Case Fatality in COVID-19; a District Perspective

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Authors' contributions

This work was carried out in collaboration among all authors. Author HK designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors FS and KH managed the analyses of the study. Author Abuzar managed the literature searches. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Objectives: To determine the case fatality rate of COVID-19 by evaluating the data of Patients died due to COVID-19.
Materials and Methods: A total of 243 patients with PCR done from the government designated Public health research laboratory of Khyber Medical University were included in a cross sectional comparative study. Chi-square test, risk analysis, probability testing and survival analysis using Kaplan Meir test was done on data sheet prepared in SPPS version 25 in accordance with the objectives of the study.
Results: Out of total 243 patients, 165 (67.90%) were negative by PCR testing and 78 (32.09%) were COVID-19 positive. The Mean age with SD was 36$\pm$17 years. Out of total 178 (73.3%) were

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males and 65 (26.7%) were females. 34 (13.99%) had age more than 55 years, where 4/5 (80%) of the deaths were recorded. The relationship of an increase in age with rate of mortality was statistically significant *(p=0.001)*. The over all probability of death in our population in age more than 55 years is 24 times higher *(OR=24,95CI: 2.6-221.24)* with relative risk of 1.1 *(rr=1.11, 95CI:1-1.24)*. Mortality rate was 6.41%. A significant correlation of mortality with case positivity *(p=0.003)* with relative risk of 1.06 *(rr=1.06, 95CI: 1.008-1.13)*. Three out of 5 of the COVID-19 positive deceased had cardiac diseases and 2/5 had respiratory disease/viral pneumonia. Using Kaplan Meir test, the survival graphs of COVID positive vs COVID negative cases had similar pattern that shows the mortality rate in the positive cases was not solely due to COVID-19, but has aggravated the pre-existing illness to cause death.

Conclusion: The mortality rate was 6.41%, more in age>55 years (80%) and almost all the deceased had chronic co-morbid conditions like CAD, CCF and COPD at time of presentation. COVID-19 is not the sole killer, it contributes killing in immune-deficient patients.

1. INTRODUCTION

COVID-19 was firstly reported to the WHO office on 31st Dec 2019. COVID-19 (Corona virus disease) was first reported from metropolitan city, Wuhan, Hubei province in China at Dec 2019, which causes severe respiratory disease/pneumonia. it is a pandemic disease infecting 5,931,963 people and killed more than 365,051 persons and 2,496,857 recoveries in almost five months span [1].

Pakistan is not an exception and the virus entered here in Feb 2020, when a student of Karachi University was reported positive for 2019nCoV by PCR with a travel history of Iran [2]. In Pakistan the literature so for covering the prevalence and incidence is deficient. In Pakistan the so for (24th July 2020) reported data from government sources declares 270,400 confirmed cases with 5763 deaths. 219783 cases are recovered so for and 1316 cases are under treatment in high dependency units countrywide. Sindh is the province with highest number of corona cases crossing 115883 [3].

There is limited known about the clinical features, presentation and even the incubation period of this deadly virus, which has an impact on the control and surveillance of an infectious disease. The incubation period of the 2019-nCoV is reported from 6 days to 12 days [4]. The risky populations are close contacts of COVID-19 infected patients, healthcare workers, family members of infected patients.

The information's available on the research documents published on Pub-Med; we found that during the period from its early outbreak in China 29th Dec 2019 till 31st March 2020, there are

750890 cases reported with 36405 deaths with a mortality rate of 4.84%. The infection was more common in male gender and morality was higher in the patient with age> 60 years [5].

Another study showed that the mortality rate in more common in cardiac compromised patients, as the predictor of fatal outcome in COVID-19 are age and underlying disorders or presence of any secondary infection as the research has shown that COVID-19 related mortality in cardiac patients could be due to virus activated cytokine storm syndrome in these patients [6].

The age and underlying diseases (hypertension, diabetes, etc.) were the most important risk factors for death of COVID-19. Bacterial infections may play an important role in promoting the death of patients [5,6].

The objectives of the study were to determine the case fatality rate of COVID-19 by evaluating the data of Patients died due to COVID-19.

2. METHODOLOGY

This comparative cross sectional study was conducted from 5th Feb 2020 to May 5, 2020 in district Nowshera and its only Medical Teaching Institution, Qazi Hussain Ahmed Medical Complex MTI Nowshera. A total of 243 patients whose PCR report was received were included in this study.

Assuming 4.3% mortality rate of COVID-19 in population from the study of Wang DW et al. [7], a sample size of 243 was calculated through open epi software, an online sample size calculator, with Absolute precision of 5%, confidence interval of 95%, and a drop out of 10%.

The sample was selected through consecutive, non-probability technique. All the patients from COVID clinics, or strong suspects with history of travel to an epidemic area or closed contacts of COVID-19 positive patients, with PCR report received forth from the Khyber Medical University, Public health research laboratory, irrespective of age and gender were randomly selected.

All patients attended in emergency or outdoor patients department were excluded. PCR Result awaiting suspects were also excluded. Similarly patients attending the COVID-19 clinic without securing the optimum marks for selection to be enrolled of PCR testing were also excluded.

All samples were sent under strict observance of protocols to the Public health research laboratory of Khyber medical university Peshawar (a designated Lab for PCR of 2019nCoV by the Government of Khyber Pukhtunkhwa).

Data was entered in SPSS version 25 and descriptive and correlation statistics were applied. The frequency and proportion of numerical and categorical variables were presented in percentages. Chi-square test was applied to show a relationship of mortality rate with age groups, co-morbidities and viral infectivity.

Our data comprised of 66 (27.2%) cases from Qazi Hussain Ahmed Medical Complex and 177 (72.8%) from district health management system analyzed by a contributing author from district health office, Nowshera.

All samples were sent under strict observance of protocols to the Public health research laboratory of Khyber medical university Peshawar (a designated Lab for PCR of 2019nCoV by the Government of Khyber Pukhtunkhwa).

All those patients whose sample was collected were isolated mainly in the isolation unit of our hospital as well as Quarantine designated by the Government or very few cases in home isolation under strict observance of the health/district administration to ensure to contain virus.

Relative risk of COVID-19 was determined in gender groups, history of travel and history of contacts in COVID-19 positive and negative groups using risk analysis statistics.

We applied Chi-square test on our population to test the relationship of Mortality due to COVID-19 with age and viral infectivity.

Kaplan Meir test was used for survival analysis to compare the mortality rate in COVID-19 positive and negative groups.

3. RESULTS

The total number of patients enrolled was 243. Out of total 165 (67.90%) were negative by PCR testing and 78 (32.09%) were COVID-19 positive. The Mean age with SD was 36+17 years, the minimum age was 2 years and maximum of 85 years with age range of 83 years. Out of total 178 (73.3%) were males and 65 (26.7%) were females. 34(13.99%) had age more than 55 years, where 4/5 (80%) of the deaths were recorded. The relationship of an increase in age with rate of mortality was statistically significant *(p=0.001)*. The over all probability of death in our population in age more than 55 years is 24 times more than age less than 55 years *(OR=24,95CI: 2.6-221.24)*. The relative risk for mortality due to COVID-19 alone was 1.11 *(rr=1.11, 95CI:1-1.24)* (Table 1). We observed that 5 out of 78 COVID-19 positive cases died with a mortality rate of 6.41%. The Fisher's exact test showed a significant correlation of mortality with case positivity *(p=0.003)*. Again the relative risk for mortality due to COVID-19 was 1.06 *(rr=1.06, 95CI: 1.008-1.13)* (Table 2).

We observed that out of the total positive 78 cases 21 (26.92%) had co-morbidities like heart and chest issues for which they were taking medication. Out of these 21 patients 5 died, which also had PCR for corona positive. 3/5 had cardiac diseases (Coronary artery disease, and Congestive cardiac failure) while two had chest problem (Chronic obstructive pulmonary disease/Asthma/Viral Pneumonia). There was a significant relationship of associated co-morbidities in COVID-19 patients with mortality. (Table 3)

Using survival statistics with time *to event analysis* on *Kaplan Meier Test*, taking age in years as time variable and disease outcome in event. We observed that survival rate in COVID-19 has an inverse relation with an increase in age. We observed the a downhill negative relationship of survival with age>55 years of age. But when we plotted the survival graphs of COVID-19 positive vs COVID-19 negative cases, a similar pattern was observed that shows the mortality rate in the cases was not solely due to COVID-19, though being an opportunistic viral infection it

would have contributed but the deceased had other co-morbidities as well like Coronary artery diseases and respiratory diseases etc. Fig. 1

4. DISCUSSION

Corona Virus disease termed as COVID-19, is an emerging highly contagious respiratory disease that is caused by novel corona virus. Its main clinical symptoms are fever, dry cough, fatigue, myalgia and dyspnea [8]. Case fatality rate of 2.3% has been reported from china that is lower than SARS (9.5%) , MERS (34.4%) and H7N9 (39%) [9].

The infectivity rate was 78/243 (32.09%) in our population. Which is higher than reported by Yang AP et al. [10] (26%). Other studies reported from Wuhan, China and other infected zones with a positivity rate of 53% and 71% respectively, using throat swab for PCR testing, as do we practice, that was higher than what we observed [11,12].

Table 1. Age and its relationship with mortality due to COVID-19

		Age categories				Total
		age<18 years	19-35 years	36-55 years	>55 years	
Disease outcome	Stable	32	108	64	34	238
	Died	0	0	1	4	5
Total		32	108	65	38	243
Chi-Square Tests						
Test		**Value**		**df**	**Asymptotic Significance (2-sided)**	
Pearson Chi-Square		16.551[a]		3	***p=0.001***	
Number of Valid Cases		243				
Risk Estimate						
		Value	**95% Confidence Interval**			
			Lower		**Upper**	
Odds Ratio for age2 (age<55 years /age> 55 years)		***24.00***	2.60		221.24	
For cohort disease outcome = Died		***1.11***	1.00		1.24	
For cohort disease outcome = stable		0.05	0.01		0.40	
N of Valid Cases		243.00				

Table 2. Viral infectivity, its correlation and relative risk for mortality

		PCR_Result		Total
		Negative	**Positive**	
Disease outcome	Stable	165	73	238
	Died	0	5	5
Total		165	78	243
Chi-Square Tests				
	Value	**df**	**Asymptotic Significance (2-sided)**	
Fisher's Exact Test	10.799[a]	1	***0.003***	
No of Valid Cases	243			
Risk Estimate				
	Value	**95% Confidence Interval**		
		Lower	**Upper**	
Relative risk	***1.068***	1.008	1.132	

Table 3. Co-morbidities in COVID-19 positive patients and its relation with mortality rate

PCR Result			Disease outcome		Total
			Stable	Died	
Negative	Co-morbidity	NIL	165	0	165
	Total		165		165
Positive	Co-morbidity	Viral Pneumonia? Asthma	3	1	4
		CAD	4	2	6
		CCF/Viral Pneumonia?	0	1	1
		COPD	12	1	13
		DM	2	0	2
		No co- morbidity	52	0	52
	Total		73	5	78
Chi-Square Tests					
PCR Result		Value	df	Asymptotic Significance (2-sided)	
Negative= 165	Pearson Chi-Square				
Positive=78	Pearson Chi-Square	39.371[c]	7	**p=0.001**	
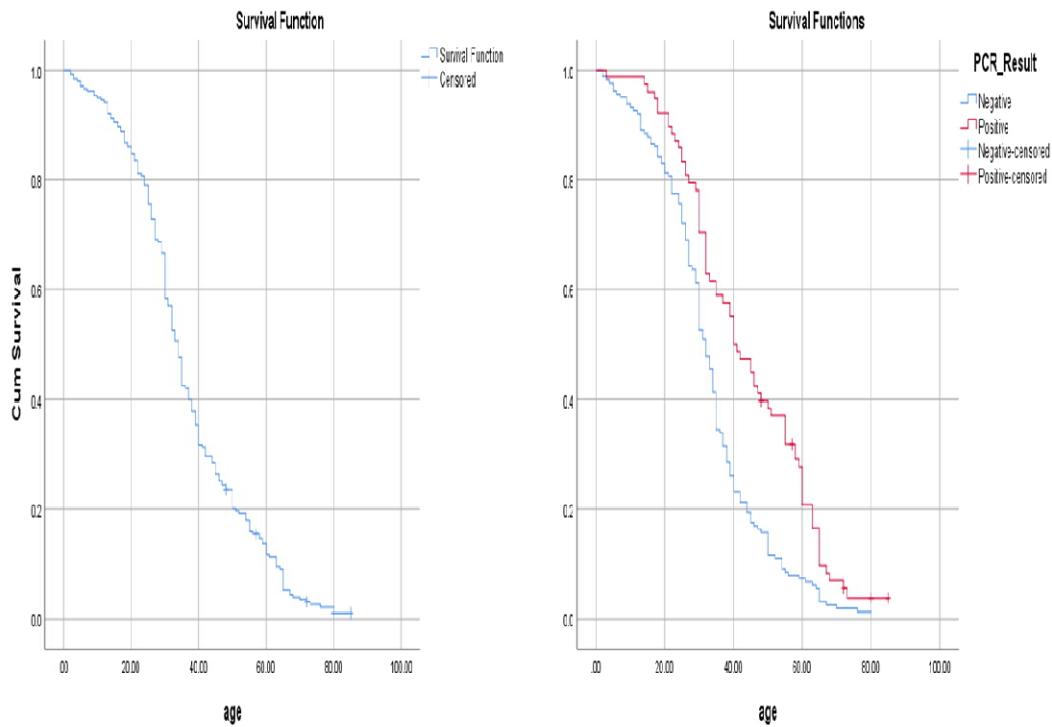
Fig. 1. Graphical representation of PCR results

We observed a mortality rate of 6.4% in our COVID-19 positive cases during the early epidemic in Nowshera, Pakistan. Which was higher than reported by Munster VJ et al. [9]. Wang DW et al. [7] reported 4.2% mortality rate. Among the Chinese patients 2873, the death rate was 3.6%, and by the end of March the death rate outside China was 1.5% [13]. Our mortality rate is higher as compared to their findings; many reasons/factor can contribute to this high mortality rate like age factors, co-

morbidities and poor implementation on the social distancing.

It was noted that 34 (13.99%) of the positive patients had age more than 55 years, where 4/5(80%) of the deaths were recorded. The relationship of an increase in age with rate of mortality was statistically significant *(p=0.001)*. The CDC reports 2019 shows that 53% of the COVID-19 infected patients that need ICU admission, and those 80% of the deaths were recorded in elderly people age>65 years, while no ICU admission or deaths were recorded in age less than 19 years of age [14]. A significant correlation of mortality with case positivity *(p=0.003)* with a relative risk for mortality due to COVID-19 *(rr=1.06, 95CI: 1.008-1.13)*was noted in present study. The severity of the infection has an impact on mortality rate. A study reported from Wuhan, the epicenter of the first outbreak reported mortality in positive patients as higher as 20% [15]. Three out of 5 of the deceased had cardiac diseases as co-morbidities and 2/5 had respiratory disease/viral pneumonia. Accumulative evidence suggests that cardiac manifestations are more common in hospitalized COVID-19 patients. Patients with CAD have more vulnerability to be infected with COVID-19 with worse outcome. In a study authored by Huang C, et al. [16]. the frequency of baseline cardiovascular disease was recorded in 14.6% of the COVID-19 patients. In another trial that comprised 416 COVID-19 patients, 19% developed cardiac injuries during hospitalization [17]. With respect of respiratory disorders in COVID-19 patients, COPD is one of the major clinical emergencies that are reported in COVID-19 patients. The possible explanation is that the host receptors of the 2019nCoV are reported to be expressed more in patients with COPD that increases the severity of the disease [18].

5. CONCLUSION

Hence we concluded that COVID-19 kills the older age patients, the mortality rate in our population (6.4%) is higher. Many factors are contributing to higher mortality like age factor, co-morbidities like pre-existing cardiac disorders and respiratory disease.

6. SUGGESTIONS

Special attention should be given to COVID-19 patients in their extreme of age (>55 years) and pre-existing conditions that causes immune dysfunction.

An accumulative integrated approach at individual, national and international level would address the problem and can reduce the burden of the disease. There is need for advocacy on social distancing, avoiding gathering, use of face masks and avoidance of travel to an epidemic area with reported COVID-19 cases.

7. LIMITATIONS OF THE STUDY

We observed only the demographic variables as it was the early epidemic and we used to collect the information from the predesigned proforma that was prepared for public health and administration use.

We used only demographic information and assessed case fatality with age and gender factors and also within the influence of the history of travel to an epidemic area and positive/family contacts.

The study limitations were that we could study the impact of age, gender and other visible factor on the mortality but could not collect the clinical data like information's about the inflammatory mediators like d-dimer, ferritin and other cytokines that play an important role to predict the severity of the disease.

Future studies should focus on the role of cytokines as predictor of severity and mortality due to COVID-19.

CONSENT

Prior informed consent was obtained from all suspects and they were assured of confidentiality.

ETHICAL APPROVAL

Ethical approval was obtained from the institutional ethical review board of Nowshera Medical College hospital administration before the execution of the study vide Notification No: 78/ERC/NMC Dated 10th Feb 2020..

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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