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Original Article

Impact of Medical Factors on Mortality in Patients With End-Stage Renal Disease in the West of Iran: A Prospective Study

Meisam Khajevand Ahmadi[1], Masoumeh Abbasi[2], Mehdi Moradinazar[1], Touraj Ahmadi Jouybari[3], Hamidreza Omrani[4], Behnam Yari Bajelani[1], Tahereh Mohammadi Majd[1*], Masoud Ghadiri[5]

[1]Clinical Research Development Center, Taleghani and Imam Ali Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran
[2]Department of Health Information Technology, School of Paramedical, Kermanshah University of Medical Sciences, Kermanshah, Iran
[3]Clinical Research Development Center, Imam Khomeini and Mohammad Kermanshahi and Farabi Hospitals, Kermanshah University of Medical Sciences, Kermanshah, Iran
[4]Cardiovascular Research Center, Health Institute, Imam Ali Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran
[5]Student Research committee, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract

Background and aims: End-stage renal disease (ESRD) is a pervasive global health challenge with high mortality rates. This prospective study aimed to identify medical factors influencing mortality in ESRD patients.

Methods: Data from 149 ESRD patients registered at Imam Khomeini hospital in Kermanshah were analyzed. Only patients with a minimum of one-year follow-up were included. Univariate and multiple regression analyses were employed, and model evaluation utilized indicators such as the area under the receiver operating characteristic (ROC) curve, sensitivity, and specificity.

Results: Among 149 ESRD patients, 88 (59.1%) were male, and 37 (24.7%) experienced mortality. The average age of deceased patients was 63.59 ± 15.74 years. Chronic glomerulonephritis was the underlying cause in 72 (48.3%) participants. Multiple regression revealed that age, diabetes, and a history of heart failure significantly correlated with mortality. ESRD patients with diabetes faced a 2.47-fold increased risk of death (95% confidence interval: 1.10 - 5.55). The model exhibited an area under the curve (AUC) of 0.70, with sensitivity and specificity of 51.35% and 75%, respectively.

Conclusion: Given the chronic nature of ESRD and elevated mortality, particularly among diabetic patients, intensified monitoring efforts are crucial for the prevention and management of diabetes in this population.

Keywords: End-stage renal disease, ESRD, Kidney disease, Mortality, Diabetes, Epidemiology

***Corresponding Author:**
Tahereh Mohammadi Majd,
Email: tahereh_mohammadi@yahoo.com

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Introduction

End-stage renal disease (ESRD), also known as terminal chronic kidney disease, is a progressive and often irreversible condition that results in the loss of normal kidney function, leading to various complications for affected individuals.[1] ESRD is characterized by a glomerular filtration rate (GFR) of less than 15 ml/min.[2] In its advanced stage, ESRD manifests symptoms such as uncontrolled blood pressure, anemia, mineral and bone disorders, and metabolic imbalances.[3] Additional symptoms include anorexia, nausea, vomiting, diarrhea, dry skin, itching, malnutrition, and platelet dysfunction.[4] A significant proportion of ESRD patients come from less developed countries, with Asia, the world's most populous continent, exhibiting the highest prevalence of chronic kidney disease.[5,6]

Globally, the prevalence of ESRD is estimated at 9.1%.[7] A meta-analysis study suggests an approximate prevalence of 11.6% in Iran.[6] Risk factors for chronic kidney diseases include age, gender, ethnicity, family history, and socioeconomic status.[8,9] Chronic conditions, notably type 2 diabetes, contributed significantly to the onset of ESRD.[10] Other factors included high blood pressure, congenital anomalies of the kidneys and urinary tract, vascular diseases, primary or secondary glomerular disorders, cystic kidneys, and unresolved acute kidney injury.[1,11]

ESRD is a substantial contributor to mortality, ranking as the 10th leading cause of death, claiming an average of 1.2 million lives annually.[7,12] The disease's mortality rate is

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estimated at 9% per year, with projections indicating a rise to 14 deaths per 100 000 general population by 2030.[13] It is also predicted that by 2040, kidney diseases will become the fifth leading cause of death worldwide.[14] Risk factors such as hyperkalemia, cardiovascular complications, infection, and sepsis contribute to increased mortality rates in ESRD patients.[15-17]

The economic burden of ESRD, stemming from re-hospitalizations and associated care costs, is substantial for patients and society.[17] Despite this, Iran lacks a precise management system for regular kidney disease screenings, especially for ESRD, leading to limited research in the field. This study aimed to determine the frequency of mortality among ESRD patients and identify contributing factors in Kermanshah province, providing crucial insights for proper planning and management of this disease.

Materials and Methods

Type of Study and Study Population

This prospective cohort study was conducted from 2022 to 2023, focusing on patients with ESRD attending the Dialysis Center of Imam Khomeini Hospital in Kermanshah. The study included the entire population of ESRD patients seeking services at this center. Ultimately, 139 patients met the inclusion criteria and were enrolled in the study.

Upon securing the necessary permits and ethical approval (IR.KUMS.REC.1399.1024), demographic and clinical information was systematically recorded by trained nurses during the patients' dialysis sessions. Before enrollment, participants were provided with a comprehensive explanation of the study's objectives, associated risks, and potential benefits. Informed verbal consent was obtained from each patient. The study specifically utilized data from patients with a minimum of one-year follow-up, with the primary outcome being the occurrence of patient death attributed to complications of ESRD during the follow-up period.

Inclusion and Exclusion Criteria

Patients clinically diagnosed with ESRD by a urologist who provided informed consent were included in the study. Exclusion criteria encompassed individuals undergoing follow-up treatment in alternative healthcare facilities and patients who had deceased from causes unrelated to ESRD.

Measurements and Study Questionnaires

The data collection utilized a standardized questionnaire and a checklist with two sections. The demographic section included variables such as age (in years), gender, education (ranging from illiterate and primary school/middle school to post-diploma/bachelor to Ph. D), employment status, marital status, economic status, and smoking habits. Clinical information included variables such as diabetes, blood pressure, vascular access for hemodialysis, family history of chronic kidney disease, history of transfusion, history of heart failure, underlying disease causing ESRD (diabetes/hypertension/chronic glomerulonephritis/urological problems and obstructive uropathies/genetic disorder), social support, and dialysis malnutrition score (DMS).

Social Support Questionnaire

The Multidimensional Scale of Perceived Social Support (MSPSS), developed by Zimet et al,[18] comprises 12 items aimed at evaluating an individual's perceived social support. The scoring system ranges from a minimum of 12 to a maximum of 60. A score falling between 12 and 20 indicates a low level of perceived social support, a score between 20 and 40 suggests a moderate level, and a score exceeding 40 signifies a high level of perceived social support. Salimi et al[19] reported Cronbach's alpha coefficients for three dimensions of social support received from family, friends, and important people in life as 89%, 86%, and 82%, respectively.

Dialysis Malnutrition Score Questionnaire

The DMS questionnaire comprises seven items, including weight change, food intake, functional capacity, gastrointestinal symptoms, comorbidities, subcutaneous fat, number of years undergoing dialysis therapy, and signs of muscle wasting.[20] Each component on the DMS form is assigned a score ranging from 1 to 5. A score of 1 is assigned if the component is entirely normal, while a score of 5 is given for the most severe adverse condition. Therefore, the DMS score for each individual can range from 7 to 35. A score of 7 to 13 indicates a normal nutritional status, a score of 14 to 23 suggests mild to moderate malnutrition, and a score of 24 to 35 signifies severe malnutrition.[21] Joukar et al[22] used the content validity ratio and content validity index (determining the validity of individual questions) to confirm the validity, and all three areas scored between 0.8 and 1 in all questions.

Statistical Analysis

Descriptive statistics, including measures of central tendency for quantitative variables and frequency and percentage for qualitative variables, were employed to characterize the study population. Initial univariate regression analysis was conducted to identify factors associated with mortality in ESRD patients and select variables for the regression model (Enter). Subsequently, multiple regression was applied to calculate adjusted odds ratio, and only variables with a P-value < 0.05 in the univariate analysis were included in the multiple regression model. Significance was set at a two-sided P value < 0.05. STATA version 14 was used to analyze all data.

Model Performance Evaluation

Three indices were computed for model evaluation in this

study: The area under the ROC curve (AUC), sensitivity, and specificity. AUC is a key metric where a value of AUC = 0.5 signifies no detection power. An AUC between 0.5 and 0.7 indicates acceptable accuracy, while an AUC between 0.8 and 0.9 reflects excellent accuracy. Moreover, an AUC between 0.9 and 1 indicates outstanding accuracy.

Results

Among the 149 patients who sought treatment at Imam Khomeini hospital, 88 (59.1%) were male, and 61 (40.9%) were female. The mortality rate was 37 (24.7%), with 25 (67.6%) deaths occurring in men and 12 (32.4%) in women. The average age of ESRD patients was 58.32 ± 15.90 years, while the average age of deceased patients was 63.59 ± 15.74 years. Chronic glomerulonephritis was the underlying cause of ESRD in 72 (48.3%) patients, and hereditary factors contributed to ESRD in 26 (17.4%) patients. The mortality rates in these two groups were higher than in the rest, at 43.2% and 18.9%, respectively.

In addition, 98 (65.8%) of the patients had high blood pressure, and 16 (10.7%) had heart failure, with mortality rates of 75.7% and 21.6%, respectively. Only 6 (4%) patients had a family history of chronic kidney disease, with one (2.7%) death among them. Additionally, 17 (11.4%) had a history of transfusion, with 2 (5.4%) deaths in this group.

After fitting the univariate regression model, three variables (age, history of diabetes, and history of heart failure) were selected for the multiple regression model ($P < 0.05$). The result of the multiple regression model revealed that, among these three variables, only the history of diabetes is significantly associated with the death of ESRD patients (Risk ratio [RR] = 2.47, confidence interval [CI]: 1.10 -5.55, $P < 0.001$). In other words, ESRD patients with diabetes had an approximately 2.47 times higher risk of death compared to those without diabetes (Table 1).

The ROC curve demonstrated an AUC of 0.7 for the multivariate regression model, indicating the model's ability to differentiate between positive and negative outcomes. Furthermore, the model exhibited a sensitivity of 51.35%, representing the proportion of true positive results, and a specificity of 75%, indicating the proportion of true negative results. These performance metrics are visually depicted in Figure 1, offering insights into the model's accuracy in correctly identifying both positive and negative cases.

Discussion

This study aimed to identify risk factors associated with the mortality of ESRD patients. Univariate analysis indicated that age, diabetes, and heart failure are significant factors, with diabetes remaining significant in the multiple regression analysis.

Notably, diabetes emerged as the most crucial factor influencing the mortality of ESRD patients. Diabetic ESRD patients exhibited an approximately 2.5 times higher mortality rate compared to their non-diabetic counterparts. This finding aligns with previous studies such as Harding et al,[23] which reported a ninefold increase in mortality among diabetic patients with acute renal failure. Similarly, Su et al [24] and Qureshi et al[15] highlighted the association between chronic co-morbidities, including diabetes, and increased mortality in chronic kidney failure patients.

The prevalence of diabetes globally, particularly in less developed countries, underscores its significant impact on ESRD mortality. In Iran, where diabetes is a public health concern, proactive measures, including symptom awareness and screening, are essential to prevent diabetes-related complications.

Univariate analysis also indicated that heart failure significantly increased the risk of death in ESRD patients. The study by Wang et al showed that increasing age, high blood pressure, cardiovascular diseases, and hyperuricemia are associated with the occurrence of kidney diseases in China and America.[25] Tonelli et al[26] similarly associated cardiovascular events with mortality due to ESRD progression. In many developed and developing countries, hypertension, glomerular disease (primary or secondary), cystic kidney diseases, and vascular disease are the leading causes of kidney diseases.[11,27] The study highlighted the role of FGF-23, secreted from osteocytes, and renal self-regulation mechanisms such as increased RAAS pathway activity and sympathetic receptor activity, contributing to cardiac fibrosis and arrhythmias.

While increasing age did not retain significance in multivariate analysis, its significant impact in univariate analysis emphasizes its role in raising the mortality rate of ESRD patients. Adeyemi et al[28] and Noh et al[29] corroborated the association between age and increased mortality in ESRD patients. Moreover, aging, often accompanied by chronic diseases, exerted a negative physiological impact, contributing to higher mortality rates.

Despite a higher proportion of male patients and deaths, gender did not significantly affect the mortality rate of ESRD patients in this study. This finding aligns with previous research,[28-32] but gender differences in the prevalence and progression of kidney diseases were reported in other studies.

In conclusion, this study underscores the critical role of diabetes in ESRD patient mortality. Addressing diabetes prevention and management is vital, given its widespread prevalence and impact on ESRD outcomes. Additionally, understanding the complex interplay of factors such as heart failure, age, and gender contributes to a comprehensive approach to managing ESRD patients.

Limitations

Several limitations should be acknowledged in this study. Firstly, the small sample size could potentially affect the generalizability of the findings to broader populations. Secondly, the relatively short follow-up period may restrict the assessment of long-term mortality trends associated with ESRD. Furthermore, the limited period of patient

Table 1. Frequency of Variables and Factors Associated With ESRD-Related Mortality: Univariate and Multivariate Regression Analysis

Variable	Subgroups	Total Frequency (%)	Total Frequency of Deaths (%)	Crude RR (95% CI)	Adjusted RR (95% CI)	*P* Valu**
Age (year)	Mean ± SD	58.32 ± 15.90	63.59 ± 15.74	1.03 (1.00-1.05)	1.02 (.99-1.05)	0.095
Gender	Male	88 (59.1)	25 (28.4)	1	-	-
	Female	61 (40.9)	12 (19.7)	0.61 (0.28 -1.35)	-	
Marital status	Single	21 (14.1)	6 (28.6)	1	-	-
	Married	128 (85.9)	31 (24.2)	0.79 (0.28 -2.37)	-	
Education	Illiterate and primary-school	72 (48.3)	22 (30.6)	1	-	-
	Middle school to post-diploma	71 (47.7)	14 (19.7)	0.55 (0.25 -1.20)	-	
	Bachelor to Ph. D	6 (4.0)	1 (16.7)	0.45 (0.05-4.12)	-	
Job	Unemployed and retired	48 (32.2)	10 (20.8)	1	-	-
	Housewife	53 (35.6)	10 (18.9)	0.88 (0.33-2.35)	-	
	Employed	48 (32.2)	17 (35.4)	2.08 (0.83 -5.19)	-	
Economic status	Weak	22 (14.8)	3 (13.6)	1	-	-
	Moderate	99 (66.4)	28 (28.3)	2.49 (0.68 -9.10)	-	
	Good	28 (18.8)	6 (21.4)	1.72 (0.37 -7.86)	-	
Smoking	Non-smoker	126 (84.6)	32 (25.4)	1	-	-
	Smoker	23 (15.4)	5 (21.7)	0.81 (0.28 -2.37)	-	
Social support	Moderate	22 (14.8)	3 (13.6)	1	-	-
	Good	127 (85.2)	34 (26.8)	2.31 (0.66 -8.32)	-	
DMS	Mild to moderate malnutrition	25 (16.8)	6 (24)	1	-	-
	Natural nutrition	122 (81.9)	30 (24.6)	1.03 (0.37 -2.84)	-	
	Severe malnutrition	2 (1.3)	1 (50)	3.16 (0.17 -5.70)	-	
Underlying disease that causes ESRD	Diabetes	17 (11.4)	5 (29.4)	1	-	-
	Hypertension	23 (15.4)	6 (26.1)	0.84 (0.20 -3.42)	-	
	Chronic glomerulonephritis	72 (48.3)	16 (22.2)	0.68 (0.21 -2.23)	-	
	Urological problems and obstructive uropathies	11 (7.4)	3 (27.3)	0.90 (0.16 -4.86)	-	
	Genetic disorder	26 (17.4)	7 (26.9)	0.88 (0.22-3.43)	-	
Diabetes	No	102 (68.5)	18 (17.6)	1	1	0.028
	Yes	47 (31.5)	19 (40.4)	3.16 (1.46-6.86)	2.47 (1.10-5.55)	
Blood Pressure	No	51 (34.2)	9 (17.6)	1	-	-
	Yes	98 (65.8)	28 (28.6)	1.86 (.80-4.33)	-	
History of Heart Failure	No	133 (89.3)	29 (21.8)	1	1	0.078
	Yes	16 (10.7)	8 (50)	3.58 (1.23-10.38)	2.73 (0.89-8.38)	
Vascular Access for Hemodialysis	No	120 (80.5)	32 (26.7)	1	-	-
	Yes	29 (19.5)	5 (17.2)	0.57 (.20 -1.62)	-	
History of CKD in Family	No	143 (96.0)	36 (25.2)	1	-	-
	Yes	6 (4.0)	1 (16.7)	0.59 (.06-5.25)	-	
History of Transfusion	No	132 (88.6)	35 (26.5)	1	-	-
	Yes	17 (11.4)	2 (11.8)	0.37 (.080-1.69)	-	
Performance Model					AUC = 0.70, CI: (0.60- 0.80) Sensitivity = 51.35 Specificity = 75	

Note. CI: Confidence interval; RR: Risk ratio; SD: Standard deviation; ESRD: End-stage renal disease; DMS: Dialysis malnutrition score; CKD: Chronic kidney disease; AUC: Area under curve.
* *P* value < 0.05: Significant.

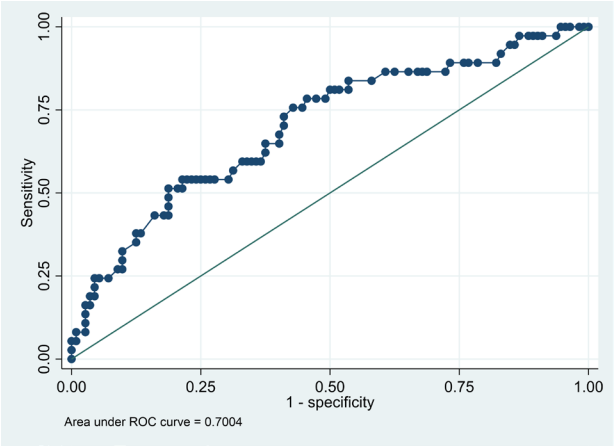

Figure 1. A Receiver Operating Characteristic for Multivariate Regression Model

evaluation might not fully elucidate the comprehensive progression of ESRD and its consequential impact on mortality over an extended timeframe. These constraints warrant cautious consideration when interpreting the results and drawing conclusions from the study.

Suggestions

For future research, it is recommended to broaden the scope by increasing the sample size and prolonging the follow-up duration. This approach would contribute to a more comprehensive understanding of mortality trends in ESRD patients. Collaborative efforts such as multi-center studies or partnerships with diverse healthcare facilities could enhance the sample size and increase the generalizability of findings. Additionally, incorporating a broader range of clinical variables and risk factors into the analysis may offer a more nuanced perspective on the factors influencing mortality in this patient population.

Conclusion

ESRD represents a significant and enduring health challenge. The observed mortality rate in this study surpassed global averages, highlighting the critical need to address contributing factors. Notably, diabetes emerged as a predominant contributor to mortality among ESRD patients, underscoring the importance of heightened vigilance by both decision-makers and healthcare professionals. These findings serve as a critical alert, urging decision-makers and specialists to enhance monitoring efforts for kidney patients. Prioritizing diabetes prevention and control, recognizing early signs of ESRD progression in high-risk individuals, and ensuring timely referrals to specialized interventions are pivotal steps for improving patient outcomes and mitigating the impact of this chronic and debilitating condition.

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Authors' Contribution

Conceptualization: Meisam Khajevand Ahmadi.
Data curation: Behnam Yari Bajelani.
Formal analysis: Tahereh Mohammadi Majd.
Methodology: Mehdi Moradinazar.
Visualization: Masoumeh Abbasi.
Writing–original draft: Meisam Khajevand Ahmadi, Touraj Ahmadi Jouybari, Hamidreza Omrani, Masoud Ghadiri.
Writing–review & editing: Meisam Khajevand Ahmadi, Mehdi Moradinazar.

Competing Interests

The authors hereby confirm that there are no competing interests associated with the publication of this research.

Ethical Approval

The Ethics Committee of Kermanshah University of Medical Sciences approved the study (IR.KUMS.REC.1399.1024). All methods were carried out in accordance with relevant guidelines and regulations. The study was conducted in accordance with the International Conference on Harmonization and the ethical principles of the Declaration of Helsinki. All participants provided written informed consent.

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