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ORIGINAL RESEARCH CORONA EXPERIENCE

Case fatality rate and survival functions of severe COVID–19 patients in intensive care unit of Bangabandhu Sheikh Mujib Medical University in Bangladesh: an observational study

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ABSTRACT

Background: Emergence of current pandemic caused by novel SARS–COV–2 has already caused over 963000 deaths. Case fatality rate (CFR) estimation helps understanding the disease severity and the lethality trend, high risk population and subsequently, optimization of quality healthcare facilities. Our observational study aimed to find out existing trends in treating the most vulnerable group with scarce medical resource allocation and to implement necessary support services to comply with the ensuing need for best possible outcomes in our ICU.

Methodology: In this observational study, all COVID–19 diagnosed patients admitted in our ICU from July 4, 2020 to September 22, 2020, were enrolled. Data were obtained from the core ICU register of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Information accumulated on predesigned data sheets comprised of particulars of patients, co–morbidities, duration of ICU stay, mode of oxygenation, organ support and quick SOFA scores. Total deaths in ICU (in hospital or referred from outside of BSMMU) were recorded.

Results: The results revealed that all patients were either very severe or critically sick with COVID–19 pneumonia at the time of ICU admission. Out of 174 patients, 46 (26.44%) were put on invasive ventilation and the rest received noninvasive ventilation in the form of NRM, high flow nasal cannula (HFNC), continuous positive airway pressure (CPAP or BiPAP), CTEX CPAP and non–invasive ventilation (NIV) as appropriate. Male and female ratio was 74:26. Age of patients ranged between 19–95y. The median age of patients was 65 y (IQR: 57–70).Quick SOFA scores were more than 2 in 65.37% of patients. Regarding co–existing organ dysfunction 13.8% had 3 or more co–morbidities; while 74.1% had 2 and 9.8% had a single systemic illness along with COVID–19. Most common diseases encountered among 135 deceased were hypertension (64%), IHD (49%), diabetes mellitus (45%), bronchial asthma or COPD (32%), renal failure (either ARF or CRF) (20%). Overall CFR due to COVID–19 pneumonia associated with co–morbidities was 77.6%. Relatively higher CFR (82.6%) was evident harboring multi–organ dysfunction especially among COVID–19 patients aged 50y or more. Gender linked CFR were 81.4% and 66.7% in males and females respectively.

Conclusion: High CFR demonstrates significant correlation with increasing age and co–morbidities and survival functions. Late presentation to the hospital and invasive mechanical ventilation also contributed to high CFR.

Keywords: Case fatality rate; CFR; COVID–19; Intensive Care Unit; Survival function

Abbreviations: CFR – Case fatality rate; NRM – Non-rebreathing mask; HFNC – high flow nasal cannula; CPAP – continuous positive airway pressure; BiPAP – Bi-level positive airway pressure; NIV – Non–invasive ventilation; IHD – Ischemic heart disease; ARF – Acute renal failure; CRF – Chronic renal failure

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1. Introduction

The case fatality rate (CFR) of a particular disease reflects the severity as well as the burden of it and highlights the capacity of existing healthcare facilities, thereby helping in policy decision making. It is calculated by measuring the number of reported deaths per total number of reported cases, but in true sense a time component is prerequisite which is absent here. COVID–19 pandemic outbreak has triggered reshuffling the public health delivery systems in about 212 countries and territories. Though first identified in Wuhan, China, the disease wave was first sensed on March 8, 2020 in Bangladesh. Since its journey, SARS–COV–2 has infected 3,14,82,606 persons and caused 9,62,298 deaths as of 04.01GMT on September 22, 2020.(1).Slow initial progression of COVID–19 in Bangladesh caused relatively low CFR but the possibility of very low number of testing and obscuring co–existing illnesses need to be considered.

In South–East Asia, including Bangladesh, the figures have been worsening as evident by securing 17th position in WORLDOMETER list. Bangladesh is one of the most densely populated (1265/ Km2) country, consisting of 4.7% of total population aged 65 y or more (2) with an average life expectancy in Bangladesh of 72.72 y (2020).(3).

CFR are subject to selection bias as more cases are tested and being treated once becoming severe symptomatically. Overall prevalence for metabolic syndrome comprising of high blood sugar, low HDL, abdominal fat, high triglycerides, high blood pressure is more in Bangladesh compared to globally estimated prevalence (30% versus 20–25%)(4).Evidence suggests that approximately 20% of SARS–COV–2 infected patients were hospitalized in China, out of which 25% needed to be treated in an Intensive Care Unit initially(5).In hospital mortality of COVID–19 patients was 77.6% in BSMMU ICU which closely resembles to those observed in many developed countries.(7-9)

Though there is a lack of adequate epidemiological information about South–East Asian countries, we tried to identify patient risk factors ensuring uniform reporting system in our ICU. Considering our experience and data trends, gradual rise of ICU admission and potential impact of misclassification of deaths, we aimed to extract CFR in this arena as an important tool to analyze, interpret and subsequently to implement rational healthcare policies.

2. Methodology

This observational study was conducted in COVID–19 ICU of our hospital, comprising of every patient confirmed to have SARS–COV–2 infection during the period from July 04, 2020 to September 22, 2020. This medical university being the first in the country has dedicated 250 isolation beds and 21 ICU beds to treat COVID–19 patients respectively. Patients were tested RT–PCR positive by approved laboratories. Data extracted from patient records from COVID–19 ICU were analyzed; including particulars of the patients, co–morbidities, length of ICU stay, vital parameters, qSOFA score, diagnosis, treatments and clinical outcomes.

Ventilation strategies comprised of non–rebreathing mask (NRM), high flow nasal cannula (HFNC), continuous positive airway pressure in the form of CPAP or BiPAP, CTEX–CPAP, non–invasive ventilation (NIV) or invasive ventilation as deemed appropriate.

Statistical analysis: Continuous variables were expressed as either means with standard deviations (SDs) or medians with interquartile range

Table 1: Demographic characteristics

Variables		Frequency n (%)	95% CI L	U
Gender	Male	129(74.1)	67.2	80.5
	Female	45 (25.9)	19.5	32.8
Age category	≤ 39 y	9 (5.2)	2.3	8.6
	40 to 69 y	111 (63.8)	56.3	70.7
	>70 y	54 (31.0)	24.1	37.9
Co–morbidities	Covid 19 pneumonia only	4 (2.3)	.6	4.6
	Single co–morbidity	17 (9.8)	5.7	14.4
	2-3 co–morbidities	129 (74.1)	67.8	80.5
	> 3 co–morbidities	24 (13.8)	8.6	19.0
Median age	65.0 (IQR: 57–70) y			

(IQRs).Frequencies and percentages were used to describe categorical variable as well. Univariable hazard ratios (HR) and 95% confidence intervals (CI) were reported. A p <0.05 was considered statistically significant. All analyses were done using SPSS V.24 (SPSS Inc., Chicago, Illinois, USA).

3. Results

This observational study enrolled 174 patients of both sexes diagnosed as very severe or critical COVID–19 at their entry to ICU. There were 174 confirmed COVID–19 patients and 135 related deaths during above mentioned period. Baseline demographic characteristics are shown in Table 1.

CFR was 77.6%. Distribution by age, highest CFR

Table 2:Gender, age, co–existing illness and outcomes of the patients

Variable	CFR
Overall	77.6%
Gender Specific CFR	
Male	81.4%
Female	66.7%
Age specific CFR	
≤ 39 yrs	11.1%
40 to 69 yrs	79.3%
>70 yrs	85.2%
≥ 50 yrs	82.6%

85.2% was evident in patients aged ≥ 70 y followed by 79.3% in aged 40 to 69 y and 11.1% in aged ≤ 39 y respectively (Table 2).

The median age of all patients was 65 y (IQR: 57–70). Precise data ranked CFR quite high (82.6%) in patients aged ≥ 50 y (Table 2). Higher CFR was obtained with more co–morbidities; 80.6% cases had 2 to 3 co–morbidities and 91.7% cases had more than 3diseases along with COVID–19 pneumonia and this demonstrated significant difference statistically (p < 0.001, Fisher's exact test) (Figure 1).

Most common co–morbids were as follows; hypertension (64%), ischaemic heart disease (49%), diabetes mellitus (45%), bronchial asthma and/COPD (32%) and renal failure (20%) respectively. Albeit, men had a higher (74%) rate of ICU admission than women (26%), the actual numbers of co–morbidities and outcomes were considered similar between the groups. 26.44% of patients were put on invasive ventilation and the rest 73.56% on non–invasive ventilation with high flow of oxygen.

Table 3 reflects a significant association between the groups in age category and the ultimate fate of the patients (p<0.001). Younger patients aged ≤ 39 y were more likely to survive (88.9% discharged) than rest of the two groups. More patients succumbed in the age categories of 40 to 69 y and ≥ 70 y respectively. We found no significant gender difference related to co–morbidities (p=0.595) but the number of comorbid condition increased with the age which was statistically significant (p<0.001) (Figure 2).

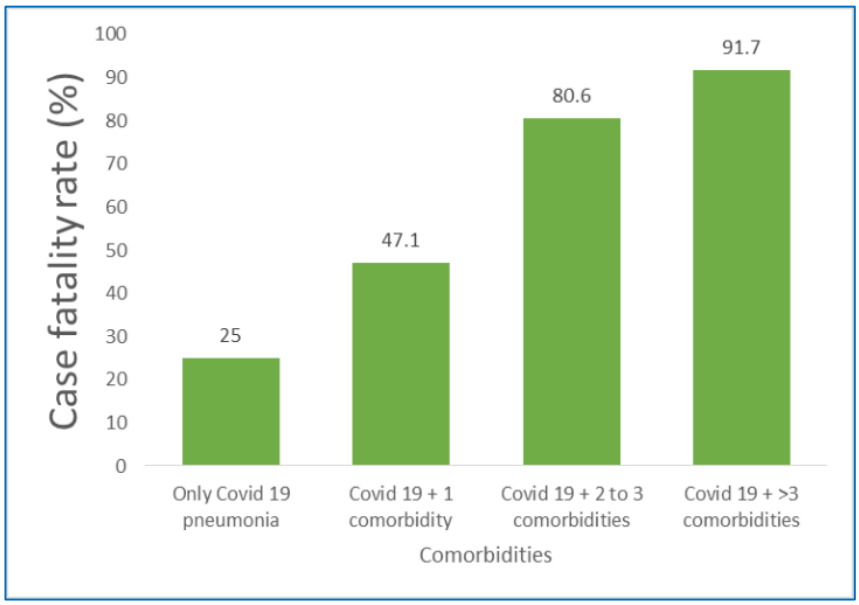

Figure 1: CFR in relation to Covid-19 plus the co-morbidities

A significant distinction (log rank test p= 0.001) in the survival between the age groups less than 50 y and ≥ 50 y were 15 days and 4 days respectively was evident (Figure3). No gender linked significant difference was accomplished pertaining to survival time that for men and women were 6 days and 4 days (log rank test p= 0.771). The median survival time of patients for the groups with single disease, 2 to 3 diseases and more than 3 diseases (p=0.04) are shown in Figure 4.

4. Discussion

COVID–19 pandemic has been associated with high morbidity and mortality since its first outbreak in China in December2019. It was on March 8, 2020, that it was first identified in Bangladesh. South Asian culture of combined family system, with the elderly and the young living in the same household, probably contributed in its acute flare up.

This is the first audit of in hospital mortality of COVID–19 infected patients in an ICU of Bangladesh, conducted during the first wave of the pandemic in the country. The CFR acquired here allude to our ICU cases and deaths related to COVID–19 pneumonia only, not the absolute national representation. Though overall CFR in Bangladesh was 1.27%, this study shows it to be 77.6% in our ICU, which correlates with the study done by Christian Karagiannidis et al. (5).

COVID–19 cumulative deaths in South–East Asia were 11% in comparison to 55% in USA and 24% in Europe as of 20 September 2020.(10). High CFR in our study requires cautious interpretation, as massive screening has not been conducted in our population and the denominator in our study was much smaller i.e. only the admitted RT–PCR positive critical cases included.

Severity of the pandemic has been extensively indicated to be affected by age, sex and concomitant diseases echoing the views of Wu Z et al. and Guan W–J et al. (11, 12). At any time point in our study, patients aged less than 50 y had 58.80% lower risk of

Table 3: Association among different age categories, co–morbidities and fate of the patients

Variables		Discharged [n (%)]	Expired [n (%)]	*p – value*
Age category	≤ 39 y	8 (88.9%)	1(11.1%)	<0.001
	40 to 69 y	23 (20.7%)	88 (79.3%)	
	>70 y	8 (14.8%)	46 (85.2%)	
Comorbidities	Covid 19 pneumonia only	3 (75.0%)	1 (25.0%)	<0.001**
	Covid 19 patient with single co–morbidity	9 (52.9%)	8 (47.1%)	
	Covid 19 patient with 2–3 co–morbidities	25 (19.4%)	104 (80.6%)	
	Covid 19 patient with more than three co–morbidities	2 (8.3%)	22 (91.7%)	

***Fisher's Exact Test; p value is significant*

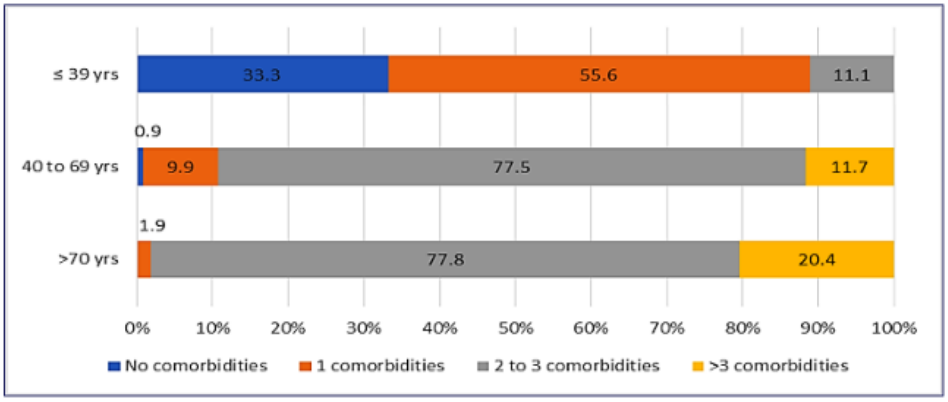

Figure 2: Distribution of co–morbidities (%) according to age category

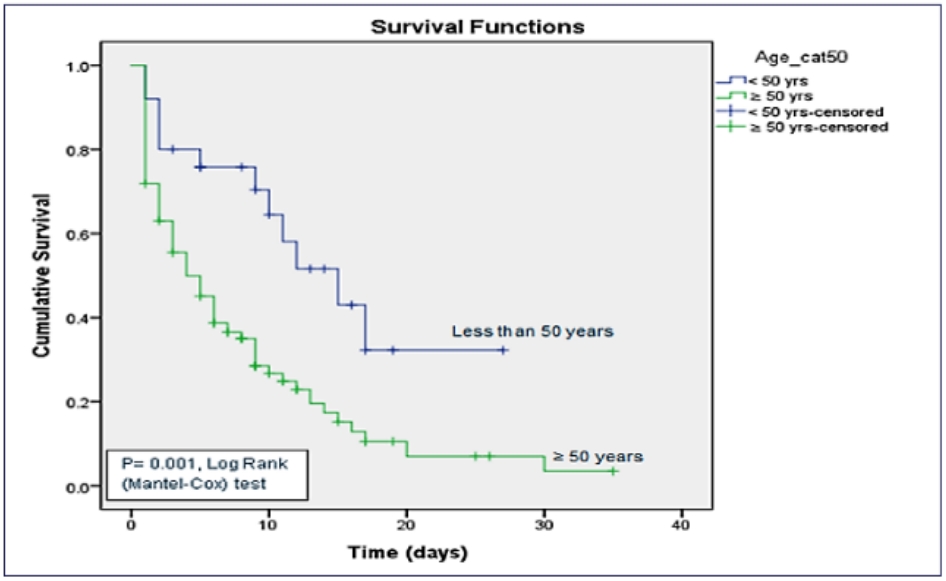

Figure 3: Survival Functions according to age

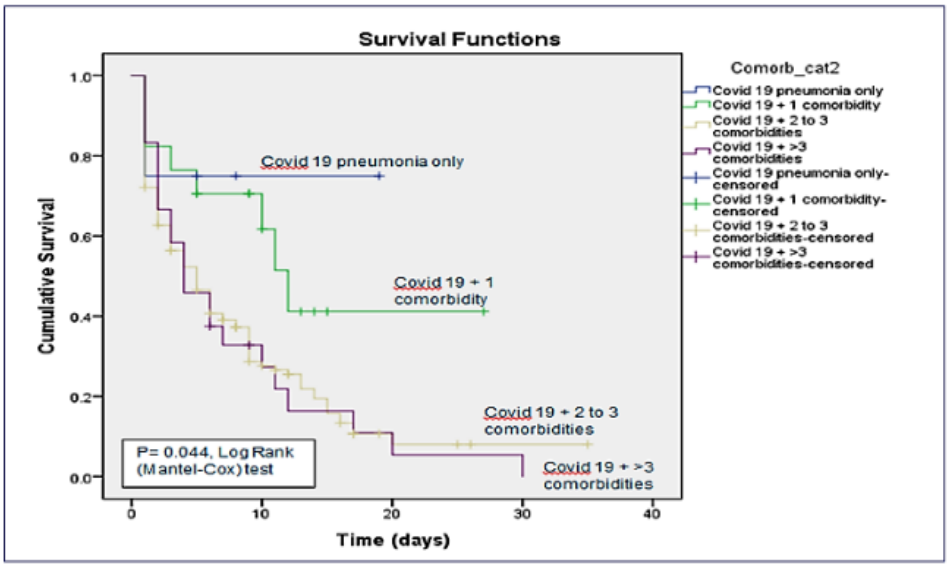

Figure 4: Survival Functions according to co–morbidities

death than those aged 50 y or more (HR= 0.412, 95% CI 0.227–0.474) which became statistically significant (p=0.004). Very high mortality of 85.2% was seen in patients aged 70 y or more that correlates with a study from UK (5). In Italy 83% were reported in patients aged 70 y or more, having a similar trend in USA and South Korea as well. 20.3% of patients aged > 70 y in England, Wales and Northern Ireland were treated in ICUs in comparison to 31.2% in our study.(6). Although men had a higher rate of ICU admission than women (74% vs. 26%), the actual numbers of co–morbidities and outcomes were considered similar between the groups. Relatively higher CFR was evident in men than women in Bangladesh which contradicts with that of India that warrants further studies regarding disparity in sex–linked mortality in this region.

Current study revealed younger patients aged ≤ 39 y were more likely to survive (88.9% discharged). A higher percentage of patients succumbed in the age categories of 40 to 69 y and ≥ 70 y respectively. Though we found no

significant gender difference related to co–morbidities (p=0.595) but the number of diseases acquired with the growing age became statistically significant (p<0.001). No patient aged less than 39 y had more than 3 co–morbidities whereas every patient aged above 70 y had several systemic diseases along with COVID–19. Most common illnesses were as follows; hypertension (64%), ischaemic heart disease (49%), diabetes mellitus (45%), bronchial asthma and COPD (32%) and renal failure (20%) respectively.

All enrolled patients had very severe or critically ill COVID–19 pneumonia with a quick SOFA score of ≥2 (65.37% of admitted patients) at their time of ICU admission. A quarter (26.44%) of the patients were ventilated mechanically and the rest (73.56%) were supported by non–invasive ventilation (NIV) in the form of NRM, HFNC, CPAP (CTEX– CPAP also) BiPAP and NIV with different modes deemed appropriate. Delayed arrival with near decompensated state and refusal to invasive mechanical ventilation were two big barriers in our ICU cases.

The median survival time for patients aged less than 50 y and ≥ 50 y were 15 days (95% CI; 8.495–21.505) and 4 days (95% CI; 2.552–5.448) respectively which revealed significant difference (log rank test p= 0.001). Median survival time for men and women were 6 days and 4 days which yielded insignificant difference (log rank test p= 0.771). The median survival time of patients decreased from those with a single disease, to 2–3 diseases and more than 3 diseases.

5. Limitations

This study was conducted during the first wave of the pandemic. It can be termed as a cross-sectional study as it included patients from a limited time period. In spite of full ICU support, deaths continued as we included all patients including elderly frail patients with multiple diseases, patients on life sustaining therapies and patients with terminal illnesses like malignancies and vital organ failure. It means the mortality was not related to COVID-19 only, but the co-morbid also played their part. Anyhow, the study highlights the importance of frequent calculation and comparisons of CFR in the same unit or with other units too.

6. Conclusion

High CFR demonstrates significant correlation with increasing age and co–morbidities and the survival functions. Among the deceased too late presentation and refusal to early invasive mechanical ventilation were the main factors. Though measuring CFR during its outbreak is not very congenial due to screening, testing and reporting inadequacy but still the dynamics of fatality rates across affected countries and territories would ameliorate the information base and provide necessary intelligence in the current prevalence of pandemic.

7. Acknowledgements

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8. Conflict of Interest

There are no potential conflicts of interest. No external or internal funding was involved in this trial.

9. Author's contribution

AKMA, MSI–Concept, protocol preparation, data analysis, manuscript writing and editing
DKB, MP, MMK–Data compiling, data interpretation and manuscript writing

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