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Predictors of long-term survival of hemodialysis patients in Hamadan province, west of Iran

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ABSTRACT

Background: Hemodialysis (HD) represents the main way of renal replacement therapy (RRT) for end-stage renal disease (ESRD) patients in Iran. Few studies have investigated the survival of HD patients in Iran.

Objectives: This study conducted to reach better understanding predictors of survival for HD patients.

Patients and Methods: This is a retrospective cohort study conducted in 1142 HD patients in Hamadan province during 11 years from 2007 to 2017. The checklist used to gather information was comprised of patient's demographic and clinical information. The analysis was carried out using Laplace regression and Cox regression model.

Results: The most prevalent causes of ESRD were reported to be high blood pressure (BP) (28.9%) and diabetes (24.34%). The probability of survival at the end of 1st, 5th, and 10th year was 0.81, 0.4 and 0.13, respectively. Results of multivariate Cox regression showed that being rural dweller, low albumin, ferritin and hemoglobin level and having positive CRP at diagnosis have a negative significant impact on survival of HD patients (P < 0.05). Conclusions: Being rural dweller, low albumin and hemoglobin level and having positive CRP at diagnosis amongst other factors were possible factors affecting the survival of HD patients in this study. Considering the low survival probability of these patients, efforts should be made to real-time diagnosis of the cause of renal diseases.

Implication for health policy/practice/research/medical education:

Due to limited and inadequate evidences of survival rate for hemodialysis patients in developing countries like Iran, this study was conducted to reach their survival compared with similar studies and achieve better understanding predictors of survival of hemodialysis patients. These findings will direct to real-time diagnosis of the cause of renal diseases.

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1. Background

Globally chronic kidney disease (CKD) is considered as a serious challenge for health systems (1). In CKD patients, reduction of glomerular filtration rate (GFR) results in renal replacement therapy (RRT), which this stage of kidney failure is often called end-stage renal disease (ESRD) (2).

In recent decade, many of developed countries had a stable or decreasing trend in incidence rate of ESRD. However, as controversy in some countries like Iran and other developing countries a rising trend in the prevalence of diabetes mellitus and hypertension as the most leading causes of ESRD are detected, which leads to increasing proportion of hemodialysis (HD) centers (3-5).

In Iran, HD represents the main way of RRT for ESRD patients (6). HD treatment for ESRD patients in this country is free of charge. Incidence and prevalence of HD in Iran follows an upward trend, and reached from 13.8 and 137 per 1 million in 1997 to 63.8 and 357 per 1 million in 2006, respectively (5,7).

Despite advances in dialysis care facilities in recent years, the survival rate of dialysis patients is shorter in comparison with general population (8). National

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evidences regarding survival rate of HD patients are rare (9,10). Five years survival rate for HD patients in Northern part of Iran was 23%, while in southern region of Iran was 46.8% (9,10).

Various factors such as albumin and hemoglobin levels, adequacy of dialysis, dialysis duration, method of RRT, body mass index (BMI), etiology of kidney failure, comorbid diseases (i.e., diabetes mellitus, cardiovascular disease), and infection rates adversely affect the survival rates of HD patients (11-17). Among all the aforementioned factors, cardiovascular disease (CVD) is considered as a leading cause of morbidity and mortality among HD patients (18,19).

2. Objectives

While growing evidence of increasing ESRD survival in developed countries was reported, however this evidence in developing countries are relatively low (9,10). To our knowledge, there has been no enough large epidemiological study regarding survival rate of Iranian HD patients. Hence to reach better understanding predictors of survival for HD patients, we aimed to investigate the survival rate and related contributors in HD patients in Hamadan province.

3. Patients and Methods

3. 1. Patients

This study is a retrospective study conducted on 1142 HD patients in Hamadan province in western Iran from March 2007 to March 2017.

Hamadan province with an area of 19493 km² in extent is located in western Iran. According to the national census held by the statistical center of Iran (https://www.amar.org.ir/english), Hamadan province had a population of 1758 268 people in 2011. Eight hospitals in the province have dialysis unit including Alimoradian,

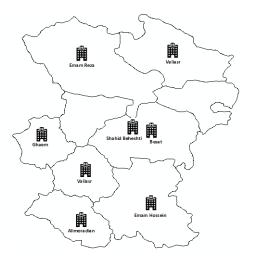


Figure 1. The hospitals with dialysis unit in Hamadan province.

Vali-asr, Ghaem, Imam Hossein, Imam Reza, Besat, Shahid-Beheshti (Figure 1).

Data were gathered by a checklist on hospital records of all ESRD patients in the province. Patients with acute renal failure (ARF) receiving transient HD and non-native patients were excluded from the study. The checklist applied in this study included patient's demographic information (age, sex, marital status, BMI, residence area, educational level, the history of tobacco use or substance abuse), and clinical information (including hemoglobin, blood urea nitrogen [BUN], creatinine, C-reactive protein [CRP] status, sodium, calcium, phosphorus, albumin and ESRD causes). Clinical and laboratory data of the before the first dialysis session were used for each patient.

3.2. Ethical issues

The research followed the tenets of the Declaration of Helsinki. Before the study, written informed consent was obtained from all patients who participated in the study. All information about individuals was coded and kept confidential. This study was approved by the Ethics Committee of Tehran University of Medical Sciences (TUMS. SPH.REC. 1395.1300).

Statistical analysis

To define the time scale in this study, we considered the time interval between the first sessions of HD to the time of patient's death. Schoenfeld's residual test was used to test the proportional hazards (PH) assumption, and univariate and multivariable (Adjusted by other variables in the model) Cox regression model was used to evaluation the impact of the simultaneous effects of variables on time scale for variables do satisfy the PH assumption. Hosmer-Lemeshow strategy was used for model building and model fitted with all variables that had P value less than 0.2. Laplace regression was used to determine survival time (month) for 5th to 45th percentiles of died patients. In fact with his approach a specific probability of the event is fixed and is the time point to be estimated. Bottai et al discussed in detail about this approach in 2010 (20). The level of 0.05 was considered significant for all statistical tests. We used the Stata software version 12 (StataCorp, College Station, TX, USA) to perform all the analytical operations.

4. Results

In this time period totally 1142 HD patients were studied, of whom 617 (54.03%) were males and 717 (62.78%) were lived in urban areas. 928 (81.26%) of them were married. In addition, the most prevalent cause of ESRD was reported to be high blood pressure (BP) (28.9%) and diabetes (24.34%). Around 385 (34.65%) of patients had CRP positive at diagnosis. Mean age at diagnosis of patients was 55.52 ± 14.65 years (range: 8-88 years). Mean hemoglobin, ferritin and serum albumin of patients were

Table 1. Effect of various predictors on survival time of HD patients using the Cox regression model in Hamadan Province from 2007 to 2017

Variable		No. (%)	Crude HR	95% CI	P value	Adjusted HR	95% CI	P value
Location	Urban	717 (62.78)	1.00			1.00		
	Rural	425 (37.22)	1.17	(0.98, 1.4)	0.09	1.26	(1.04, 1.52)	0.02
Marital status	Single	107 (9.37)	1.00			1.00		
	Married	928 (81.26)	1.18	(0.55, 2.51)	0.67	1.87	(0.94, 1.52)	0.11
	Widow	94 (8.23)	1.35	(0.61, 3.00)	0.45	2.62	(1.18, 5.85)	0.018
	Divorce	13 (1.14)	3.45	(1.16,10.3)	0.03	2.43	(0.8, 7.31)	0.12
Substance	No	977 (85.55)	1.00			1.00		
addiction	Yes	165 (14.45)	1.31	(1.04, 1.64)	0.02	1.31	(1.03, 1.65)	0.021
	Hypertension	330 (28.9)	1.00			1.00		
	Diabetes	278 (24.34)	1.15	(0.91, 1.44)	0.23	1.19	(0.94, 1.52)	0.15
	Urologic & obstructive diseases	105 (9.2)	1.14	(0.82, 1.58)	0.42	1.28	(0.91, 1.8)	0.15
ESRD cause	Polycystic kidney	45 (3.94)	1.24	(0.77, 2.00)	0.37	1.27	(0.77, 2.08)	0.35
	Glomerulonephritis	77 (6.74)	1.12	(0.68, 1.83)	0.65	0.67	(0.39, 1.15)	0.14
	Diabetes & hypertension	125 (10.95)	1.04	(0.79, 1.42)	0.69	1.05	(0.78, 1.42)	0.76
	Unknown	182 (15.94)	0.97	(0.72, 1.32)	0.87	1.05	(0.76, 1.44)	0.78
Serum albumin	>3.5	660 (60.7)	1.00			1.00		
(g/dL)	<3.5	427 (39.3)	3.14	(2.61, 3.77)	< 0.001	2.05	(1.67, 2.51)	< 0.001
Hemoglobin	>11	588 (53.6)	1.00			1.00		
(g/dL)	<11	509 (46.4)	3.48	(2.86, 4.24)	< 0.001	3.12	(2.51, 3.88)	< 0.001
CRP	Negative	726 (65.35)	1.00			1.00		
(mg/L)	Positive	385 (34.65)	8.18	(6.6, 10.16)	< 0.001	3.57	(2.90, 4.39)	< 0.001

10.6 g/dL, 334.75 ng/mL and 3.66 g/dL, respectively. The effects of prognostic factors on hazards ratio of diagnosis to death of patients have been demonstrated in Table 1. Rural dweller patients had 26% higher hazard of death compare with urban dwellers (P = 0.02) and substance abuser patients had 31% higher hazard of death (P=0.021). The mortality risk for patients with an albumin level of less than 3.5 g/dL was 2.05 times higher compared with those with higher amounts of albumin (P < 0.001). CRP positive patients had 3.57 higher hazard of death in comparison with CRP negative patients (P < 0.001) and patients with hemoglobin level less than 11 g/dL had 3.12 fold higher risk of death compared to normal range (P < 0.001). Also patients with diabetes, urologic and obstructive diseases and polycystic kidney disease as ESRD causes had 1.19 (P=0.15), 1.28 (P=0.15) and 1.27 (P=0.35) higher risk of death in comparison with patients with hypertension as the cause

of ESRD.

The probability of survival at the end of 1st, 5th, and 10th year was 0.81, 0.4 and 0.13; respectively (Table 2). As shown in Table 3, the first 10, 20, 30 and 40 percentile of HD patients were died at 5.63, 13.43, 22.27 and 33.13 months after diagnosis, respectively.

5. Discussion

This is a retrospective cohort study regarding the survival rate and its predictors of 1142 HD patients in Hamadan province during 11 years period (March 2007 to March 2017). The majority of patients were married and urban dweller. BP and diabetes were most prevalent cause of ESRD. Being rural dweller, low albumin, ferritin and hemoglobin levels and having positive CRP at diagnosis amongst other factors are proved to have significant effect on survival probability. The survival probability in 1st, 5th, and 10th years were 81%, 40%, and 13%

 $\textbf{Table 2.} \ \text{Survival time of diagnosis to death in HD patients in Hamadan province from 2007 to 2017}$

Survival time (y)	Total	Death	Censored	Survival probability	95% CI
1	1142	189	245	0.81	(0.79,0.84)
2	708	108	137	0.68	(0.65, 0.71)
3	463	64	78	0.57	(0.54, 0.61)
4	321	47	53	0.48	(0.45, 0.52)
5	221	35	38	0.4	(0.36, 0.44)
6	148	18	27	0.35	(0.3, 0.39)
7	103	13	24	0.3	(0.25, 0.34)
8	66	7	15	0.26	(0.22, 0.31)
9	44	11	11	0.19	(0.14, 0.24)
10	22	5	8	0.13	(0.09, 0.19)

Table 3. Survival time (month) from diagnosis to death in different percentiles of HD patients in Hamadan province from 2007 to 2017

Percentile	Survival time (month)	Robust SE	95% CI	P value
Percentile 5	3.20	0.39	(2.43, 3.97)	< 0.001
Percentile 10	5.63	0.51	(4.63, 6.63)	< 0.001
Percentile 15	8.74	0.78	(7.20, 10.28)	< 0.001
Percentile 20	13.43	1.00	(11.45, 15.40)	< 0.001
Percentile 25	17.33	1.09	(15.19, 19.47)	< 0.001
Percentile 30	22.27	1.28	(19.75, 24.79)	< 0.001
Percentile 35	27.47	1.69	(24.14, 30.80)	< 0.001
Percentile 40	33.13	1.58	(30.03, 36.22)	< 0.001
Percentile 45	38.50	1.72	(35.13, 41.87)	< 0.001

respectively.

This study showed that the 5-year survival of HD patients was 40%. This proportion was lower than that reported from France and Brazil with the 5 year survival equal 87% and 63.32% (21,22). However, the survival of our patients is more than that of the study conducted in Ethiopia by 14.8% (23). According the United States Renal Data System (USRDS) report in 2009, 5-year survival rate of non-diabetic ESRD patients were between 30%-50%, relatively similar with results of this study (24). Free HD charges and affordable costs of medical therapy for HD patients in Iran can encourage them to receive timely medical care and compliance with treatment.

Consistent with our finding, several studies have also shown that low hemoglobin levels were strongly associated with higher risk of mortality in HD patients (25,26). Evidence shows that maintaining the hemoglobin level of HD patients at the normal range, is associated with increase in quality of life (27), improvement of cardiac and brain function (28,29) and decrease in hospitalization and cost of treatment (30).

Our study confirmed the previous findings that, low serum albumin is related with severe survival (14,31,32). Combe et al showed that decreased serum albumin over time correlated with increased CVD death (33). In dialysis patients, low serum albumin level applied commonly as an surrogate of malnutrition and reflected visceral protein stores (34).

Our finding highlighted that the positive inflammatory marker CRP was the strong mortality predictor in HD patients. Inflammation usually is in relation with insulin resistance, oxidative stress, wasting, infections and endothelial dysfunction (35). Omae et al showed that HD renal cancer patients with elevated CRP levels had lower performance status and higher graded tumors (36). In fact inflammation has an important effect in the pathogenesis of malnutrition and atherosclerosis and causes higher cardio-vascular disease (CVD) mortality in these patients (37).

6. Conclusion

Being rural dweller, low albumin and hemoglobin level and having positive CRP at diagnosis amongst other factors were possible factors affecting the survival of HD patients in this study. Considering the low survival probability of these patients, efforts should be made to real-time diagnosis of the cause of renal diseases.

Limitations of the study

One of the limitations of this study was missing data due to incomplete hospital records because of lack of some laboratory tests in some hospitals; therefore complete GFR, intact parathyroid hormone (iPTH) and total iron binding capacity (TIBC) were rarely done and could not be used for this study. Also because of the retrospective nature of the study it was not possible to verify quality control of the data. Therefore, further studies with prospective follow-up are suggested. Addiction and smoking status of patients was based on their self-report and was prone to information bias.

Authors' contribution

In this study, MAM as corresponding author and supervisor conducted the study. MY and VS as an advisors contributed to the experimental design. SK analyzed the results and interpreted data. SA and MAM wrote the manuscript. MY, VS and SK collected the data.

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Conflicts of interest

The authors declare no conflict of interest.

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