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ORIGINAL RESEARCH CORONA EXPERIENCE

A retrospective, observational study to assess the intermediate-term clinical outcomes of COVID-19 patients in a tertiary hospital in Khyber Pakhtunkhwa, Pakistan

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ABSTRACT

Background & Objective: There is limited data from lower middle-income countries to describe the outcomes of COVID-19 and the prevalence of patients requiring critical care. We aim to assess and compare the demographics, clinical course and mortality of COVID-19 patients admitted to the intensive care unit (ICU) and those admitted to the specialized COVID unit (SCU).

Methodology: A single-center, retrospective, observational study in which all patients admitted to Lady Reading Hospital (LRH), Peshawar (Pakistan) with laboratory-confirmed COVID-19 from March 25, 2020 to December 31, 2021 were included. Study data were retrieved through the Pakistan Registry of Intensive Care (PRICE).

Results: Of 699 patients, 448 were critically ill, and 251 did not require ICU admission. Of those admitted to ICU, 61.8% were male, with a median age of 55 y. ICU mortality was significantly higher (P = 0.001) among those on IMV and those aged 60 y; whereas 68.9% of the non-ICU patients were male, with a median age of 57 y. While the median duration of hospitalization was significantly longer (P = 0.001), the chances of recovery were substantially better (P = 0.001) compared with the critically ill population.

Conclusion: The major risk factors contributing to the increased mortality in COVID-19 patients are age and the requirement for IMV.

Keywords: COVID-19; Intensive Care Unit; Lower Middle Income Country; Mortality; SARS-CoV-2

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1. INTRODUCTION

Over the last few years, the world has faced one of the most challenging times recorded. Coronavirus Disease (COVID-19) emerged from Wuhan, China, in December 2019,[1] and rapidly enveloped several countries causing a pandemic.[2] The virus responsible was isolated and

identified as the seventh member of the coronavirus family, Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2).[3] The outbreak raised concerns regarding the incubation period, transmission, and clinical course of the disease. The incubation period was estimated to be 5−6 days,[4] while droplet and airborne communications were considered critical routes of spread.[5] COVID-19 is a potentially fatal disease that manifests with varying symptoms ranging from being asymptomatic to the development of severe pneumonia with acute respiratory distress syndrome (ARDS), shock, and multi-organ failure.[6] The most commonly observed signs were dyspnea, hypoxemia, and acute respiratory failure. The disease progresses to a critical stage 7–13 days after symptom onset and patients requiring intensive care have a higher mortality rate.[7]

The first COVID-related death in Pakistan was reported in March 2020.[8] The increasing number of cases that followed, exerted significant pressure on the healthcare system to accommodate and provide care to the critically ill.[9] It also highlighted the importance of adequate intensive care resources for patient management.[9,10] As of March 2022, 489 million cases and over 6 million deaths had been documented globally,[11] with Pakistan recording 1,524,973 confirmed cases and 30,359 reported deaths.[12]

Although extensive efforts have been made at a global scale to better understand the high transmissibility rate of the virus and its clinical implications; there is scarce data from lower middle-income countries regarding the outcomes and clinical course of patients admitted with COVID-19. Thus, the primary objective of this study was to determine the outcomes of all patients admitted to a tertiary care hospital with laboratory-confirmed COVID-19. Mortality was defined as death during the intensive care unit (ICU) or specialized COVID unit (SCU) stay. The secondary objective was to map the clinical course and compare the characteristics of the patients who were shifted to the ICU from the SCU.

2. METHODOLOGY

2.1. Study design and participants

This was a single-center, retrospective, observational study carried out at Lady Reading Hospital (LRH), Peshawar, Pakistan. It is an 1800-bed tertiary care hospital with 30 ICU beds and 220 SCU beds. During the study period, from March 25, 2020 to December 31, 2021, 699 patients were enrolled. The patient population included individuals of all ages with laboratory-confirmed SARS-CoV-2 virus recruited from four ICUs and the SCU. The infection was confirmed using reverse transcription-polymerase chain reaction (RT-PCR) analysis of nasopharyngeal swab samples (NPSW). The approval was sought by the Ethical Review Committee of LRH before the commencement of the study.

2.2. Data collection

Data of admitted COVID-19 patients, including demographics, outcomes; and clinical characteristics comprising age, gender, comorbidities, need for mechanical ventilation and requirement of antibiotics, were reviewed.

To efficiently carry out the objectives of the study, data were retrieved from the Pakistan Registry of Intensive Care (PRICE), which is based on the Network for Intensive Care Systems and Training (NICST) registry. PRICE is a cloud-based web portal that commenced in 2017. It facilitates the collection of real-time granular healthcare data of patients admitted to ICUs that form part of a network. This creates an opportunity for critical care setups to evaluate and improve the quality and delivery of patient care, along with creating opportunities for research.[13] PRICE is operational in all four provinces of Pakistan, including Islamabad.

2.3. Statistical analysis

All statistical analyses were performed using STATA/IC Mac version 16.1 (StataCorp LP, Texas, USA). For descriptive analysis, mean ± SD (standard deviation) was computed for quantitative variables; whereas the percentages were calculated for qualitative variables. Continuous data were tested for normality using the Shapiro-Wilk normality test for those variables that were not normally distributed. The non-parametric Wilcoxon rank-sum test (Mann–Whitney U-test) and the chi-square test were used to compare continuous and nominal data, respectively. Statistical significance was set at a $P \leq 0.05$.

3. RESULTS

The cohort included 699 patients, with 342 (48.9%) admitted to ICU and 357 (51.1%) admitted to SCU. Of the SCU patients 106 were transferred to the ICU, bringing the total to 448 ICU patients. Of these, 143 (31.9%) were discharged alive from the ICU, and 72 (16.1%) went home clinically improved. Out of the 251 patients admitted to the SCU, 173 (68.9%) survived and 68 (27.1%) expired (Figure 1).

Table 1 reports the clinical characteristics of the 448 critically ill patients admitted with confirmed COVID-19, during the study period. The cohort comprises 277 (61.8%) male and 171 (38.2%) female patients, with no significant difference in mortality between the two groups (P = 0.394) (Figure 2). The median age was 55 y (IQR, 45-65), with a significantly higher mortality rate observed in patients with a median age of 60 y (60 [IQR,

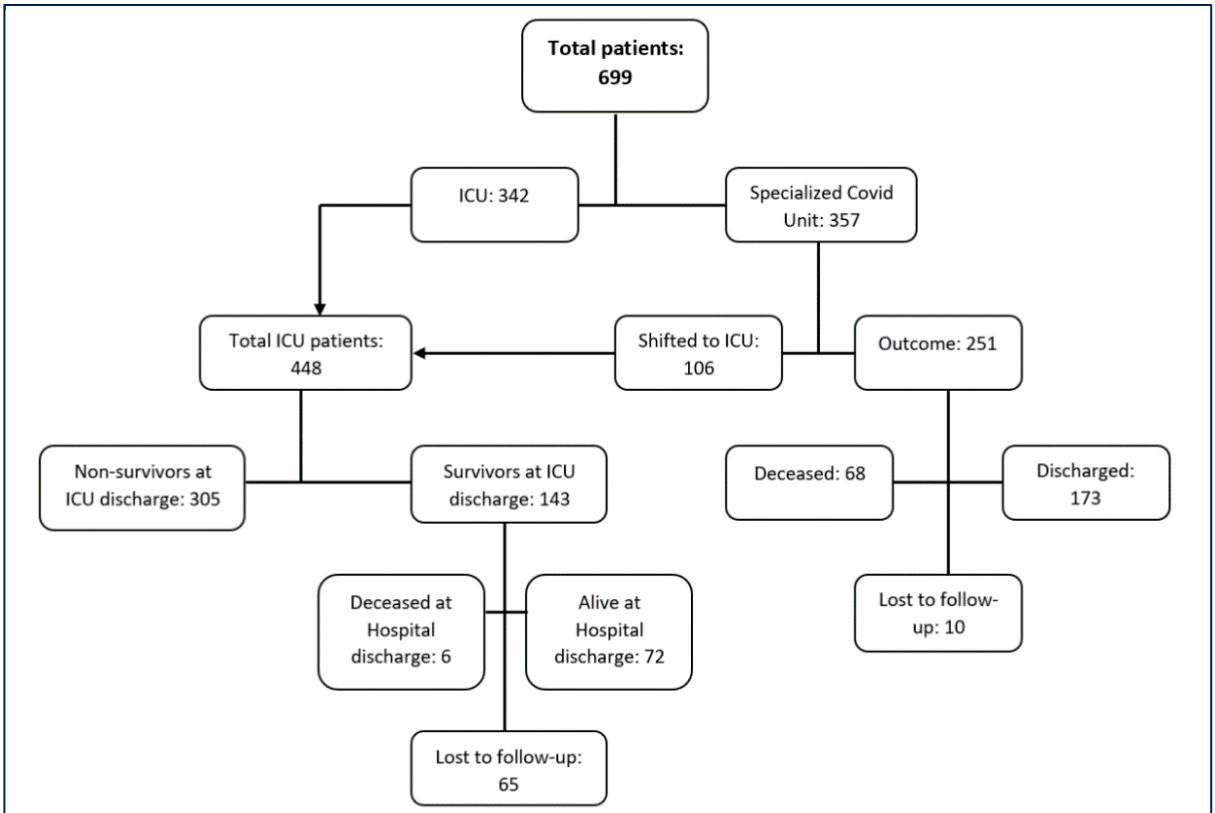

Figure 1: Distribution and follow-up of the patients

50-65] vs 53 [38-60] P < 0.001). Majority of patients presented with at least one co-morbidity (n = 243, 54.2%), with hypertension being the most prevalent (n = 168, 37.5%), followed by diabetes (n = 75, 16.7%) (Figure 3). During the first hour of ICU admission, 322 patients (86.1%) required invasive mechanical ventilation, and the number of patients who did not survive was significantly higher than those who did [258 (94.2%) vs 64 (64%); P < 0.001]. Out of the 52 patients receiving non-invasive ventilatory support and 82 patients on cardiovascular support, it was observed that the number of patients who were discharged alive was significantly higher than those who expired; [36 (36%) vs 16 (5.8%); P < 0.001] and [37 (25.9%) vs. 45 (14.8%); P + 0.006], respectively. The median length of ICU stay was 4 days (IQR, 2−7), and in-ICU mortality was 68.1%.

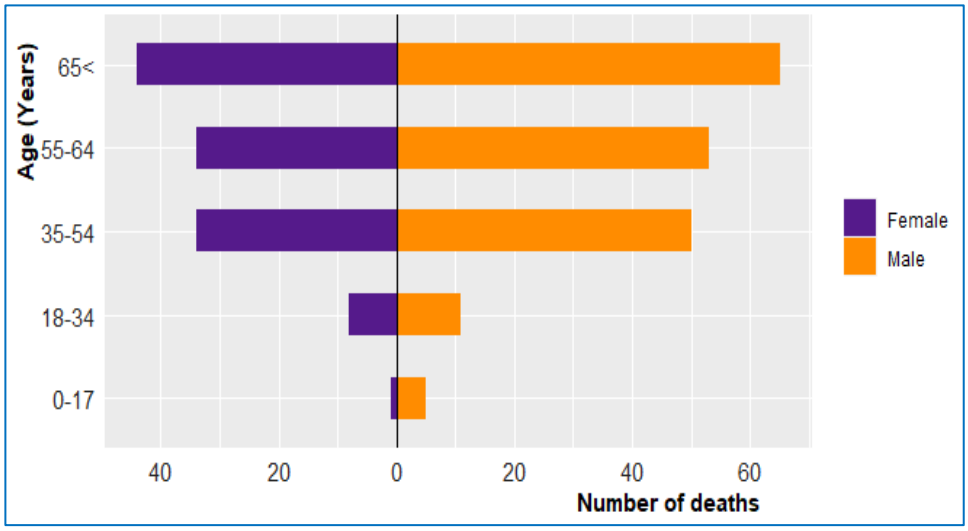

Figure 2: Comparison of the number of deaths of patients with confirmed COVID-19

Table 1: Characteristics of COVID-19 patients admitted to ICU, according to in-ICU death

Characteristics	Patients admitted to ICUs n = 448	Survivors at ICU discharge n = 143	Non-survivors at ICU discharge n = 305	P -value*
Age, y, median (Q1, Q3)	55 (45-65)	53 (38-60)	60 (50-65)	< 0.001*
0−17	7 (1.6)	1 (0.7)	6 (2.0)	
18−34	50 (11.2)	31 (21.7)	19 (6.2)	< 0.001*
35−54	136 (30.4)	52 (36.4)	84 (27.5)	
55−64	122 (27.2)	35 (24.5)	87 (28.5)	
> 64	133 (29.7)	24 (16.8)	109 (35.7)	
Gender				
Male *n (%)*	277 (61.8)	93 (65.0)	184 (60.3)	0.394
Female *n (%)*	171 (38.2)	50 (35.0)	121 (39.7)	
Comorbidities (Top 12), n (%)				
Hypertension	168 (37.5)	48 (33.6)	120 39.3)	0.283
Diabetes	75 (16.7)	33 (23.1)	42 (13.8)	0.020*
Type 2 Diabetes	74 (16.5)	10 (6.99)	64 (21.0)	< 0.001*
Depression	26 (5.8)	14 (9.79)	12 (3.93)	0.024*
Cardiovascular disease	11 (2.5)	2 (1.4)	9 (2.95)	0.515
Angina	9 (2.01)	2 (1.4)	7 (2.30)	0.725
Type 1 Diabetes	7 (1.6)	-	7 (2.30)	0.102
Asthma	3 (0.7)	1 (0.7)	2 (0.66)	1
Renal failure (mild)	3 (0.7)	1 (0.7)	2 (0.66)	1
Respiratory disease (mild)	2 (0.5)	1 (0.7)	1 (0.33)	0.537
Congestive heart failure	1 (0.2)	-	1 (0.33)	1
Renal failure (moderate to severe)	1 (0.2)	1 (0.7)	-	0.319
No comorbidities**	205 (45.8)	75 (52.4)	130 (42.6)	0.065
Organ support at the first hour of admission n (%)				
Invasive respiratory support	322 (86.1)	64 (64.0)	258 (94.2)	< 0.001*
Non-invasive respiratory support	52 (13.9)	36 (36.0)	16 (5.8)	< 0.001*
Prone ventilation	96 (25.5)	37 (29.1)	59 (23.6)	0.298
Cardiovascular support	82 (18.3)	37 (25.9)	45 (14.8)	0.006*
Renal replacement therapy	16 (3.7)	2 (1.45)	14 (4.76)	0.154
Antibiotics at admission, n (%) Prescribed at admission	442 (98.7)	140 (97.9)	302 (99.0)	0.606
Length of ICU stay in days, median (Q1, Q3)	4 (2-7)	5 (3-8.5)	3 (2-7)	< 0.001*

**Chi-square (categorical variables) or Mann–Whitney (continuous variables) tests (α = 0.05); **Patients had no comorbidity*

Table 2 compares patients' demographics, comorbidities, and outcomes in the ICU with those in the SCU. Similar trends were observed where the majority of patients (68.9%) were male with a median age of 57 y (IQR, 45−65), and the most commonly seen comorbidities were hypertension (67.2%) and diabetes (57.3%). It was noticed that a significantly higher number of patients with no known comorbidities were admitted to the ICU than to the SCU; 45.8% vs 17.2% (P < 0.001). The mortality rate of the SCU was significantly lower; 28.2% vs 81.2% (P < 0.001), while the median length of stay was significantly longer (P < 0.001).

4. DISCUSSION

The rapidly escalating population affected by COVID-19 created an enormous burden on hospital systems worldwide. A tertiary care hospital in New York, USA converted all available operating rooms and post-anesthesia care units to ICUs to accommodate the

Table 2: Demographics, medical history, and outcome of admitted patients with confirmed COVID-19

Characteristics	ICU patients n = 448	SCU patients** n = 241	P value*
Age at admission (y) Median (Q1−Q3)	55 (45−65)	57 (45−65)	0.518
Gender, n (%)			
Male	277 (61.8)	166 (68.9)	0.079
Female	171 (38.2)	75 (31.1)	
Comorbidities, n (%)			
Hypertension	168 (37.5)	162 (67.2)	<0.001*
Diabetes	75 (16.7)	138 (57.3)	<0.001*
Type 2 Diabetes	74 (16.5)	-	<0.001*
Depression	26 (5.8)	31 (12.9)	0.002*
Cardiovascular disease	11 (2.5)	2 (0.8)	0.238
Angina	9 (2.01)	-	0.031*
Type 1 Diabetes	7 (1.6)	-	0.102
Asthma	3 (0.7)	18 (7.5)	<0.001*
Renal failure, Mild	3 (0.7)	7 (2.9)	0.038*
Respiratory disease, Mild	2 (0.5)	1 (0.4)	1
Congestive heart failure	1 (0.2)	8 (3.3)	0.001*
Hepatic disease, Mild	-	2 (0.8)	0.122
No comorbidities ***	205 (45.8)	42 (17.2)	<0.001*
Outcome at hospital discharge, *n (%)*	**n = 383**	**n = 241**	
Alive	72 (18.8)	173 (71.8)	0.001*
Deceased	311 (81.2)	68 (28.2)	
Length of stay in the hospital (days) Median (Q1−Q3)	n = 338 4 (2−8)	n = 241 6 (4−10)	<0.001*

**Chi-square (categorical variables) or Mann–Whitney (continuous variables) tests (α=0.05)*
***Patients who expired while in the SCU or were discharged home.*
****Patients had none of the listed comorbidities*

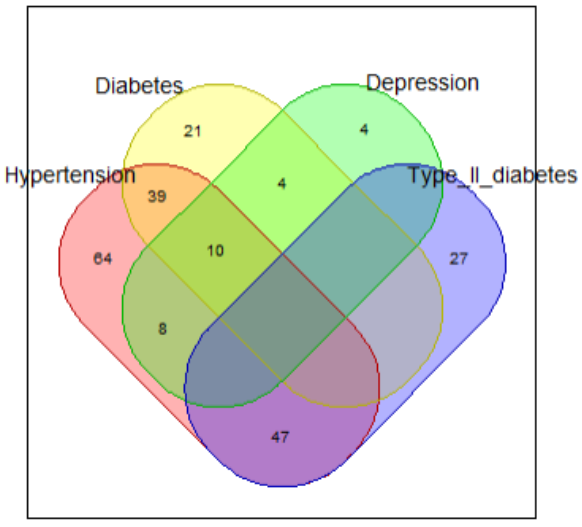

Figure 3: Distribution of patients with confirmed COVID-19 among the top 4 comorbidities

increasing patient load.[14] Our study showed 305 (68.1%) patients expired in the ICU; this data is similar to a case series in the USA, where the mortality rate was 67%.[15] The common characteristics contributing to high mortality in both studies were age and the requirement for mechanical ventilation. The mean age in the USA was 70 y, while the median age of 60 y (IQR, 50−65) was observed in LRH. The results are coherent with other studies conducted during the early phase of the pandemic, reporting a 61.5% mortality rate in China.[9]

A previous study shows that males are more likely than females to contract severe SARS-CoV-2 infection.[1] The higher susceptibility could be attributed to the fact that several genes responsible for immunity are located on the X chromosome, making females more resistant to viral disease.[16] However, our study showed no significant difference between males and females (P 0.394) in severity, need for critical care, and mortality, with 60.3% male and 39.7% female ICU non-survivors.

Among the critically ill COVID-19 patients included in the study, the highest mortality (35.7%) was noted in those over 64 y of age. Patients with a median age of 60 y (IQR, 50−65) had a significantly higher mortality rate than those aged 53 y (IQR, 38−60). This trend has been observed in nationally and internationally conducted studies where the median age was 64.5 y (IQR, 54−70) and 56 y (IQR, 46−67), respectively.[17,18] Data from this study confirms a decrease in survival chances as age increases. The cohort included seven patients who were less than 17 y old, out of which 86% were deceased at ICU discharge. Previously collected data shows that while children are not severely affected and do not require critical care, infants can have a more severe presentation.[19] In this data set, the difference between infants and children has not been defined. There was no significant difference in the median age of patients (0.518) admitted to the SCU (57 y [IQR, 45−65]) and those admitted to intensive care 55 y [IQR, 45−65]), with both groups comprising adults belonging to older age groups.

In this cohort of patients admitted to the ICU, 54.2% presented with at least one comorbidity, a comparatively high number than data retrieved from Wuhan (23.7%)[6]. Hypertension was the most common underlying disease followed by diabetes, as observed in a previously conducted international study.[20] The data from this study highlights that a significant proportion of patients with pre-existing Type II diabetes did not survive ($P < 0.001$). A compromised immune response in diabetics, including chronic inflammation and impaired cell-mediated immunity, could be contributing factors to the severity of disease.[21] Further studies from LMICs are required to characterize the severity and risk of death among patients with different comorbidities.

Analysis of treatment modalities showed that the administration of antibiotics had no significant difference in the clinical outcome. For patients receiving organ support, 94.2% of patients who expired in the ICU were on invasive respiratory support, indicating a higher mortality rate in intubated patients. Of the 13.9% of patients receiving non-invasive ventilation, 69.2% were discharged alive from the ICU. However, due to limited data, the study does not describe the heterogeneity in number with other studies on mechanical ventilation.

18.3% of patients needed cardiovascular support including inotropes and vasopressors. Renal replacement therapy (dialysis) was given to 3.7% of patients in our cohort, which is relatively low compared to the results of a study conducted in China which revealed the necessity of RRT in 17% of patients.[7] Patients admitted to the SCU had a significantly better prognosis (P), where 71.8% of patients were discharged home alive. A study conducted in the geriatric wards in Paris reported the in-hospital mortality as 31%.[22] Their population comprised the elderly (70 y or older) which could be a factor for the higher mortality rate in comparison to our sample of patients with a median age of 57 y.

Analysis of the length of stay shows that ICU non-survivors had a significantly shorter length of stay. This, in turn, creates a significant difference in the median length of hospital stay when compared to the patients admitted to the SCU. The quick deterioration and severity of critical patients can explain the short length of stay. This study also shows that the longer length of hospital stay for patients admitted to the SCU can be due to the significant prevalence of co-existing clinical illnesses (82.6%).

Our study shows that the overall mortality rate is higher than the survival rate for patients admitted to the ICU. In reference with the ISARIC clinical data reporting,[23] this study assesses the outcomes of patients admitted to non-intensive care units, which can be considered as a strength since limited data is available otherwise.

5. LIMITATIONS

A limitation of this study is that it was a single-center study with few patients, and we cannot determine that the results are representative of our population. Furthermore, there is no information on the type of COVID-19 variants associated with higher mortality. As the data is minimal, further multi-center studies are required to define more risk factors and their broader application to critically ill COVID patients.

6. CONCLUSION

The results of our study suggest that the need for invasive mechanical ventilation significantly increases the mortality rate in patients admitted to the intensive care unit. The other main factor that influenced the small number of survivors was increasing age. Patients who were aged 64 y or older were more at risk of developing critical illness leading to increased mortality compared to the younger population. Patients that were discharged from the specialized COVID ward had a lower mortality rate but a longer length of hospital stay.

7. Data availability

The numerical data generated during the course of this study is available with the authors and can be available on a reasonable request.

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Pakistan Registry of Intensive CarE (PRICE): Expanding a lower middle-income, clinician-designed critical care registry in South Asia. Journal of the Intensive Care Society 2018 0 (0) 1–6, and Beane A et al. Establishing a critical care network in Asia to improve care for critically ill patients in low-and middle-income countries. Critical Care. 2020 Oct 15;24 (1).

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10. Conflict of Interest

All authors declare no competing interest.

11. Authors contribution

SA conceptualized and designed the study and had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. SA and AH contributed to the writing of the report. AH contributed to the critical revision of the report. AH, DG and MS contributed to the statistical analysis. All authors contributed to data acquisition, data analysis, or data interpretation, and reviewed and approved the final version.

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