemodialysis as a predictor of adverse outcomes. Frailty tends to increase with disease progression, persisting after therapy. The occurrence of frailty is prevalent in dialysis patients, accounting for 30-73% of cases.[14]

Frailty is accompanied by symptoms such as sarcopenia, fatigue, weakness, slow gait speed, low physical activity, and increased energy expenditure. In CKD patients, frailty leads to cognitive impairment, delirium, susceptibility to diseases, increased dependence on others, higher hospitalization rates, elevated fall risk, disability, and increased mortality. Frailty is mediated by underlying causes, environmental factors, and genetic mechanisms leading to cellular aging, mitochondrial dysfunction, worsening digestive system permeability, and microglial hyperactivity. These collectively contribute to physiological changes, including the emergence of comorbidities, stress responses, and sarcopenia.[14] CKD is a pro-inflammatory condition, evidenced by increased CRP, IL-6, and pro-coagulation markers, heightening frailty risk. The inflammatory burden and catabolic conditions in CKD contribute to muscle mass decline and cachexia.[16]

Commonly associated frailty risk factors include age, race, occupation, gender, education, body mass index, CKD severity, biological morbidity, depression, disability, albumin, and smoking habits. Additionally,

comorbidities like COPD, obesity, endothelial dysfunction, and arthritis double the risk of frailty. Psychiatric disorders and disabilities triple the risk.[17]

Gender is a crucial factor influencing frailty, with a higher prevalence in women despite their longer life expectancy.[18] The impact of age on frailty remains inconsistent, with associations typically found in individuals above 60 years, especially ≥70 years.[19] Comorbidities significantly contribute to accelerating frailty onset in the CKD population.[16]

Physical activity is closely linked to frailty; regular physical activity enhances both physical and psychological health, reversing the adverse effects of chronic diseases and maintaining functional autonomy in the elderly.[20] Reduced physical activity accelerates the catabolic process, leading to disability. Abnormal nutritional status reduces muscle mass and strength, affecting the immune system and lowering resistance to infections. Age-related anorexia and weight loss play a role in frailty pathophysiology.[21]

A systematic review and meta-analysis focusing on frailty as a negative predictor of health outcomes in CKD patients indicate that frailty predicts increased mortality, hospitalization, and falls. Frailty is identified as a cause of mortality, hospitalization, and falls.[22] The progression of CKD stage and the need for haemodialysis increase in frail CKD patients.[23]

In this study, a significant association was found between age and frailty in stage 5 CKD patients. Research by Joseph et al. (2023) supports this, indicating a significant relationship between age and frailty, particularly with advancing age.[24] Similar findings are reported in studies by Yang et al. (2023) and Chang et al. (2022), emphasizing that increasing age raises frailty risk in CKD patients.[25,26]

Gender does not emerge as a significant risk factor for frailty in CKD patients, consistent with Joseph et al.'s (2023) study, which states that gender is not a significant frailty risk factor in CKD patients.[24] Yang et al. (2023) also found no association between gender and frailty in CKD patients.[25] However, Xu et al. (2022) and Li et al. (2021) show a strong correlation between gender and frailty in the geriatric population.[27,28] The theoretical perspective supports the idea that frailty risk often increases in females.[17]

Nutritional status is a significant risk factor with a strong correlation. Luo et al.'s (2022) study demonstrates a strong relationship between frailty occurrence and nutritional status, using the MNA. Poor nutritional status increases the risk of cognitive frailty, with the study recommending a Mediterranean diet to reduce cognitive decline risk.[29] This is supported by Xu et al.'s (2022) research, showing a strong correlation between low vegetable and fruit consumption and frailty risk in the geriatric population.[28] Li et al. (2021) found that a BMI ≥ 30 increases frailty risk.[29]

Comorbidity based on the CCI score is a risk factor with a strong correlation. Yang et al. (2023) demonstrates a significant relationship between CCI score and frailty in CKD patients.[25] Chang et al. (2022), Xu et al. (2022), and Li et al. (2022) also mention a strong correlation, with higher CCI scores indicating increased frailty incidence. CKD patients often suffer from various other chronic diseases.[26-28]

Functional status based on the ADL score is a strong risk factor. A review by Wu et al. (2019) citing Lee et al.'s research shows a strong correlation between disability and frailty in stage 5 CKD patients undergoing dialysis.[17] Yang et al. (2023) also indicates a significant relationship between physical activity, measured by grip strength and daily step count, and frailty in CKD patients.[25] This is supported by Xu et al.'s (2022) research, showing that low physical activity increases frailty risk, and Li et al.'s (2021) study demonstrating the relationship between ADL scores and frailty risk in the elderly.[27,28] This increased risk is primarily associated with advancing age, where individuals tend to experience a decline in

walking speed and grip strength, affecting ADL scores.[27]

Mental status analysis based on the MMSE score is a strong risk factor, supported by Li et al. (2022), indicating that dementia increases frailty risk in the geriatric population.[27] However, Bansal et al.'s (2022) study suggests that MMSE score is not a significant factor influencing frailty in CKD patients.[30]

Depression analysis using the GDS score as a risk factor shows a strong correlation. Chang et al.'s (2022) study indicates a strong correlation between depression and frailty in CKD patients.[26] Additionally, Xu et al. (2022) and Li et al. (2021) show a strong correlation between depression and frailty in the geriatric population.[27,28]

Multivariate analysis in this study indicates that CCI, MMSE, and ADL are the most influential factors on frailty simultaneously. This suggests that patients with multiple comorbidities, impaired mental status, and severe dependency can collectively impact frailty by 80.1%. While no previous study has analysed the combined effect of these three factors on frailty in CKD patients, referring to previous research by Chang et al. (2022), Xu et al. (2022), and Li et al. (2022) suggests that a higher CCI score depicting comorbidity increases frailty incidence.[26-28] Previous studies by Wu et al., Yang et al., and Xu et al. demonstrate that as age advances, dependence in daily activities tends to increase, contributing to the rising prevalence of frailty.[17,25,28] Li et al. also shows that patients with dementia tend to have high frailty scores.[27]

The relationship between CKD and bone-mineral disease (BMD) is caused by systemic disturbances in bone and mineral metabolism. This is triggered by kidney decline, leading to secondary hyperparathyroidism characterized by hyperphosphatemia, decreased calcitriol, and hypokalaemia, resulting in PTH secretion and hyperparathyroidism in advanced CKD cases. Additionally, increased FGF23 levels in hyperparathyroidism exacerbate kidney function. Klotho, a transmembrane protein on FGF23, plays a role in CKD-MBD homeostasis (PTH, phosphate, FGF23, and calcitriol). FGF23's inability to neutralize phosphate levels through PTH secretion is observed in patients with high PTH levels due to klotho deficiency. This leads to mineral metabolism disorders, secondary hyperparathyroidism, vascular calcification, and cardiac hypertrophy. Wnt (portmanteau of wingless and int) inhibitory mechanisms also play a role in CKD-BMD pathogenesis by decreasing bone formation and reversing induced osteodystrophy and vascular calcification. Activin-A, found in damaged kidney fibroblast tissue, contributes to CKD-BMD through vascular and skeletal components.[31,32] The link between BMD and frailty is often associated with aging factors that increase the risk of falls, fractures, and dominance of incapacity, especially in women. This is due to a decline in sex hormones, primarily oestrogen, with oestrogen playing a role in maintaining calcium in bones and preventing BMD. Osteoporosis is the most common BMD, increasing the risk of fractures and hospitalization. Osteoporosis is often associated with decreased oestrogen levels in women experiencing menopause. This affects bone remodelling and frailty through muscle mass loss and muscle strength reduction.[33]

The strengths of this study lie in the comprehensive analysis of numerous factors, serving as a benchmark for identifying influences on frailty scores. The examination of comorbidities in the samples, referring to the CCI, provides a detailed overview of common chronic diseases in the elderly. Moreover, the multivariate analysis conducted in this research is a notable advancement, as previous studies have not explored the simultaneous impact of various factors on frailty, making it a valuable contribution to understanding the factors most affecting frailty.

However, some limitations need consideration. The study lacks identification

of the duration of frailty in patients, potentially introducing bias, especially in distinguishing between those who have been undergoing haemodialysis for an extended period and those who are new to the treatment. Furthermore, the research is conducted at a single location, limiting its ability to represent the entire Indonesian sample, and thus, generalizations should be made cautiously.

CONCLUSION

The study reveals a positive correlation between age and frailty scores, indicating that advancing age increases frailty. While no significant gender-frailty correlation was found, nutritional factors showed an inverse relationship, suggesting better nutrition lowers frailty scores. Comorbidities positively correlated with frailty, with most subjects experiencing diabetes with end-organ damage, contributing to frailty. Functional status exhibited an inverse correlation, signifying that improved functionality corresponds to lower frailty scores. Mental status displayed a positive correlation, implying that better mental health reduces frailty. Depression was positively associated with frailty, as depressed elderly individuals often experience reduced appetite and nutritional decline. The multivariate analysis identified CCI, MMSE, and ADL as the most influential factors, jointly explaining 80.1% of frailty variance. Further research should explore additional factors impacting frailty, and gender-related analyses should ensure equal male and female sample representation to prevent biases.

Declaration by Authors

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