

Epidemiological Factors and Clinical Course of COVID-19 in Patients Who Died Following the Disease in Dedicated COVID Hospital, Rewa District, Madhya Pradesh - A Retrospective Study

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ABSTRACT

BACKGROUND

The clinical spectrum of SARS-CoV-2 infection encompasses asymptomatic infection, mild upper respiratory tract infection, and severe viral pneumonia with respiratory failure and even death. This study attempts to estimate the time interval between symptoms onset to severity, time taken for hospitalization, length of stay in hospital along with demographic and clinical characteristics of deceased patients infected with Covid-19.

METHODS

This retrospective study was conducted in SSMC associated Dedicated Covid Hospital, Rewa district, India. Covid-19 positive deaths (112) that occurred from May 2020 to January 2021 in this institute were considered for this study. Information regarding socio-demographic profile, systemic diseases / underlying medical conditions, signs and symptoms of the disease, clinical course, and investigations were collected and analysed. Time duration variables included were time from the initial symptom to breathlessness, time taken to seek treatment, delay in hospitalization, and length of stay in the hospital.

RESULTS

Elderly males with 2 or more comorbid conditions were found to be at higher risk of mortality. Median duration from onset of initial symptom to treatment seeking / hospitalization in DCH was 5 days. While mean duration from onset of initial symptoms to onset of breathlessness was 2 days 6 hrs. There was a delay of 3 days in hospitalization after experiencing breathlessness. 90 % patients had bilateral lung involvement at the time of admission. More than half of the patients had multiple organ involvement. Positive correlation was observed in delay in hospitalization, with syndrome severity at the time of admission and negative correlation with length of stay in hospital.

CONCLUSIONS

Delay in hospitalization is observed as an important factor which affects clinical course. Disease severity increases and length of stay decreases with delayed presentation at the time of admission. It should be addressed with awareness generation activities in community and self-assessment tool appropriate and suitable for implementing in general population.

KEYWORDS

Covid 19, Covid Infection, Mortality, Time Delay, Length of Stay (LoS)

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BACKGROUND

On 31 December 2019, the WHO China Country Office of WHO was informed of cases of pneumonia of unknown cause detected in Wuhan City, Hubei Province of China.¹ On January 7, 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was isolated by Chinese scientists from patients with the disease.² This new virus causing respiratory disease was officially named as Severe Acute Respiratory Syndrome Novel coronavirus 2 (SARS-CoV-2) disease 2019 (COVID-19) by the World Health Organization (WHO) in February.³ Subsequently, on 11 March 2020, WHO formally declared the novel coronavirus outbreak a pandemic and issued guidelines for pandemic response.^{4,5}

Thereafter, it was confirmed that the virus spreads from person to person both in hospital settings and among families.⁶ The clinical spectrum of SARS-CoV-2 infection encompasses asymptomatic infection, mild upper respiratory tract infection, and severe viral pneumonia with respiratory failure and even death.^{7,8} Despite the favourable clinical course for most cases, a mortality rate of 30 – 70 % was evidenced for COVID-19 patients treated on intensive care unit (ICU).^{9,10} Coronavirus disease-19 (COVID-19) has spread rapidly around the world, and many risk factors including patient demographics, social determinants of health, environmental variables, underlying health conditions, and adherence to social distancing have been hypothesized to affect case and death rates. Developing new therapies, identifying risk factors, and minimizing spread through social distancing remain top priorities in the fight against COVID-19. Time delay in diagnosis and seeking treatment is not only important for transmission and control of disease but it also affects clinical course and severity of disease.^{11,12}

There may be rapid progression of clinical course in some patients from onset of initial symptoms to Multiple organ dysfunction. Therefore, early diagnosis, triage and timely treatment of critical cases are of utmost importance.¹³

Limited knowledge exists currently about time interval between first symptoms appearing to progression towards severity, not on the length of stay in hospitals in India. Not only estimated number of patients but Length of Stay in hospital is important for planning and managerial purposes to predict the number of required hospitals and logistics, both in High dependency units (HDU) and ICU.^{14,15} Socio demographic and clinical characteristics, presence or absence of chronic conditions might affect clinical course of disease and decision for seeking medical care. There may be complex interaction of these variables which affects the outcome of patient.

Objectives

1. To find out
 - a. The time interval between onset of symptoms and appearance of severe symptoms
 - b. The time interval between onset of breathlessness and hospitalization
 - c. The duration of stay in the hospital

2. To identify the demographic and clinical characteristics of patients who had died of COVID 19.

METHODS

This retrospective study was conducted in SSMC associated hospital, Rewa district, India, a tertiary care centre which was identified as Dedicated Covid Hospital for providing care and treatment for covid-19 disease. It caters to population of four adjoining districts. Covid-19 positive patients diagnosed by RTPCR or Rapid Antigen Test (RAT) at the time of admission and remained positive throughout their clinical course and died (112) from May 2020 to January 2021 in this institute were considered for this study. Thus Study population comprised of 112 deceased.

Data Collection Methods

The death reviews on every covid deaths were designed to provide an understanding of the causes and clinical course of patients. Data was collected and filled in the prescribed format. Study variables include socio-demographic profile, pre hospitalization history, systemic diseases / underlying medical condition, sign and symptoms of disease, clinical course, investigations and procedures performed. Information was collected by reviewing Referral notes, case sheets, lab reports and interviewing treating physician. Researchers verified the information by telephonic interview of deceased family members. Best respondents were interviewed regarding socio demographic profile, pre hospitalization clinical condition after obtaining informed consent.

Time Duration Variables

The date of symptoms onset, time taken for seeking medical care, date of admission in DCH and date of death were recorded accurately. Time duration between onset of initial symptoms to onset of breathlessness and duration from onset of breathlessness to hospitalization were considered as separate variables as each had its independent effect on clinical course. Breathlessness warrants most important symptom in the clinical course of disease as it reflects the clinical condition of patient. It compels patient to realize severity of situation and decision to take medical care. Therefore, time duration from breathlessness to hospitalization was considered as delay in this study.

Clinical Syndrome (Infection Severity) Classification

Clinical syndrome as per the infection severity with which patient presented at the time of admission were recorded from the clinical records and thereafter coded for analysis ranging from 1 to 5 with increasing severity of clinical condition. 1. Sepsis, 2. Respiratory Failure with sepsis, 3. Acute Respiratory Distress Syndrome (ARDS) with Sepsis, 4. Multiple Organ Dysfunction Syndrome (MODS) with ARDS

and 5. Multiple Organ Failure (MOF) Laboratory parameters C-Reactive protein and D-Dimer levels and radiological findings were also considered in this research paper.

Ethical Consideration

Informed consent was obtained from best respondents of the deceased patients. The anonymity and confidentiality of all the deceased persons and persons interviewed were maintained. Ethical clearance was obtained from institutional ethical committee.

Statistical Analysis

The data was then analysed using computer software Stata and MS excel 2016 Qualitative or categorical variables were presented as percentages and proportion. chi square test and t test was applied for testing significance. All quantitative variables such as age, Hospital stay, Time taken for seeking treatment, laboratory values were estimated using measures of central location (mean, median, IQR). The associations between the different variables including time duration variables with syndrome severity were evaluated using Spearman's rank correlation coefficient.

RESULTS

A total of 820 covid-19 positive patients were admitted between May 2020 to January 2021. Among these total 112 deaths were recorded during this period which corresponds to fatality rate of 13.7 % in the hospital. Out of 112 deaths 28 were females and 80 were males. Among 112 COVID deaths investigated, the leading cause was COVID induced severe pneumonia and Acute Respiratory failure (97). In Rest 15 cases causes of death were due to acute exacerbation of co-morbid illnesses they were already having, that is Cerebro Vascular Accident, Chronic Kidney Disease and Coronary Artery Disease.

4 patients were admitted in this facility for indications other than covid-19 related symptoms and they had been diagnosed incidentally of having covid infection as per routine procedures performed. These patients had been excluded from analysis as time variables could not be calculated and clinical spectrum was clearly different from Covid 19.

Most of the covid positive patients who died belonged to 41 - 70 yrs. age group. (Min 14 and max 90 yrs. old). The mean age of deceased patients was 60.5 years, while it was 61. 7 years for males and 57.04 years for females. (t value 1. 58, P value. 117, NS) 43.5 % were residents of Rewa district followed by 36.1 % belonging to Satna district. Half of the Deaths (53 %) occurred during the month of September 2020. 44.4 % patients came directly to SGMH (DCH) for treatment / health check-up. 55.6 % came here upon referral, main indications being breathlessness, worsening of symptoms and deteriorating condition.

The demographic and clinical information of deceased patients is summarized in Table I.

	Class	Number	Percentage
Age	0 - 40	7	6.5
	41 - 50	20	18.5
	51 - 60	23	21.3
	61 - 70	37	34.3
	71 - 80	14	12.9
	80 - 90	7	6.5
Sex	Class	Number	Percentage
	Male	80	74.1
	Female	28	25.9
District	Rewa	47	43.5
	Satna	39	36.1
	Sidhi	10	9.2
	Singrauli	10	9.2
	Panna, Mumbai	11	1.8
Month of Death	Jan	3	2.8
	Dec	4	3.7
	Nov	5	4.6
	Oct	10	9.2
	Sept	58	53.7
	Aug	19	17.6
	July	7	6.5
	June	0	0
	May	2	1.8
Patients having chronic co morbid condition N = 77 (71.3 %)	≥ 3 co morbidities	24	22.2
	2 co morbidities	25	23.2
	1 co morbidity	28	25.9
	None	31	28.7
Chronic conditions (N = 77)	DM	54	70.1
	HTN	34	31.5
	CKD	14	13.0
	Morbid Obesity	10	9.3
	Heart diseases	12	11.1
	Moderate / Severe Anaemia	13	12
	Chronic Lung Disease	07	6.5
	CVA	07	6.5
	Cancer	05	4.6
	Liver and GB Ds	04	3.7
	Hypothyroidism	03	2.8
	Others*	04	3.7
Initial symptoms (multiple symptoms)	Fever	68	63
	Cough	71	65.7
	Fever with chills	15	13.9
	Generalized weakness	32	29.6
	Breathlessness	06	5.5
	Loss of appetite	10	9.3
	Pain in abdomen	9	8.3
	Diarrhoea	5	4.6
	Chest pain	4	3.7
	Altered Sensorial	22	20.4
Clinical Syndrome present at the time of admission	MOF	14	13
	MODS with ARDS Given in Material methods	27	25
	ARDS with Sepsis	35	32.4
	RF with Sepsis	24	22.2
	Sepsis	08	7.4
	C-Reactive Protein Level (mg / lt)	Mean = 29.86, Median = 8.31, Mode = 3.12, IOR = Q3 - Q1 = 34.77 - 3.12 = 31.65	Normal range = 0.2 to 6
	D - Dimer (ng / ml)	Mean = 1116.28, Median = 433.22, Mode = 2776.87, IOR = Q3 - Q1 = 1143.77 - 250.71 = 893.05	Normal value < 500
	*Others=parkinsons1, osteoarthritis 1, Polio 1, BPH 1, Infections 02 typhoid, UTI		
	Clinical Characteristics (Table 1)		
	Mean = 60.5 yrs., Median = 61. 3, S D = 13. 55 Min = 14, Max = 90, IQR = 69.5 - 50.25 = 19.25		

Table 1. Demographic Information and Clinical Characteristics

*Others=parkinsons1, osteoarthritis 1, Polio 1, BPH 1, Infections 02 typhoid, UTI
Clinical Characteristics (Table 1)
Mean = 60.5 yrs., Median = 61. 3, S D = 13. 55 Min = 14, Max = 90, IQR = 69.5 - 50.25 = 19.25

71.3 % patients were suffering from 1 or more chronic diseases. 22.2 % cases had 3 or more chronic diseases. However, 28.7 % cases did not have any co morbid condition. Co morbidities including diabetes, hypertension, CKD, Heart disease and obesity were observed more frequently.

Most common initial symptoms were fever (76.9 %) followed by cough in 65.7 % patients. Generalized weakness was experienced as presenting symptom in 29.6 % while breathlessness as initial symptom was reported by only 5.5 % cases. Other symptoms include pain in abdomen, diarrhoea, loss of appetite and chest pain. Subsequently all

patients developed breathlessness. About 22 patients presented with altered sensorium at the time of admission in DCH. 4 patients presented with indication of Renal transplant therapy (Dialysis).

Severity of covid infection among study cases at the time of admission was classified into five clinical syndromes. Laboratory parameters indicated increased level of inflammatory markers. (Table 1)

Radiographic Findings and Distribution on Baseline Chest X-Ray at the Time of Admission		Number (%)
Type of parenchymal opacity	X Ray Could Not Be Done	05 (4.6 %)
	Consolidation	87 (80.5 %)
	Ground glass opacity	04 (3.7 %)
	Nodular Infiltrations	10 (9.2 %)
	Pleural effusion	01 (0.9 %)
	pneumothorax	00
Distribution in Lungs	Diffuse Fibrocavitary lesions	01 (0.9 %)
	Peripheral predominant	00
	Perihilar predominant	00
	Diffuse	101 (93.5 %)
	Right lung	03 (2.7 %)
Involved lung field	Left lung	01 (0.9 %)
	Bilateral lungs	96 (88.8 %)
	Single zone involvement	03 (2.6 %)
	Multiple zone involvement	98 (90.7 %)
	Right upper zone	76 (70.3 %)
	Right middle zone	61 (56.4 %)
	Right lower zone	101 (93.5 %)
	Left upper zone	42 (38.8 %)
	Left middle zone	63 (58.3 %)
	Left lower zone	98 (90.7 %)

Table 2. Radiographic Findings and Distribution on Baseline Chest X-Ray at the Time of Admission (N = 108)

Radiological findings were shown in Table - 3. In x-ray most common parenchymal abnormality at the time of admission was consolidation, which was present in 80.5 %, with diffuse distribution (93.5 %), bilateral multiple zone involvement, in 90.7 % patients. Apart from consolidation nodular infiltrations were present in 9.2 % patients, and ground glass opacity was present in 3.7 % patients. Only

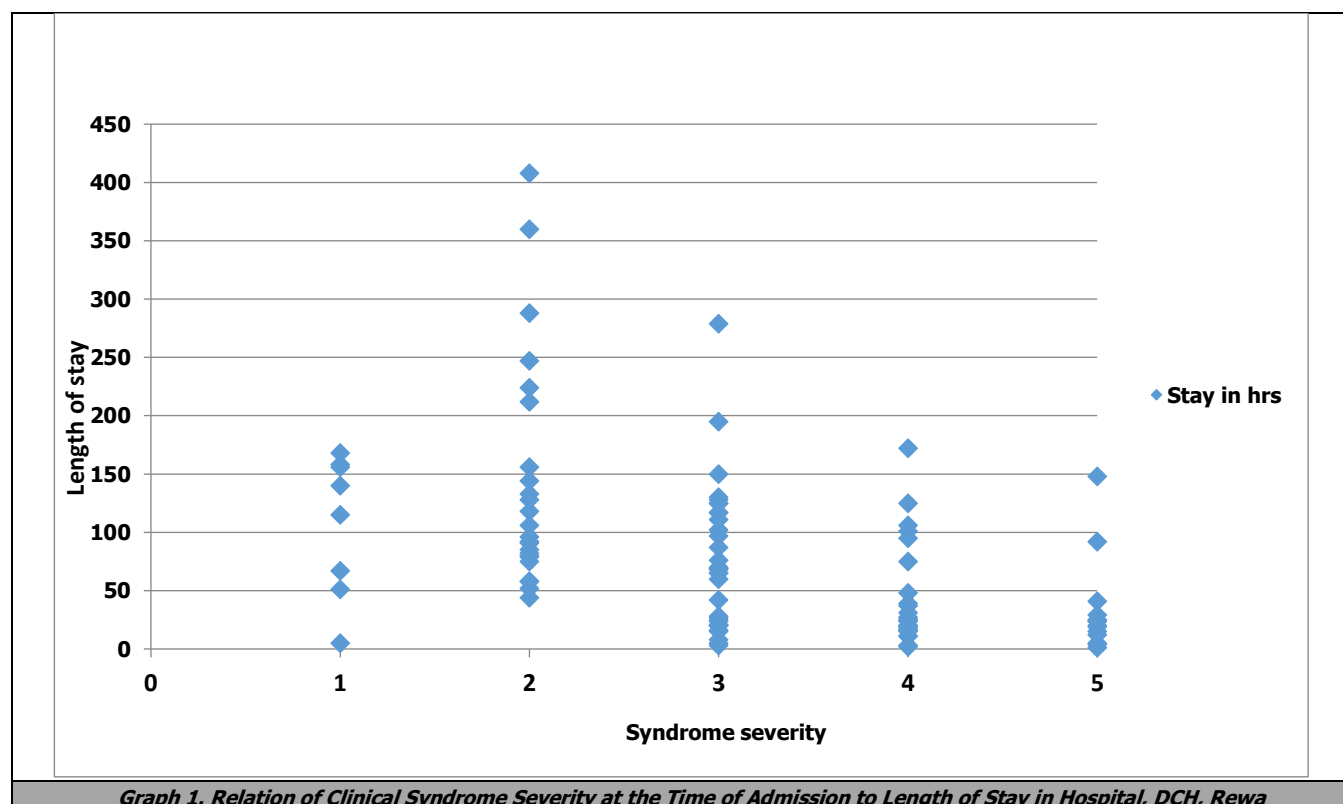
one patient had left sided pleural effusion, and one patient had diffuse fibrocavitary lesions in chest x ray. At the time of admission Right lower zone (93.5 %) and left lower zone (90.7 %) were most frequently involved lung fields.

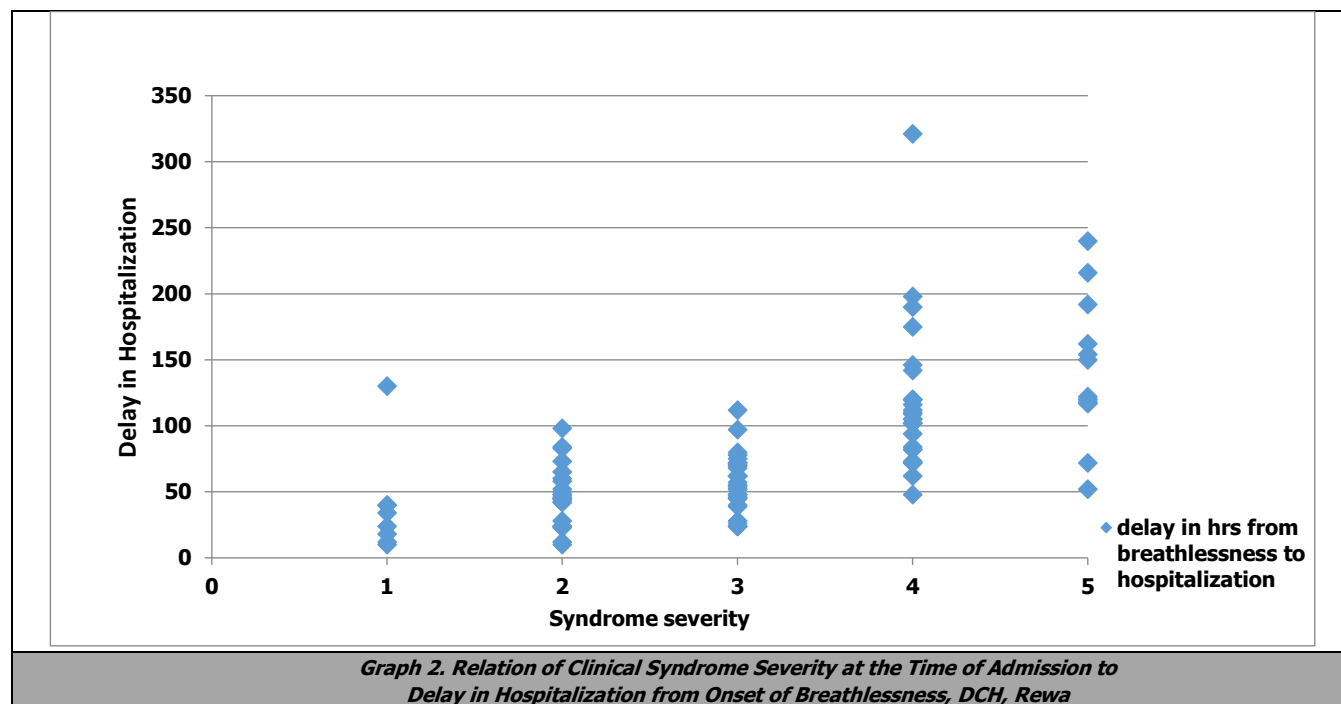
Time Duration Variables

The Mean length of stay in a hospital amounted to 3 days 6 hrs while Median stay was about 2 days 10 hrs. Median duration for the onset of first symptoms and admission to DCH or presentation to the health facility was 5 days. Median duration from onset of initial symptoms to onset of breathlessness was 1 day 18.5 hrs, Delay in Hospitalization from onset of Breathlessness was 2 days 22 hrs and Median length of stay in hospital was 2 days 13.5 hrs.

Class	No	Percent	
Length of Stay in Hospital (SGMH)	< 1Day	34	31.5
	1 - < 3Days	27	25
	> 3 - 7 Days	38	35.2
	> 7 Days	9	8.3
Mean = 78.12 hrs, Median 62.5 Min = 1hr, Max = 408 IQR = Q3 - Q1 = 96			
Class	No	Percent	
Time interval from initial symptoms onset to 1 st visit	< 1 Day	13	12.04
	1 - < 3 Days	29	26.9
	> 3 - 7 Days	51	47.2
	> 7 Days	15	13.9
Min = 1, Max = 14, Mean = 4.7 days, Median = 5days, IQR = 5 days			
Class	No	Percent	
Time from appearance of initial symptoms to Hospitalization in DCH, Rewa	< 1 Day	3	2.8
	1 - < 3 Days	25	23.1
	> 3 - 7 Days	59	54.6
	> 7 Days	21	19.4
Min = 1, Max = 15, Mean = 5.5 days, Median = 5 days, IQR = 4			
Class	No	Percent	
Duration from onset of initial symptoms to onset of Breathlessness	< 1 Day	42	38.9
	1 - < 3 Days	40	37.1
	> 3 - 7 Days	21	19.4
	> 7 Days	05	4.6
Min = 0, Max = 360, Mean = 53.57 hrs, Median = 42.5, IQR = 59.5			
Class	No	Percent	
Delay in Hospitalization from onset of Breathlessness, DCH, Rewa	< 1 Day	13	12
	1 - < 3 Days	49	45.4
	> 3 - 7 Days	39	36.1
	> 7 Days	07	6.5
Min = 10, Max = 321, Mean = 79.2hrs, Median = 70, IQR = 54.28			

Table 3. Time Duration Variables





		1*vs.2 †	1vs.3‡	1vs.4●	1vs.5	1vs.6**
Spearman r	r	0.7645	0.1489	0.006210	-0.5699	-0.02419
	95 % confidence interval	0.6697 to 0.8349	-0.04693 to 0.3336	-0.1884 to 0.2004	-0.6881 to -0.4223	-0.2176 to 0.1710
P value	P (two-tailed)	<0.0001	0.1242	0.9491	<0.0001	0.8037
	P value summary	****	ns	ns	****	ns
	Significant? (alpha = 0.05)	Yes	No	No	Yes	No
	Number of XY Pairs	108	108	108	108	108

Table 4. Spearman Correlation between Different Variables

* Clinical Syndrome at the time of admission
† Delay in Hospitalization from onset of Breathlessness, DCH, Rewa
‡ Age
● No of comorbid conditions
|| Length of stay in hospital
** Gender, Male and Female

Spearman correlation rank test was applied in Table 4 depicts, length of stay in hospital ($r = -0.5699$, P value = < 0.0001) shows negative correlation with clinical syndrome at the time of admission. Patients who presented with less severe clinical condition had longer length of stay in hospital. Delay in hospitalization shows a strong positive correlation with severity of clinical syndrome at the time of admission. As delay increases severity increases. ($r = 0.7645$, P value = < 0.0001) Although age and number of co morbid conditions had no significant values they showed a weak positive relation with severity of syndrome.

DISCUSSION

This study attempts to find out the epidemiological and clinical characteristics of patients who died due to COVID-19. Fatality rate of covid in our tertiary care hospital was 13.7 %. A multicentric study reported the average mortality rate as 26.84 %.¹⁷ Heterogeneous mortality rates were

observed in different countries of the world. This might be due to different age composition, clinical condition of patient at the time of presentation and government preparedness for the pandemic. Majority of deaths occurred in the month of September which corresponds with increasing phase of epidemic in the month of September observed in India with overburdened hospitals. In our study, data revealed that majority of the covid patients who died were males with age 60 or more and suffering from 2 or more chronic diseases. Other studies corroborate these findings.^{16,17} Majority of the patients, 71.3 % had one or more co morbidity. However less than 30 % did not have any co morbidity. Similar findings were reflected in other studies: Most common chronic diseases found in our cohort were Diabetes mellitus, Hypertension, CKD and obesity. Most common presenting symptom was fever followed by cough.^{17,18} Several predictors responsible for the death of the covid patients were identified in meta-analysis,¹⁹ various regressions and other models.^{14,20,21} Our study cohort characteristics were in concordance with these studies. Various laboratory parameters were included in many studies as marker of organ damage and predictors of severity of disease. In our study we found that level of CRP and D Dimer were raised and comparable with the levels reported in critically ill patients included in various studies.^{17,20}

Majority (90 %) of the patients had Bilateral Zone involvement at the time of admission. Study conducted by Zhang B et al. reported all patients had bilateral involvement of lungs, majority of them were severely ill.¹⁷

Further an attempt was being made to find the chronology of onset of first symptoms to breathlessness and time taken for seeking medical care and death. Median time from onset of symptoms to hospitalization or first contact with health care facility was 5 days while other studies in different countries revealed it may be as short as 2.6 days in Singapore to 5.14 days in UK.¹⁵ Some countries reported

5 to 7 days and 4.6 days between symptom onset and hospital admission.^{2,14} Median durations between initial symptom and breathlessness was found to be 1 day 18.5 hrs in our study which was quite short. Huang C et al.² reported that severely ill patients may develop ARDS in 2 days. This finding indicates that disease may adopt acute severe course in high risk group. 76 % patients in our study experienced breathlessness within 3 days of initial symptoms, however only 39 % presented to the health care facility for medical care. Another study reported 75 % patients were hospitalized within 8 days after symptom onset.¹⁵

The delay in our study refers to the delay in recognizing symptoms especially breathlessness and making a prompt decision to seek care. Median period of delay for hospitalization or seeking care was 2 days and 22 hrs. This is the duration patients took even after the appearance of breathlessness which is a matter of concern. Alaa A et al.¹⁴ in their study documented that later hospital admission was an independent risk factor for mortality. Reducing this delay is particularly important in covid disease in which symptoms can worsen within hours and limited information is available regarding its clinical course. The main factor behind this type of delay could be lack of knowledge and underestimation of signs, symptoms, and severity of the problem.

38 % patients in our study presented to the tertiary care hospital with multiple organ involvement. A Study documented patients in deceased group were susceptible to multiple organ failure, especially heart and respiratory failure.²² Another study reported much higher involvement of multiple organs.¹⁷

Median Length of stay of deceased patients in our hospital was 2 and a half days. More than half (56.5 %) of the deceased had length of stay not more than 3 days. Faes C et al.¹⁵ in their study reported The Median Length of stay in a hospital from 3 to 10.4 days and LoS increasing with age. However, their study included both survivors and non survivors. Shorter Length of stay might be due to the severe presenting condition of patients. Majority of the patients were hypoxemic having multiple organ involvement with ARDS and Sepsis in our study.

After applying spearman rank correlation test, we found a significant correlation between severity of clinical syndrome at the time of admission, delay for hospitalization and length of stay in hospital. As the delay increases severity of syndrome increases. Shorter Length of stay was observed in cases having severe syndrome. It is reported in various studies that time elapsed for seeking care is crucial and has survival value.^{12,14,15} Damage to the multiple organs can be prevented and treated if the patient reaches the health care facility on time and gets appropriate and quality care. Also, a well-equipped health facility with a good referral network plays an important role in preventing the mortality. There were 63 cases (56.3 %) for whom the first place to seek care was DCHC or private practitioners. Although statistically significant difference was not observed between mean duration of contacting the first place of care to DCH but every hour counts in acute diseases like covid infection.

CONCLUSIONS

Elderly persons with underlying chronic illnesses are more likely to contract the virus and become severely ill. In this study we identified delay in hospitalization even after having breathlessness to be life threatening. If respiratory symptoms develop, it is important to seek immediate care. Thorough assessment of underlying causes of death and contributing factors provide useful data for planning various interventions and strategies. Awareness about risk factors should develop in the community. Self-assessment tool could be developed taking into account the predictors of mortality. It must be appropriate and suitable for implementation in general population. This can help individuals to assess their individual risk for covid-19 infection. Timely identification of symptoms, risk stratification and interventions, prompt referral where necessary are the key factors in the reduction of mortality.

Limitation

Firstly, the study group comprised of deceased patients which depicts limited clinical picture. Further studies in community settings are needed to get a full picture of the spectrum of clinical severity. Secondly, Time variables in the study depend on the symptoms reported. However, symptoms are self-reported and subject to recall bias. So these variables need more validation with study population including mild to severely ill patients.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

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