ORIGINAL RESEARCH

EMERGENCY ROOM VISITS IN PATIENTS WITH LEFT VENTRICULAR DYSFUNCTION RECEIVING HEMODIALYSIS : A CASE CONTROL STUDY

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ABSTRACT

Introduction: Chronic kidney disease (CKD) prevalence in Saudi Arabia has been rising over the past few years. The risk of developing left ventricular dysfunction is high in patients with CKD on hemodialysis. Our aim is to study the frequency of emergency room visits and the length of ER stay in patients LVD on hemodialysis.
Methods: All patients who were on hemodialysis between the period of January 2011 and November 2016 were included in our study. Patients' demographic, medical and laboratory data were extracted for all patients. Patients were classified into three groups according to their ejection fraction (EF<40%, EF= 40-49% and EF≥50%). Descriptive statistics were done for all variables. Logistic regression was used to assess the outcome while adjusting for confounder.
Results: Analysis included 333 patients. Two-hundred and fifty seven patients had an EF ≥50% and 36 patients with EF 40-49% and 40 patients with EF <40 %. Age was significantly higher in patients with EF<50% compared to patients with EF ≥50% (P=0.002). Comorbidities were more prevalnt in patients with EF<40% and EF 40-49%. Number of ER visits and length of stay were significantly different between the three groups (P=0.005, P=0.023) ICU admissions shows a statistically significant diffrence between the three groups (P=0.013).
Conclusion: Patients with low EF on hemodialysis have a higher rate of ER visits and length of stay in ER when compared to patients with EF≥50.
KEY WORDS: LVD, renal failure, mortality, emergency room, ICU

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INTRODUCTION

Chronic kidney disease (CKD) prevalence in Saudi Arabia has been rising markedly over the past few years. (1) In 2016, the report of the Saudi Center for Organ Transplantation (SCOT) showed a total of 17,687 dialysis patients, of which 16,315 of them are treated by hemodialysis (HD) and the remaining 1,372 by peritoneal dialysis (PD). (2) The definition of Left ventricular dysfunction (LVD) is left ventricular ejection fraction (LVEF) half of that of the systolic capacity of the left ventricle. Hemodialysis patients are at high risk of developing left ventricular dysfunction (LVD) compared to the general population. (3-5). Heart failure (HF) is defined as inability of the cardiac muscle to generate sufficient cardiac output to meet the body need. In the presence of symptoms and signs of heart failure, heart failure is classified into; HF with left ventricular ejection fraction (LVEF) less than 40%, (reduced ejection fraction), HF with LVEF between 40% to 49% (moderately-reduced ejection fraction) and HF with LVEF more than 50% (preserved ejection fraction).(6) Causes of CHF include left ventricular hypertrophy, ischemic heart disease, systolic failure (7) and diastolic dysfunction (8) In the United States it is estimated that more than 8 million people will suffer from HF by 2030. (9-10) Those patients will have a mortality rate of 50% within five years of the diagnosis. (11)

In patients treated using hemodialysis for CKD the prevalence of cardiovascular disease is high. (8) It is estimated to be two to ten-fold higher than those with normal functioning kidney and the risk of cardiovascular disease morbidity and mortality is abnormally high in all stages of CKD [8,12,13]. A common cardiovascular disease in this group is congestive heart failure (CHF). (5) CHF and LVD are considered as prognostic indicators for mortality when present once end-stage renal disease therapy is initiated. (14) Once CHF is present at the time of dialysis initiation, mortality is estimated to occur within 90 days (15)

The US Renal Data System (USRDS) showed that the mortality rate in patients on dialysis is 83% at 3 years after HF with the hazard ratio being adjusted for mortality of 2.1 (95% confidence interval, (1.80- 2.45) (16) Another study estimated that 40% of deaths in dialysis patients are caused by cardiac diseases (17-18) Deaths during hospital admissions and according to USRDS for patients on hemodialysis were caused by CHF in 8.7% of patients, 6.6% due to pulmonary edema and 4% due to volume overload (8)

Future guidelines and protocols in dealing with this group of patients must be designed to improve the outcomes and survival among these patients. Our aim is to assess the clinical characteristics, comorbidities, rate of emergency room visits, duration of stay in the ER and the outcomes among hemodialysis patients in King Abdulaziz University Hospital (KAUH) - Hemodialysis Unit, Jeddah, Saudi Arabia according to their ejection fraction level.

METHODS

Design. We conducted this hospital-based case-control study in the Department of Medicine at King Abdulaziz University Hospital (KAUH) in Hemodialysis Unit, Jeddah, Saudi Arabia between January 2017 and May 2018, using electronic and paper-based patient records. Ethical approval was obtained from the Department of Bioethics.

Participants. All patients who were ≥18 years old, who were admitted to KAUH between January 2011 to November 2016 and were on hemodialysis in KAUH for 3 months or more were included. Patients were then divided into 3 groups according to their EF results. The Cut-off points for EF were EF <40% , EF between 40-49% and EF ≥ 50%.

Variables and data measurements. Using standardized and pretested data extraction sheet, we collected data from electronic hospital records for cases and controls. We extracted data on age, gender, nationality, history of diabetes mellitus, ischemic heart disease, dyslipidemia, body mass index, height, weight, cause of end-stage renal disease, since when was the patient on dialysis, number of ER visits, average stay in ER in each visit, outcome of last visit, intensive care unit (ICU) stay, last echocardiography reports, lipid profile, complete blood count, coagulation profile and INR, cardiac enzymes, medications (Anti-diabetes, anti-hypertension, anti-coagulant, anti-dyslipidemia).

Reducing bias. To reduce selection bias, we only included patients with echocardiography reports and EF results in all patients.

Sample size. Considering a reported population of 16315 patients on hemodialysis in Saudi Arabia (19) with 95% confidence interval and a 5% margin of error. The minimum sample size required was 375 patients.

Statistical methods. We used percentages to represent the categorical data. If the numerical data was normally distributed, we used the mean and standard deviation and used the median and interquartile range if not. A chi-squared test was used when comparing the categorical variables. For the numerical variables, if the data was normally distributed, the comparisons were carried out using a one-way analysis of variance. A Kruskal-Wallis test was used if it was not normally distributed. To adjust for potential confounding variables, multiple logistic regression models were constructed. The variables with > 10% missing data were excluded from the regression model. IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA) was used, and for all of the statistical tests, a p-value of < 0.05 was defined as the level of significance. The Statistical Package for the Social Sciences (SPSS) version 21.0 for Windows was used.

RESULTS

Analysis included 333 patients who were on hemodialysis. Two-hundred and fifty seven patients had an EF ≥50% and 36 patients with EF 40-49% and 40 patients with EF <40 %. Age was significantly higher in patients with EF<50% compared to those with EF ≥50% (P=0.002). The mean age in patients with EF<40% was 61.08 (±16.1 and for those with EF 40-49% the mean age was 60.9 (±13.9 compared to 53.43(±16.8) in those with EF≥50%. Gender was also significantly different when comparing the three groups (P=0.025) (Table 1.1).

Table 1.1: General Characteristics of patients according to their EF.

Parameter	EF= <40% (N=40)	EF= 40-49% (N=36)	EF=50-100% (N=257)	P value
Age				
Mean (±)	61.08 ± 16.1	60.9 ±13.9	53.43 ± 16.8	0.002
Median				
Gender N (%)				
Males	26 (14.8)	24 (13.6)	126 (71.6)	0.025
Females	14 (9)	11 (7.1)	131(84)	
Comorbidities N (%)	37 (92.5)	31 (86.1)	177 (68.9)	<0.001
Body mass index				
Mean (±)	27.2 (±6.15)	24.8 (±5.24)	26.67 (±7.90)	0.373
Diabetes mellitus N (%)	28 (70)	19 (52.8)	79 (30.7)	<0.001
Hypertension N (%)	35 (87.5)	29 (80.6)	163 (63.4)	0.002
Dyslipidemia N (%)	5 (12.5)	1 (2.8)	13 (5.1)	0.122
Ischemic heart disease N (%)	16 (40)	11 (30.6)	20 (7.8)	<0.001

When comparing comorbidities, 92.5% (N=37) and 86.1% (N=31) of patients with EF <40% and EF between 40-49%, respectively had one or more of the comorbidities compared to only 69% (N=177) of patients with EF≥50% (P<0.001). Diabetes mellitus (DM) was prevalent in 70% (N=28) of patients with EF <40% and 53% (N=19) of patients with EF 40-49% compared to only 31% (N=79) of those with EF≥50%.(P<0.001). Hypertension (HTN) was also more prevalent in patients with EF<50%, with 88% (N=35) of patients with EF <40% had HTN and 81% (N=29) of patients with EF 40-49% compared to only 63% (N=163) of those with EF≥50%.(P=0.002) Ischemic heart disease (IHD) were also significantly prevalent in patients with EF<50% (P<0.001). 40% (N=16) of patients with EF <40% had IHD and 30% (N=11) of patients with EF 40-

49% compared to only 8% (N=20) of those with EF≥50%.(Table 1.1).

The mean number of ER visits in patients with EF<40% was 3.2 (± 3) and in patients with EF 40-49% 2.8 (± 3.5) compared to 2.1 (± 3.6) in patients with EF≥50% (P=0.005). The mean average of stay between the three groups was also significantly different (P=0.023). Patients with EF<40% had a mean of 2.15 (±2.6) and 3.1(±6) in patients with EF 40-49% and 1.44 (±2.3) in patients with EF ≥50% (Table 1.2). ICU admissions shows a statistically significant diffrence between the three groups (P=0.013). 58% (N=23) and 53% (N=19) of patietns with EF <40% and EF 40-49% respictivily required ICU admission compared to 37% (N=94) of patients with EF≥50%.(Table 1.2)

Table 1.2: ER visits and outcomes of patients according to their EF. *Length of stay **Intensive care unit

Parameter	EF <40% (N=40)	EF 40-49% (N=36)	EF 50-100% (N=257)	P value
Number of ER visits				
Mean (±)	3.18 ±2.9	2.8 ±3.5	2.13 ±3.6	0.005
LOS* in ER				
Mean (±)	2.15 ±2.6	3.08 ±5.8	1.44 ±2.3	0.023
ICU Admission, N (%)**	23 (57.5)	19 (52.8)	94 (36.6)	0.013
Death, N (%)	20 (50)	16 (44.4)	68 (26.5)	0.002

Linear regression analysis was done to examine the factors affecting the number of ER visits. ICU admission was significantly associated (P<0.001) and positively correlated to the number of ER visits (Beta=0.312) (Table 2).

Table 2: Linear Regression Model and Correlation for Number of ER Visits.

	Coefficients[a]						
Model	Unstandardized Coefficients		Standardized Coefficients	t	P value	95.0% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	3.640	2.834		1.284	0.201	-1.953	9.233
Ejection fraction	.011	.037	.046	.294	0.769	-.061	.083
Age	-.010	.015	-.053	-.648	0.518	-.039	.020
Gender	.417	.443	.067	.942	0.348	-.457	1.291
Comorbidities	-.401	1.085	-.049	-.369	0.712	-2.542	1.741
Hypertension	.413	.965	.055	.428	0.669	-1.492	2.318
Ischemic heart disease	.561	.615	.071	.913	0.363	-.652	1.774
Diabetes mellitus	.275	.540	.044	.510	0.611	-.790	1.341
Dyslipidemia	1.913	.934	.143	2.049	0.042	.071	3.755
Body Mass Index	-.046	.032	-.101	-1.441	0.151	-.108	.017
Intensive Care Unit admission	1.969	.455	.312	4.331	0.000	1.072	2.866
Left Atrium Size	.895	.325	.214	2.758	0.006	.255	1.536
Left Ventricle Size	-.655	.389	-.172	-1.683	0.094	-1.423	.113
Fractional shortening	-.086	.060	-.224	-1.418	0.158	-.205	.034

In the linear regression model for the average length of stay in the emergency room, none of the variables showed a statistically significant association with the length of ER stay. (Table 3)
Logistic Regression Model was conducted to examine the association between the need for ICU admission and other variables. DM was strongly associated with increased ICU admission with odds ratio of 3.610 and a p value of 0.002. Number of ER visits had also a significant association with ICU admission (P<0.000, O.R.: 1.302). Body mass index (BMI) and was significantly associated with ICU admission (P=0.016, OR: 1.067) (Table 4).

DISCUSSION
Our study shows the increased prevalence of comorbidities (diabetes mellitus, hypertension and ischemic heart disease) in patients with EF <50%. It is worth noting that the lower the patient's EF was in the classification, the higher the prevalence of the above mentioned comorbidities which may reflect the poor cardiovascular profile for those patients. Stack AG et al. showed that patients with LVD, as well as chronic kidney failure on dialysis had higher morbidity and mortality in comparison to those with normal EF(20).

Table 3: Linear Regression Model and correlation for the average length of ER stay.

Model		Coefficients						
		Unstandardized Coefficients		Standardized Coefficients	t	P Value	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	-4.362	3.153		-1.383	0.168	-10.584	1.861
	Ejection fraction	0.054	.041	.221	1.339	0.182	-.026	.135
	Age	0.003	.016	.017	.196	0.845	-.029	.036
	Gender	-0.187	.493	-.029	-.379	0.705	-1.159	.786
	Comorbidities	0.114	1.208	.013	.094	0.925	-2.269	2.497
	Hypertension	.211	1.074	.026	.196	0.845	-1.909	2.330
	Ischemic heart disease	1.324	.684	.160	1.936	0.054	-.025	2.673
	Diabetes mellitus	.367	.601	.056	.611	0.542	-.819	1.553
	Dyslipidemia	-.707	1.039	-.050	-.681	0.497	-2.757	1.343
	Body mass index	-.046	.035	-.097	-1.301	0.195	-.116	.024
	Intensive care unit	.548	.506	.082	1.084	0.280	-.450	1.546
	Left Atrium Size	.593	.361	.135	1.643	0.102	-.119	1.306
	Left Ventricle Size	.681	.433	.170	1.572	0.118	-.174	1.535
	Fractional shortening	-.038	.067	-.093	-.558	0.577	-.170	.095

Our findings go in accordance with number of studies, such as Jassal s et al. which showed the increased prevalence of comorbidities and mortality in patients with severe congestive heart failure and low EF (5, 4). This can be attributed to the increased duration of end-stage renal disease (ERSD) and the associated changes that may happen to the cardiovascular system as a result, like uremic pericarditis and volume overload, which may eventually lead to the development of LVD or HF, which is considered a factor to increasing mortality in dialysis patients(4, 21). Previous literature shows that diabetes and ischemic heart disease, in addition to smoking and advanced age were associated with increased risk of death. (5, 22, 23) An interesting finding by Goodkin DA et al. was that hypertension was associated with lower risk of death in dialysis patients(22). Sharabas I et al. found that hypertension increases mortality in dialysis patients(24). Our results also demonstrated that patients with EF=40-49% have an increased rate of ER visits and do have a worse prognosis than those with EF≥50%. Previous

literature shows that cardiovascular disease were the most common cause of death in patients on dialysis and amounting to 39.4% of all-cause death in the population under study(13).

ICU admissions were significantly associated with increased number of ER visits but not with the average length of stay in the ER. A previous study found that long hospital stay, prior to ICU admission was associated with poor outcome (25). Other risk factors such as, dyslipidemia, age and EF were not found to be statistically significant Independent risk factors for the number of ER visits and ER length of stay. However, in our study DM was found to be a significant independent risk factor for increase the need for ICU admission in our patients. Number of ER visits was also found to be an independent risk factor for increase the need for ICU admission and this could reflect the poor health condition of those patients and the need to optimize their care to prevent further deterioration of their condition.

Table 4: Logistic Regression Model for ICU Admission.

	P Value	Odds Ratio	95% C.I.for OR	
			Lower	Upper
Age	0.349	0.989	0.966	1.012
Gender	0.536	0.799	0.393	1.626
Hypertension	0.025	0.373	0.158	0.881
Ischemic heart disease	0.427	0.672	0.253	1.789
Diabetes mellitus	0.002	3.610	1.572	8.292
Dyslipidemia	0.283	0.435	0.095	1.987
Body mass index	0.016	1.067	1.012	1.125
Number Of ER Visits	0.000	1.302	1.134	1.495
Left Atrium Size	0.207	0.707	0.412	1.212
Left Ventricle Size	0.686	0.875	0.458	1.672
Fractional shortening	0.632	0.976	0.883	1.078
Ejection fraction	0.462	0.978	0.922	1.037

A study by Douglas s et al. showed that heart failure patients who got discharged from the ER had a higher risk of early death than those who got admitted to the hospital(26). Interestingly, that study found that old age was associated with increased incidence of admission. One possible explanation for our results may be a patient related. For example, elderly patients may not have the same response to the disease as younger patients, so they might not go to the hospital as frequently. Our study also found that the lower the EF the higher the rate of ER visits. Another interesting finding is that the mean length of stay in ER was higher in the EF 40-50% patients in comparison to patients with EF<40%. This increase in the length of ER stay which was even longer than patients with lower EF which may be explained by the variable nature of that groups which was not classified until recently by the European Society of Cardiology in order to better understand how to manage this special group of patients(27). As such physicians may not choose to admit them, but in the same time they might not be able to discharge them due to their variable nature.

One of the limitations of our study is its being done in a single center. Another is the relatively small sample size in comparison to other studies. Our study lacked the cause-specific visit to the ER. It may be interesting if ER visits and length of stay in patients on hemodialysis were compared to those on peritoneal dialysis in terms of EF under the same classification that we did. A study that encompasses most major centers in the region may have a better representation and understanding of our population.

CONCLUSION

Our study showed that the lower the EFs of patients on hemodialysis the higher their number of ER visits and patients with EF 40-49% have higher length of stay which might show the need to study this population to come up with a better understanding and a way to manage such patients.

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AUTHORS' CONTRIBUTIONS

The participation of each author corresponds to the criteria of authorship and contributorship emphasized in the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals of the International Committee of Medical Journal Editors. Indeed, all the authors have actively participated in the redaction, the revision of the manuscript and provided approval for this final revised version.

SPONSORSHIP

Declared none.

COMPETING INTERESTS

The authors declare no competing interests.

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