ORIGINAL ARTICLE

Clinical Features and In-hospital Outcomes in COVID-19 Patients: An observational study from Tertiary Care Hospital Karachi, Pakistan

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ABSTRACT

Objective: The aim of this study is to determine the demographics, comorbidities, presenting complaints, laboratory parameters, and factors associated with patients' outcomes of the hospitalized patients with COVID-19 from one of the largest teaching institute of Karachi.

Methodology: This was single center retrospective study conducted in Liaquat National Hospital Karachi, Pakistan. Records of all the COVID-19 positive patients who were hospitalized during April, 2020 to June, 2020 were studied. The diagnosis of COVID-19 was confirmed based on guidelines issued by WHO and standard laboratory test of real time PCR on a nasopharyngeal swab.

Results: Total 208 records were completely retrieved and analyzed. Overall age of study participants was 54.60 ± 13.77 years. Most of the admitted patients were males (68.3%). Majority of the patients were symptomatic (94.2%) and frequent symptoms were fever(75%), shortness of breath (58.7%) and cough (54.3%). Out of 252 patients, In-hospital mortality was observed on approximately quarter of the analyzed sample (26%) patients. Disease severity, presence of comorbid, higher hospital stay, NLR ratio and CRP levels were associated with significantly higher odds of mortality. On multivariable analysis, increasing age (aOR=1.18, 95% CI: 1.08 - 1.29), ICU admission (aOR=43.44, 95% CI: 5.49 - 343.8) and increasing creatinine (aOR=1.55, 95% CI: 1.00 - 2.39) were also independent predictors of mortality.

Conclusion: The current study provides evidence that increasing age and ICU admission and increasing age were chief predictors of mortality in our settings. Presence of comorbidity and initial diseases severity are also important factors to triage patients.

Keywords: COVID-19, pandemic, intensive care unit, mortality, Karachi,

INTRODUCTION

The Coronavirus disease was first reported in Wuhan, China in December 2019. It is caused by SARS-CoV-2, a novel member of the corona virus family known to cause respiratory illnesses. Since then, it has been declared a pandemic affecting more than 14 million worldwide in more than 200 countries and resulting in 612, 054 deaths as of 22 July 2020^{1.}

In Pakistan, first case was reported on 26th February 2020 and over months the reported number of cases have increased exponentially crossing 250,000 by mid of July 2020. The rate of infection in Karachi has exceeded other part of country because of its dense population and it has been reported up to 25% of all the national cases2. This has caused a considerable burden on the already fragile health care system of the country.

COVID-19 spectrum of ranges asymptomatic cases to critical illness with Sepsis and multi organ dysfunction. A substantial number of patients require hospitalization sometimes for prolonged periods with significant complications, morbidity and mortality³⁻⁷.

This study aimed to define the epidemiological and clinical characteristics, treatment given and factors associated with patients' outcomes of patients with proven COVID-19 disease admitted at Liaquat National Hospital,

one of the biggest tertiary care hospitals in Karachi, the epicenter of the outbreak in Pakistan. Having a comprehensive review of these characteristics will help clinicians develop a better understanding of the disease and also benefit in management, especially when locally reported literature in this regard is sparse.

METHODOLOGY

This was single center retrospective study conducted in Liaquat National Hospital which is one of the largest tertiary care hospitals in Karachi. The study was conducted after acquiring approval from Hospital Ethics Committee. Records of all the COVID-19 positive patients hospitalized during April-2020 to June-2020 were studied. The diagnosis of COVID-19 was confirmed based on guidelines issued by World Health organization and standard laboratory test of real time polymerase chain reaction test on a nasopharyngeal swab. The study was reviewed and approved by Hospital Ethical Committee. The data was retrieved from patients' medical record file.

Patients' demographics including age and gender, clinical features such presenting symptoms, presence other chronic illness, disease severity, biomarkers upon patients admission including hemoglobin, neutro-lymphocyte ratio (NLR), platelets, creatinine, sodium, potassium, C-reactive

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protein (CRP) levels, D-dimer, ferritin, Lactic acid dehydrogenase (LDH), admitting ward and smoking history were recorded from their medical files.

Patients were categorized as mild, moderate, severe and critical upon their admission in accordance with the criteria suggested by Wu et al8. Patients were considered mild if they had mild clinical symptoms, no indications of pneumonia on radiological investigation. Patients were laballed as moderate with appearance of symptoms such as cough, dyspnea, fever and positive radiological signs for pneumonia. Severe classification was done when there was respiratory distress with ≥ 30 breaths per minute; PaO2 / FiO2 ≤ 300 mmHg or resting oxygen saturation in air ≤93 %. Patients identified as critical if there was need of mechanical ventilation or any organ failure which required admission intensive care unit. Primary study outcome was in-hospital mortality while secondary study outcomes included ICU stay, mechanical ventilation requirement and occurrence of complications.

Retrieved data was entered into IBM SPSS (version 21) for statistical analysis of data. Categorical variables were presented as frequency and percentage. Continuous variables with Gaussian distribution were presented as mean ± standard deviation whereas non-normally distributed variables were summarized as median (IQR: inter-quartile range). Shapiro-Wilk test was used Chisquare or Fisher-exact test was used to compare study variables between survivors and non-survivors. Continuous variables were compared among two using either independent t-test or Man-Whitney U test depending on the normality of the data. Association of variables with inhospital was determined through binary logistic regression. Univariable logistic regression was applied to compute odd ratio and their 95% confidence interval. Variables that had p<0.25 were considered to be entered in the final effect model. Statistical significance on final effect model defined for p<0.05.

RESULTS

Patients Characteristics: Total 252 records were reviewed. Out of 252, 18(7.14%) patients left against medical advised and 26 (10.31%) patients were excluded because of missing data. Therefore, total 208 records were completely retrieved and analyzed. Overall age of study participants was 54.60 ± 13.77 years. Most of the admitted patients were (68.3%). Almost all of the infected patients had no history of smoking (96.6%). More than half of the patient effected with COVID-19 had comorbidity (68.8%). The most frequent comorbidity was hypertension (48.1%) followed by diabetes (35.6%), chronic kidney disease (6.7%) and asthma (6.7%) and any malignancy (1.9%). Majority of the patients were symptomatic (94.2%) and the commonest symptom was fever 75%) followed by shortness of breath (58.7%), cough (54.3%), myalgia (9.1%), diarrhea (9.1%), sore throat (8.2%), weakness (5.8%), vomiting (4.3%), loss of appetite (2.9%) and abdominal pain (1.9%). Most of the patients admitted through emergency (87%) while 13% were elective admissions. Nearly one-fourth of the patients presented in their mild stage of the disease (26%) whereas some presented as moderate (33.3%) and severe (32.7%) diseases and few presented with critical disease (8.2%).

Nearly half of the patients were admitted to ICU (43.8%). In-hospital mortality was observed on 26% patients. Frequency of mortality in different units is presented in Figure 1.

Comparison of patients' characteristics between survived and non-survived patients: Comparison of participants' characteristics is depicted in Table 1. Gender distribution (p=0.769),smoking status symptomatic presentation (p=0.192), were not significantly different among survivors and non-survivors. Mean age for survived and non-survived patients 52.03 ± 13.24 and 61.91 ± 12.67. Average age of patient who didn't survived was significantly high as compared to those who were alive (p<0.001). Comorbidities were significantly high among expired patients as compared to survivors (85.2% vs 63%) (p=0.002). The frequency comorbidity of diabetes was significantly higher for non-survivors as compared to survivors (55.6% vs 28.6%) (p<0.001). All of malignant patients expired (p<0.001). Expired patients significantly higher in proportion who experienced shortness of breath as a disease symptom as compared to non-survivors (75.9% vs 52.6%) (p=0.003). Proportion of patients with severe and critical presentation at the time of admission was significantly higher in expired patients as compared to alive (p<0.001). Expired patients included higher proportion of ICU admissions as compared patients who survived (85.2% vs 29.2%) (p<0.001).

Table 2 is displaying comparison of length of stay and laboratory investigation between alive and dead patients. Expired patients had significantly higher median longer length stay (p=0.020), higher neutrophil lymphocyte ratio (p=0.007), creatinine (p=0.002), CRP levels (p<0.001), Ddimer (p<0.001), serum ferritin (p=0.002) and lactate dehydrogenase (p<0.001).

Univariable and multivariable association of factors with in-hospital mortality: Univariable and multivariable associations of risk factors with mortality are presented in Table 3: On univariable analysis, it was identified that increasing agedeath (OR= 1.06, 95% CI: 1.03 - 1.09), presence of commodity (OR= 3.38, 95% CI: 1.49 - 7.66), ICU stay (OR= 16.26, 95% CI: 6.84 - 38.69), increasing length of stay (OR=1.06, 95% CI: 1 - 1.12), increase in NLR (OR= 1.08, 95% CI: 1.02 - 1.15), CRP levels (OR= 1.05, 95% CI: 1.02 - 1.08) were associated with the higher odds of death. The degree of severity on patient presentation was also associated with higher odds death. Patients who presented in severe condition were significantly more likely to be non-survivors as compared to those who had mild condition when they presented (OR= 21.78, 95% CI: 4.91 -96.73). The significantly higher odds of death were also observed in patients whose condition were severe at the time of presentation as compared to those who were mild when presented (OR= 21.78, 95% CI: 4.91 - 96.73). The likelihood of death was also higher in patients who presented with critical condition (OR= 121.33, 95% CI: 18.44 - 798.35) as compared to mild disease patients (Table 3).

Final multivariable was built with age, smoking status, comorbid, being symptomatic, severity status on presentation, ICU stay, overall length of stay, hemoglobin levels, neutron-lymphocyte ratio, creatinine, potassium, CRP levels. Age (aOR= 1.18, 95% CI: 1.08-1.29), ICU stay

(aOR= 43.44, 95% CI: 5.49-343.8) and creatinine (aOR= 1.55, 95% CI: 1-2.39) were independent predictors of death

on final effect model after adjusting the model for other covariates (Table 3).

Table 1:Distribution of participants' characteristics

	Total	Alive	Expired	P-value		
Participants' Characteristics	(n=208)	(n=154)	(n=54)			
Age (in years)#	54 ± 13.77	52.03 ± 13.24	61.91 ± 12.67	**<0.001		
Gender; n(%)						
Male	142(68.3)	106(68.8)	36(66.7)	0.769		
Female	66(31.7)	48(31.2)	18(33.3)	0.769		
Smoking status; n(%)		•		<u>.</u>		
Former	4(1.9)	2(50)	2(50)			
Current	3(1.4)	1(33.3)	2(66.7)	†0.103		
Never	201(96.6)	151(75.1)	50(24.9)			
Comorbid; n(%)	, ,			•		
Yes	143(68.8)	97(63)	46(85.2)	**0.000		
No	65(31.2)	57(37)	8(14.8)	**0.002		
Specific comorbidities; n(%)	, ,	1 , ,	, , ,	•		
Diabetes	74(35.6)	44(28.6)	30(55.6)	**<0.001		
Hypertension	100(48.1)	68(44.2)	32(59.3)	0.056		
Chronic kidney disease	14(6.7)	9(5.8)	5(9.3)	†0.363		
Asthma	14(6.7)	12(7.8)	2(3.7)	10.527		
Malignancy	4(1.9%)	0(0)	4(7.4%)	**<0.001		
Symptomatic; n(%)	1(11070)	1 0(0)	1 ((::,,,,			
Yes	196(94.2)	143(92.9)	53(98.1)			
No	12(5.8)	11(7.1)	1(1.9)	 †0.192		
Specific symptoms; n(%)	.=(0.0)	1()	1 .()			
Fever	156(75)	113(73.4)	43(79.6)	0.361		
Shortness of breath	122(58.7)	81(52.6)	41(75.9)	**0.003		
Cough	113(54.3)	87(56.5)	26(48.1)	0.289		
Myalgia	19(9.1)	15(9.7)	4(7.4)	†0.786		
Diarrhea	19(9.1)	16(10.4)	3(5.6)	†0.413		
Loss of appetite	6(2.9)	5(3.2)	1(1.9)	†1.00		
Sore throat	17(8.2)	15(9.7)	2(3.7)	†0.248		
Abdominal pain	4(1.9)	3(1.9)	1(1.9)	†1.00		
Vomiting	9(4.3)	7(4.5)	2(3.7)	†1.00		
Weakness	12(5.8)	8(5.2)	4(7.4)	†0.514		
Severity on presentation; n(%)	12(0.0)	J 0(0.2)	ן די ו ודי	10.014		
Mild	54(26)	52(33.8)	2(3.7)			
Moderate	69(33.2)	62(40.3)	7(13)			
Severe	68(32.7)	37(24)	31(57.4)	**<0.001		
Critical	17(8.2)	3(1.9)	14(25.9)			
ICU stay; n(%)	11(0.2)	[J(1.3)	17(20.3)			
Yes	91(43.8)	45(29.2)	46(85.2)			
No	117(56.2)	109(70.8)	8(14.8)	**<0.001		
	117 (30.2)	109(70.0)	0(14.0)			
Complication; n(%) Yes	120(57.7)	73(47.4)	47(87)			
				<0.001		
No	88(42.3)	81(52.6)	7(13)			

^{†:}Fisher-exact test is reported; #: age is presented at mean ± standard deviation, ICU=intensive care unit, *Significant at p<0.05, **Significant at p<0.01

Table 2:Laboratory investigations upon patients' admission

Table 2.Laboratory investigation	nis upon patients aumission				
	Total	Alive	Expired	P-value	
	(n=208)	(n=154)	(n=54)	1 -value	
Hospital stay‡	7 (5 – 12)	7 (5 - 11.25)	9.50 (5.75 - 13.25)	*0.020	
Hemoglobin levels‡	12.45 (10.83 – 13.7)	12.7 (10.84 - 13.80)	11.90 (10.63 - 13.23)	0.110	
NLR‡	4 (2.64 – 7.06)	3.8 (2.46 - 5.50)	4.86 (3.33 - 8.60)	**0.007	
Platelets‡	209.50 (150 – 286.75)	212 (150 - 282.75)	199.50 (148 - 291)	0.853	
Creatininelevels‡	0.99 (0.80 – 1.3)	0.93 (0.80 - 1.17)	1.21 (0.89 - 1.87)	**0.002	
Sodiumlevels‡	138 (136 – 141)	138 (136 - 141)	138 (134 - 141)	0.538	
Potassiumlevels‡	3.8 (3.6 – 4.1)	3.80 (3.60 - 4.10)	3.90 (3.46 - 4.35)	0.415	
CRP levels	12.36 (2.46 – 24.50)	9.53 (1.96 - 21.69)	21.27 (7.23 - 28.34)	**<0.001	
D dimer‡	1.34 (0.69 – 5.16)	1.01 (0.58 - 3.57)	3.58 (1.13 - 9.74)	**<0.001	
Ferritin levels	809 (417.75 – 1494.50)	719.50 (396.25 - 1215.25)	1231 (556.50 - 2164)	**0.002	
LDHlevels‡	454 (326.25 – 660)	408.50 (309 - 561)	668.50 (443.25 - 919)	**<0.001	

CRP= C-reactive protein, LDH= Lactic acid dehydrogenase, NLR= Neutrophil-lymphocyteratio, ‡: variable is summarized as median (interquartile range), *Significant at P<0.05, **Significant at P<0.05

Table 3: Association of risk factors with in-hospital mortality

Table 5. Association of the	sk lactors with in-hospital mortality				
	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value	
Age	1.06 (1.03 - 1.09)	**<0.001	1.18(1.08-1.29)	**<0.001	
Gender					
Male	0.91 (0.47 - 1.75)	0.769	=	=	
Female	Ref	<u> </u>	-	-	
Smoking Status	<u> </u>			•	
Former	3.02 (0.42 - 22.00)	0.275	1.63(0-447366.97)	0.939	
Current	6.04 (0.54 - 68.04)	0.146	44.34(0.02-78986.63)	0.321	
Never	Ref	,		Ref	
Comorbid	•				
Yes	3.38 (1.49 - 7.66)	**0.004	0.46(0.08-2.64)	0.381	
No	Ref			Ref	
Symptomatic					
Yes	4.01 (0.51 - 32.34)	0.184	0.14(0.01-3.88)	0.248	
No	Ref	•	Ref	'	
Severity on presentation	n				
Mild	Ref		Ref		
Moderate	2.94 (0.58 - 14.75)	0.191	0.55(0.04-8.34)	0.669	
Severe	21.78 (4.91 - 96.73)	**<0.001	4.31(0.33-55.94)	0.264	
Critical	121.33 (18.44 - 798.35)	**<0.001	19.76(0.84-463.61)	0.064	
ICU stay		J.		II.	
Yes	16.26 (6.84 - 38.69)	**<0.001	43.44(5.49-343.8)	**<0.001	
No	Ref			Ref	
Hospital stay	1.06 (1 - 1.12)	*0.036	0.97(0.88-1.08)	0.620	
Hemoglobin levels	0.90 (0.78 - 1.04)	0.157	0.98(0.74-1.31)	0.895	
NLR	1.08 (1.02 - 1.15)	*0.013	1.03(0.9-1.17)	0.679	
Platelets	1 (0.99 - 1)	0.625	- '	-	
Creatinine	1.11 (0.94 - 1.30)	0.216	1.55(1-2.39)	*0.048	
Sodium levels	0.97 (0.91 - 1.03)	0.269	- '	-	
Potassium levels	1.41 (0.85 - 2.37)	0.187	0.38(0.12-1.24)	0.109	
CRP levels	1.05 (1.02 - 1.08)	**<0.001	1.02(0.98-1.07)	0.328	
D-dimer	1 (0.99 - 1)	0.763	-	-	
Ferritin levels	1 (1 - 1)	0.065	-	-	
LDH levels	1 (1 - 1)	0.090	-	-	
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CRP= C-reactive protein, ICU= intensive care unit, L= Lactic acid dehydrogenase, NLR= Neutrophil-lymphocyteratio, aOR= adjusted odd ration; OR = odd ration; Ref= reference category; CI: confidence interval, *Significant at P<0.05**Significant at P<0.01

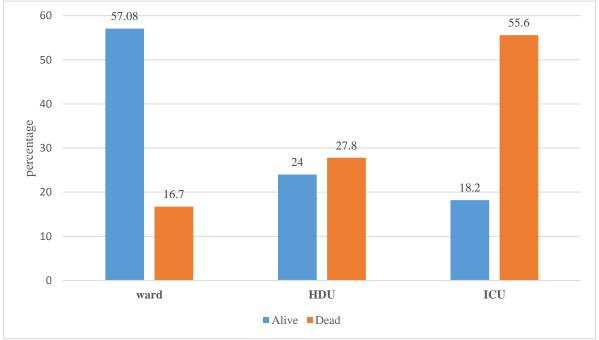


Figure 1: Frequency of mortality among different patient care areas

DISCUSSION

SARS-CoV-19 disease imposed new challenges and burdens on the healthcare system around the world. The guidelines to manage the COVID-19 infected patients were modified rapidly as day by new researches were emerging related to this lethal virus. The nature of disease is still not completely explored and yet under studied. Moreover, vaccines against the virus are still under the developmental and trial phase, in this context it becomes highly important to study the outcomes of infected patients and uncover the factors associated with mortality and share our experience and disease trend in Pakistani hospitalized population.

The current study presented the data of COVID-19 patients from the peak of virus in the city to about end of the first peak. Like other parts of the world, most of the admitted patients in our facility were males^{9, 10}. The reason of higher proportion of infected males in our local setting is obvious that males are likely to be engaged in outdoor activities than females for a variety of reasons which exposed them to the higher risk of acquiring infection than females. Researchers also suggested that males are more likely to develop severe outcomes than females due to immunological differences and higher smoking prevalence among men which negatively impacts disease severity 11. However, in our study we didn't find gender-based differences in mortality ratio which is in line with the findings reported in other similar studies9, 10, 12. Some researchers also reported that there was higher risk of inhospital mortalities in COVID-19 infected males than females but the total records analyzed in those studies was quite largerthan investigations that didn't find the significant association of male gender with mortality which could be the cause of conflicting finding^{13, 14}.

Similar literature around the globe reported that admitted patients on an average were middle aged or older patients. Mohammed et al conducted a study to investigate risk factors associated with COVID-19 mortality and reported median age of patients was 50 years¹⁵. Another study conducted in Pakistan reported mean age of 52.58±15.68 years¹². The studies conducted in China reported an average of age of 57.6±13.7 years of COVID-19 hospitalized patients¹². A study from United States reports that 67.3% of COVID-19 hospitalized patients were older than 60 years 16. 66.34% patients admitted in our hospital were 50 years or above. The most probable justification for middle age or elderly hospitalized patients is the fact that SARS-CoV-2 is more fatal for individuals with weaker immune system or for immunocompromised patients. This is well known fact that patients with co-existing severe comorbidities are likely to exhibit complications than healthy young adults. Furthermore, in our admitted patients, increasing age was identified as independent risk factor of in-hospital mortality on multivariable analysis which is in agreement with other studies as well^{9, 15, 17}.

Majority of the patients admitted through emergency and most of them were severe or critical at the time of admission. Results of the study also indicated that disease severity was significantly associated with adverse outcomes of the patients. The average age of severe and critical patient was near to sixty years. Moreover 69.1% of severe had comorbidities and 88.2% critical patient had

comorbidities which might be the reason of worse disease for this group. However, another important factor is health seeking behavior of the people. A survey was conducted in Pakistan during COVID-19 pandemic which reported that one in six adult consider that they and their families are safe from SARS-CoV-2 even without taking any preventive measure. It was also reported in a survey that 68% Pakistani population had perception that it is highly probable to survive with the disease. Furthermore, it was also reported that seven out of 10 citizens were reluctant to visit hospitals and clinics¹⁸. The findings of the survey are undoubtedly relatable with ignorant health seeking behavior and patients' presentation with worsen disease.

Clinical presentation of COVID-19 may vary from asymptomatic to severe condition. As stated by CDC, dyspnea and cough with at least any one of the symptom of fever, headache, body ache, chills, sore throat, lack of taste and/or smell or any gastrointestinal symptoms including vomiting, nausea, anorexia or diarrhea are indications of COVID-19^{19.} Almost all of the hospitalized patients in our setting were symptomatic with frequently reported symptoms of fever, shortness of breath and cough which are similar to features reported in Chinese and Italian and population^{9, 12.} However, being symptomatic was not found to be the significant risk factor of mortality which is consistent the findings of Giacomelli et al9. Comparable to the clinical features of COVID-19 hospitalized patients reported by Almaeezidi et al and Singh AK et al, our patients had also frequent comorbid of diabetes and hypertension^{20, 21}. However, in our settings, the presence of any comorbidity was not found to be significantly associated with in-hospital mortality when model was adjusted for other covariates. Presence of underlying diseases was found to be independent predictor of mortality in other studies on multivariable model^{15, 22}. Yet again the basis for negative finding in our study may be due to less number of patients though other studies analyzed records of more than thousand patients^{15, 22}.

In our study, overall median hemoglobin, platelets, creatinine, sodium, potassium, LDH were lying in normal ranges on patient presentation but NL ratio, CRP levels, ferritin and d-dimer were elevated upon patient presentation with significant rise in non-survivors. Almazeedi in his study reported d.dimer and CRP levels were elevated in 36.6% and 14.6% respectively. Elevated CRP levels upon initial presentation were identified as independent risk factor of adverse outcomes in COVID-19 patients by Luo et al¹⁷and Giacomelliet al⁹. In our study, none of the biomarker was identified as significant predictor of mortality on multivariable logistic regression model. However, increase in CRP levels was found to be associated significantly associated with the ICU admission.

The current study presents the experience of a single center institute in Karachi. A multi-center study may be conducted to better understand the factors associated COVID-19 in-hospital mortality in our population.

CONCLUSION

The current study provides evidence that increasing age and ICU admission and increasing age were chief predictors of mortality in our settings. Presence of

comorbidity and initial diseases severity are also important factors to triage patients.

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