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CLINICAL FEATURES AND OUTCOME OF END-STAGE RENAL DISEASE PATIENTS ON MAINTENANCE HEMODIALYSIS ADMITTED TO MEDICAL INTENSIVE CARE UNIT

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Abstract:
Background: The increasing prevalence of end-stage renal disease (ESRD) has resulted in a growing number of maintenance hemodialysis (MHD) patients, particularly among older individuals with conditions such as diabetic nephropathy and microvascular disease. MHD patients face a higher risk of medical complications, which often leads to their admission to the intensive care unit (ICU). However, there is a notable gap in data regarding the outcomes of MHD patients admitted to ICUs. This study addresses this gap by providing insights into the clinical features and outcomes of MHD patients admitted to the medical ICU.
Objective: This study investigates the epidemiology and outcomes of MHD patients admitted to the ICU, explicitly focusing on assessing the predictive accuracy of the Simplified Acute Physiology Score II (SAPS II) in determining mortality.
Methodology: A prospective observational study was conducted at Bahria International Hospital Lahore, involving 189 consecutive MHD patients admitted to the ICU from January 2021 to December 2022. Data collection included recording patient diagnoses, SAPS II variables, organ system failures (OSFs), and additional laboratory parameters. Multivariate logistic regression analysis was utilized to identify significant predictors of survival at ICU discharge.
Results: Among the 189 patients studied, the average age was 61.2 ± 12.8 years, with a male predominance. Diabetic nephropathy emerged as the most prevalent primary renal disease. ICU mortality showed an upward trend with each additional OSF at admission. Univariate analysis revealed significant associations between non-survivor status and higher SAPS II scores, increased OSFs, longer mechanical ventilation duration, and abnormal serum phosphorus levels. Multivariate

analysis confirmed OSFs and mechanical ventilation duration as significant predictors of ICU mortality.

Conclusion: This study sheds light on the changing demographic of MHD patients and underscores the importance of OSFs and mechanical ventilation duration as critical determinants of ICU mortality. The limited predictive utility of SAPS II in this cohort highlights the necessity for tailored prognostic indicators for critically ill MHD patients. These findings offer valuable insights for clinicians managing this vulnerable patient population in the intensive care setting.

Introduction:

Over the past two decades, there has been a significant rise in the number of patients with end-stage renal disease (ESRD), mainly due to an increase in older patients with diabetic nephropathy and vascular renal disease [1]. This trend is expected to continue, and the incidence of ESRD is projected to double in the next decade [2]. Most of these patients will require dialysis. In the last decade, the number of patients treated for chronic uremia has increased worldwide, with Europe experiencing an average annual increase of 4% in the incidence and prevalence of dialysis-treated ESRD patients [3]. The demographic of chronic maintenance hemodialysis (MHD) patients is changing, with a greater number of patients being older and sicker [4]. These patients are more susceptible to developing cardiovascular complications, gastrointestinal bleeding, bacterial infections, and other medical problems, which are a significant cause of morbidity and death [5, 6]. Consequently, there is an increased risk of multi-organ dysfunction in MHD patients, which requires admission to the intensive care unit (ICU). According to reports, 2% of MHD patients require ICU admission every year. Additionally, acute medical/surgical complications are a common cause of dialysis discontinuation before death [7, 8].

It is crucial to understand the epidemiology and outcome of ICU patients to help MHD patients and their families plan for critical illness. However, there is a lack of data on the outcome of MHD patients admitted to ICUs. Existing studies mostly compare patients with ESRD and those with acute renal failure, and different scoring systems are used to assess prognosis [9]. The Simplified Acute Physiology Score II (SAPS II) is a scoring system that grades the severity of individual ICU patients. While most studies show good SAPS II discrimination, several report calibration as disappointing [10].

Generic scores may not predict outcomes in ICU-admitted MHD patients since they allocate high points for several clinical and laboratory data that are usually out of the physiological range of MHD patients, irrespective of the acute event leading to ICU admission [11]. In a case-control study involving a relatively small number of MHD patients, SAPS II was found to be inadequate in predicting outcomes, but calibration was not tested. This study aims to describe the clinical features and outcomes of MHD patients admitted to an ICU and to determine whether SAPS II is a valid predictor of hospital mortality for this specific cohort.

Methodology:

This is a prospective observational study conducted at Bahria Town Hospital Lahore, known as Bahria International Hospital Lahore. All patients with consecutive end-stage kidney disease on maintenance hemodialysis (MHD) admitted to the ICU between January 2021 and December 2022 were included in the study. In the case of readmission to the ICU during the study period, only the first admission was considered. Patients undergoing renal replacement therapy with intermittent hemodialysis received the treatment approximately every other day during their stay in the ICU. In most cases, permanent arteriovenous fistulas were used as vascular accesses for hemodialysis, while dialysis catheters were used for the remaining patients. The hospital's Ethics Committee reviewed the study design and approved it. Although informed consent from patients was not required, they were informed about the study.

On admission to the ICU, we recorded the diagnosis, the variables required to calculate SAPS II, and the number of organ system failures (OSFs) during the first 24 hours.

SAPS II (Simplified Acute Physiology Score II) is a severity-of-illness score based on 17 physiological and six disease-related variables. The variables are measured during the first 24 hours of ICU admission, and the score was calculated using a pre-defined equation. The maximum score is 163, with higher scores indicating greater severity of illness and a higher risk of mortality. The score is widely used in critical care medicine to predict hospital mortality and guide clinical decision-making. OSF was defined according to specific criteria. Cardiovascular failure was identified by heart rate <54/min, mean arterial blood pressure <50 mmHg, ventricular tachycardia (VT), ventricular fibrillation (VF), and serum pH <7.24 with PaCO2 of <49 mmHg. Respiratory failure was identified by respiratory rate <8/min or >40/min, PaCO2 >50 mmHg, AaDO2 >350 mmHg (alveolar-to-arterial oxygen difference, calculated as $AaDO_2 = ((FiO_2)$ (Atmospheric pressure - H_2O pressure) - $(PaCO_2/R)) - PaO_2$), and the need for mechanical ventilation (MV). Hematological failure was identified by white blood cell count <1000/mm3, platelet count <20,000/mm3, and hematocrit <20%. The neurological loss was determined by a Glasgow coma score <6 without sedation. We assigned one point for each OSF, resulting in a range of 0 to 4 OSFs per patient. We also collected additional laboratory data on serum uric acid, phosphorus, and serum cholesterol levels before a new dialysis. Severe sepsis was defined according to Bone et al. [10]. The criteria developed by Bone et al. to define severe sepsis include the presence of infection and at least one systemic manifestation of infection, such as fever, tachycardia, or leukocytosis, along with evidence of organ dysfunction. Examples of organ dysfunction include altered mental status, low blood pressure, decreased urine output, abnormal liver function tests, and abnormal blood clotting tests. These criteria help to identify patients with severe sepsis, which is a life-threatening condition that requires immediate medical intervention. We gathered information about the causes of renal disease, the length of time a person had chronic kidney disease (CKD), and the type of dialysis they underwent. We also noted if they had diabetes mellitus or cardiovascular disease. In addition, we documented the use and length of mechanical ventilation (MV), how long they stayed in the ICU, and whether they survived until the time of hospital discharge. All medical data were collected according to a standardized procedure. Two physicians recorded the data, which was then systematically audited by a third physician. The quality assessment included SAPS II variables, duration of hospitalization, ICU and hospital discharge outcomes, and the use and duration of mechanical ventilation (MV).

All values were presented as means ± SD. The analysis of chronic dialysis (MHD) patients' variables, including the Simplified Acute Physiology Score II (SAPS II) score, involved using chi-square or Fisher tests when necessary for comparing categorical variables. For continuous variables, the Mann–Whitney U-test was employed. Multivariate logistic regression analysis was conducted to discern significant predictors of survival at Intensive Care Unit (ICU) discharge. In this analysis, the dependent variable was survival at ICU discharge, and the independent variables included those identified in the univariate analysis with a P-value of <0.15 for survivors and non-survivors. This statistical approach aims to elucidate the factors that significantly contribute to the survival outcome at ICU discharge among MHD patients.

Data analyses and statistical analysis were performed using SPSS version 25. A p-value of less than 0.05 was considered statistically significant.

Results:

The study population comprised 189 chronic kidney disease (MHD) patients. The average age is 61.2 years, with a male-to-female ratio of 1.1:1. Predominant primary renal diseases include diabetic nephropathy (28.6%), glomerulonephritis (20.6%), and vascular renal disease (17.5%). The average duration of renal replacement therapy is 36.1 ± 12.7 months. Notably, 63.5% of patients have cardiovascular disease, and 36.5% have diabetes mellitus, offering a concise overview of the population's profile. (Table 1)

Table 1: Demographic of study population:

Demographic Characteristics	**MHD Patients**	**Percentages**
Number	189	100
Age (years)	61.2 ± 12.8	
Sex Ratio (Male/Female) (n)	(97/92)	
Primary Renal Disease (n)		
Diabetic Nephropathy	54	28.6
Glomerulonephritis	39	20.6
Vascular Renal Disease	33	17.5
Polycystic Kidney Disease	24	12.7
Other Hereditary Renal Disease	18	9.5
Reflux Nephropathy	12	6.3
Chronic Interstitial Nephritis	6	3.2
Systemic Disease and Other Miscellaneous	3	1.6
Previous Duration of Renal Replacement Therapy (months)	36.1 ± 12.7	
Cardiovascular Disease	120	63.5
Diabetes Mellitus (n)	69	36.5

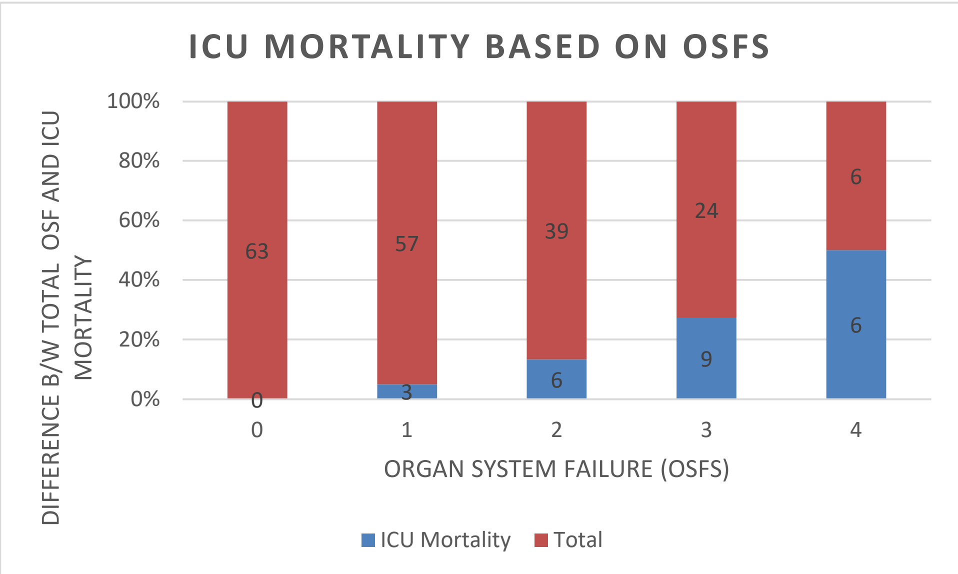

Figure 1: Shows ICU mortality based on organ system failures

Table 2: ICU Mortality Based on OSFs on Admission

No. of OSFs	**ICU Mortality**	**Total**
0	0	63
1	3	57
2	6	39
3	9	24
4	6	6
Total	**24**	**189**

Table 2 shows ICU mortality by number of OSFs (excluding renal failure) at admission. Patients with no OSFs had no mortality. 3 out of 57 patients in the 1 OSF category died. In the 2 OSFs group, 6 out of 39 patients died. In the 3 OSFs group, 9 out of 24 patients died. All 6 patients in the 4 OSFs group died (Figure 1).

The table provides a comprehensive picture of the relationship between the number of OSFs on admission and ICU mortality. As the count of OSFs increases, there is a discernible escalation in the likelihood of mortality during the ICU stay. These findings underscore the importance of assessing and managing OSFs in critically ill patients, as they appear to be closely linked to clinical outcomes in the ICU setting.
Out of the total patients, 12.6% (24) expired, while 165 survived. We analyzed different variables to assess the association with poor outcomes between the survivors and non-survivors (Figure 2).

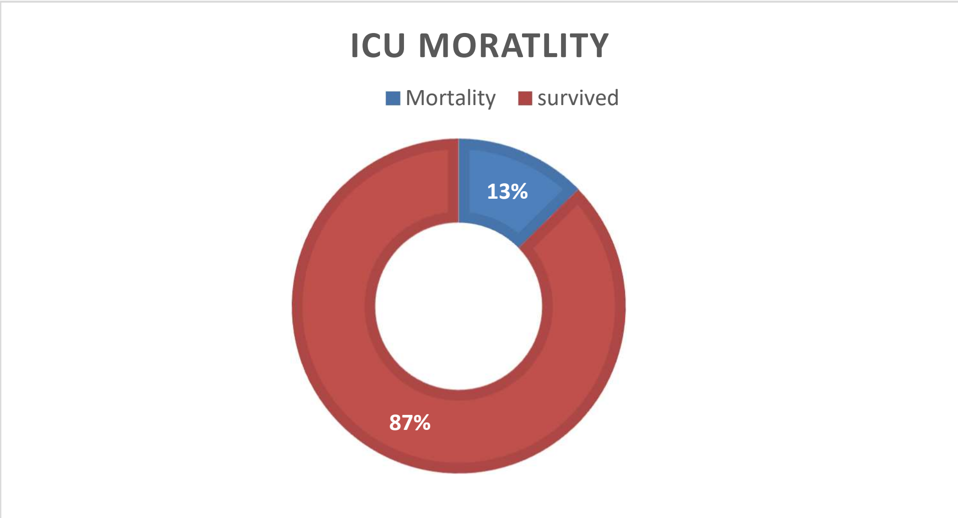

Figure 2: ICU mortality in patients of MHD

Table 3: Comparison of Variables in Non-Survivors and Survivors with Associated P-values

Variable	Non-survivors (24)	Survivors (165)	P-value
Age (years) (mean ±SD)	60.2±13.6	61.4±15.2	0.69
Sex (dead/alive) (n)			
Males	11	86	0.36
Females	13	79	
SAPS II (mean ±SD)	69.3±31.1	33.1±11.3	**<0.001**
Dialysis duration before admission (months) (mean ±SD)	60.5±38.1	72.2±47.2	0.66
Number of OSFs (mean ±SD)	2.6±0.9	0.8±0.6	**<0.001**
Cardiovascular disease (n)			
No	05	91	0.33
Yes (one or more)	19	74	
Diabetes mellitus			
No	06	86	0.67
Yes (one or more)	18	79	
Length of stay (days) (mean ±SD)	7.9±7.3	7.4±11.1	0.96
Duration of Mechanical ventilation (MV) (days) (mean ±SD)	5.1±3.6	1.3±2.3	**0.006**
Serum uric acid (mg/dl) (mean ±SD)	7.1±1.5	6.8±1.7	0.61
Serum phosphorus (n)			
Normal serum level (1.20–2.5 mmol/l)	02	130	**<0.001**
Abnormal serum level (<1.20 or >2.5 mmol/l)	22	35	
Serum cholesterol			
0–2.0 mmol/l	12	82	0.87
>2.0 mmol/l	12	83	

Table 3 presents a comprehensive analysis of various factors in patients who did not survive (non-survivors) compared to those who survived (Survivors). The mean age of non-survivors was 60.2 years (±13.6), while survivors had a slightly higher mean age of 61.4 years (±15.2), with a non-significant p-value of 0.69. The sex distribution did not show a significant difference between the two groups, with 11/24 males among non-survivors and 86/165 among survivors (p-value = 0.36). The Severity Acute Physiology Score (SAPS II) revealed a substantial difference, with non-survivors having a mean SAPS II of 69.3 (±31.1) compared to survivors with a significantly lower mean of 33.1 (±11.3) (p-value <0.001).

Regarding pre-admission dialysis duration, no significant difference was observed between non-survivors (60.5±38.1 months) and survivors (72.2±47.2 months) with a p-value of 0.66. However, the number of organ system failures (OSFs) exhibited a marked distinction, with non-survivors having a higher mean of 2.6 (±0.9) OSFs compared to survivors with a mean of 0.8 (±0.6) OSFs, and this difference was statistically significant (p-value <0.001). Additionally, the presence of cardiovascular disease and diabetes mellitus did not demonstrate a significant association with mortality. At the same time, the duration of mechanical ventilation showed a notable difference (p-value = 0.006), with non-survivors having a longer mean duration (5.1±3.6 days) compared to survivors (1.3±2.3 days). The serum uric acid and serum cholesterol levels did not show significant differences between the two groups, but abnormal serum phosphorus levels were significantly associated with non-survivors (p-value <0.001). These findings highlight the importance of SAPS II, OSFs, and mechanical ventilation duration as potential mortality indicators in critically ill patients.

Table 4: Multivariate analysis for variables as predictors of ICU mortality

Variables	**OR**	**(95% CI)**	**P-value**
SAPS II	1.64	0.96–1.31	0.66
Number of OSFs	4.22	1.21–22.88	0.02
MV duration (days)	1.12	1.08–1.51	0.04
Phosphorus	2.95	0.97–16.96	0.09

Table 4 shows the results of a multivariate analysis of variables, including SAPS II, number of organ system failures (OSFs), duration of mechanical ventilation (MV), and serum phosphorus levels. The odds ratio for SAPS II is 1.64, but it is not statistically significant (p = 0.66). The number of OSFs has a substantial association with the outcome. Each additional OSF significantly increases the odds of the event, indicating a potential link between the severity of organ system failures and the outcome. The odds ratio for the number of OSFs is 4.22 with a 95% CI of 1.21–22.88 and a p-value of 0.02. Additionally, the duration of mechanical ventilation (MV) shows significance, with an odds ratio of 1.12 (95% CI: 1.08–1.51) and a p-value of 0.04. This suggests that as the duration of MV increases, the odds of the event also increase, pointing to the importance of considering MV duration in predicting outcomes.

The odds ratio for serum phosphorus is not statistically significant at 0.05. The number of OSFs and MV duration significantly predict the outcome, providing valuable insights for clinicians managing critically ill patients.

Discussion:

The increasing number of people with end-stage disease (ESRD) has led to a rise in the population of patients undergoing maintenance hemodialysis (MHD). This poses challenges when it comes to managing these patients in critical care situations. In this discussion, we will explore aspects of our study, including the changing demographics of MHD patients, how organ system failures (OSFs) affect outcomes in the care unit (ICU), and the limitations and implications of using the Simplified Acute Physiology Score II (SAPS II) to predict mortality for this particular group.

The demographic shift observed among MHD patients admitted to the ICU reflects trends seen in an aging population and a higher prevalence of nephropathy and vascular renal disease. These factors contribute to an incidence of ESRD. It is worth noting that our study group had an age of 61.2 years with diabetic nephropathy being the common primary cause of kidney disease. This change in demographics highlights the importance of understanding. Addressing the challenges faced by older and frailer MHD patients receiving critical care.

Our investigation into the outcomes of patients in the care unit (ICU) in relation to the number of organ system failures (OSFs) at admission yields information regarding the challenges involved in managing individuals with multiple organ health issues. The documented rise in ICU mortality rates as the number of OSFs increases emphasizes how vulnerable these patients are to experiencing dysfunction across organs. This underscores the significance of identifying and intervening in their cases [16, 17].

This finding emphasizes the necessity for a comprehensive approach to critical care that encompasses renal aspects and considers the broader physiological impact on various organ systems.

Our study also highlights the significant impact of mechanical ventilation (MV) duration on patient outcomes, with longer durations correlating with poorer outcomes. This underscores the importance of timely interventions and the management of respiratory support in this patient population.

Assessing SAPS II as a predictor of hospital mortality in MHD patients admitted to the ICU reveals interesting observations. While SAPS II is widely used as a severity-of-illness score, its applicability to MHD patients is questioned due to its unique physiological profile. Our study indicates limited predictive accuracy of SAPS II for this specific cohort, suggesting the need for tailored scoring systems that better align with the clinical nuances of MHD patients [10].

Comparing our study's mortality rates with those reported in similar studies highlights potential differences attributed to variations in patient populations and medical complexity. Understanding these distinctions is crucial for interpreting and contextualizing our findings.

Several limitations should be considered when interpreting our study. The single-center nature of the study may limit generalizability, and future research employing multi-center approaches could enhance the robustness of our conclusions. Additionally, the observational design introduces potentially confounding variables, underscoring the need for further research employing randomized controlled trials to provide more definitive insights.

Conclusion:

This study provides valuable insights into the changing demographics of patients with MHD and highlights the importance of factors such as OSFs and mechanical ventilation duration in affecting ICU mortality. The usefulness of SAPS II as a predictive tool was limited in this group, thus emphasizing the need for customized prognostic indicators for critically ill MHD patients. These findings can assist clinicians in better managing this vulnerable patient population in the intensive care setting.

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