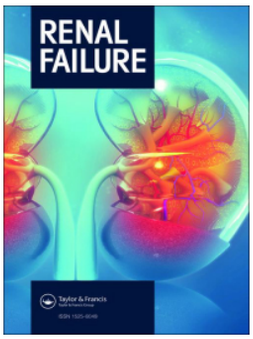

Renal Failure

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/irnf20

Transferrin levels are associated with malnutrition markers in hemodialysis patients in KwaZulu-Natal, South Africa

Sherilene Benjamin & Alain Assounga

To cite this article: Sherilene Benjamin & Alain Assounga (2024) Transferrin levels are associated with malnutrition markers in hemodialysis patients in KwaZulu-Natal, South Africa, Renal Failure, 46:1, 2337292, DOI: 10.1080/0886022X.2024.2337292

To link to this article: https://doi.org/10.1080/0886022X.2024.2337292

Published online: 14 Apr 2024.

RENAL FAILURE
2024, VOL. 46, NO. 1, 2337292
https://doi.org/10.1080/0886022X.2024.2337292

Taylor & Francis
Taylor & Francis Group

CLINICAL STUDY

Transferrin levels are associated with malnutrition markers in hemodialysis patients in KwaZulu-Natal, South Africa

Sherilene Benjamin[a] and Alain Assounga[b]

[a]Department of Biomedical and Clinical Technology, Durban University of Technology, Durban, South Africa; [b]Department of Nephrology, Nelson R. Mandela School of Medicine, University of KwaZulu-Natal, Durban, South Africa

ABSTRACT

Introduction: Malnutrition is a global phenomenon and may be contributing to the increasing size of the hemodialysis (HD) population in South Africa and is affecting morbidity and clinical outcomes. Our study assessed whether transferrin could be a possible marker for malnutrition in the HD population.

Methods: Clinical parameters (including skinfold thickness and mid-upper arm circumference [MUAC]) and laboratory markers (including transferrin and hemoglobin) were measured during a six-month period in a sample of 59 HD patients.

Results: Linear regression analysis showed that MUAC ($p = 0.027$) as well as skinfold thickness ($p = 0.021$) had a significant association with transferrin levels within the HD participants. There was no significant association between transferrin levels or MUAC with hemoglobin levels ($p = 0.075$). Furthermore, the study found that decreased transferrin levels (< 2.15 g/dL to 3.80 g/dL) were closely related to malnutrition in the malnutrition distribution groups within the study, with 97.7% of HD participants being classified in one of the malnutrition groups.

Conclusion: Thus, transferrin levels are a valuable marker for malnutrition within the HD patient population and can be included along with clinical assessment parameters such as MUAC and skinfold thickness as primary indicators for malnutrition.

ARTICLE HISTORY
Received 2 July 2023
Revised 25 March 2024
Accepted 27 March 2024

KEYWORDS
Transferrin; transferrin saturation; malnutrition; hemodialysis; erythropoietin

1. Introduction

Malnutrition is a global issue among end-stage kidney disease (ESKD) patients on hemodialysis (HD) and is a significant contributor to morbidity and mortality in both developing and industrialized nations [1,2]. Malnutrition often occurs in the setting of acute or chronic sickness in affluent countries, while in underdeveloped countries it is also linked with low socioeconomic conditions [1].

The subjective global assessment (SGA) nutritional assessment tool is a valuable, economical, and noninvasive composite tool in clinical practice [3,4]. The SGA is recommended for the evaluation of acute malnutrition in adults and has been used to monitor patients' nutritional status in acute settings [5]. Low body mass index (BMI) BMI < 18.5 kg/m2 (underweight) is generally associated with mid-upper arm circumference (MUAC) cutoffs in the range of 23 cm to 25.5 cm [6–8]. In severe malnutrition, both fat and muscle are reduced in the upper arm [9].

Plasma transferrin is a glycoprotein with two iron-binding domains and is synthesized by the liver. It is the most important vehicle for transporting iron into cells and preventing iron-mediated free radical toxicity. Approximately 3 mg of iron (0.1% of total body iron stores) circulates in the plasma and is bound to transferrin [10]. The sum of all iron binding sites on plasma transferrin is known as total iron binding capacity (TIBC). A decrease in the percentage of transferrin that transports iron (< 20%) implies iron deficiency, either absolute or functional [11].

Albumin has been criticized as a marker in nutritional assessment due to its lack of specificity and long half-life (approximately 20 days) [12]. Protein malnutrition can result in decreased transferrin and hypoalbuminemia [13]. Since transferrin has a much shorter half-life (8 days) than albumin (19–20 days), measurement of the transferrin level may be a more sensitive indicator of protein malnutrition than albumin measurement [14,15]. Transferrin rises in the presence of an iron shortage and falls in the presence of an iron surplus or protein-energy malnutrition [11, 16]. As a primary plasma

CONTACT Alain Assounga assoungaa@ukzn.ac.za Renal OPD, Inkosi Albert Luthuli Central Hospital, Private Bag X03, Mayville, 4058, South Africa

transport protein for distributing iron, it serves as a reserve by preserving extracellular iron until it is needed and then enables it to reach target tissues [17,18]. Circulating iron is attached to transferrin and permeates non-intestinal cells by receptor-mediated endocytosis after engaging with the transferrin receptor (TfR) [19]. Upregulation of TfRs occurs in iron deficiency anemia [11]. The absolute amount of transferrin catabolised daily is substantially smaller than albumin which is due to the more significant plasma concentration of albumin; the relative catabolic rate of transferrin and, on average, twice as great as that of albumin [20].

End stage kidney disease decreases the uptake of dietary iron in the duodenum and the small and large intestines [21]. This contributes to fewer numbers of iron molecules available to bind to transferrin (TIBC) [22]. Poor regulation of iron homeostasis is a major factor in development of ESKD [23].

Hemodialysis patients' nutritional status cannot be accurately assessed by a single measurement [24]. Early identification of malnutrition is critical for providing enough nutritional support, managing the illness effectively, and preventing the associated adverse clinical outcomes [25,26]. Due to increased blood losses, especially in HD patients, as well as potentially compromised gastrointestinal iron absorption, ESKD patients present with functional iron deficiency, which is the inability to deliver sufficient iron to the site of erythroblast production even in the presence of adequate stores [27].

Transferrin saturation (TSat) is related to the ratio of serum iron and TIBC which is how much serum iron is actually bound. In ESKD, erythropoiesis may be disrupted by iron unavailability [28]. The optimization of iron therapy in patients with ESKD contributes to the treatment for complications and potentially allows modification of disease progression [29]. Iron repletion protocols used by most dialysis organizations in the United States specify a TSat target range of 30% to 50% [27]. The Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend TSat to be no greater than 30% and serum ferritin of 500 ng/mL during iron therapy, independently of ESKD status and erythropoietin stimulating agent (ESA) use [30].

The aim of this study was to assess the association of clinical (anthropometric measurements) and laboratory markers (transferrin levels) as factors affecting malnutrition with ESKD patients with a glomerular filtration rate < 15 mL/min/1.73 m^2 (eGFR) [31,32].

2. Methodology

Malnutrition as a contributing factor affecting erythropoiesis in ESKD with eGFR < 15 mL/min/1.73 m^2 among patients in KwaZulu-Natal, South Africa. A prospective, experimental and quantitative methodology was employed.

The nutritional status of the patients was assessed by anthropometric analysis monitoring transferrin and albumin blood levels. The utilization of the patient's iron and ferritin levels for erythropoiesis were assessed. The effect of iron and ferritin levels on erythropoiesis was by HB monitoring.

2.1. Sample population

The sample size was 59 participants with ESKD on HD, selected from Addington and King Edward (KEH VIII) hospitals in eThekwini, KwaZulu-Natal, South Africa,

2.2. Inclusion criteria

a. Hemodialysis patients (ESKD).
b. All patients, irrespective of sex, culture, or race.
c. Patients receiving treatment at Addington or KEH VIII hospitals.
d. Patients who are 18 to 50 years old.

2.3. Exclusion criteria

a. Acute HD patients.
b. Patients who are pregnant.
c. Patients who are aware and awaiting a living donor transplant in the next few months to a year.
d. Patients who have severe cases of immunological disorders.

2.4. Ethical considerations

Before the commencement of the actual investigation, ethical approval was obtained from the Durban University of Technology Ethical Committee and permission was also obtained from the Higher Degree Committee and the Department of Nephrology, Hemodialysis Units at Addington and KEH VIII. To facilitate the study, the research plan was presented to the Departments of Nephrology as well as the hemodialysis units and the nursing staff at Addington and KEH VIII.

A letter requesting permission to conduct the study at Addington and KEH VIII was sent to KZN Health Ethekwini District for an ethical clearance certificate. The study commenced after obtaining this certificate.

A letter of information and consent form in English and IsiZulu was presented to all patients participating in the study. Patients were informed regarding the purpose and the requirements of the study, that participation in the trial was entirely voluntary, and that they were entitled to withdraw at any point without affecting the medical treatment rendered to them. They were also informed that all information used in the research would remain confidential and that any data reported in scientific journals or published would not include information identifying them by name.

Patients who were willing to participate signed the consent form were randomized into the control or experimental groups and continued their treatments as usual. The HD participants had blood tests once a month for six months. Anthropometric analysis was performed post-HD each month for six months. Recombinant erythropoietin (RHuEPO) doses were monitored for the study period.

2.5. Anthropometric measurements

Anthropometric measurements were performed on the participants selected for the study as described in previous studies for ESKD patients on HD [33–35]. The height, weight, MUAC and skinfold thickness were measured (in duplicate) monthly post dialysis for six months by the researcher to ensure standardization of the technique.

2.6. Blood samples

An extra 10 mL of blood was taken in duplicate with the routine monthly blood tests and was used for the study-related ELISA tests. The blood tubes were marked using numbers to protect the participant's identity. The samples were centrifuged (Nelson Mandela School of Medicine) to separate the serum from blood components. Blood was spun down at 1750x g for 10 min. Samples were collected, labeled accordingly, and stored at −70 °C.

2.7. Laboratory tests

The patients were recruited to the study following informed consent. Hemoglobin (Hb), transferrin (Tfr), albumin (Alb), iron (Fe), and ferritin (Ferr) were obtained from the participants' routine monthly blood tests for six months. Blood was drawn from the arterial blood lines of the HD circuit at the commencement of the procedure.

2.8. Statistical analysis

Descriptive methods providing means and standard errors of the means were applied to analyze the data. The IBM SPSS version 27 (IBM, New York, USA) was used. The test of the association between relevant variables using linear univariate regression analysis, with transferrin as the dependent variable, was performed with p-values of < 0.05 being regarded as significant.

3. Results

Table 1 shows the descriptive statistics for demographic, clinical and laboratory data for the HD portion of the sample.

3.1. Clinical parameters

Table 2 depicts the clinical parameters for the HD participants.

3.2. Laboratory parameters

Table 3 depicts the laboratory parameters of the HD participants.

3.3. Association between selected clinical and laboratory parameters

The clinical parameter of MUAC [38.74 cm ± 0.65 cm] was analyzed (univariate regression) for association with selected laboratory parameters, as shown in Table 4. The only significant association was with transferrin levels [1.45 g/dL ± 0.5 g/dL, $p = 0.027$].

The laboratory parameter of transferrin [1.45 g/dL ± 0.5 g/dL] was analyzed (univariate regression) for association with selected clinical and laboratory parameters, as shown in Table 5. There was a significant association between transferrin and MAUC [38.74 cm ± 0.65 cm, $p = 0.027$], skinfold thickness [22.86 mm ± 2.06 mm, p-value = 0.021], albumin 32.49 g/L ± 0.92 g/L, $p = 0.007$), and dry weight [73.6 kg ± 4.6 kg, $p = 0.20$].

3.4. Transferrin levels

The concentration levels of transferrin of HD participants were recorded as being between 1 g/dL and 2.5 g/dL, as shown in Figure 1. The control group of healthy individuals were within the normal range.

Table 1. Descriptive statistics patients ($n = 59$).

	N statistic	Min statistic	Max statistic	Mean statistic	Mean Std. error	Std. deviation statistic
Gender Male (m) and Female (f)	59	–	–	–	0.066	0.504
Age (yr)	59	20.00	71.00	45.373	1.738	13.353
Height (m)	50	1.09	1.85	1.627	0.016	0.111
MUAC (cm)	50	16.00	36.00	28.743	0.651	4.607
Skin fold thickness(mm)	50	1.40	77.80	22.862	2.059	14.559
HB (g/dL)	49	4.60	14.30	10.025	0.278	1.946
Ferritin (µg/L)	49	19.00	1650.00	941.265	68.453	479.174
Albumin (g/L)	49	15.00	42.00	32.490	0.917	6.423
Transferrin (g/dL)	48	0.95	2.25	1.451	0.046	0.316
Transferrin saturation (%)	45	5.00	73.00	30.956	2.336	15.673
ESR (mm/h)	30	7.00	140.00	37.033	5.410	29.632
CRP (mg/dL)	30	6.00	288.00	31.870	9.776	53.545
Dry weight (kg)	22	52.00	108.00	72.782	3.704	17.375
EPO Weekly dosage (IU)	55	0.00	18000.00	8007.273	840.169	6230.863
Erythropoietin level (mU/mL)	34	4.20	143.80	22.668	5.407	31.528
Urea (mg/dL)	37	9.40	45.50	24.746	1.397	8.495

Table 2. Clinical parameters patients ($n = 59$).

Variables	Means ± (SEM)
Skin fold thickness (mm)	22.86 ± 2.06
(MUAC (cm)	38.74 ± 0.65
Height (m)	1.63 ± 0.02
Weight (kg)	73.6 ± 4.6
Age (yr)	45.37 ± 1.74
Systolic Bp (mmHg)	153.0 ± 2.8
Diastolic Bp (mmHg)	89.4 ± 1.9
Mean arterial pressures (mmHg)	110 ± 2.0

Table 3. Laboratory parameters patients ($n = 59$).

Variables	Means ± (SEM)
Hemoglobin (g/dL)	10.03 ± 0.28
Ferritin (µg/L)	941.30 ± 68.45
Transferrin (g/dL)	1.45 ± 0.05
Transferrin saturation (%)	30.96 ± 2.34
Albumin (g/L)	32.49 ± 0.92
EPO levels (mU/mL)	22.67 ± 5.41
EPO weekly dose (IU)	8007 ± 840.2

Table 4. Univariate linear regression analysis (MUAC as dependent variable) $N = 59$.

Variable	Odds Ratio	Confidence Interval	p value
Transferrin (g/dL)	4.578	[0.532–8.625]	0.027*
Albumin (g/L)	0.052	[−154 to 0.259]	0.616
C Reactive Protein (CRP) mg/dL	0.003	[−0.030 to 0.036]	0.849
Hemoglobin (Hb)	0.277	[−0.402 to 0.955]	0.416

*significant at the p = < 0.05 level.

Table 5. Univariate linear regression analysis (transferrin as dependent variable) $N = 59$.

Variable	Odds ratio	Confidence Interval	p value
MUAC (mm)	0.22	[0.03–0.042]	0.027*
Skin fold thickness(g/dL)	0.004	[0.002–0.11]	0.021*
Ferritin (µg/L)	−8.16E	[0–0]	0.930
Transferrin saturation (%)	−0.01	[0.07–0.04]	0.608
ESR (mm/h)	0.002	[0.02]	0.251
Urea (mg/dL)	−0.09	[0.021]	0.155
Albumin (g/L)	0.019	[0.005–0.032]	0.007*
Hemoglobin (g/dL)	0.043	[0.004–0.090]	0.075
Dry Weight (kg)	0.010	[0.002–0.019]	0.020*

*significant at the p = < 0.05 level.

Figures 2 and 3 are scatter plot graphs showing the relationship between transferrin and skinfold thickness and MUAC, respectively.

3.5. Clinical distribution of malnutrition

Clinical malnutrition was distributed in relation to normal ranges for MUAC (clinical malnutrition 1) (Figure 4) and skinfold thickness (clinical malnutrition 2) (Table 6).

Figure 5 shows the distribution of transferrin levels according to the normal range (< 2.15 g/dL to 3.80 g/dL) in the HD sample. Transferrin levels < 200 g/dL were grouped according to severity of malnutrition [16].

4. Discussion

4.1. Clinical malnutrition and anthropometric measurements

We associated the distribution of MUAC data with clinical malnutrition 1 (Figure 4). The findings were that the MUAC parameters of 16% of males and females were associated with clinical malnutrition 1. These findings confirmed the existence of clinical malnutrition 1 in the HD sample. Our results support the notion that MUAC can be a dependable marker for malnutrition among the HD population in Ethekwini. As reported by Das et al. [36], MUAC can be a reliable and accurate nutrition screening tool in impoverished states, communities, and clinics, which would then reduce the amount of time and technical proficiency required for the assessment of malnutrition [36]. Musa et al. [37] conducted a study in Sudan and reported that 51.1% of arm circumferences in both genders were malnourished using a MUAC cutoff of 25.5 cm for both genders with a BMI of less than 18.5 kg/m^2 [37]. Further studies conducted with children concluded that edema might increase a limb's circumference, but it is not usually a problem of the upper arm [38]. However, researchers concur that MAUC may only consistently identify HD patients with adequate nutrition as one element of a composite nutritional score derived from SGA including also BMI, per cent of a reference weight, triceps skinfold, mid-arm muscular size, and serum albumin [3, 38].

Further analysis of MUAC using linear regression demonstrated that MUAC had a significant ($p = 0.027$) association with transferrin levels within the HD participant sample (Table 5).

We also associated the distribution of skinfold thickness with clinical malnutrition 2 (Table 6), where our data indicated that 14% of male and 48% of female participants fell within this group. In our sample there was a prevalence of clinical malnutrition 2, and these results confirm that skinfold thickness can contribute to the early detection of malnutrition. Our findings correlate with other study findings that skinfold thickness and SGA have a favorable track record as a marker for early detection malnutrition [39,40]. However, skinfold thickness testing can be inconsistent considering techniques, methodology, staffing availability, etc. We suggest therefore that the MUAC can be a more reliable clinical assessment. Further, our findings did not correlate with previous studies such as [38] which reported that SGA, which included triceps skinfold thickness, MAUC and serum albumin, were not reliable in identifying malnutrition [38]. Subsequent studies confirm that available anthropometric measurements for body composition, which include biochemical markers, are an integral component of nutrition management and decreased mortality in HD patients [41].

Furthermore, this study found that there is a significant correlation between skinfold thickness and transferrin ($p = 0.021$) (Table 5).

Dry weight was assessed over a period of six months in the HD sample group in the current study, with the results being significantly ($p = 0.007$) associated with transferrin (Table 5).

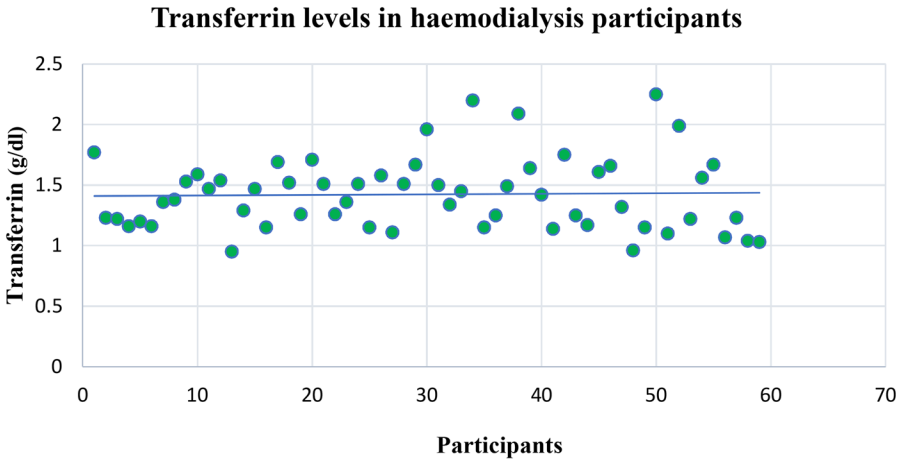

Figure 1. Scatter plot graph depicting transferrin levels in the HD participants ($n = 59$).

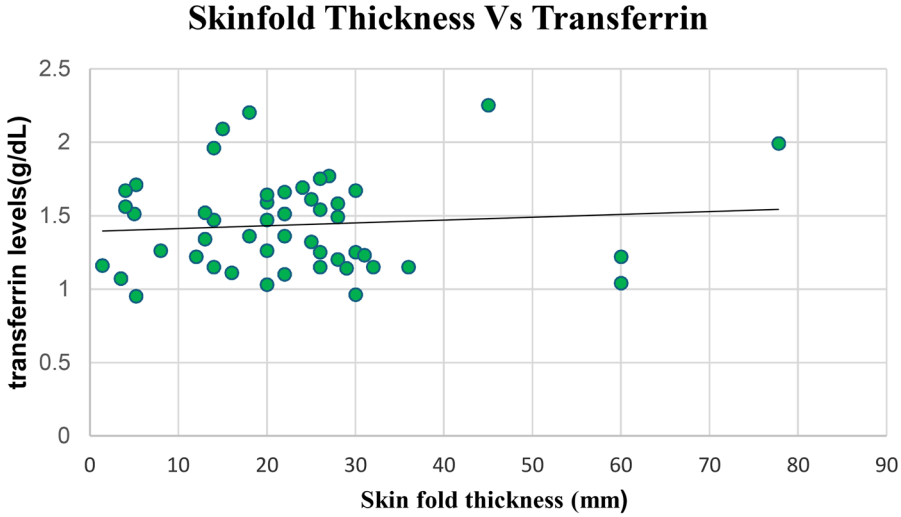

Figure 2. Scatter plot graph depicting the relationship of skinfold thickness with transferrin levels.

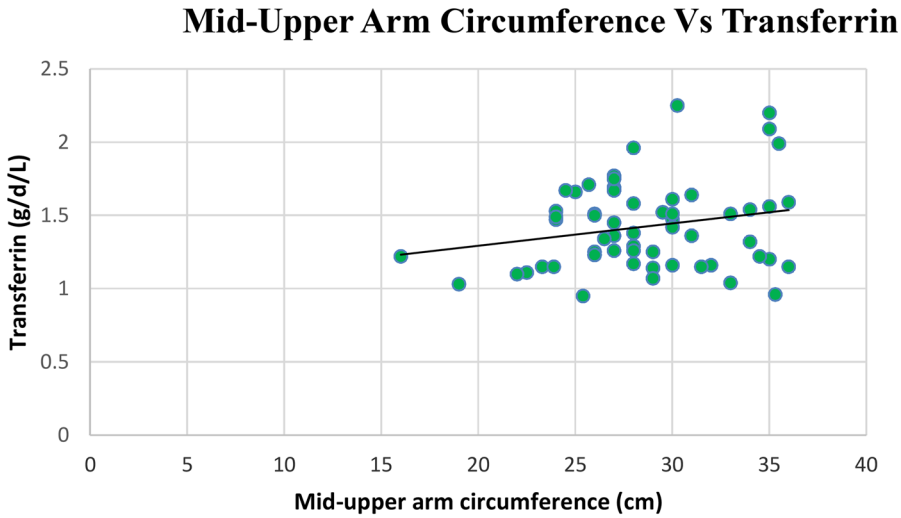

Figure 3. Scatter plot graph depicting the relationship of MUAC with transferrin level.

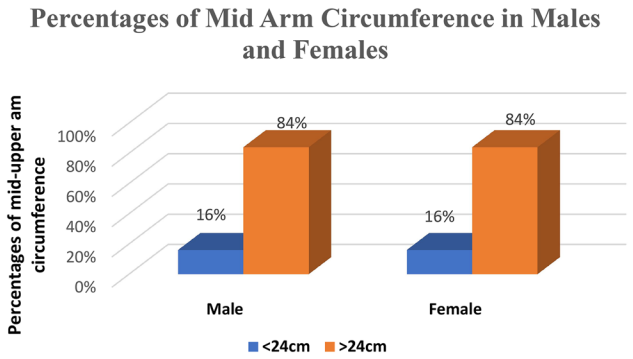

Figure 4. Percentages of MUAC in males and females.

Table 6. Showing the percentages of skin fold thickness in males and females using the appropriate reference ranges for evidence of malnutrition.

Skin fold thickness ranges (males) for malnutrition		Skin fold thickness (females) for malnutrition	
< 14 mm	24%	< 23 mm	48%
> 14 mm	76%	> 23 mm	52%

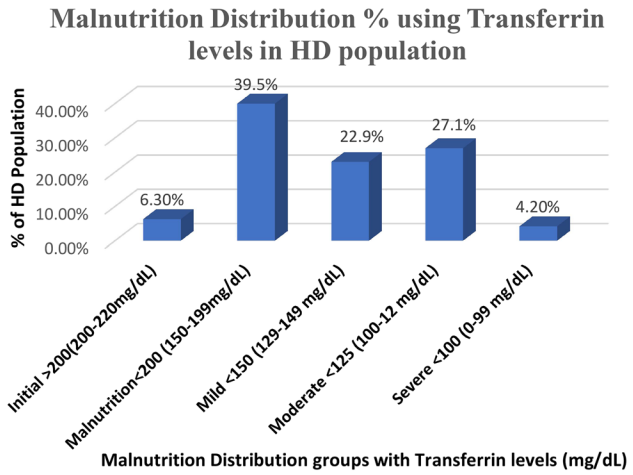

Figure 5. Showing distribution of transferrin levels in malnutrition groups.

In this study univariate regression analysis revealed that age, height and gender of the HD participant sample were not significantly associated with transferrin therefore with malnutrition (Table 5). Other studies have shown the significance of age in relation to malnutrition due to medical co-morbidities with the progression of ESKD [42]. The HD participants in the current study had a mean age of 45.37 years ± 1.74, a much younger group of participants compared to other studies [43].

The transferrin levels in the HD participants ranged between 1 g/d/L and 2 g/d/L, with the prevalence of malnutrition being substantial. Using transferrin levels we applied a group distribution based on the guideline range of 215 mg/dL to 380 mg/dL for malnutrition, with less than < 200 mg/dL corresponding with malnutrition in HD patients [44,45]. In the current study, only 6.3% of HD participants had transferrin levels above 200 mg/dL (Figure 5). Other results were: malnutrition-39.5%, mild-22.90%, moderate-27.10% and severe-4.20%. Furthermore, this study revealed that there was a significant association between transferrin levels and certain clinical anthropometric variables as well as laboratory variables. Univariate linear regression analysis with transferrin as a dependent variable revealed a significant association with MUAC ($p=0.027$), skinfold thickness ($p=0.027$) and albumin ($p=0$ 007). These findings concur with studies that have found serum transferrin levels to be low in patients with both mild and severe ESKD; with the lowest levels being found in patients in a poor nutritional state [46]. The prevalence of malnutrition has been estimated in hospitals in Western countries to be 30% to 50% and in long-term care facilities up to 85% [13]. Clinical assessments of malnutrition can contribute to reducing further complications with malnutrition.

4.1.1. Transferrin as a laboratory marker

Our finding was that transferrin is a valuable marker for malnutrition in our HD participants. Its significant that this recommendation with anthropometric markers supports this recommendation. Anthropometric markers are well established malnutrition markers. Anthropometric measurements require expertise and consistency in the technique. Furthermore, transferrin being serum-based tests, it can be easily monitored in larger and remote population groups. Severely deficient levels of transferrin are a result of protein-energy malnutrition and have been observed in diabetic foot studies as an accurate indicator of severe protein-energy malnutrition in readings lower than 100 mg/dL [16].

Transferrin levels have certain limitations in terms of reliability as a marker for malnutrition because these can be affected by other conditions such as acute or chronic infection, inflammation and iron deficiency [10, 47]. Additionally, transferrin decreases with an increase in ferritin concentration and is higher in patients with heavier body weights [48]. Nevertheless, a study among orthopedic patients with a relatively high prevalence of nutritional issues among patients undergoing elective orthopedic surgery used transferrin level and albumin level as indicators for nutrition status [49]. The significance of transferrin is that it can detect iron deficiency [10].

So, early screening or detection for transferrin levels could contribute to the management of malnutrition in HD patients. Transferrin has a short life of an average of 8 days, whereas albumin is 19 days [5, 50].

4.2. Other laboratory parameters

The mean ferritin result in our HD group was 941.30 ug/dL. Univariate analysis regression analysis revealed no significant association between ferritin and either MUAC or transferrin. Kuragano et al. [51] in their study of 805 patients undergoing maintenance HD found that high serum levels of ferritin with decreased TSats required different ranges to identify their high and low levels. The authors defined dysutilisation of iron for erythropoiesis in patients with lower TSats (< 20%) and higher ferritin (≥ 10 ug/dL) levels.

The mean hemoglobin level in our HD group was 10.03 g/dL. Low levels of hemoglobin in patients are usually an indication of malnutrition [52]. Univariate analysis regression analysis revealed no significant association between hemoglobin and either MUAC or transferrin (Tables 4 and 5). The significance of association between transferrin and hemoglobin was close, with $p = 0.075$. This could be further explored with a larger sample size.

The TSat mean of the HD group in this study was 30.96%. Univariate linear regression analysis revealed no significant association between TSat and transferrin. Our TSat% was close to the low end of the acceptable range; the KDIGO recommendation is that iron supplements should be used to treat anemia associated with kidney disease (CKD) if the TSat index is less than 30% and serum ferritin is less than 500 ng/ml [51]. High TSat (> 55%) increases the risk of cardiovascular mortality [53].

Retrospective analyses of erythropoietic responsiveness showed that maximum erythropoietic response is achieved at TSat levels greater than 30% with ferritin being in the range of 350 ng/mL to 500 ng/mL; this range was associated with the maximum Hb response to ESA dose [54]. Other studies claimed serum ferritin no longer represents iron that can be utilized during erythropoiesis so TSat is a poor biomarker of iron availability to the bone marrow [55].

Conversely, some investigations have found that patients with low ferritin (100 ng/mL) and low TSat (20%) levels did not have a notably higher risk of adverse events or mortality. The risk of mortality was greater in individuals with high ferritin levels (> 100 ng/mL) and low TSat levels (20%) who were suspected of iron dysutilisation for erythropoiesis [51].

The mean albumin level in our HD group was 32.49 g/dL (Table 3). Univariate linear regression analysis revealed a significant association between albumin and transferrin levels ($p = 0.007$). Low serum albumin levels, age, low BMI, and duration of HD are independent risk factors for malnutrition development including due to reduced renal function [26,27]. Further to all of our findings it has been reported that malnutrition in HD needs to be individualized and country-specific malnutrition treatment solutions found [56].

5. Conclusion

This study shows that transferrin levels can also contribute to malnutrition assessment. As it is significantly associated with anthropometric measurements in our study. A larger sample size and a longer time frame would improve the clarity of our results regarding the association of clinical parameters (MUAC and skinfold thickness) and laboratory markers (transferrin) with malnutrition in HD patients.

Disclosure statement

No potential conflict of interest was reported by the author(s).

References

[1] Iorember FM. Malnutrition in chronic kidney disease [mini review]. Front Pediatr. 2018;6:1. doi: 10.3389/fped.2018.00161.

[2] Martin-Alemañy G, Valdez-Ortiz R, Olvera-Soto G, et al. The effects of resistance exercise and oral nutritional supplementation during hemodialysis on indicators of nutritional status and quality of life. Nephrol Dial Transplant. 2016;31(10):1712–9. doi:10.1093/ndt/gfw297.

[3] Dai L, Mukai H, Lindholm B, et al. Clinical global assessment of nutritional status as predictor of mortality in chronic kidney disease patients. PLoS One. 2017; 12(12):e0186659. doi:10.1371/journal.pone.0186659.

[4] Detsky AS, McLaughlin JR, Baker JP, et al. What is subjective global assessment of nutritional status? JPEN J Parenter Enteral Nutr. 1987;11(1):8–13. Jan-Feb doi:10.1177/014860718701100108.

[5] Serón-Arbeloa C, Labarta-Monzón L, Puzo-Foncillas J, et al. Malnutrition screening and assessment. Nutrients. 2022;14(12):2392–2401. Jun 9 doi:10.3390/nu14122392.

[6] Tang AM, Chung M, Dong KR, et al. Determining a global mid-upper arm circumference cut-off to assess underweight in adults (men and non-pregnant women). Public Health Nutr. 2020;23(17):3104–3113. Dec doi:10.1017/S1368980020000397.

[7] Tang AM, Dong K, Deitchler M, et al. Use of cutoffs for mid-upper arm circumference (MUAC) as an indicator or predictor of nutritional and health-related outcomes in adolescents and adults: a systematic review. Washington DC: Food and Nutrition Technical Assistance III Project (FANTA); 2013.

[8] Yang Y, Wu Y. The association between skinfold thicknesses and estimated glomerular filtration rate in adolescents: a cross-sectional study. BMC Nephrol. 2022; 23(1):96. doi:10.1186/s12882-022-02709-7.

[9] Addo OY, Himes JH, Zemel BS. Reference ranges for midupper arm circumference, upper arm muscle area, and upper arm fat area in US children and adolescents aged 1–20 y. Am J Clin Nutr. 2016;105(1):111–120. doi:10.3945/ajcn.116.142190.

[10] Ogun AS, Adeyinka A. Biochemistry, transferrin. StatPearls. Treasure Island (FL): StatPearls Publishing, Copyright © 2022, StatPearls Publishing LLC.; 2022.

[11] Bermejo F, García-López S. A guide to diagnosis of iron deficiency and iron deficiency anemia in digestive diseases. World J Gastroenterol. 2009; Oct 715(37):4638–4643. doi:10.3748/wjg.15.4638.

[12] Levitt DG, Levitt MD. Human serum albumin homeostasis: a new look at the roles of synthesis, catabolism, renal and gastrointestinal excretion, and the clinical value of serum albumin measurements. Int J Gen Med. 2016;9:229–255. doi:10.2147/IJGM.S102819.

[13] Keller U. Nutritional laboratory markers in malnutrition. J Clin Med. 2019;8(6):775.

[14] Grüngreiff K, Gottstein T, Reinhold D, et al. Albumin substitution in decompensated liver cirrhosis: don't forget zinc. Nutrients. 2021;13(11):4011. doi:10.3390/nu13114011.

[15] Kim B-J, Zhou J, Martin B, et al. Transferrin fusion technology: a novel approach to prolonging biological half-life of insulinotropic peptides. J Pharmacol Exp Ther. 2010;334(3):682–692. 05/01 doi:10.1124/jpet.110.166470.

[16] Litchford MD. Chapter 8-nutritional issues in the patient with diabetes and foot ulcers. In: bowker JH, Pfeifer MA, editors. Levin and neal. The diabetic foot. (Seventh Edition). Philadelphia: Mosby; 2008. p. 199–217.
[17] Mackenzie EL, Iwasaki K, Tsuji Y. Intracellular iron transport and storage: from molecular mechanisms to health implications. Antioxid Redox Signal. 2008;10(6):997–1030. 2008/06/01 doi:10.1089/ars.2007.1893.
[18] Siddiqui K, Rafiq M, Bhutto MA, et al. Red blood indices, platelet count and transferrin levels in celiac patients with and without type 1diabetes mellitus in Hyderabad Sindh. Pakistan. Khyber Med Univ J. 2021;13(1):25–29.
[19] Velaga RM. Elucidating the role of mitoferrin (mfrn), iron regulatory proteins (IRP1 and IRP2) and hephaestin (heph). In Iron metabolism by TagSNP and protein-protein interaction (PPI). Analysis: London Metropolitan University; 2014.
[20] Crowe A, Morgan EH. Iron and transferrrin uptake by brain and cerebrospinal fluid in the rat. Brain Res. 1992;592(1–2):8–16. doi:10.1016/0006-8993(92)91652-u.
[21] Batchelor EK, Kapitsinou P, Pergola PE, et al. Iron deficiency in chronic kidney disease: updates on pathophysiology, diagnosis, and treatment. J Am Soc Nephrol. 2020;31(3):456–468. Mar doi:10.1681/ASN.2019020213.
[22] Gutiérrez OM. Treatment of iron deficiency anemia in CKD and end-stage kidney disease. Kidney Int Rep. 2021; Sep6(9):2261–2269. doi:10.1016/j.ekir.2021.05.020.
[23] Zhao L, Zou Y, Zhang J, et al. Serum transferrin predicts end-stage renal disease in type 2 diabetes mellitus patients. Int J Med Sci. 2020;17(14):2113–2124. doi:10.7150/ijms.46259.
[24] Aguilera A, Bajo MA, Espinoza M, et al. Gastrointestinal and pancreatic function in peritoneal dialysis patients: their relationship with malnutrition and peritoneal membrane abnormalities. Am J Kidney Dis. 2003;42(4):787–796. doi:10.1016/s0272-6386(03)00920-x.
[25] Saad MEN, Ragab U, Salah AM, et al. Study of nutritional status among end stage renal disease patients on regular hemodialysis in zagazig university hospitals. Egypt J Hosp Med. 2022;87(1):1407–1413. doi:10.21608/ejhm.2022.224890.
[26] Weekes C, Spiro A, Baldwin C, et al. A review of the evidence for the impact of improving nutritional care on nutritional and clinical outcomes and cost. J Hum Nutr Diet. 2009;22(4):324–335. doi:10.1111/j.1365-277X.2009.00971.x.
[27] Gaweda AE. Markers of iron status in chronic kidney disease. Hemodial Int. 2017; Jun21 Suppl 1(Suppl 1):S21–s27. doi:10.1111/hdi.12556.
[28] Patino E, Akchurin O. Erythropoiesis-independent effects of iron in chronic kidney disease [article. Pediatr Nephrol. 2022;37(4):777–788. doi:10.1007/s00467-021-05191-9.
[29] Richard C, Verdier F. Transferrin receptors in erythropoiesis. Int J Mol Sci. 2020;21(24):9713. doi:10.3390/ijms21249713.
[30] Del Vecchio L, Locatelli F. Clinical practice guidelines on iron therapy: a critical evaluation. Hemodial Int. 2017;21 Suppl 1(S1):S125–S131. doi:10.1111/hdi.12562.
[31] Martínez-Castelao A, Górriz JL, Segura-de la Morena J, et al. Consensus document for the detection and management of chronic kidney disease. Nefrologia. 2014;34(2):243–262.
[32] Kuo IC, Lin HY, Niu SW, et al. Glycated hemoglobin and outcomes in patients with advanced diabetic chronic kidney disease. Sci Rep. 2016;6(1):20028. Jan 28 doi:10.1038/srep20028.
[33] Kalantar-Zadeh K, Kleiner M, Dunne E, et al. Total iron-binding capacity–estimated transferrin correlates with the nutritional subjective global assessment in hemodialysis patients. Am J Kidney Dis. 1998;31(2):263–272. doi:10.1053/ajkd.1998.v31.pm9469497.
[34] Steiber AL, Kalantar-Zadeh K, Secker D, et al. Subjective global assessment in chronic kidney disease: a review. J Renal Nutr. 2004;14(4):191–200. doi:10.1016/S1051-2276(04)00139-6.
[35] Woodruff B, Duffield A. Anthropometric assessment of nutritional status in adolescent populations in humanitarian emergencies. Eur J Clin Nutr. 2002;56(11):1108–1118. doi:10.1038/sj.ejcn.1601456.
[36] Das A, Saimala G, Reddy N, et al. Mid-upper arm circumference as a substitute of the body mass index for assessment of nutritional status among adult and adolescent females: learning from an impoverished indian state. Public Health. 2020;179:68–75. Feb doi:10.1016/j.puhe.2019.09.010.
[37] Musa IR, Omar SM, Adam I. Mid-upper arm circumference as a substitute for body mass index in the assessment of nutritional status among adults in Eastern Sudan. BMC Public Health. 2022;22(1):2056. 2022/11/10 doi:10.1186/s12889-022-14536-4.
[38] Jones CH, Wolfenden RC, Wells LM. Is subjective global assessment a reliable measure of nutritional status in hemodialysis? J Ren Nutr. 2004;14(1):26–30. doi:10.1053/j.jrn.2003.09.006.
[39] Rodrigues N, Sala P, Horie L, et al. Bioelectrical impedance analysis and skinfold thickness sum in assessing body fat mass of renal dialysis patients. J Ren Nutr. 2012;22(4):409–415.e2. 03/30 doi:10.1053/j.jrn.2012.01.024.
[40] Sheikh RY, Samoon HJ, Bhat NA, et al. Malnutrition and inflammatory parameters in patients with chronic kidney disease stages 3–5 from Northern India. Egypt J Intern Med. 2022; 2022/09/1334(1):70. doi:10.1186/s43162-022-00149-1.
[41] Duong TV, Wu PY, Wong TC, et al. Mid-arm circumference, body fat, nutritional and inflammatory biomarkers, blood glucose, dialysis adequacy influence all-cause mortality in hemodialysis patients: a prospective cohort study. Medicine (Baltimore). 2019;98(12):e14930. Mar doi:10.1097/MD.0000000000014930.
[42] Guenzani D, Buoli M, Caldiroli L, et al. Malnutrition and inflammation are associated with severity of depressive and cognitive symptoms of old patients affected by chronic kidney disease. J Psychosom Res. 2019; 2019/09/01/124:109783. doi:10.1016/j.jpsychores.2019.109783.
[43] Bramania P, Ruggajo P, Bramania R, et al. Nutritional status of patients on maintenance hemodialysis at muhimbili national hospital in Dar Es Salaam, tanzania: a Cross-Sectional study. J Nutr Metab. 2021;2021:6672185–6672187. doi:10.1155/2021/6672185.
[44] Bhattacharjee K, Das D, Rabha P, et al. A study on hematological profile in patients of chronic renal failure with special reference to serum iron profile. JEBMH. 2015;2(46):8212–8219. doi:10.18410/jebmh/2015/1107.
[45] Roy LG, Manjunath S, Urooj A, Department of Studies in Food Science and Nutrition, University of Mysore,

Mysore, India. Screening of malnutrition using clinical, dietary and anthropometric variables in an indian hemodialysis population. JMED. 2015;2015:1–14. doi:10.5171/2015.847823.

[46] Ooi BS, Darocy A, Pollak V. Serum transferrin levels in chronic renal failure. Nephron. 1972;9(4):200–207. doi:10.1159/000180151.

[47] Abdelaleem NE, Elsaeed W, Abdelfatah M. Evaluation of serum transferrin receptor level in children undergoing regular hemodialysis. Egypt J Hosp Med. 2022;86(1):66–72. 2022-01-01;86:66-66-72. doi:10.21608/ejhm.2021.209981.

[48] Kwiatkowska E, Opara M, Kwiatkowski S, et al. Is transferrin saturation a useful marker of iron metabolism in patients with chronic kidney disease treated with hemodialysis? TOUNJ. 2019;12(1):77–82. doi:10.2174/1874303X01912010077.

[49] Cross MB, Yi PH, Thomas CF, et al. Evaluation of malnutrition in orthopaedic surgery. J Am Acad Orthop Surg. 2014;22(3):193–199. doi:10.5435/JAAOS-22-03-193.

[50] Worwood M, May AM, Bain BJ. Iron deficiency anaemia and iron overload. Dacie Lewis Pract Haematol. 2016;(12):165–186.

[51] Kuragano T, Joki N, Hase H, et al. Low transferrin saturation (TSAT) and high ferritin levels are significant predictors for cerebrovascular and cardiovascular disease and death in maintenance hemodialysis patients. PLoS One. 2020;15(9):e0236277. doi:10.1371/journal.pone.0236277.

[52] Majeed A, Hameed A, Aftab I, et al. Soluble serum transferrin receptor (STFR) levels in hemodialysis patients. Annals KEMU. 2016;22(4):290–295. doi:10.21649/akemu.v22i4.1463.

[53] Wells BJ, Mainous AG, 3rd, King DE, et al. The combined effect of transferrin saturation and low density lipoprotein on mortality. Fam Med. 2004;36(5):324–329. May

[54] Gaweda AE, Bhat P, Maglinte GA, et al. TSAT is a better predictor than ferritin of hemoglobin response to epoetin alfa in US dialysis patients. Hemodial Int. 2014;18(1):38–46. Jan doi:10.1111/hdi.12078.

[55] Besarab A, Drueke TB. The problem with transferrin saturation as an indicator of iron 'sufficiency' in chronic kidney disease. Nephrol Dial Transplant. 2021; Jul 2336(8):1377–1383. doi:10.1093/ndt/gfaa048.

[56] Sahathevan S, Khor BH, Ng HM, et al. Understanding development of malnutrition in hemodialysis patients: a narrative review. Nutrients. 2020;12(10):3147. Oct 15 doi:10.3390/nu12103147.