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ORIGINAL ARTICLE

Association of hand grip strength and laboratory markers with frailty in patients on maintenance hemodialysis

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ABSTRACT

Background: Frailty is a common yet under-recognised problem in end-stage renal disease.
Objective: To assess the association between frailty and hand grip strength and to evaluate laboratory parameters as predictors of frailty in patients on maintenance hemodialysis.
Methods: This study was conducted at Combined Military Hospital, Lahore, from January to February 2025, among adolescent and adult patients with end-stage renal disease undergoing maintenance haemodialysis. Key exclusion criteria included physical disabilities, poor functional status, acute kidney injury, and unwillingness. Before the start of the mid-week haemodialysis session, hand grip strength was tested on both sides three times using a handheld digital dynamometer, and the best value was recorded. The Short Physical Performance Battery (SPPB) was also administered to all patients, with scores <10 indicating frailty. Blood samples were also collected to check haemoglobin, serum calcium, phosphate, albumin, creatinine, potassium, C-reactive protein, and bicarbonate levels. Statistical analyses were performed using Spearman's rank correlation test, binary logistic regression, and receiver Operating Characteristic (ROC) curve analysis.
Results: A total of 105 patients with a mean age of 55.00 ± 14.96 years were included. The mean hand grip strength was 14.32 ± 6.80 kg, below the normal reference values (>28 kg for males and >18 kg for females). Mean hand grip strength was 15.11 ± 6.95 kg on the right side and 13.52 ± 6.96 kg on the left side. The median (IQR) SPPB score was 8.00 (4.50–10.00). SPPB score showed a significant correlation with hand grip strength ($r^2 = 0.311$; $p < 0.001$). A hand grip strength cutoff of ≥16.95 kg demonstrated a sensitivity of 65.71% and specificity of 81.43% for discriminating non-frail status (SPPB ≥10) (AUC = 0.781; $p < 0.001$). None of the laboratory parameters were independent predictors of frailty ($p > 0.05$).
Conclusion: Hand grip strength is associated with frailty and can discriminate non-frail status, while laboratory parameters are not independent predictors of frailty.

Key Words: Chronic Kidney Failure, Frailty, Hand Strength, Physical Functional Performance, Renal Dialysis

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INTRODUCTION

End-stage renal disease (ESRD) is a major global health challenge, with millions of patients dependent on maintenance haemodialysis (HD) for survival. In Pakistan alone, the prevalence of chronic kidney disease (CKD) among adults stands at 21.2%, with reports ranging from 12.5% to 29.9% in different studies.[1] According to the National Kidney Foundation's latest guidelines, CKD is defined as "kidney injury or glomerular filtration rate <60ml/min/1.73m^2 for at least 3 months". CKD has five stages, with the lower stages (1-3) typically asymptomatic. More advanced stages (4-5) commonly present with symptoms such as albuminuria (>30mg/day), electrolyte imbalances, and structural or histological abnormalities.[2]

As CKD progresses, functional ability is reduced by immobility, decreased appetite leading to malnourishment, and muscular atrophy and myopathy, driven by deterioration of the contractile machinery, protein modifications that impair muscle contraction, and a reduction in type 2 fibres. This phenomenon is called sarcopenia, the gradual loss of muscle bulk and strength. Sarcopenia can act as a direct measure of frailty, which is a multidimensional syndrome characterised by reduced physiological capacity and increased susceptibility to stressors, making patients more likely to succumb to falls, hospitalisations, and other complications. Frailty is more common in ESRD patients than in non-ESRD patients, being prevalent in 60-97% of patients on maintenance HD.[3] In another study, a rise in prevalence of frailty was seen with increasing vintage of haemodialysis amongst patients undergoing maintenance HD.[4]

Understanding the importance of frailty is of little value if it cannot be detected promptly and distinguished from normal age-related muscle atrophy.[5] Currently, there are a variety of tests available to evaluate functional capacity. It is important to note that a single test might not apply to all patients. A popular tool for this is the Frailty Scale, which is effective at assessing frailty in under 5 minutes.[6] There is still a need for a practical bedside and easy-to-use measure to assess frailty better and faster, which is why we intended to investigate hand grip strength (HGS), the short physical performance battery (SPPB) test, and laboratory parameters in the assessment of frailty in ESRD patients on maintenance HD. CKD has been described as an accelerated form of metabolic aging characterized by persistent inflammation and oxidative stress. Specific markers of chronic inflammation could have a significant value in predicting worse outcomes and frailty.[7]

Although frailty is common among patients with ESRD, several essential knowledge gaps and practical challenges remain. Protocols for measuring HGS are heterogeneous, and cut-offs specific to ESRD are not clearly defined.[8] The routinely available laboratory markers show inconsistent associations with frailty, and most evidence is from cross-sectional studies, rather than longitudinal.[7] There are limited datasets from low- and middle-income countries. These gaps highlight the need for locally conducted studies that combine standardised functional testing with laboratory biomarkers to improve the detection and management of frailty in ESRD. This study aimed to investigate the association between frailty as assessed by SPPB and handgrip strength, and to identify laboratory parameters predictive of frailty and poor functional status in ESRD patients on maintenance HD. A better understanding of these relationships would clarify how to measure fragility in this vulnerable population and how to improve health outcomes for ESRD patients on maintenance HD.

METHODS

This cross-sectional study was conducted over 2 months, from January to February 2025, at the nephrology unit of Combined Military Hospital Lahore, Pakistan. The sample size was calculated using G*Power software (version 3.1.9.7). A priori power analysis was performed for a bivariate correlation (exact test). Based on a previously reported correlation coefficient of 0.473 between hand grip strength and frailty[9] assessed by SPPB scores, with a two-tailed alpha level of 0.05 and a power of 80%, the minimum required sample size was calculated to be 33 participants. Written consent was obtained from all the patients included in this research. We also ensured that the confidentiality of all patients and the data was maintained. This study included patients aged 13-84 years old. They were diagnosed with ESRD and have been undergoing maintenance HD for more than three months as outpatients. Key exclusion criteria included physical disability, poor functional status (an inability to perform usual physical activities related to basic self-care), acute kidney injury, and patients who refused to cooperate.

Data collected from patients included demographic information, type of vascular access, duration of HD, and dialysis frequency. HGS was measured using a handheld digital dynamometer before the start of the mid-week haemodialysis session. Before the test began, the dynamometer was calibrated for accuracy, and it was ensured that the patients were not feeling exhausted/fatigued. Patients were asked to sit in a chair with arms that rested easily on their thighs. The dynamometer was to be held in their palms, with their fingers wrapped around the instrument's handle. The interphalangeal joints of the fingers were flexed to 90°, and the thumb was abducted to 90°. The elbow was bent to 90° for the most accurate measurements. The patients were instructed to squeeze the dynamometer with maximal force for 3-5 seconds, with the force gradually increased. The test was repeated three times, and measurements were taken for both the left and right hands; the highest value (in kilograms) on each

side was recorded for analysis. Rest was advised for 30-60 seconds between attempts to prevent exhaustion from affecting the results. Hand grip strength less than 28 kg for males and less than 18 kg for females is considered reduced strength in South Asians.[10]

Frailty was assessed using the SPPB, a lower-limb strength test. It is a validated tool to evaluate physical performance.[11] There are three major components: the standing balance test, the gait speed test, and the chair stand test. Balance tests were performed first, including the side-by-side, semi-tandem, and tandem stand tests. These were performed for 10 seconds each. The second component of the SPPB involved analysing walking speed by having the patient walk 4 meters at their normal pace. The test was repeated twice, and the fastest reading was recorded. The third component assessed lower extremity strength. Patients were asked to sit in a chair with their hands crossed over their shoulders and then instructed to stand from the chair (single-chair stand). It was then repeated five times at the patient's fastest pace. Patients were asked to perform the tests independently, without support. However, depending upon their condition, support was provided.

SPPB Scores from each test were summed to yield a cumulative score ranging from 0 to 12. A cumulative score of 10-12 was considered normal. In contrast, lower SPPB scores (less than 10) indicated frailty, using cut-offs employed in previously published studies.[12] A blood sample was collected within 5 minutes of initiating the HD session to analyse haemoglobin, serum calcium, phosphate, albumin, creatinine, potassium, CRP, and bicarbonate levels.

Participants were categorized into three age groups based on the study cohort's age quartiles to enable comparison of frailty and functional performance across age strata. The lower quartile comprised participants aged 13-54 years (Group 1), the middle quartile comprised participants aged 55-62 years (Group 2), and the upper quartile comprised participants aged 63-84 years (Group 3). This data-driven grouping ensured approximately equal numbers of participants in each category, minimizing bias and enabling meaningful statistical comparisons of HGS and SPPB scores across age strata

Ethical Approval

The Institutional Review Board of the Combined Military Hospital Lahore approved the protocol for this study on 1st January 2025 (IRB no. #607/2025).

Statistical Analysis

Data analysis was done using SPSS version 24. All continuous variables were expressed as mean±standard deviation if they followed a normal distribution or as median and interquartile ranges if not normally distributed. Categorical variables were expressed as frequencies/percentages. Descriptive statistics were calculated for age, HGS, SPPB scores, and frailty for patients in each group. Comparison of the statistical significance for the differences between the three age groups was done using One-Way ANOVA and Kruskal-Wallis. The Spearman correlation test was used to assess the relationship between HGS and frailty in the overall study population and in the three age groups. Binary logistic regression was performed to determine whether laboratory parameters could predict frailty. This was done in two stages: all variables were included in the univariate stage, and all variables with a p-value < 0.250 at that stage were included in the multivariate model, in accordance with standard statistical practice.[13] Receiver operating characteristic (ROC) curve was generated to assess the sensitivity and specificity of HGS for predicting frailty.

RESULTS

The study included 105 patients, with a mean age of 55.00±14.96 years. Baseline characteristics of the study population are shown in Table 1.

HGS was more on the right side (15.11 ± 6.95 kg) compared to the left side (13.52 ± 6.96 kg), as shown in Table 2. Higher HGS scores were associated with better physical performance, as evidenced by a significant positive correlation between HGS and SPPB ($r2 = 0.558$; $p < 0.001$) across the entire study population (Figure 1).

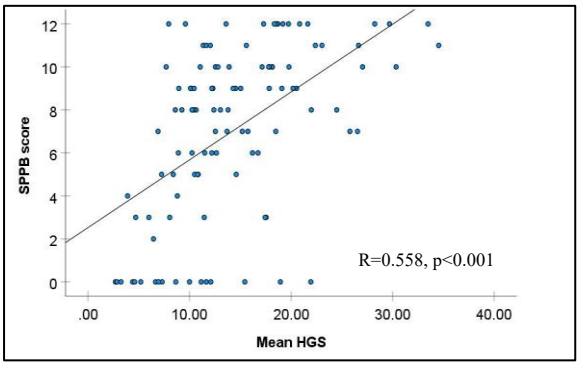

Figure 1: *Correlation of handgrip strength with frailty. SPPB=short physical performance battery*

When stratified by age, the frequency of frailty increased significantly across groups (p=0.003), with 45.7% in group 1 (younger), 71.4% in group 2 (middle), and 82.9% in group 3 (oldest) (Table 3). Median (IQR) SPPB scores also declined progressively with age, from 10 (IQR 8–12) in the youngest group, 7 (5- 10) for the middle group, and 6 (IQR 0–9) among the oldest (p < 0.001), indicating poor physical performance with advancing age (Table 4) across age groups, the differences were not statistically significant (p > 0.05). A significant positive correlation was observed between HGS and SPPB scores across all age groups (p<0.05), indicating that greater grip strength was consistently associated with better physical performance (Table 4). The ROC curve for HGS as a marker of frailty showed an area under the curve of 0.780 (95% confidence interval 0.688, 0.872; p< 0.001) (Figure 2).

Table 1: Baseline characteristics of the study population

Variables	n (%)
Gender	
Male	58 (55.24%)
Female	47 (44.76%)
Frequency of haemodialysis	
Twice a week	61 (58.10%)
Thrice a week	44 (41.90%)
Type of vascular access	
Arteriovenous fistula	67 (63.81%)
Tunnelled catheter	38 (36.19%)
Variables	**mean ± SD**
Age (years)	55.0 ± 14.9
Hemoglobin (gm/dL)	9.55 ± 1.70
Serum calcium (mmol/L)	2.10 ± 0.24
Serum phosphate (mmol/L)	1.43 ± 0.63
Serum albumin (gm/L)	35.4 ± 5.57
Serum potassium (mmol/L)	4.91 ± 0.87
Serum bicarbonate (mmol/L)	20.2 ± 5.97
Variables	**median (IQR)**
Education (years)	10 (5- 12)
Hemodialysis vintage (months)	8.00 (3.00- 30.00)
Serum creatinine (µmol/L)	599 (433.5- 755.5)
Serum C-reactive protein (mg/L)	9.10 (2.50- 32.00)

HGS ≥16.95 kg showed a sensitivity of 65.71% and a specificity of 81.43% for predicting SPPB scores>10. Logistic regression analysis revealed no statistically significant association between laboratory measurements and frailty. Lower serum albumin was associated with an increased odds of frailty in the unadjusted analysis, but this association lost statistical significance after adjustment, suggesting confounding by other factors (Table 5).

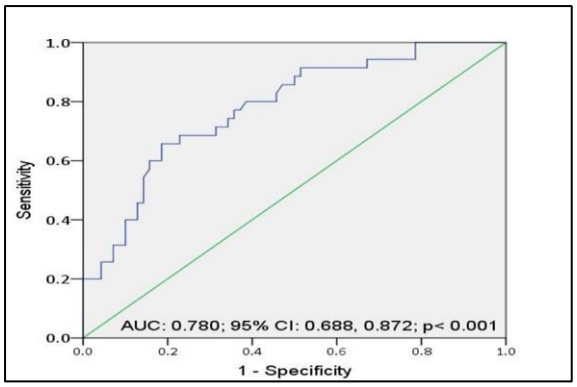

Figure 2: *ROC curve for handgrip strength as a marker of frailty.*

Table 2: Handgrip strength measurements of the study population

Variables	mean ± SD
Handgrip strength right (kg)	15.11 ± 6.95
Handgrip strength left (kg)	13.52 ± 6.96
Handgrip strength of right and left (kg)	14.32 ± 6.80

Table 3: Comparison between age-based groups

Variable	Group 1 (n=35)	Group 2 (n=35)	Group 3 (n=35)	p-value
Frailty (SPPB<10)	**n (%)** 16 (45.71)	**n (%)** 25 (71.43)	**n (%)** 29 (82.86)	0.003*
Variables	**mean ± SD**	**mean ± SD**	**mean ± SD**	
Age (years)	37.97±11.6	58.31± 3.19	68.71±5.96	<0.001[a]*
HGS (kg)				
Mean	15.25±7.42	14.37± 6.38	13.33±6.61	0.694
Right	16.18±7.63	15.23± 6.22	13.92±6.96	0.931
Left	14.32±7.57	13.51± 6.83	12.74±6.54	0.445
Variable	**median (IQR)**	**median (IQR)**	**median (IQR)**	
SPPB score	10 (8- 12)	7 (5- 10)	6 (0- 9)	<0.001[b]*

HGS=handgrip strength; SPPB=short physical performance battery; [a]One-way ANOVA and; [b]Kruskal-Wallis test were applied; p<0.05 was considered statistically significant. Group 1=13-54 years, Group 2= 55-62 years, Group 3= 63-84 years.*

Table 4. Correlation between handgrip strength and SPPB scores across age groups

Age group	Rho	p value
Group 1 (13-54 years)	0.444	0.008
Group 2 (55-62 years)	0.635	<0.001*
Group 3 (63-84 years)	0.522	0.001*

*HGS=handgrip strength; SPPB=short physical performance battery. Spearman correlation was applied. * p<0.05 was considered statistically significant.*

Table 5. Regression analysis of laboratory parameters with frailty in end-stage renal disease

Variable	B	p value	Unadjusted OR (95% CI)	95% CI		B	p value	Adjusted OR (95% CI)	95% CI	
				Lower	Upper				Lower	Upper
Haemoglobin	-0.183	0.144	0.833	0.652	1.065	-0.090	0.524	0.914	0.692	1.207
Serum calcium	-0.086	0.923	0.918	0.162	5.214			-		
Serum phosphate	-0.105	0.749	0.900	0.473	1.714			-		
Serum albumin	-0.128	0.007*	0.879	0.802	0.965	-0.101	0.059	0.904	0.815	1.004
Serum creatinine	-0.001	0.196	0.999	0.998	1.000	-0.001	0.999	0.999	0.998	1.001
Serum potassium	-0.057	0.811	0.944	0.589	1.513			-		
Serum C-reactive protein	0.008	0.134	1.008	0.998	1.018	0.004	0.391	1.004	0.995	1.013
Serum bicarbonate	-0.005	0.879	0.995	0.930	1.065			-		

*OR=Odds ratio; CI= confidence interval; All values calculated using binary logistic regression analysis; *p<0.05 was considered statistically significant.*

DISCUSSION

To assess the association between frailty and hand grip strength and to evaluate laboratory parameters as predictors of frailty in patients on maintenance hemodialysis.

The present study found a significant positive association between HGS and frailty, a reliable indicator of frailty. However, none of the laboratory parameters tested were predictive of the patients' frailty. Previous studies have shown that HGS is a valuable and trusted marker for assessing residual muscle function.[14] HGS can not only serve as an excellent prognostic marker of frailty in ESRD patients, but also benefit all medical inpatients.[15] Frailty has been a prognostic marker for patients on long-term haemodialysis for a long time. Still, discussions on its impact on patient care have only recently begun.[16] While frailty and sarcopenia are closely linked together, they represent separate clinical situations. Frailty is a much broader term for conditions characterized by decreased resilience and increased susceptibility to stressors, potentially due to multiple causes, including sarcopenia.[17] Frailty under its broader umbrella has also been linked to lower psychological reserves leading to poor outcomes, showing that frailty can not only stem from conventional diseases rather involves psychological aspects as well.[18] Complex nature of this frailty in ESRD might explain why any of the isolated static laboratory values could not predict frailty in our cohort.

For these reasons, efforts have consistently sought to identify a reliable bedside method or an easily accessible laboratory parameter that predicts frailty. Unfortunately, we were unable to prove whether any static biochemical laboratory parameter could confirm this. A systematic review showed that hemoglobin and serum albumin levels were negatively correlated with frailty. In line with disparities in results in this arena, research showed that biomarkers such as C-reactive protein could not predict frailty, although they are good predictors of mortality.[19]

Therefore, decreased hand grip strength and, by extension, low SBBP scores can be excellent predictors of the prognosis of long-term ESRD patients on HD. These markers are known to have a strong correlation with increased hospitalisation and mortality.[15,20] Consequently, physicians and clinicians can use these dynamic tests in comparison with static biochemical markers in the day-to-day evaluation of these patients. For this purpose, we have established an HGS threshold of>16.95kg to indicate normal physical function (SPPB > 10), which aligns closely with clinical studies that identify specific HGS cutoffs indicating mobility limitations and disability in patients with CKD.[21] Our observation that laboratory measurements did not predict frailty emphasises the need to do complete clinical examinations rather than depending primarily on biochemical indicators. This supports the approach which emphasises how important it is to keep in mind to analyse different health domains while detecting frailty in ESRD.[22]

Exercise programs, dietary optimisation, and comorbidity management can help mitigate frailty in ESRD patients and may improve patient outcomes.[23] It is also pertinent to note that the presence of sarcopenia needs to be promptly identified and managed accordingly. However, the safety of various exercise regimens in these patients remains understudied and warrants further investigation.

Several confounding variables may have contributed to the disparity between our results and those of

previous research. There is a high risk of observer bias in tests such as the SPPB, which are observer-dependent. Our total cohort of 105 patients may be sufficient to establish a preliminary correlation; however, more extensive data collection would be needed to confirm it. Our data have also not been stratified by population characteristics, such as ethnicity. It has already been shown that frailty in elderly adults varies by ethnic background.[24] They clearly showed how frailty had a positive correlation with African American ethnicities as compared to other population backgrounds.

The established HGS threshold serves as a useful screening tool for identifying patients at risk of frailty in clinical settings. While standard laboratory measurements showed no significant relationships with frailty in our population, further research on novel biomarkers and comprehensive assessment methodologies is needed. These findings contribute to the growing body of evidence that routine assessments of muscular strength and physical performance in ESRD patient care can enhance clinical outcomes.

CONCLUSION

Hand grip strength is a simple, rapid, and noninvasive measure for identifying frailty in patients with end-stage renal disease undergoing long-term hemodialysis. In contrast, the laboratory parameters evaluated do not independently predict frailty.

Limitations and future recommendations

Laboratory parameters were measured at a single time point, and emerging biomarkers and hormonal factors were not assessed, limiting the scope of this study. Future multicenter, longitudinal studies are needed to evaluate dynamic laboratory changes and novel biomarkers, and to determine their potential role in identifying and monitoring frailty in clinical practice.

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AUTHOR'S CONTRIBUTIONS:

AM: Study design, data acquisition and analysis, manuscript drafting, final approval of the version to be published.

ARA: Conception of the study, interpretation of data, critical revision of the manuscript, final approval of the version to be published.

AM: Data collection, data analysis, manuscript drafting, final approval of the version to be published.

RY: Interpretation of results, critical review of the manuscript, final approval of the version to be published.

All authors approved the final version to be published and agreed to be accountable for all aspects of the work, ensuring that any questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

CONFLICT OF INTEREST:

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DATA SHARING STATEMENT:

The data are available from the corresponding author upon reasonable request.

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