Frequency and outcome of adverse events in hospitalized critically ill patients

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Abstract

Objectives

To identify Frequency and outcome of adverse events in hospitalized critically ill patients

Methods

This is a retrospective case-control study of critically ill ICU patients was conducted from January-December 2019 at the Aga Khan University Hospital (AKUH) in Pakistan. Data was collected from patients' medical records using a pre-approved pro forma. Variables included demographics, patient and hospitalization characteristics and laboratory investigations. Any adverse event during the admission was also noted. Outcome measures included in-hospital mortality and length of stay.

Results

773 patients met the inclusion criteria and were included in the study; 504 (65.2%) were males and 269 (34.8%) females; mean age was 57.3 ± 16.6 years. Overall mortality rate was 33%. The most common adverse events during a patients hospital stay were acute kidney injury (22%), shock (18%) and electrolyte imbalance (18%). Risk factors for mortality in these patients included mechanical ventilation, septic shock, acute kidney injury, thrombocytopenia, seizures, acute liver failure, ARDS and metabolic acidosis.

Conclusion

Our study reveals a high mortality rate for critically ill ICU patients. Adverse events during admission were frequent and also associated with increased mortality. We hope this study sets the stage for larger scale studies in developing countries to drive improvements in accurate risk stratification and optimal patient management.

Keywords
Critical care, ICU, shock, outcome

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Introduction

An Intensive Care Unit (ICU) caters to patients with serious illnesses in order to provide the treatment critical for their survival such as mechanical ventilation, frequent invasive monitoring and vasopressor supports.[1] Accidental or poor outcomes in a health care setting are described as adverse events. These are quite frequent in ICU patients and can be the result of the vulnerabilities of patients' health condition due to pre-existing risk factors or comorbidities; complications of care; or the large number of procedures to which ICU patients are subjected such as the insertion of central lines, hemodialysis catheters and bronchoscopies.[2]

There are approximately 4 million ICU admissions per year in the United States with reported average mortality rates ranging from 8-19%.[3] In comparison, a 2017 study carried out in Pakistan, a developing country, showed a mean mortality rate of 50% with the highest mortality observed in patients admitted due to neurotrauma (72%) followed by patients with pulmonary diseases (68%).[4]

While there are many studies of the reasons for high mortality rates in ICUs in developed countries there is limited data on the situation in developing countries. Moreover, although ICUs are high-mortality areas, data on the predictors of mortality in an ICU setting is quite low. We have therefore conducted this study to determine the risk factors leading to high mortality rates among patients on an ICU ward in a developing country.

The prognosis of a patient admitted to ICU depends on their comorbidity status, existing risk factors and history of recurrent hospital admissions. Some of the most significant contributors to hospital mortality were the presence of comorbidities and advanced age.[5] The prevalence of comorbid conditions may predispose patients to a range of complications or organ dysfunction. The most common comorbid conditions encountered in an ICU setting are diabetes mellitus (DM), hypertension, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD) and chronic liver disease.[6] The patient's prognosis is therefore determined by the severity of their presenting illness and the existence of additional chronic diseases as the presence of comorbidities leads to an increase in the risk of adverse outcomes and any complications the patient may experience during their stay at the ICU. This may increase the length of their stay in the ICU and the hospital and in turn lead to an even greater risk of health care associated infections.

Methodology

Study Setting

The study was approved by the Institutional Review Board at Aga Khan University, Karachi. We included all adult ICU patients admitted to AKUH from January to December 2019. Patients who left against medical advice were excluded from the study. Data was collected from the medical records of all included patients using a pre-approved pro forma. Data variables included demographics, patient and hospitalization characteristics and laboratory investigations. Any adverse event during the admission was also noted. Outcome measures included in-hospital mortality and length of stay.

Data Analysis

IBM SPSS statistics 21 was used for data analysis. Chi square test was used for the comparison of categorical variables. Demographic characteristics were identified using descriptive statistics and the odds ratio was calculated to check for any association between mortality and risk factors. In

order to measure the significance of the results, a P-value of <0.05 was considered to be statistically significant.

Results

822 ICU patients were admitted to AKUH from March 2019 to December 2019. 773 (94%) patients met the inclusion criteria and were studied in detail. 504 (65.2%) were males and 269 (34.8%) females; mean age was 57.3 ± 16.6 years. The overall demographics, patient and hospitalization characteristics are presented in **Table 1**. Comorbid conditions like ischemic heart disease (p = <0.001), hypertension (p = <0.001), chronic kidney disease (p = 0.001) and chronic liver disease(p = 0.001) are significantly associated with increased mortality. In addition, mechanical ventilation, septic shock, acute kidney injury, thrombocytopenia and leukocytosis were among a range of hospitalization factors strongly associated with mortality (p = <0.001). Logistic regression analysis was carried out on the risk factors to evaluate their ability to correctly predict the outcome **(Table 2)**. The following risk factors were significant predictors of mortality: sepsis (OR=7.4, P = <0.001), seizures (OR=5.7, , P = 0.004), respiratory failure (OR = 10.6, , P = <0.001), metabolic acidosis (OR= 48.0, , P = <0.001).

Table 3 shows that complications can significantly affect mortality rates as indicated by their high chi square values and P-values of <0.001. Acute liver failure was linked with the highest mortality risk (95.2%) followed by ARDS (90.2%) and septic shock (88.7%).

Discussion

Historically, several attempts have been made to identify the predictors of mortality. However, these studies have been very specific; taking only one or two variables into account.[7,8] Our study looks at several factors to define the various predictors of mortality from the time of admission to the time of discharge. It shows that hypertension, diabetes and ischemic heart diseases are the most prevalent comorbid conditions in our participants. This finding is consistent with previous studies conducted in Asia and particularly, Pakistan.[9,10] It may be attributed to low awareness and limited understanding of these diseases among individuals and thus poor management of these diseases. Moreover, comorbid conditions like chronic kidney disease and chronic liver disease increase the risk of mortality. Several epidemiological studies suggest that even a mild increase in the serum creatinine is correlated with a higher mortality risk.[11] According to a study carried out in 2017, liver cirrhosis is the 13th most common cause of death around the world.[12] The high prevalence of hepatitis B and Hepatitis C in developing countries could be a contributing factor in the majority of chronic liver disease cases in our study population.[13] Mechanical ventilation is also strongly associated with increased mortality due to related complications such as oxygen toxicity, barotrauma and hemodynamic compromise.[14] The ultimate goal of mechanical ventilation should be to provide life-sustaining gas exchange while limiting or minimizing ventilator-induced lung damage. Various ventilation strategies such as low tidal volumes and higher positive end-expiratory pressures (PEEPs) have been used to minimize mechanical ventilation damage and have yielded positive outcomes.[15,16] Larger studies are needed to further validate these results.

Electrolytic imbalances are also frequently found in ICU settings as 37.5% of the patients who died and were included in our study developed electrolyte imbalances during their stay. There can be several reasons for this. A study carried out in 2010 shows medications as one of the possible causes as drugs may interfere with electrolytic absorption, modify hormonal responses influencing homeostasis and directly influence the function of an organ responsible for the preservation of the electrolyte balance.[17]Despite improvements in supportive care, ARDS also contributes to a high

mortality rate. In order to manage ARDS, a number of interventions especially around the use of ventilators have been proposed but their implementation is hampered under recognition of ARDS by clinicians.[18]

The logistic regression model explains 54.7% (Nagelkerke R^2 = 0.547) of the variance in the outcome and correctly classified 85.3% of the cases after adjusting for age, gender and Charlson index. Metabolic acidosis is a commonly occurring acid-base disorder in ICU settings.[19] **Table 2** shows that patients with metabolic acidosis were 48 times more likely to die compared to those without it. Similarly, patients with either sepsis, respiratory failure or seizures were also at greater risk of dying than those without these conditions. Thus, our study clearly shows the importance of closely monitoring patients with the complications mentioned above to avoid adverse outcomes in a critical care setting.

Our results showed that commonly occurring acute kidney injury and septic shock were associated with increased mortality. **Table 3** shows that 88.7% of patients who developed septic shock died of it while 71.7% of those with acute kidney injuries did not survive. These percentages are concerning in a critical care unit setting. Patients surviving an episode of acute kidney injury are most likely to have recurrent episodes which could lead to increased risk of mortality.[20]

Analysis of the cohorts' lab results such as hemoglobin levels, total leukocyte count, platelet count and sodium levels revealed anemia as the most prevalent underlying condition. A recent 2020 study shows that hepcidin overexpression exists in critically ill patients which may lead to decreased utilization of iron and is the most likely cause of anemia in these patients.[21] Another significant finding in our analysis is the insignificance of the charlson comorbidity index as a mortality indicator in our study population. This needs to be explored in detail with further studies based on a larger sample size.

Our findings provide a general indication of the factors determining the prognosis of ICU patients and can offer a basis for the planning of directed treatment of patients admitted to critical care units to help mitigate adverse outcomes.

Our study however has certain limitations as the sample group contained adult population and thus the findings cant be extended or generalized to pediatric population. Moreover, This study is limited to one centre and might not representative of the entire population.

Conclusion

Our study reveals a high mortality rate for critically ill ICU patients at a large tertiary hospital in a developing country. There were frequent adverse events during the patients stay in the ICU and these were in turn associated with increased mortality. We hope this study sets the stage for larger scale studies of the factors affecting patient mortality in an ICU setting in developing countries to deliver improvements in accurate risk stratification and optimal management of ICU patients.

Conflicts of interest

The authors declare that there are no conflicts of interest in this study.

Source of funding

None.

Data Availability: The datasets generated during and/or analysed during the current study are not publicly available but are available from the corresponding author on reasonable request.

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Table 1: Characteristics of patients (n = 773)

Characteristics	**Overall (N = 773)**	**Expired (N = 253)**	**Survived (N = 520)**	**P value**
Mean age (years)	57.3 ± 16.6	51.4 ± 18.9	60.1 ± 14.6	<0.001
Gender				0.524
Male	504 (65.2)	161 (64%)	343 (66%)	
Female	269 (34.8)	92 (36%)	177 (34%)	
Comorbid conditions				
Charlson score	3.08 ± 2.1	2.94 ± 2.4	3.14 ± 2.0	0.267

Diabetes Mellitus	351 (45.4%)	98 (38.7%)	253 (48.7%)	0.009
Hypertension	440 (56.9%)	107 (42.3%)	333 (64%)	<0.001
Ischemic heart disease	287 (37.1%)	48 (19%)	239 (46%)	<0.001
Chronic Kidney Disease	84 (10.9%)	41 (16.2%)	43 (8.3%)	0.001
Chronic Liver Disease	26 (3.4%)	16 (6.3%)	10 (1.9%)	0.001
Chronic Obstructive Pulmonary Disease	52 (6.7%)	12 (4.7%)	40 (7.7%)	0.125
Hospitalization factors				
Mechanical Ventilation	152 (19.7%)	130 (51.4%)	22 (4.2%)	<0.001
Hyponatremia	265 (34.4%)	82 (32.4%)	183 (35%)	<0.001

Leukocytosis	370 (47.9%)	177 (70.0%)	192 (37%)	<0.001
Thrombocytopenia	244 (31.6%)	163 (64.5%)	81 (15.5%)	<0.001
Anemia	456 (59.1%)	213 (84.2%)	244 (47%)	<0.001

Table 2: Frequency of adverse events in critically ill patients (N =773)

Complication (n)	**Outcome**		**$\chi 2$**	**P-value**
	Alive %	**Expired %**		
Septic shock **YES (133)** **NO (640)**	15 (11.3) 505 (78.9)	118 (88.7) 135 (21.1)	228.74	<0.001
Hospital Acquired Infections **YES (42)** **NO (729)**	12 (28.6) 506 (69.4)	30 (71.4) 223 (30.6)	30.042	<0.001
Acute Kidney Injury **YES (159)** **NO (612)**	45 (28.3) 473 (77.3)	114 (71.7) 139 (22.7)	137.37	<0.001
Acute Liver Failure **YES (21)** **NO(752)**	1 (4.8) 519 (69)	20 (95.2) 233 (31)	38.31	<0.001
Electrolyte imbalance **YES (132)** **NO (641)**	37 (28) 483 (75.4)	95 (72) 158(24.6)	111.32	<0.001
ARDS **YES (61)** **NO (712)**	6 (9.8) 514 (72.2)	55 (90.2) 198 (27.8)	99.22	<0.001

Table 3: Odds of mortality in critically ill patients (N= 773)

Risk Factor	OR	Confidence interval (95%)		P value
		Lower	Upper	
Sepsis	7.443	3.3	16.7	<0.001
Metabolic acidosis	48.0	24.3	94.8	<0.001
Respiratory failure	10.6	4.4	25.6	<0.001
RTI	1.1	0.5	2.6	0.790
Stress ulcers	10.5	0.9	127.2	0.064
Seizures	5.7	1.7	19.0	0.004

Nagelkerke $R^2 = 0.547$