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Investigation of Factors Affecting Clinical Outcome of Peritoneal Dialysis Patients

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Abstract

Background: End-stage kidney disease (ESKD) is a global issue. Although the use of kidney replacement therapy measures has improved outcomes for patients with ESKD, the mortality rate remains significant. Identifying modifiable factors that affect patient outcomes can help improve their survival. The aim of this study was to investigate the factors affecting the clinical outcome of peritoneal dialysis patients.

Methods: This prospective cohort study was conducted between 2018 and 2021.

Participants: Patients aged between 18 and 75 years with a history of peritoneal dialysis (PD) for at least six months were included. Demographic data, kt/v ratio, medical history, serum levels of albumin, creatinine, triglycerides, total cholesterol, calcium, phosphorus, parathyroid hormone, hemoglobin, and ferritin were recorded before starting PD and during the follow-up period, along with clinical outcomes. To describe the data, the central index of mean, frequency, and relative frequency was used, and for analytical statistics, Chi-square test, analysis of variance, and Kruskal-Wallis were used.

Results: A total of 64 patients with a mean age of 51.78 ± 15.31 years were included. Of these, 27 (42.18%) had a history of diabetes mellitus, and 38 (59.37%) had a history of hypertension (HTN). 48 (75%) patients survived until the end of the study, while 47 (73.4%) participants experienced peritonitis. Our findings indicate that variables such as sex, marital status, weight, history of HTN, and serum levels of hemoglobin and ferritin significantly affect outcomes.

Conclusion: We found that factors including sex, marriage, normal weight, HTN, normal hemoglobin, and ferritin can lead to better survival in PD patients. Recurrent peritonitis was the most crucial cause of PD to HD shifts.

Keywords: Peritoneal Dialysis, Survival, End-stage kidney disease

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Introduction

End-stage kidney disease (ESKD) is a global health issue that affects people in both developing and developed regions, with increasing incidence and prevalence worldwide (1). Along with significant morbidity and mortality, CKD and ESKD result in high healthcare costs (2).

The increased prevalence of diabetes mellitus (DM) and hypertension (HTN), the main underlying etiologies of CKD and ESKD, along with improved survival of these patients from non-renal causes, are suggested as reasons for the rising prevalence of ESKD (1).

Despite improvements in the management of ESKD and the use of kidney replacement therapy (KRT), the mortality rate of these patients remains noteworthy (3). 5-year survival for ESKD patients is approximately 50% (4).

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↑What is "already known" in this topic:
Peritoneal dialysis (PD) is a form of KRT. Previous studies have suggested that several factors, such as sepsis, fluid overload, low ultrafiltration volume, higher age, and low urine output, can increase the risk of death among patients undergoing peritoneal dialysis (PD).

→What this article adds:
This study suggests that factors including sex, marriage, normal weight, HTN, normal hemoglobin, and ferritin can lead to better survival in PD patients. Recurrent peritonitis was the most crucial cause of PD to HD shifts.

Peritoneal dialysis (PD) is a form of KRT used in acute and chronic kidney injury (5). The lower cost of PD compared to hemodialysis (HD) and the preservation of remnant renal function are two main benefits. However, improving survival for patients undergoing PD is still a challenging issue (6).

Previous studies have suggested that several factors, such as sepsis, fluid overload, low ultrafiltration volume, higher age, and low urine output, can increase the risk of death among patients undergoing peritoneal dialysis (PD) for acute and chronic kidney injury (AKI/CKD) (5-7). However, there is an ongoing discussion regarding the role of other factors that may affect the prognosis of these patients.

Recognizing modifiable factors that impact the prognosis of ESKD patients undergoing kidney replacement therapy (KRT) is crucial to enhancing their quality of life and survival. Therefore, this study aims to assess the potential association of laboratory values with the clinical outcomes of ESKD patients on PD therapy.

Methods

This prospective cohort study was conducted over a three-year period from August 2018 to September 2021 at the PD centers affiliated with Kerman University of Medical Sciences. Our statistical population included all patients who were introduced to PD centers in Kerman to start PD in August 2018. Sampling was done by census and all patients who were referred to start peritoneal dialysis in the mentioned time period were evaluated for entry.

Inclusion and exclusion Criteria: The study included all patients who had undergone PD for at least six months since August 2018. Study participants were between the ages of 18 and 75 years. Patients with a previous history of malignancy or heart failure and those who underwent kidney transplantation during the follow-up period were excluded. Informed consent was obtained from each participant.

Data Collection: Patient data, including age, sex, marital status, previous history of diabetes mellitus (DM) and hypertension (HTN), serum levels of albumin, creatinine (Cr), triglycerides (TG), and total cholesterol (Chol), calcium, phosphorus, parathyroid hormone, hemoglobin, and ferritin before starting PD were recorded. During the patients' visits after a 10-hour fasting period, 5 cc of venous blood was collected from each peritoneal dialysis (PD) patient. The blood samples were promptly transferred to the same laboratory. Hemoglobin levels were measured using the Sysmex KX-21N hematology auto-analyzer (Sysmex Corporation, Kobe, Japan). Serum ferritin levels were determined using the ELISA method (Monobind, CA, USA). Creatinine, calcium, phosphorus, TG, Chol, and albumin levels were measured using a commercially available kit (Pars Azmoon Co., Iran). The patients' total calcium levels were adjusted based on their albumin levels using the formula: corrected total calcium = measured serum calcium (mg/dL) + (4 - ALB serum [g/dL]) × 0.8. PTH levels were assessed using the new PTH (1-84) kit (Fardavar Co., Iran). Patients' weights were measured using a digital scale (Seca, Germany) with minimal clothing.

The results were recorded in the data collection form. we categorized study participants into four categories based on their DM history and serum albumin levels (7) as follows: A) positive history of DM and serum albumin level ≥ 3.5 g/dl, B) negative history of DM and serum albumin level ≥ 3.5 g/dl, C) positive history of DM and serum albumin level < 3.5 g/dl, and D) negative history of DM and serum albumin level < 3.5 g/dl.

To assess the adequacy of dialysis in peritoneal dialysis patients, the Kt/V calculator was utilized, employing the relevant formulas. All the above tests and Kt/V ratio were repeated every three months during the follow-up period. The patients' outcomes were also documented.

Clinical Outcome

Patients' outcomes including survival or death, complications such as PD-related peritonitis (as the amount of more than 100 white blood cells or more than 50% of neutrophils in the output fluid of PD or positive culture of peritoneal fluid), and the need for switching to hemodialysis were recorded. For the survival model in this study, the time interval between the time of the patient's first dialysis and the time of the patient's death in case of death and in the case of the patient's death, until the time of the patient's last visit to the center was entered in a checklist.

Data Analysis

he collected data was analyzed using IBM SPSS Statistics Software (IBM Corporation; version 25). To describe the data, the central index of mean, frequency, and relative frequency was used, and for analytical statistics, Chi-square test, analysis of variance, and Kruskal-Wallis were used.

Tests such as Kaplan-Meier Survival Analysis, Log-Rank Test, and Cox Regression Analysis were used for this purpose.

Results

A total of 64 patients with a mean age of 51.78 ± 15.31 years were included in the study, of whom 54.7% were female and 45.3% were male. Among them, 27 (42.18%) and 38 (59.37%) participants had a prior history of DM and HTN, respectively.

Given that previous studies have shown that albumin levels and a history of diabetes are effective in the survival of PD patients, we categorized study participants into four categories based on their DM history and serum albumin levels as follows: A) positive history of DM and serum albumin level ≥ 3.5 g/dl (20 cases), B) negative history of DM and serum albumin level ≥ 3.5 g/dl (32 cases), C) positive history of DM and serum albumin level < 3.5 g/dl (7 cases), and D) negative history of DM and serum albumin level < 3.5 g/dl (5 cases). The patients' mean weight and mean body mass index (BMI) were 60.89 ± 10.18 kg and 19.82 ± 3.23 kg/m2, respectively (Table 1). Data regarding laboratory values are reported in Table 2.

During the study, 16 (25%) deaths occurred among the patients, with 5, 5, 4, and 2 participants from groups A-D, respectively (p-value: 0.46). Cardiovascular events (7 (43.8%) cases), newly diagnosed malignancies (6 (37.5%)), and infections (3 (18.8%)) were the main causes of death.

Table 1. Patients' demographic data

Variable		Group 1 DM+ albumin ≥ 3.5 g/dl	Group 2 DM- albumin ≥ 3.5 g/dl	Group 3 DM+ albumin < 3.5 g/dl	Group 4 DM- albumin < 3.5 g/dl	Total	*P*-Value
Sex	Male	40 (8)	43.8 (14)	71.4 (5)	40 (2)	45.3 (29)	0.524
	Female	60 (12)	56.2 (18)	28.6 (2)	60 (3)	54.7 (35)	
Marriage	No	35 (7)	43.8 (14)	42.9 (3)	40 (2)	40.6 (26)	0.939
	Yes	65 (13)	56.2 (18)	57.1 (4)	60 (3)	59.4 (38)	
History of Diabetes Mellitus	Yes	100 (20)	0	100 (7)	0	43.8 (28)	0.159
	No	0	100(32)	0	100 (5)	56.2 (36)	
History of Hypertension	Yes	40 (8)	68.8 (22)	57.1 (4)	80 (4)	59.4 (38)	0.001
	No	60 (12)	31.2 (10)	42.9 (3)	20 (1)	40.6 (26)	
Age (years)		55.85±15.2	46.03±15.32	59.57±5.15	61.4±12.9	51.78±15.31	0.159
Body Mass Index (kg/m^2)		23.65±15.3	21.08±3.45	20.94±2.07	19.82±3.23	19.82±3.23	0.021
Weight (kg)		64.49±11.34	59.49±9.23	60.21±6.62	57.40±14.34	60.89±10.18	0.018

Based on the chi-square test and analysis of variance and the Kruskal-Wallis H test

Table 2. Evaluated laboratory values for each patient

Variable	Group 1 DM+ albumin ≥ 3.5 g/dl	Group 2 DM- albumin ≥ 3.5 g/dl	Group 3 DM+ albumin < 3.5 g/dl	Group 4 DM- albumin < 3.5 g/dl	Total	*P*-Value
Kt/v	17.74±0.47	1.48±0.41	1.76±0.41	1.57±0.41	1.6±0.44	0.150
1st Creatinine	7.24±2.85	7.89±3.23	5.24±2.16	4.96±3.08	7.17±3.11	0.070
1st Albumin	4.29±0.48	4.23±0.65	3.02±0.22	3.18±0.26	4.03±0.71	0.001
1st Cholesterol	149.2±43.03	164.71±65.1	145.42±55.93	238±60.63	163.51±60.91	0.023
1st Triglyceride	163.10±69.87	182.43±90.33	142±67.83	207.6±69.43	173.93±80.68	0.452
2nd Creatinine	7.49±2.94	8.10±3.62	5.74±2.09	6.75±2.74	7.55±3.25	0.338
2nd Albumin	4.37±1.6	4.12±0.63	3.32±0.42	3.42±0.31	4.06±1.06	0.070
2nd Cholesterol	150.48±8.63	184.95±21.45	173.18±17.70	183.04±25.61	172.74±11.42	0.621
2nd Triglyceride	173.27±72.74	173.44±77.21	125.72±56.24	176.56±64.18	168.41±72.94	0.449
Hemoglobin	10.49±1.45	10.58±1.32	12.14±1.16	9.03±0.36	10.62±1.43	0.004
Parathyroid Hormone	366.66±13.49	265.89±45.75	130.18±29.58	102.4±30.43	270.09±49.72	0.371
Calcium	8.80±0.79	8.58±0.93	8.55±0.32	8.47±0.46	8.64±0.80	0.743
Phosphorus	5.03±0.80	5.48±1.17	4.61±1.17	3.93±0.78	5.12±1.12	0.012
Ferritin	354.55±58.02	288.01±50.95	244.94±55.67	271.1±72.42	302.77±32.19	0.729

Based on the analysis of variance and the Kruskal-Wallis H test. Data presented as Mean ± standard division

Of the 64 patients, 48 (75%) survived until the end of the study (15, 27, 3, and 3 participants from groups A-D). Patients' mean survival duration was 16.03 months, with durations of 13.9, 17.03, 17.42, and 16.2 months for groups A, B, C, and D, respectively. The difference in the survival duration between groups A and C was not statistically significant ($P = 0.676$).

By the end of the study, 20 patients (31.25%) were still on peritoneal dialysis (groups A = 8, B = 10, and D = 2), but this difference was not statistically significant ($P = 0.234$). A total of 28 patients (43.75%) switched to HD (7, 17, 3, and 1 participant from groups A to D), but this difference was also not statistically significant ($P = 0.220$).

A total of 47 (73.4%) patients had a history of PD-related peritonitis, with a mean number of episodes of peritonitis of 1.42 ± 0.15. The fourth group had the highest mean number of peritonitis (2.8 ± 0.66), while the first group had the lowest mean number (1.10 ± 0.85). This difference was statistically significant ($P = 0.005$).

Recurrent peritonitis in 18 patients (62.1%) was the main cause of switching to HD, followed by peritoneal insufficiency in 9 patients (31%) and catheter failure in 2 patients (6.9%). In the first group, the highest cause of death was related to peritoneal insufficiency (n = 4), while recurrent peritonitis was seen in (n = 12, 2, 1) cases in B, C, and D groups, respectively ($P = 0.644$).

According to the Kaplan-Meier test (Figure 1), the average survival time in all subjects was 16.03 months (group A 13.9 months, B 17.03 months, C 17.42 months, and D 16.2 months). The highest average survival time was observed in group C and the lowest average survival time was found in group A. This difference was not statistically significant ($P = 0.676$).

According to the Cox Regression analysis, variables

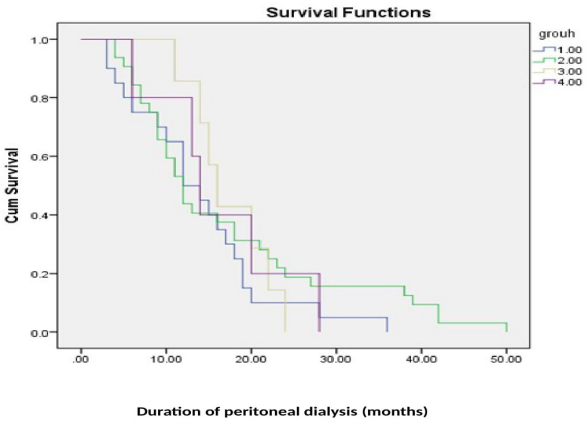

Figure 1. Survival analysis graph of the investigated subjects in the 4 studied groups.
Based on the Kaplan-Meier test

Table 3. The relationship between each variable and patients' outcomes

Variable	*P*-Value	Relative Risk	Confidence Interval
Age	0.830	1	1.04-0.96
Sex	0.014	0.30	0.78-0.11
Weight	0.010	0.92	0.98-0.86
Marital Status	0.041	0.36	0.96-0.13
Diabetes Mellitus	0.191	0.52	1.39-0.19
Hypertension	0.020	0.29	0.82-0.10
Body Mass Index	0.511	1.07	1.32-0.87
Kt/v	0.561	0.7	2.35-0.20
1st Creatinine	0.062	0.84	1.01-0.70
1st Albumin	0.582	1.27	3.05-0.53
1st Cholesterol	0.142	0.99	1-0.98
1st Triglyceride	0.082	1	1.01-0.99
2nd Creatinine	0.682	0.96	1.13-0.82
2nd Albumin	0.973	1	1.48-0.68
2nd Triglyceride	0.351	0.99	1-0.99
2nd Cholesterol	0.771	0.99	١-0.99
Hemoglobin	0.006	0.61	0.87-0.43
Parathyroid Hormone	0.861	1	١-0.99
Calcium	0.301	0.74	1.31-0.42
Phosphorus	0.532	1.15	1.83-0.73
Ferritin	0.011	0.99	١-0.99

Based on the Cox regression test

including sex, marriage, normal weight, HTN, normal hemoglobin, and ferritin had a significant positive impact on the outcome (Table 3).

Discussion

According to the findings of this prospective cohort study, factors such as patients' sex and marital status, body weight, history of HTN, and serum levels of hemoglobin and ferritin had a significant impact on the outcome of PD cases.

PD is one of the main forms of KRT for patients suffering from ESKD. This method offers several advantages, including portability, fewer dietary restrictions, lower medical costs, and better preservation of residual renal function (8, 9).

However, PD failure over time and the need to shift to HD is a major problem (10). Only a small number of patients remain on PD for more than five years (11). Several factors related to the patient, healthcare provider, and healthcare monitoring system may contribute to the decision to stop PD (12). A large proportion of PD patients switch to HD each year, with reported rates exceeding 35% (11). Unfortunately, the rate of return to PD after switching to HD is very low (13). In our study, recurrent peritonitis was the most common reason for this shift.

Patients on PD may experience various complications, such as PD-related peritonitis - which is the primary cause of transition to hemodialysis - (14), catheter dysfunction, edema and ultrafiltration failure, hernias, hypertriglyceridemia, and hyperglycemia, all of which can affect their outcome (8).

Recent studies have reported that low albumin is an important factor causing decreased survival of PD patients (7). However, in our study, the number of people with low albumin was low, and thus no association was found between low albumin and survival.

In addition to the aforementioned complications, other factors may also influence the prognosis and outcome of cases undergoing PD. For instance, hypertriglyceridemia is one of the PD-related complications that can affect patients' outcomes. Huang et al. showed that hypertriglyceridemia could be a risk factor for treatment failure in PD-related peritonitis (15). Wan and colleagues found that the serum TG level at the beginning of PD therapy is a risk factor for early-onset peritonitis and can worsen these patients' prognosis (16). Xia and colleagues revealed that an increased ratio of serum TG to HDL cholesterol can negatively affect patients' outcomes, resulting in reduced survival (17). However, we found no significant correlation between serum TG levels and patients' outcomes. This difference could be attributed to the lower mean TG level in our study compared to other studies.

The association between serum ferritin levels and the prognosis of patients undergoing PD has not been widely studied. Our results showed that a serum ferritin level of 250-350 was a positive factor influencing patients' outcomes ($P = 0.01$, RR = 0.99, CI = 1-0.99). A study by Fu et al. found that an elevated serum ferritin level, as a marker of systemic inflammation, can increase the risk of cardiovascular and all-cause mortality in cases undergoing PD (18). However, their study had lower ferritin levels than our study.

According to our literature review, the impact of fluctuations in hemoglobin levels on the prognosis of ESKD patients is a matter of debate (19). Chen and colleagues recommend correcting anemia in patients without a previous history of cardiovascular disease who undergo PD to improve their outcomes (19). We found that normal serum hemoglobin levels were another factor that may positively affect patients' outcomes.

Similar to our study, a study by Danneville et al. suggested that women undergoing PD are at lower risk of peritonitis and need to switch to HD compared to men (20). In contrast, ROS and colleagues concluded that women undergoing PD are at an increased risk of mortality secondary to infectious complications compared to men (21).

There were some limitations to our study. First, the study was carried out at a single center, so it may include a center-specific effect. On the other hand, it can also be an advantage that all laboratory measurements are performed at one facility. Second, due to international sanctions in our country and the reduction of PD requirements, the choice of PD as an RRT method has decreased in recent years, and therefore, the sample size of our study was small. Third, the duration of our follow-up was shortened due to COVID-19 restrictions and patient limitations.

Implications for Clinical Practice and Conclusion

Our findings indicate that several factors, including gender, marital status, normal weight status, hypertension (HTN), normal hemoglobin levels, and ferritin levels, are associated with improved survival in patients undergoing PD. Additionally, preventing recurrent peritonitis may reduce the need for switching from PD to HD. As such, implementing interventions aimed at managing these modifiable factors can potentially enhance the survival outcomes of PD patients.

Ethical Approval and consent to participate

The Ethics Committee of Kerman University of Medical Sciences approved this research. The approval code was IR.KMU.AH.REC.1398.170.

Authors' contributions

Authorship: NS and ME researched literature and conceived the study. NS,AD, JA, and BD were involved in protocol development, gaining ethical approval, patient recruitment, and data analysis. NS wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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Conflict of Interests

The authors declare that they have no competing interests.

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