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The effect of workability-related factors in patients with end-stage kidney disease undergoing hemodialysis

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Abstract

Background The disability of patients with end-stage kidney disease (ESKD) and the possibility of reducing the ability to work for patients who are receiving hemodialysis require extensive investigations worldwide. In this regard, we aimed to investigate employment status and its effect on a large group of work ability-related factors in these patients.

Methods A total of 191 patients with ESKD who were referred to the dialysis department of Guilan Educational and Medical Centers, Rasht, Iran, in 2023 participated. The demographic and occupational data, clinical characteristics, and laboratory findings of the patients were recorded. A work ability index questionnaire was used to record the ability to work.

Results According to the results, 37.7% of people undergoing hemodialysis were employed, 45.4% of those who were not employed, lost their jobs before, and 54.6% lost their jobs after starting hemodialysis. Patients with lower values of work ability index found to be significantly older, illiterate, with lower job satisfaction and high frequency of absence from their job. Also, they were unemployed individuals with high rates of disability and no history of job change ($P<0.05$ for all).

Additionally, current unemployment, history of job changes, and packed red blood cell transfusion were predictive variables of the ability to work in hemodialysis patients ($P<0.001$, $P=0.046$, $P=0.046$).

Conclusions Our results illustrated that the employment rate is low among patients with ESKD even before starting hemodialysis. Patients with higher age, less education, disability and anemia are at higher risk of weak ability to work.

Keywords Workability, Kidney failure, chronic, Hemodialysis

Background

In United States, there is a steady increase of 20,000 cases of end-stage kidney disease (ESKD), the final stage of chronic kidney disease (CKD), every year [1]. The prevalence of ESKD is about 24,000 cases in Iran and it has increased significantly in recent years [2, 3]. The condition of patients with ESKD is very debilitating, so patients' quality of life and their job and social status are affected [4]. In most cases, due to the severe condition of ESKD patients, death occurs in the absence of dialysis or transplantation [1]. To prevent uremia and its

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complications, patients need kidney replacement therapy, such as hemodialysis and peritoneal dialysis, for the remainder of their life [5]. Hemodialysis prolongs life for many patients and affects their quality of life. The overall employment rate among ESKD patients, especially those undergoing hemodialysis, is low. Half of the patients who develop ESKD are of working age (less than 65 years), and most are at risk of losing their jobs [6–8].

Patients undergoing hemodialysis have frustrating problems such as frequent hospitalization, difficult vascular access, and physical and mental problems that can result in disability [9]. In the USA, the unemployment rate among ESKD patients was reported to be approximately 10% or less [8]. Few studies have investigated the factors affecting the employment status of patients undergoing hemodialysis. Some studies have shown that young and educated peritoneal dialysis patients have better employment status [10]. According to the Work Ability Index (WAI) questionnaire, the effectiveness of interventions for workers and risk factors for disability caused by work can be assessed [11].

Awareness of the ability to work provides a good perspective for occupational health physicians to identify at-risk workers for better clinical and social management through effective interventions to enhance the ability of these patients to work. In this regard, we aimed to perform a comprehensive investigation of the employment status and ability to work in patients with ESKD undergoing hemodialysis in dialysis centers in Rasht, Iran.

Methods

Study design and sample collection

This cross-sectional study was conducted on 191 ESKD patients in the two largest dialysis units (Razi Hospital Hemodialysis Center and Caspian Hemodialysis Center) of Rasht, from March 2023 to December 2023. Rasht city is the capital of Guilan province, north-central Iran, and this city offers relatively reasonable job opportunities compared to smaller cities in the region. However, it's important to note that this is within the context of Iran's overall challenging employment situation.

All patients with ESKD who were working before contracting this disease and who were undergoing hemodialysis in 2023 were included in the study. We calculated the sample size based on the study of Erickson et al. [12] and the sample size formula below. The minimum sample size was estimated to be 168. In order to increase the validity of the results, we assessed about 191 patients.

$$n = \frac{(z_{1-\alpha})^2 p(1-p)}{d^2}$$

$$\frac{(1.96)^2 0.23(0.77)}{0.069^2}$$

$$n = 168$$

a=0.05.
P=23%.
d=0.3p.

Patients with malignancies, advanced heart failure, dementia, incomplete data or who did not want to be interviewed were excluded from the study. Written informed consent was obtained from all participants. ESKD was considered the 5th stage of CKD classification and included patients with a GFR less than 15 ml/min per 1.73 m^2 of body surface or patients who needed hemodialysis regardless of the GFR.

All demographic and occupational data, clinical characteristics, and laboratory findings were noted based on the patients' medical records, and the checklists were completed after interviewing each patient in the dialysis center.

The same person responsible for documenting the medical records of all patients also conducted interviews with them to verify the accuracy of the data in a private environment.

To determine whether a job was physical, mental, or a combination of both (physical and mental), the interviewer assessed the nature of tasks involved in a job. A physical job involves manual labor and requires physical strength, while a mental job includes tasks that require analytical thinking and cognitive skills in an office setting. A physical-mental job requires a mix of both physical and cognitive abilities, such as for those who work in healthcare professions.

A measure to assess job satisfaction among patients undergoing hemodialysis was developed in consultation with an experienced occupational medicine specialist and a nephrologist. We asked the patients if they experienced negative emotions due to poor working conditions (low), felt neutral with a balance of positive and negative aspects of their job (middle), or experienced positive emotions such as happiness in their work (high) [13, 14].

Disability in patients was defined by asking whether any physical, mental, sensory, or cognitive impairment affected their ability to work.

We recorded the last calculated values of laboratory findings charted in patients' medical records. Dialysis adequacy was evaluated using Kt/V > 1.2.

WAI questionnaire

The WAI questionnaire which assesses the ability to work of the patients, was completed by the interviewer. The WAI has seven items, including the ability

to perform current work compared to its golden time (scores from 0 to 10), ability to work related to physical and mental job needs (scores from 1 to 5), ability to work due to illness (scores from 1 to 6), number of workplace absences due to illness during the last year (scores from 1 to 5), ability to work in the next two years (scores from 1 to 4 or 7), intellectual and mental abilities (scores from 1 to 4), and diagnosed diseases by a specialist (scores from 1 to 7). A total of 7 to 27, 28 to 36, 37 to 43, and 44 to 49 cores are considered weak, average, good, and excellent performance, respectively (Table 1) [15]. The reliability and validity of the WAI questionnaire have been previously determined [16, 17].

Statistical analysis

All the statistical analyses were performed using SPSS software for Windows, version 16. 0 (SPSS Inc., Chicago, IL, USA). A significance level less than 0.05 was considered to indicate statistical significance. Numbers and percentages were used to report the frequency of variables. We used the chi-square test and Fisher's exact test to determine the associations between qualitative variables and the ability to work, one-way ANOVA to compare the means of ability to work groups, and logistic regression (odds ratio (OR) with 95% confidence intervals) to determine the associations between variables. In logistic regression analysis, ability to work status was considered a dependent variable. Age, level of education, job satisfaction, workplace absenteeism, history of job changes, underlying disease, history of packed red blood cell transfusion, previous renal transplantation, history of diabetes, and current unemployment were considered independent variables. The data are reported as odds ratios [18] with 95% confidence intervals (CIs), and a significance level of 5% was considered.

Results

The participants of this study had a mean age of 53/32 ± 13/85 years, and 74.9% of them were men and 25.1% were women. In regard to the level of education, the participants' distribution was as follows: 12.6% were illiterate, 5.2% had completed elementary school, 33.5% had a high school education, 31.9% held a diploma, 4.7% had a bachelor's degree, and 11% possessed a master's degree.

According to our results, out of 191 patients with ESKD, patients with a greater mean age had significantly lower WAI scores ($P=0.005$). The frequencies of WAI scores among patients were 93 (48.7%), 52 (27.2%), 31 (16.2%), and 15 (7.9%), corresponding to weak, moderate, good, and excellent, respectively.

The demographic and occupational characteristics of patients with ESKD undergoing hemodialysis according to their WAI are reported in Table 2. The results illustrated that older patients and those with lower level of education, current unemployment, greater disability, and those with no history of job changing had significantly lower WAI scores ($P<0.05$ for all).

Also, patients with less satisfaction and absence from work had significantly less ability to do work ($P<0.001$). However, there was no statistically significant association between the shift work status of the patients and their ability to work ($P>0.05$). In our study, all patients were covered by insurance, and employed patients were more likely to have mental jobs than physical jobs (48% vs. 28.3%). However, there was no statistically significant difference between the types of insurance and these jobs in terms of the ability to work ($P>0.05$).

Hypertension (45.8%) and diabetes (33.8%) were the most frequent comorbidities among the participants. Patients with a history of packed red blood cell transfusion and who underwent hemodialysis in evening shifts had weak WAI scores ($P<0.05$) (Table 3). The serum level of Hb was significantly lower among patients with weak ability to work ($P<0.05$), while KT/V, TIBC, Fe and

Table 1 Items of the WAI questionnaire and the range of each item's score

	Item	Range of score
1	Current work ability compared with the lifetime best	0–10
2	Work ability in relation to the demands of the job	2–10
3	Number of current diseases diagnosed by physician	1–7
4	Estimated work impairment due to diseases	1–6
5	Sick leave during the past 12 months	1–5
6	Personal prognosis of work ability 2 years from now	1–7
7	Mental resources	1–4
WAI score		7–49

Table 2 Demographical and occupational data of participants according to their work ability index

Variables		Work ability index *N* (%)				*P* value
		Weak (27 – 7)	Moderate (36 – 28)	Good 37–43))	Excellent (44–49)	
Gender	Male	69 (48.3)	42 (29.4)	21 (14.7)	11 (7.7)	0.606*
	Female	24 (50.0)	10 (20.8)	10 (20.8)	4 (8.3)	
Age, years (Mean ± SD)		56/13 ± 14/4	53/65 ± 11/7	47/09 ± 13/6	47/6 ± 12/6	*P* = 0/005**
Level of education	Illiterate	18 (75.0)	1 (4.2)	5 (20.8)	0 (0.0)	< 0.001***
	Elementary school	6 (60.0)	2 (20.0)	2 (20.0)	0 (0.0)	
	High school	28 (43.8)	19 (29.7)	13 (20.3)	4 (6.2)	
	Diploma	30 (49.2)	22 (36.1)	4 (6.6)	5 (8.2)	
	Bachelor	2 (22.2)	4 (44.4)	22 (22.2)	1 (11.1)	
	Master	9 (42.9)	4 (19.0)	5 (23.8)	3 (14.2)	
Type of job	Physical	39 (41.9)	31 (33.3)	15 (16.1)	8 (8.6)	0.606***
	Mental	30 (55.6)	12 (22.2)	8 (18.2)	3 (6.8)	
	Physical-Mental	24 (54.5)	9 (20.5)	8 (18.2)	3 (6.8)	
Level of job satisfaction	Low	38 (66.7)	13 (22.8)	6 (10.5)	0 (0.0)	< 0.001***
	Medium	34 (35.4)	34 (35.4)	22 (22.9)	6 (6.2)	
	Much	21 (55.3)	5 (13.2)	3 (7.9)	9 (23.7)	
Absence from work	Yes	88 (52.4)	45 (26.8)	27 (16.1)	8 (4.8)	< 0.001***
	Not in past month	5 (21.)	7 (30.4)	4 (17.4)	7 (30.4)	
	Not in past three month	14 (17.5)	33 (41.2)	19 (23.8)	14 (17.5)	
Work shifts	Fixed morning	23 (41.1)	19 (33.9)	11 (19.6)	3 (5.4)	0.482***
	Fixed night	5 (62.5)	1 (12.5)	2 (25.0)	0 (0.0)	
	Shifts in circulation	65 (51.2)	32 (25.2)	18 (14.2)	12 (9.4)	
Employment status	Employed	7 (9.7)	26 (36.1)	26 (36.1)	13 (18.1)	< 0.001***
	Not employed	86 (72.3)	26 (21.8)	5 (4.2)	2 (1.7)	
Disability	Yes	78 (78.0)	18 (18.0)	4 (4.0)	0 (0.0)	< 0.001***
	No	15 (16.5)	34 (37.4)	27 (29.7)	15 (16.5)	
Job change	Yes	31 (75.6)	9 (22.0)	1 (2.4)	0 (0.0)	< 0.001***
	No	62 (41.3)	43 (28.7)	30 (20.0)	15 (10.0)	

*Chi square test

**One-way ANOVA test

*** Fisher's exact test

ferritin were not significantly different ($P > 0.05$) (Table 4). After logistic regression analysis, variables, including a history of job change, a history of packed red blood cell transfusion, and current unemployment, were found to be predictors of the ability to work ($P < 0.05$) (Table 5). Moreover, current unemployment ($P = 0.0001$), a history of job changes ($P = 0.046$), and blood transfusion in one's past medical history ($P = 0.046$) increased the probability of not being able to do work (weak and moderate WAI) by 14.7, 10.19 and 2.7 times, respectively.

Discussion

Recent studies indicate that among patients undergoing hemodialysis, those with lower socioeconomic status, particularly those who are unemployed, face a heightened risk of mortality [19]. This finding reveals that social factors, such as employment, play a crucial role in the prognosis of patients undergoing dialysis, alongside their medical condition, and it underscores the critical need to identify the factors contributing to unemployment in these patient population. Therefore, in this study, we conducted a comprehensive investigation into this matter and explored a wide range of factors affecting the ability to work in patients on dialysis.

Our results showed that most patients with ESKD undergoing hemodialysis had a weak ability to work according to the WAI (scores of 7–27). According to the results of our study, disability and current unemployment were significantly higher among patients with weak ability to work, which is in line with the findings of previous

Table 3 Medical hallmarks of patients with ESKD according to their work ability index

Variables		Work ability index *n* (%)				*P* value
		Weak (27 – 7)	Moderate (36 – 28)	Good 37–43))	Excellent (44–49)	
History of pack cell infusion	Yes	67 (60.4)	29 (26.1)	10 (9.0)	5 (4.5)	< 0.001***
	No	26 (32.5)	23 (28.8)	21 (26.2)	10 (12.5)	
Dialysis at mid-afternoon	Yes	61 (46.2)	43 (32.6)	16 (12.1)	12 (9.1)	0.016***
	No	32 (54.2)	9 (14.3)	15 (25.4)	3 (5.1)	
Dialysis at evening	Yes	23 (76.7)	4 (13.3)	2 (6.7)	1 (3.3)	0.011***
	No	70 (43.5)	48 (29.8)	29 (18.0)	14 (8.7)	
Dialysis at morning	Yes	30 (53.6)	9 (16.1)	15 (26.8)	2 (3.6)	0.01***
	No	63 (46.7)	43 (31.9)	16 (11.9)	13 (9.6)	
Kidney transplantation	Yes	6 (37.5)	8 (50.0)	0 (0.0)	2 (12.5)	0.069***
	No	87 (49.7)	44 (25.1)	31 (17.7)	13 (7.4)	
Access of dialysis	Arteriovenous fistula	51 (46.8)	27 (24.8)	19 (17.4)	12 (11.0)	0.093***
	Permacath	41 (53.2)	21 (27.3)	12 (15.6)	3 (3.9)	
	Cortex	1 (20.0)	4 (80.0)	0 (0.0)	0 (0.0)	
Duration of dialysis (month)		45.69 ± 33.59	40.57 ± 28.69	30 ± 18.21	44.33 ± 36.12	0.103**
Duration of every session of hemodialysis (hour)		3.55 ± 47.0	3.47 ± 0.47	3.51 ± 0.49	3.43 ± 0.45	0.643**
Number of hemodialysis sessions per week		2.79 ± 0.53	2.67 ± 0.55	2.77 ± 0.56	2.8 ± 0.41	0.622***

** One-way ANOVA test

*** Fisher's exact test

Table 4 Laboratory findings of patients with ESKD according to their work ability index

Variables	Work ability index Mean ± SD				*P* value
	Weak (27 – 7)	Moderate (36 – 28)	Good 37–43))	Excellent (44–49)	
Hb (g/dL)	10.05 ± 1.77	10.74 ± 2.0	10.37 ± 1.72	11.35 ± 0.99	0.024**
Fe	45.74 ± 76.24	57.7 ± 107.08	52.51 ± 37.59	64.46 ± 65.16	0.760**
(mg/dl) Cr	8.05 ± 2.85	8.93 ± 3.0	10.03 ± 3.12	10.26 ± 3.05	0.002**
Ferritin (µg/L)	456.5 ± 448.0	539.4 ± 655.0	488.2 ± 459.5	369.9 ± 473.5	0.668**
KT.V	1.51 ± 0.29	1.46 ± 0.19	1.51 ± 0.19	1.46 ± 0.24	0.669**
TIBC (µg/dL)	265.53 ± 61.58	274.82 ± 100.08	273.09 ± 56.79	272.06 ± 45.2	0.885**

Hb hemoglobin, *Fe* iron, *Cr* creatinine, *KT/V* clearance time/volume, *TIBC* total iron-binding capacity

***One-way ANOVA test*

studies. Assessing the association between disability and clinical outcomes in patients receiving maintenance hemodialysis in 2020 demonstrated that 15.2%, 25.8%, and 31.4% of patients in the nondisabled, moderately disabled, and highly disabled groups, respectively, experienced a decrease in their ability ($P < 0.001$). The physical and mental activity scores decrease with increasing degree of disability [20].

Our results, in agreement with previous studies, show that older patients with lower level of education have weak ability to work [21]. Generally, the possibility of employment in older patients is low [17, 19, 22, 23], With increasing age, the possibility of reducing the function of regulatory systems, pathologic conditions, and chronic diseases increases, so it is natural to expect a decrease in the ability to work of older patients [6]. In line with the results of our study, it was shown that educated patients were more likely to be employed among patients undergoing hemodialysis [24]. Patients with a high level of education can have more mental and less physical work. Additionally, the salaries of these patients are greater than the fair benefits that the government allocates to

Table 5 Association between work ability and study variables in patients with ESKD

Variables		OR	*P*-value	95% CI	
				Lower	Upper
Age	< 40	-	0.533		
	41–50	−0.470	0.521	0.149	2.621
	51–60	−0.598	0.426	0.126	2.402
	61–70	−1.298	0.114	0.055	1.364
	> 70	−1.357	0.240	0.027	2.471
Level of education	illiterate	-	0.788	-	-
	Elementary school	−0.712	0.590	0.037	6.552
	High school	−0.346	0.719	0.108	4.660
	Diploma	−0.859	0.379	0.063	2.869
	Bachelor	−0.815	0.514	0.038	5.126
	Master	0.478	0.663	0.188	13.807
Job satisfaction	Low	-	0.367	-	-
	middle	0.620	0.345	0.513	6.728
	High	1.102	0.158	0.653	13.871
Without absence from work		0.476	0.500	0.403	6.434
History of job change		2.322	0.046	1.040	99.928
Dialysis complications		0.307	0.659	0.348	5.304
Pack cell infusion		1.016	0.046	1.018	7.488
Kidney transplantation		2.181	0.072	0.824	95.131
Diabetics		0.806	0.116	0.820	6.118
Not employed		2.690	0.000	5.001	43.377
Constant		−7.536	0.000	--	

disabled patients; for this reason, they are more likely to stay employed.

According to the results of our study, 37.7% of patients undergoing hemodialysis were employed, and among those who were not employed, 45.4% and 54.6% of patients lost their jobs before and after starting hemodialysis, respectively. The unemployment of these patients can be attributed to several factors, including physical problems like fatigue, mental health issues like depression and anxiety, and the fact that these patients need several hours per week for their dialysis, making it difficult for them to schedule their job times [25–27]. To help unemployed patients return to their job, clinicians should help the patients with the consultation of an occupational specialist by controlling the aforementioned associated factors. To provide an overview of employment rates in other countries, it's noted that in the United States patients on dialysis have an employment rate of about 18.9%, while Finland and India reported higher employment rates of 33% and 29.9%, respectively, than the United States [28]. These figures are more aligned with our findings. Economic pressures can drive employment rates among different countries. In countries with less social safety nets, individuals may feel a greater need to continue working despite health challenges. Also, governments of high-income countries provide more funding of care for CKD patients than other countries [29]. A study conducted by Erickson et al. demonstrated that the employment rate was lower in patients with lower-than-average incomes and decreased from 42% before the onset of ESKD to 13% within six months after the onset of the disease. The low employment rate of patients even before the start of ESKD showed that patients with CKD faced many physical, psychological, and social challenges and problems even before the start of hemodialysis, which made it difficult for them to be employed [12].

Patients with physical jobs tended to lose more jobs than did those with mental jobs, similar to our findings [10], which indicated that mental jobs were more frequent among employed patients. According to our results, previous kidney transplantation was not significantly related to the ability to work, which was in line with previous studies [30, 31]. However, it is important to consider that in our study, patients with a history of kidney transplantation were those whose transplantation had been rejected and who are currently receiving hemodialysis treatment.

In the present study, the duration of hemodialysis significantly affected the patients' ability to work. Most of

our participants stated that the hemodialysis care team cooperated with them to schedule their hemodialysis based on their work time. In contrast, it was stated in a previous study that those who underwent hemodialysis in the last hours of the evening had a higher employment rate [22]. Moreover, vascular access for hemodialysis has been reported to have direct and indirect effects on the experience of dialysis and quality of life related to the health and symptoms of patients [32]. Hemodialysis access and its complications were among the determining factors of unemployment in patients undergoing hemodialysis [9], which was not different in our study. The complications of dialysis include intradialytic hypotension, muscle cramps, dialysis disequilibrium syndrome, infection, anaphylactic reactions, hemolysis, air embolism and aneurysm or stenosis of arteriovenous fistula or graft [33].

According to our results, patients with higher Hb levels had better ability to work, but no significant relationships were found between the levels of Fe, ferritin, and TIBC. All of our patients were on regular treatment with erythropoietin. In one study, it was reported that those with anemia who were treated with erythropoietin had a higher employment rate at the start of hemodialysis. Treating anemia by improving fatigue and enhancing the feeling of well-being in patients with ESKD can help them maintain their job [8]. Patients with a history of packed red blood cell transfusion had less ability to work, probably due to deterioration of their general condition and more severe anemia. The Cr level was significantly different between the WAI subgroups, but the Kt/V ratio was not significantly different, which was in line with the findings of a previous study on ESKD patients [24]. A history of packed red blood cell transfusion, current unemployment status, and job changes are predictive variables of the ability to work in patients undergoing hemodialysis. Obviously, in unemployed patients, less ability to work is expected, and the association between the ability to work and employment has been reported in many previous studies [21, 34, 35].

Moreover, those who have a history of changing jobs are usually individuals who have tried to explore different types of work to secure employment, but due to their disease condition, they were not successful.

According to our investigation, no study has accurately reported all the demographic data, clinical characteristics, and laboratory findings affecting the ability to work of patients with ESKD undergoing dialysis. In this regard, the present study examined a large number of related variables. On the other hand, each country has its own social and infrastructure to support patients with ESKD, which raises the need to conduct studies in different countries, and our study is the first comprehensive study to evaluate the ability of work-related factors among patients with ESKD in Iran.

Limitations

One of the limitations of this study was the lack of a control group; no comparison was made between the employment rate in the general population and ESKD patients. On the other hand, variables related to employment were reported by the patients; therefore, recall bias may have occurred. We did not collect patient demographics for those who were approached but did not participate. Patients receiving hemodialysis treatment usually have more than one underlying disease. A wide range of underlying diseases was found in our sample, making it difficult to detect a significant association between any disease and the ability to work. Another limitation of this study is the method used to assess job satisfaction. As job satisfaction was not the primary variable of interest, we did not employ a standardized instrument that has been validated in the literature. Instead, we developed a classification system in consultation with colleagues. In future research, it would be beneficial to utilize a standardized and well-validated instrument to measure job satisfaction. Moreover, future multi-center studies with larger sample sizes would be beneficial to support our results.

Conclusion

The results of this study showed that the employment rate and ability to work in dialysis patients are low, and some of these patients lose their jobs even before starting dialysis. These findings indicate the importance of early initiation of therapeutic interventions and rehabilitation services in ESKD patients before they start dialysis. In this study, older, less educated and anemic patients as well as those who had disability or low levels of satisfaction in their job, were more prone to lose it. Therefore, patients who have a history of these cases are prioritized for receiving rehabilitation services. We need more studies in the future focusing on identifying the types of treatment methods and rehabilitation services and testing the effectiveness of these methods so that they can help hemodialysis patients maintain their employment.

Abbreviations

ESKD	End stage kidney disease
CKD	Chronic kidney disease
WAI	Work ability index
OR	Odds ratio
CIs	Confidence intervals
Hb	Hemoglobin
Fe	Iron
Cr	Creatinine
KT/V	Clearance time/volume
TIBC	Total iron-binding capacity

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Authors' contributions
M.M. conceived and designed the experiments, performed the experiments, contributed reagents,materials, analysis tools or data and wrote the paper. M.A. conceived and designed the experiments, contributed reagents, analysis tools or data, wrote the paper. E.R. performed the experiments, analyzed and interpreted the data, contributed reagents, materials, analysis tools or data. All authors read and approved the final manuscript.

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Data availability
The dataset of this study is available from the corresponding author on reasonable request.

Decelerations

Ethics approval and consent to participate
This research design was approved by the Ethics Committee of Guilan University of Medical Sciences with the ethics code of I.R.GUMS.REC.1400.149.

Consent for publication
None.

Competing interests
The authors declare no competing interests.

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