

# Clinical Determinants of Frailty in End-stage Renal Disease

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## ABSTRACT

This cross-sectional analytical study was carried out to determine the frequency of frailty in patients on haemodialysis and to identify predictive clinical parameters. Patients were selected using convenience sampling. Exclusion criteria included acute kidney injury, non-compliance to hemodialysis, limited physical mobility due to cerebrovascular or rheumatological diseases, acute infections and unwillingness. Frailty was assessed using a short physical performance battery (SPPB). Handgrip strength and triceps skin fold thickness were also measured. There were 79 patients enrolled in the study with mean age of 51.86±14.85 years, including 44 (55.70%) males. The median SPPB score was 8 (4-11). Frailty was observed in 51 (64.56%) patients. SPPB score had significant correlation with handgrip strength ( $R^2 = 0.309$ ;  $p < 0.001$ ) and triceps skin fold thickness ( $R^2 = 0.060$ ;  $p = 0.030$ ). On univariate analysis, increasing age, female gender, triceps skin fold thickness and hand grip strength were predictive of frailty. However, only increasing age ( $p < 0.001$ ) was predictive of frailty in multivariate analysis.

**Key Words:** Haemodialysis, Physical performance, Renal replacement therapy.

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The prevalence of end-stage renal disease is increasing progressively over time. In addition to the different biochemical abnormalities and associated effects on specific organ systems, patients with chronic kidney disease have a generalized impairment of health, characterized by loss of muscle mass and poor physical performance status. Frailty has been linked to various factors including poor psychological health and inadequate social support. Renal impairment independently increases the risk of frailty and is associated with worse outcomes such as more frequent emergency department attendances, greater need for indoor care and higher mortality. There is ample data to suggest that frailty is associated with the progressive worsening of patient-reported quality of life over time in patients undergoing maintenance hemodialysis.<sup>1</sup> A recent systematic review and meta-analysis has described a 46% prevalence of frailty in haemodialysis-dependent patients.<sup>2</sup>

Different screening tools have been used previously to assess frailty depending upon the practicality and patient's benefit.

SPPB is one such objective tool developed by National Institute on Aging. This is based on the assessment of balance, gait speed and lower limb strength. It does not need much equipment to perform and can easily be applied in a clinical setting. It is a reliable predictor of illness and mortality, with good validity and reliability already documented in many previous publications.<sup>3</sup>

Despite ample data from the rest of the world to prove a strong association of frailty with poor outcomes, the true prevalence of frailty in Pakistani hemodialysis-dependent patients has not been sufficiently described before. This study was therefore carried out to document statistics from the dialysis unit of a tertiary care hospital and to identify clinical parameters that could predict this. This would in turn identify patients requiring more aggressive management to improve long-term outcomes via a focused management approach.

This cross-sectional analytical study was conducted at the Dialysis Unit of Combined Military Hospital Peshawar from October to December 2021. The Ethics Review Committee for Medical and Biomedical Research of this hospital approved the study protocol before the start of data collection. All patients with a minimum duration of three months on hemodialysis were enrolled, based on the provision of written consent. They were selected via convenience sampling. Exclusion criteria included acute kidney injury, non-compliance to hemodialysis, limited physical mobility due to cerebrovascular or rheumatological diseases, acute infections and unwillingness expressed by patients.

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**Table I: Comparison between frail and robust patients.**

Parameter	Frail patients (n=51)	Robust patients (n=28)	p
Age (years)	57.96± 13.03	40.75± 11.15	<0.001*
Gender			
Males	22 (43.14%)	22 (78.57%)	0.002***
Females	29 (56.86%)	6 (21.43%)	
Hemodialysis frequency			
Twice a week	41 (80.39%)	27 (96.43%)	0.049***
Thrice a week	10 (19.1%)	1 (3.57%)	
Hemodialysis vintage (months)	14 (4-36)	7.5 (3-22.5)	0.212**
Triceps skin fold thickness (mm)	9 (6-12)	12 (10-15.75)	0.004**
Hand grip strength (kg)	5 (3-13)	27.50 (12.25-47.00)	<0.001**
SPPB score	5 (1-8)	11.50 (10.25-12.00)	<0.001**

Comparisons were made using \*independent samples t-test, \*\*independent samples Mann-Whitney U test and \*\*\*Chi-square test.

Data was collected just before the start of the mid-week hemodialysis session. Hand grip strength was measured twice with a digital dynamometer and the best of two readings was recorded. Balance tests, gait speed tests and chair stand tests were then done by the third and fourth authors as part of SPPB. Haemodialysis was carried out for three and a half hours using Fresenius 4008S machines. Triceps skinfold thickness was finally measured with a standard calliper at the end of the haemodialysis session.

All analyses were done with IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp, Armonk, NY). Continuous variables were described as mean± standard deviation or median and interquartile ranges, depending on the normality of distribution as assessed by Shapiro-Wilk test. Patients were divided into frail and robust groups based on SPPB scores <10 or higher. Different variables were compared between the two groups using independent samples t test, independent samples Mann-Whitney U test and Chi-square test. Linear regression analysis was done to determine the relationship of SPPB with handgrip strength and triceps skin fold thickness. Binary logistic regression analysis was performed for the evaluation of the relationship between different clinical parameters and frailty. Level of statistical significance was set at <0.05.

There were total 79 patients with mean age of 51.86 ± 14.85 years. Thirty-five (44.30%) were females and 44 (55.70%) were males. Majority of them (68, 86.08%) were on twice-a-week hemodialysis, whereas, the rest got dialysed three times a week. The mean hemodialysis vintage was 13 (3- 33) months. The median SPPB score was 8 (4-11). Frailty was observed in 51 (64.56%) patients. Mean triceps skin fold thickness was recorded as 10 (6-13) mm. Median hand grip strength was 12 (3-27) kg. There was a significant correlation of SPPB score with handgrip strength ( $R^2=0.309$ ;  $p<0.001$ ) and triceps skin fold thickness ( $R^2=0.060$ ;  $p=0.030$ ). The comparison of different parameters amongst frail and physically robust patients is shown in Table I. It can be clearly seen that the two groups had different age and gender distributions. On univariate analysis, increasing age ( $p<0.001$ ), female gender ( $p=0.004$ ), triceps skin fold thickness ( $p<0.032$ ), and hand grip

strength ( $p<0.001$ ) were predictive of frailty. However, only increasing age was ( $p<0.001$ ) predictive of frailty on multivariate analysis, whereas the other parameters lost statistical significance.

SBBP is effective in determining frailty in groups with higher prevalence such as elderly patients on hemodialysis where other indices like Fried phenotype do not estimate its true prevalence.<sup>4</sup>

Previous literature suggest frailty to be dynamic and thus changes over time are generally seen amongst patients with end-stage renal disease. The results of this study have thus provided hope that effective interventions could improve health-related outcomes in selected patients. Elderly patients are especially likely to benefit from exercise training programs. There were higher proportion of females in the frail cohort. Still, female gender was not predictive of frailty in the overall model identified in this study. Whereas most of the published data suggest an association of the female gender with frailty, results similar to ours have also been reported elsewhere.<sup>5,6</sup>

Patients with CKD on hemodialysis often have a loss of muscle mass driven by inflammation and cachexia. This problem is frequently compounded by poor appetite attributable to uraemia and medications. Comorbidities such as anaemia and coronary heart disease every so often limit physical activity. Moreover, proximal myopathy is also seen in these patients. All these factors contribute to frailty.

This was a cross-sectional study, with no follow-up to study the association of frailty with long term outcomes. Moreover, we did not evaluate dynamic changes in frailty over time. This study involved a relatively small number of patients, primarily consistent with the workload at this dialysis unit. We would suggest multi-centre studies involving a larger number of patients to validate our results.

In conclusion, frailty is a major concern in patients on maintenance hemodialysis for end-stage renal disease. Increasing age is an important pointer towards this problem, and special emphasis should thus be placed on appropriate patient groups to improve long-term outcomes.

**DISCLOSURE:**

This data was presented as an e-poster (Abstract no 1049) titled 'Clinical parameters predicting frailty in haemodialysis dependent patients' at the 42nd Annual Meeting of the Korean Society of Nephrology, held in Seoul, South Korea from 26- 29 May 2022.

**ETHICAL APPROVAL:**

The study protocol was approved by Ethics Review Board for Medical and Biomedical Research of Combined Military Hospital Peshawar prior to the initiation of data collection.

**PATIENTS' CONSENT:**

All participants provided written consent.

**COMPETING INTEREST:**

The authors declared no competing interest.

**AUTHORS' CONTRIBUTION:**

ARA: Conception of study, data analysis, and critical revision.

NS: Study design, data interpretation, and critical revision.

SU: Data acquisition, data analysis, and drafting.

MS: Data acquisition and drafting.

All the authors have approved the final version of the manuscript to be published.

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