ORIGINAL ARTICLE

Causes of Mortality in End Stage Renal Disease Patients in a Single Haemodialysis Center

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ABSTRACT

Objective: To determine the frequency of various causes of mortality in hemodialysis dependent patients of end-stage renal disease (ESRD).

Study Design: An observational study.

Place and Duration of Study: The study was conducted at the dialysis unit of Karachi Institute of Kidney Diseases, Karachi, Pakistan from March 2022 to September 2022.

Materials and Methods: Patients of age 30 to 70 years of either gender having end-stage renal disease on hemodialysis for at least 3 months were included in the study. All patients were follow up on every session of hemodialysis and in case of death, the cause of death was noted. All collected data were analyzed using SPSS version 25.

Results: The mean age was 56.3 ± 11.3 years and mean BMI was 21.6 ± 3.5 kg/m^2. Out of 178 patients, 55.1% had diabetic nephropathy as cause of ESDR and 28.7% had hypertension. It was found that most common cause of mortality was sepsis (63.5%), followed by acute pulmonary edema or fluid overload (22.5%). There was a significant association between the duration of hemodialysis and causes of end-stage renal disease with all causes of mortality ($p<0.05$).

Conclusion: Sepsis is the leading cause of mortality in haemodialysis patients of end-stage renal disease, and special attention should be given to such patients of end-stage renal disease (ESRD).

Keywords: *Cause, ESRD, Haemodialysis, Mortality.*

Introduction

Chronic kidney disease is a severe condition for which the standard of therapy includes active monitoring for indicators of disease progression and early referral to experts for hemodialysis or prospective renal transplantation.[1,2] Almost 1.9 million individuals are undergoing for renal transplantation globally every year, wherein 648,000 individuals belong from developing countries.[3]

Renal transplant is a curative therapeutic option for end-stage renal disease (ESRD) patients; however, not all ESRD patients receive a transplant owing to numerous circumstances. In most of the developing countries, there is a lack of renal transplantation therapies, which is the reason of almost 2.3 to 7.1 million premature mortalities.[4] In Pakistan, the incidence rate of ESRD is 150 per million individuals every year.[5] Aside from that, arranging a kidney transplant is a laborious task. For this reason, dialysis is a regularly used treatment modality.[6] Dialysis therapy not only delays death but also improves a number of clinical indications of end-stage renal disease. Nonetheless, hemodialysis patients have a very high fatality rate as well, particularly in the first three months after starting dialysis. According to

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estimates, the annual death rate is 9% per year and five-year survival rate is up to 50%.[7]

Numerous causes have been identified that increase the odds of mortality in ESRD patients. Amongst this most common cause is a cardiovascular event (that accounts for more than half of the deaths), followed by infection and sepsis.[8] de Arriba G et al. identified sepsis as the most frequent cause of death in hemodialysis patients (20%), followed by cardiac event (18%).[9] Song et al. also revealed that 33.8% of the patients with ESRD had sepsis and 25% had a major cardiac event.[10]

In Pakistan, the maintenance of the mortality register is still not a commonly practiced clerical work. This lack of documentation is a huge hurdle for the health management departments to plan for coping with various disease burdens. This study was, therefore, conducted to determine the frequency of various causes that lead to mortality in ESRD patients so that an institutional directory is to formulate. Additionally, it would provide the evidence that would help clinicians ~~to~~ pay special attention to the causes that are associated with the highest mortality.

Materials and Methods

An observational study was conducted at the dialysis unit of Karachi Institute of Kidney Diseases, Karachi, Pakistan from March 2022 to September 2022 after obtaining approval from the ethical committee of the institution. Sample size of 178 was calculated using WHO sample size calculator 1.1 by assuming a confidence level of 95%, taking statistics of cardiac event as 18%[9] and absolute precision as 5.7%. Admitted patients of age 30 to 70 years of either gender having end-stage renal disease on hemodialysis for at least 3 months were included in the study. Patients who had a history of malignancy, patients having COVID-19 or ischemic heart disease and patients who died of unnatural causes (like road traffic accidents) were not part of the study. Non-probability consecutive sampling was used for sample selection.

Prior to enrollment, objectives, risks and benefits of the study were explained to the participants. Patients or their families provided written informed consent. Data regarding sociodemographic factors, BMI, duration and frequency of hemodialysis, modality of access and etiology of ESRD were recorded. Causes of mortality in patients with ESRD

were;

1. Sepsis

Patient having 2 or more of following;

a. Temperature >38°C or < 36°C
b. Heart rate >90 beats/minute
c. Respiratory rate >20 breaths/minute
d. TLC (total leukocyte count >12,000 or <4,000 plus Infection (known or suspected source)

2. Acute pulmonary edema or fluid overload:

Patient having excess fluid in the lungs, clinically bilateral fine crackles at lung bases and x-ray chest shows bilateral infiltrates and/or blunting of costophranic angles.

3. Cardiac cause

a. Atrial fibrillation

Presence of all three of the following on standard 12-lead ECG will be consider as a case of atrial fibrillation.

i. Absent p waves.
ii. Replacement of P waves by rapid oscillations of fibrillatory waves of varying size, shape, and interval between two consecutive waves.
iii. An irregular ventricular response

b. Acute myocardial infarction

Patient having myocardial ischemia ECG changes (ST elevation) or ST depression and subsequent release of biomarkers of myocardial necrosis. (Positive troponin-I (>0.30ng/dl) at the time of presentation and 6 hours later).

4. GI hemorrhage

Bleeding in the gastrointestinal tract, from the mouth to the rectum in the form of hematemasis and/or melena, Nasogastric tube shows fresh blood coffee ground aspirate, and digital rectal examination shows black tarry foul smelling watery stool.

Patients were monitored for three months for morality and if mortality occurred then causes of mortality was identified and reported on pe-designed questionnaire.

Data was analyzed using SPSS version 25. Mean and SD were reported for age, BMI, duration of hemodialysis and frequency of hemodialysis. Frequency and percentage were reported for gender, mode of access, cause of ESRD, mortality and cause of mortality. Data was stratified by age, gender, BMI, duration of hemodialysis, frequency of hemodialysis, mode of access and cause of ESRD. Chi square test

was applied and *p* ≤0.05 was taken as significant.

Results

The mean age was 56.3 ± 11.3 years and mean BMI was 21.6 ± 3.5 kg/m². The mean duration of hemodialysis was 4.14 years. Of 178 patients, 59% patients were males and 41% patients were females. Almost 73% of the patients had hemodialysis two times per week. Most of the patients had arteriovenous fistula mode of access (47.2%), followed by permanent catheter (27%). Out of 178 patients, 55.1% had diabetic nephropathy as cause of ESDR and 28.7% had hypertension. (Table 1)

When it comes to frequency of various causes of mortality, it was found that most common cause of

Table 1: Baseline characteristics of study variables (n=178)

Variables	Statistics Mean ± SD*
Age in years	56.3 ± 11.3
BMI in kg/m2	21.6 ± 3.5
Duration of hemodialysis in years	4.14 ± 1.3
Gender	**n (%)**
Male	105 (59)
Female	73 (41)
Frequency of hemodialysis	**n (%)**
Twice a week	130 (73)
Thrice a week	48 (27)
Mode of access	**n (%)**
Arteriovenous fistula	84 (47.2)
Permanent catheter	48 (27)
Double lumen	46 (25.8)
Causes of ESDR	**n (%)**
Diabetic nephropathy	98 (55.1)
Chronic glomerulonephritis	10 (5.6)
Chronic interstitial nephritis	1 (0.6)
Vasculitis	4 (2.2)
Obstructive uropathy	11 (6.2)
Polycystic kidney disease	3 (1.7)
Hypertension	51 (28.7)
*Standard Deviation	

mortality was sepsis (63.5%), followed by acute pulmonary edema or fluid overload (22.5%), cardiac cause (2.2%) and GI hemorrhage (2.2%), demonstrated in figure 1.

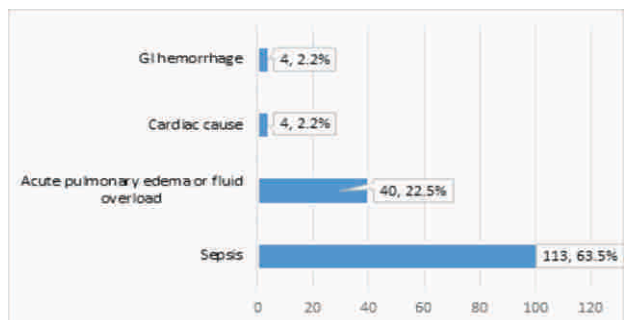There was significant association between duration of hemodialysis and causes of ESRD with all causes of

Fig 1: Frequency of causes of mortality (n=178)

mortality (*p*<0.05). (Table 2)

Discussion

Hemodialysis is the primary treatment in patients

Table 2: Stratified analysis of causes of mortality (n=178)

	Cause of mortality (n %)			
Gender	Sepsis	Acute pulmonary edema/ fluid overload	Cardiac cause	Gastrointestinal hemorrhage
Male	66	26	3	3
	37.07%	14.60%	1.68%	1.68%
Female	47	14	1	1
	26.40%	7.86%	0.56%	0.56%
p-value	0.744	0.785	0.746	0.74
BMI (kg/m²)				
17-24	71	30	2	3
	39.88%	16.85%	1.12%	1.68%
24.1-30	42	10	2	1
	23.59%	5.61%	1.12%	1.12%
p-value	0.34	0.345	0.342	0.347
Duration of hemodialysis (years)				
1-4	71	25	3	0
	39.88%	14.04%	1.68%	0%
5-7	42	15	1	4
	23.59%	8.42%	0.56%	2.24%
p-value	0.008*	0.009*	0.01*	0.001*
Frequency of hemodialysis				
2/week	77	33	4	2
	43.25%	18.53%	2.24%	1.68%
3/week	36	7	0	2
	20.22%	3.93%	0%	1.12%
p-value	0.136	0.137	0.135	0.145
Mode of access				
Arteriovenous fistula	55	19	1	3
	30.89%	10.67%	0.56%	1.68%
Permanent catheter	32	10	1	1
	17.97%	5.61%	0.56%	0.56%
Double lumen	26	11	2	0
	14.60%	6.17%	1.12%	0%
p-value	0.744	0.746	0.744	0.742
Causes of ESRD				
Diabetic nephropathy	68	17	2	2
	38.20%	9.55%	1.12%	1.12%
Chronic glomerulonephritis	7	2	0	1
	3.93%	1.12%	0%	0.56%
Vasculitis	2	2	0	0
	1.12%	1.12%	0%	0%
Obstructive uropathy	4	3	2	1
	2.24%	1.68%	1.12%	0.56%
Polycystic kidney disease	2	1	0	0
	1.12%	0.56%	0%	0%
Hypertension	30	15	0	0
	16.85%	8.42%	0%	0%
p-value	0.042*	0.04*	0.047*	0.046*
* *p* ≤0.05 was taken as significant.				

with ESRD. If ESRD is not treated timely then it can be deadly.[11-14] Hemodialysis helps to improve the quality of life in ESRD patients and its evaluation is continuously needed to enhance treatment outcomes.[8,13,15-17] Research on outcomes can help improve the management of ESRD patients and can lessen undesirable results. Hence, we aimed to assess the causes of mortality in ESRD patients presenting at a tertiary care hospital, Karachi, Pakistan.

There is still scarcity of data in terms of etiologies of ESRD in Pakistan. A Pakistani study showed that diabetes mellitus, high blood pressure and chronic glomerulonephritis were the leading causes of ESRD.[18] In our study, we found diabetic nephropathy was the most frequent cause of ESRD (55%), followed by hypertension (29%), whereas chronic glomerulonephritis was present in only 5.6% of the cases. The fact that diabetes and hypertension were appeared to be the main causes of ESRD in our study can be because these are the major disorders in Asian population.[19-21] Sarmento et al. revealed that the unknown causes of the ESRD was found in 35.3%, followed by diabetes in 26% of the cases and hypertension in 23% of the cases, respectively.[22]

In the current study, sepsis was the most frequent cause of mortality in ESRD patients (63.5%), followed by acute pulmonary edema/fluid overload (22.5%). Lakshminarayana GR et al. revealed that the leading causes of mortality were cardiac event (52%), infections (27%), termination of dialysis (2.9%), advanced cancer (3%), poly trauma following an accident (1.5%) and cerebral bleeding (1.5%). While, in 13.2% of cases, the reason of death was unclear.[23] In a systematic review by Bem et al. also found relationship between long interval of dialysis and mortality in patients of hemodialysis.[24] Desta et al. observed that the incidence of mortality in ESRD patients with sepsis was 3 folds higher as compared to ESRD patients without sepsis.[15] Hence, deaths due to infections are generally because of common pathogens, but may also happen because of unusual pathogens.[25] Lastly, it was also observed in our study that duration for which patient was on dialysis and preceding cause that led to development of ESRD significantly affected the frequency of causes that result in mortality in haemodialysis dependent patients of ESRD.

Numerous intriguing new facts have emerged as a result of the systematic analysis of the causes of fatalities in our hemodialysis-dependent ESRD patients. While the drawbacks of our study included the small sample size, short follow-up period, and inclusion of only patients from one institution. Larger prospective studies should be carried out in the future to evaluate the elements that contribute to morality and survival among hemodialysis-dependent ESRD patients.

Conclusion

Sepsis is the leading cause of mortality in haemodialysis patients of end-stage renal disease and special attention should be given to such patients.

REFERENCES

1. Acosta-Ochoa I, Bustamante-Munguira J, Mendiluce-Herrero A, Bustamante-Bustamante J, Coca-Rojo A. Impact on Outcomes across KDIGO-2012 AKI Criteria According to Baseline Renal Function. Journal of Clinical Medicine. 2019; 8: 1323. doi: 10.3390/jcm8091323.

2. Scott IA, Scuffham P, Gupta D, Harch TM, Borchi J, Richards B. Going digital: a narrative overview of the effects, quality and utility of mobile apps in chronic disease self-management. Australian Health Review. 2020; 44: 62-82. doi: 10.1071/AH18064

3. Workie SG, Zewale TA, Wassie GT, Belew MA, Abeje ED. Survival and predictors of mortality among chronic kidney disease patients on hemodialysis in Amhara region, Ethiopia, 2021. BMC Nephrology. 2022; 23: 193. doi: 10.1186/s12882-022-02825-4

4. Liyanage T, Ninomiya T, Jha V, Neal B, Patrice HM, Okpechi I, et al. Worldwide access to treatment for end-stage kidney disease: a systematic review. Lancet. 2015; 385: 1975-82. doi: 10.1016/s0140-6736(14)61601-9

5. Hamid A, Dhrolia MF, Qureshi R, Imtiaz S, Ahmad A. Clinical Characteristics of Patients on Long-term Hemodialysis. Journal of the College of Physicians and Surgeons Pakistan. 2019; 29: 328-32. doi: 10.29271/jcpsp.2019.04.328

6. Tang SCW, Lai KN. Peritoneal dialysis: the ideal bridge from conservative therapy to kidney transplant. Journal of Nephrology. 2020; 33: 1189-94. doi: 10.1007/s40620-020-00787-0.

7. Dr. A. What are Survival Rates for Patients on Dialysis? Renal Fellow Network. 2018.

8. Bello AK, Okpechi IG, Osman MA, Cho Y, Htay H, Jha V, et al. Epidemiology of haemodialysis outcomes. Nature Reviews Nephrology. 2022; 18: 378-95. doi: 10.1038/s41581-022-00542-7

9. de Arriba G, Avila GG, Guinea MT, Alia IM, Herruzo JA, Ruiz BR, et al. Mortality of hemodialysis patients is associated with their clinical situation at the start of treatment. Nefrología (English Edition). 2021; 41: 461-6. doi: 10.1016/j.nefroe.2021.10.006

10. Song S, Cho C, Park SY, Cho HB, Yoo JH, Kim MG, et al. Cause of postoperative mortality in patients with end-stage renal disease. Anesthesia and Pain Medicine. 2022; 17: 206-12. doi: 10.17085/apm.21080

11. Murdeshwar HN, Anjum F. Hemodialysis. [Updated 2022 Jun 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563296/.

12. Alemu H, Hailu W, Adane A. Prevalence of Chronic Kidney Disease and Associated Factors among Patients with Diabetes in Northwest Ethiopia: A Hospital-Based Cross-Sectional Study. Current Therapeutic Research. 2020; 92: 100578. doi: 10.1016/j.curtheres.2020.100578

13. Hashemi MS, Irajpour A, Abazari P. Improving Quality of Care in Hemodialysis: a Content Analysis. Journal of caring sciences. 2018; 7: 149-55. doi: 10.15171/jcs.2018.024

14. Hsu Cy, Parikh RV, Pravoverov LN, Zheng S, Glidden DV, Tan TC, et al. Implication of Trends in Timing of Dialysis Initiation for Incidence of End-stage Kidney Disease. JAMA Internal Medicine. 2020; 180: 1647-54. doi: 10.1001/jamainternmed.2020.5009

15. Derseh BT, Dadi AF. Mortality and predictors of Chronic Kidney Diseases (CKD) in selected dialysis centers in Addis Ababa, Ethiopia. medRxiv. 2022. doi: 10.1101/2022.01.27.22269879

16. Gao D, Jing S, Wu J, Wu G. Economic Burden and Medical Insurance Impact of the Different Dialysis for End-stage Renal Diseases. Iranian Journal of Public Health. 2018; 47: 1675-80.

17. Saleem I, Dhrolia M, Qureshi R, Nasir K, Ahmad A. 'Haemodialysis burden'overweighs the associations of demographic, social and clinical factors on quality of life: A single centre study from Pakistan. Journal of the Pakistan Medical Association. 2022; 72: 886-90.

18. Khan S, Hussain T, Salahuddin N, Mehreen S. Risk Factors of End Stage Renal Disease in Peshawar, Pakistan: Odds Ratio Analysis. Open Access Macedonian Journal of Medical Sciences. 2016; 4: 381-7. doi: 10.3889/oamjms.2016.068.

19. Hasan M, Sutradhar I, Gupta RD, Sarker M. Prevalence of chronic kidney disease in South Asia: a systematic review. BMC Nephrology. 2018; 19: 291.'10.1186/s12882-018-1072-5

20. Shrestha N, Gautam S, Mishra SR, Virani SS, Dhungana RR. Burden of chronic kidney disease in the general population and high-risk groups in South Asia: A systematic review and meta-analysis. PLoS One. 2021; 16: e0258494. doi: '10.1371/journal.pone.0258494

21. Alicic RZ, Rooney MT, Tuttle KR. Diabetic Kidney Disease: Challenges, Progress, and Possibilities. Clinical Journal of the American Society of Nephrology (JASN). 2017; 12: 2032-45. doi: 10.2215/cjn.11491116

22. Sarmento LR, Fernandes P, Pontes MX, Correia DBS, Chaves VCB, Carvalho CFA, et al. Prevalence of clinically validated primary causes of end-stage renal disease (ESRD) in a State Capital in Northeastern Brazil. Brazilian Journal of Nephrology. 2018; 40: 130-5. doi: 10.1590/2175-8239-jbn-3781

23. Lakshminarayana GR, Sheetal LG, Mathew A, Rajesh R, Kurian G, Unni VN. Hemodialysis outcomes and practice patterns in end-stage renal disease: Experience from a Tertiary Care Hospital in Kerala. Indian Journal of Nephrol. 2017; 27: 51-7. doi: 10.4103/0971-4065.177210

24. Bem D, Sugrue D, Wilding B, Zile I, Butler K, Booth D, et al. The effect of hyperkalemia and long inter-dialytic interval on morbidity and mortality in patients receiving hemodialysis: a systematic review. Ren Fail. 2021; 43: 241-54. doi: 10.1080/0886022x.2020.1871012

25. Prasad N, Patel MR. Infection-Induced Kidney Diseases. Frontiers in medicine. 2018; 5: 327. doi: 10.3389/fmed.2018.00327

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