

Clinico-Laboratory Profile of Deaths in COVID-19 Positive Patients: A Retrospective Study from a Tertiary Care Hospital in India

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Abstract

Introduction: COVID-19 infections have caused millions of deaths around the world. This study gives a detailed insight into the demographic and clinico-laboratory profile of deaths among COVID-19 patients over a period of one year admitted in a tertiary care COVID hospital.

Methodology: In this retrospective observational study, medical records of admitted COVID-19 positive deaths in adult patients over a period of one year from 1st April 2020 to 31st March 2021 were retrieved. The data includes the co-morbidities present, symptoms, duration of symptoms to admission time, duration of hospital stay, clinical examination findings and laboratory reports.

Results: Medical records of 445 COVID-19 positive deaths were studied. The mean age was 55 ± 18.49 years and the majority were in the age group of 41 - 60 years. Around 61% were males and 39% were females. Diabetes and hypertension were the most common co-morbidities present. The average duration of symptoms before hospitalization was 5.26 ± 4.5 days. Breathlessness was the most common presenting symptom. The average duration of stay in the hospital was 6.73 ± 7.18 days. The serum ferritin, C-reactive protein (CRP), serum lactate dehydrogenase (LDH) and D-dimer were increased in the majority of patients.

Conclusion: An early admission and optimal management during the initial period of COVID-19 disease is critical and may help in decreasing the mortality. The raised CRP, high serum LDH and serum ferritin can be used as predictors of poor prognosis.

Key words: COVID-19, prognostic markers, clinical profile in COVID-19, laboratory profile in COVID-19, deaths in COVID.

Introduction

The novel corona virus 2019-nCoV or COVID-19 has infected people all over the world in a short span of time. On March 11, 2020, WHO declared COVID-19 as a pandemic. There have been about 609 million confirmed COVID-19 cases with over 6.5 million deaths globally¹. Around 5.2 lakh deaths occurred due to this pandemic in India, and about 26,499 deaths have been reported in the capital city of New Delhi². COVID-19 has a varied spectrum of presentation ranging from asymptomatic cases to severe pneumonia to acute respiratory distress syndrome (ARDS) with multiple organ failure and death. In a study from China by Wang K *et al*, the major cause of death in COVID-19 patients was found to be acute respiratory failure and sepsis³. On one hand, the case fatality ratio (CFR) has been quite high in some countries like Yemen (18%), Sudan (7.84%), Syria (5.53%), Somalia (5%), and Mexico (4.7%), on the other some countries have very low CFR such as Bhutan (0.03%), Singapore (0.09%), and New Zealand (0.11%). Among the countries with maximum confirmed cases, India has a CFR of about 1.1% compared to Russia (1.88%), Brazil (1.98%), USA (1.1%) and global CFR of 1%¹. This variation in mortality

rates has been postulated to be due to various factors such as racial differences, population age composition, health facilities availability, hospitalisation criteria and local administrative policies⁴.

It has been observed that lymphopenia, high NLR (Neutrophil lymphocyte ratio), raised D-dimer and high C-reactive protein (CRP) are poor prognostic factors in COVID-19⁵. However, there is a relative lack of literature on demographic, clinical and other laboratory factors associated with the disease severity and mortality in COVID-19. Hence, the present study was conducted to identify the same.

Methodology

This retrospective observational study was conducted at Department of Medicine of a dedicated tertiary level COVID-19 care hospital of New Delhi, India. The medical records of COVID-19 positive deaths during the period of one year from 1st April 2020 to 31st March 2021 were retrieved after obtaining Institutional Ethics Committee approval. All adult patients (>18 years of age) who were admitted and died with confirmed COVID-19 infection [confirmed by

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positive reverse transcriptase polymerase chain reaction (RT-PCR) or cartridge based nucleic acid amplification test (CBNAAT) or rapid antigen test (RAT) of nasopharyngeal/oropharyngeal swab] were included in the study. The data including age, gender, co-morbidities, duration of symptoms, duration of hospital stay, clinical examination findings, laboratory reports and treatment given (as mentioned in case sheets) was recorded as per the study proforma.

Statistical Package for Social Sciences (SPSS) version 16 (Chicago, USA) software was used for statistical analysis. All quantitative variables were expressed as Mean \pm Standard Deviation and Median. Qualitative variables were expressed as proportion. The Cox proportion analysis was applied to identify the significant risk factors.

Results

Over a period of one year, from 1st April 2020 to 31st March 2021, around 1,843 patients with COVID-19 positive report were admitted in COVID wards/Intensive care units (ICU)/high dependency units (HDU) of our hospital. The medical records of 445 COVID-19 positive deaths during this period were retrieved from the medical records section, and data collected from case records was subsequently analysed.

Among the 445 COVID-19 positive deaths observed, 271 (60.9%) were males and 174 (39.1%) were females. The mean age of the study population was 55 ± 14.89 years, ranging from 18 - 94 years. The majority (47.41%) were in the age group of 41 - 60 years (Table I).

Table I: Age-wise distribution of patients.

AGE (in years)	Males	Females	Total
≤ 25	5	11	16 (3.59%)
26-40	41	19	60 (13.48%)
41-60	126	85	211 (47.41%)
61-80	89	57	146 (32.80%)
≥ 81	10	2	12 (2.69%)
TOTAL	271	174	445

About 76% of the patients had one or more co-morbidities. Diabetes and hypertension were the most common co-morbidities observed, followed by coronary artery diseases (CAD) and chronic kidney disease (CKD) (Table II). The routine blood investigations and examination findings are presented in Table III.

The average duration of symptoms before hospitalisation was 5.26 ± 4.53 days, with the median time being 4 days.

Breathlessness was the most common presenting

symptom, seen in 80% (356 of 445) of patients, followed by fever in 270 patients (60.6%) and cough in 196 patients (44%). Other common symptoms observed were vomiting, diarrhoea, sore throat and chest pain.

Table II: Distribution of patients based on the co-morbidities.

Co-morbidity	N(%)
Diabetes	188 (42.24)
Hypertension	176 (39.55)
Coronary Artery Disease (CAD)	61 (13.70)
Chronic Kidney disease(CKD)	53 (11.91)
Chronic obstructive Pulmonary Disease (COPD)/ Bronchial Asthma	25 (5.61)
Chronic liver disease (CLD)	16 (3.59)
Thyroid disorders	16 (3.59)
Others(HIV, CNS disorders, Rheumatic heart Disease, Malignancy, Rheumatoid arthritis, depression, etc.)	31 (6.96)

Table III: Routine blood investigation and examination findings

Parameter	N	Mean \pm SD
Systolic Blood Pressure (mmHg)	423	116.98 \pm 29.97
Diastolic Blood Pressure (mmHg)	408	74.29 \pm 15.22
Respiratory rate (per minute)	263	25.92 \pm 6.88
Oxygen saturation at room air SpO ₂ (%)	366	80.48 \pm 15.69
Haemoglobin (gm/dl)	380	11.11 \pm 2.63
Total Leucocyte Count (per mm ³)	379	12338 \pm 9343.54
Neutrophils (per mm ³)	318	83.11 \pm 8.90
Lymphocytes (per mm ³)	247	13.39 \pm 8.64
Neutrophil lymphocyte Ratio (NLR)	247	9.21 \pm 8.6
Platelet count (lacs/mm ³)	376	2.02 \pm 0.98
Random Blood sugar (mg/dl)	69	223.52 \pm 144.27
Blood Urea (mg/dl)	379	80.71 \pm 71.31
Serum Creatinine (mg/dl)	379	2.51 \pm 3.53
Total Bilirubin (mg/dl)	295	1.25 \pm 2.84
Aspartate transaminase (AST)(U/L)	367	105.86 \pm 304.04
Alanine Transaminase (ALT) (U/L)	367	73.79 \pm 245.94
Alkaline Phosphatase (ALP) (U/L)	315	131.40 \pm 105.77
Serum Sodium (mmol/l)	378	138.07 \pm 7.91
Serum Potassium (mmol/l)	376	4.39 \pm 1.06

The average duration of stay in the hospital, (i.e., the time from hospital admission to death) was 6.73 ± 7.18 days.

Around 25% deaths occurred within the first 24 hours of admission and another 12% in the next 24 hours, (i.e., more than one-third people died within the first 48 hrs of admission) (Table IV). It was observed that elderly patients had shorter hospital stay and died early (Table V).

Table IV: Distribution of patients based on duration of hospital stay.

Duration of hospital stay	N (%)
Less than 12 hours	45 (10.11%)
12 - 24 hours	63 (14.15%)
24 - 48 hours	53 (11.9%)
3 - 5 days	86 (19.32%)
5 - 10 days	102 (22.92%)
11 - 14 days	42 (9.43%)
≥ 15 days	54 (12.13%)

Table V: Mean duration of hospital stay according to age.

Age (in years)	Mean duration of hospital stay (in days)
≤ 25	7.81
26 - 40	7.45
41 - 60	6.64
61 - 80	6.71
≥ 81	3.25

The mean NLR ratio (N = 247) was 9.21 ± 8.6 . Around 59% patients (146/247) had NLR > 5.9 at the time of admission. The cut-off of NLR > 5.9 was taken as it was found to be associated with high in-hospital mortality in patients hospitalised for COVID-19 pneumonia in a validation analysis by Yildiz *et al*⁶. The mean serum ferritin level (N = 107) was 639.09 ± 562 ng/ml. (Normal value in males: 18 - 464 ng/ml and females < 50 years: 6 - 137 ng/ml and females > 50 years: 11 - 264 ng/ml). 66% (71 of 107) patients had raised serum ferritin levels. 30.8% patients (33 of 107) had very high levels (greater than 1,000 ng/ml) of serum ferritin.

CRP levels were available for 101 patients. CRP was elevated (> 6 mg/l) in 83.16% (84 of 101) of patients with mean CRP being 104.45 ± 99.85 mg/l.

Similarly, serum lactate dehydrogenase (LDH) was raised (> 450 U/L) in 94.4% (135 of 143) of patients with mean value of 1077.75 ± 704.88 U/L. Twelve patients had serum LDH levels greater than 2,000 U/L.

35 of 37 patients had increased D-dimer level of more than 250 ng/ml. Of this, 9 patients had d-dimer levels

more than 2,500 ng/dl. Highest level observed was 10,000 ng/dl.

Almost 70 per cent of patients (272/391) had bilateral infiltrates on chest X-ray. 31 of 391 (8%) had unilateral infiltrates/consolidation on X-ray and around 22% (88 of 391) had normal X-ray findings.

Invasive ventilation was given to 36% (162) patients. Non-invasive ventilation in the form of BI-PAP and high flow nasal cannula (HFNC) were applied to 8.8% (39) and 4.3% (19) of total patients respectively.

Steroids were given to 284 patients (63.8%) and low molecular weight heparin (LMWH) was given to 285 patients (64%). 22 patients received Remdesivir.

The Cox-Proportional Analysis showed that those with breathlessness had (hazard risk HR - 1.15, 95% confidence interval CI - 1.02 - 1.29) ($p = 0.021$) indicating higher mortality in those who had dyspnoea. The CRP levels had a (HR 1.002, 95% CI 1.001 - 1.003) ($p = 0.003$) indicating higher CRP levels were associated with increased mortality. Use of steroids and LMWH showed hazard risk of 0.083 ($p < 0.001$) and 0.084 ($p < 0.001$), respectively suggesting that their use was associated with less mortality.

Discussion

This is one of the largest study of COVID-19 related mortality spread over a period of one year.

The mortality among hospitalised patients was found to be higher as compared to overall mortality in the country, as most of the patients who were admitted to the hospital had moderate-to-severe COVID-19. Patients with mild COVID-19 were managed at home or COVID-19 care centres.

A male predominance was seen, with about 61% males among the total deaths. Asirvatham *et al* also reported a higher proportion of deaths (71%) among men⁷. The gender disparity in morbidity and mortality associated with COVID-19 is attributed to increased expression of angiotensin converting enzyme-2 (ACE-2) in lungs which is regulated by male sex hormones⁸. ACE-2 enzymes have been postulated in the pathogenesis of COVID-19. Viral interaction with the ACE-2 receptor causes endothelial injury and thus, increased risk of thrombosis. Another reason for higher mortality among males is due to the increased presence of risk factors such as smoking and alcohol use which is not common in Indian females. In a study by Li Y *et al*, X chromosome and sex hormones were attributed in providing innate and adaptive immunity to females and thus, lower mortality in women with COVID-19⁹.

The mean age was 55 ± 14.89 years with a median of 55 years. In a similar study from Mumbai, the median age was

64.8 years¹⁰. Higher mortality rates were observed with advancing age due to poor lung functions, presence of co-morbidities and reduced innate and adaptive immune response.

The most common co-morbidities observed were diabetes and hypertension. Around 70% of patients had one or more co-morbidities. Previous studies have also shown that there is higher mortality in COVID-19 patients with co-morbidities compared to patients without any co-morbidities^{11,12}.

The median time duration from symptom onset to hospitalisation was 4 days which was same as reported by Asirvatham *et al* in their study⁷. In a similar study from Italy, the reported mean interval between symptom onset and hospitalisation was 3.6 ± 3.2 days¹³.

Breathlessness was the most common symptom observed (in about 80% of patients) followed by fever in about 60% of patients. Tambe *et al* reported that breathlessness was the most common symptom observed followed by cough and fever¹⁴.

The average duration of hospital stay, (i.e., period from hospital admission to death) was 6.73 days (median time duration was 5 days). In a study from China during the initial phase of the pandemic, Chen *et al* reported a median time of 16 days from disease onset to death¹⁵. However, a study from India reported the median time interval of 4 days⁷.

It was observed that the duration of hospital stay was shorter for elderly population. The average duration of hospital stay was just 3.25 days for patients greater than 81 years of age as compared to 7.81 days for patients less than 25 years of age. Londhey *et al* also observed around 27% (209/763) deaths in first 24 hours and 52% deaths between 24 - 72 hours¹⁰. Goel *et al* also reported 33% deaths within first 72 hours of hospital admission¹⁶. A study from Sudan reported around 63.64% of deaths within first 24 hours of admission¹⁷. The early deaths post-hospitalisation may be due to delay in seeking healthcare. The reasons for this delay include ignorance of severity of disease, fear of sealing of the residential area, quarantine of other family members and lack of transport facilities because of nationwide lockdown. Infact, in many of these patients there was rapid deterioration of the disease due to so called "Happy Hypoxaemia syndrome" - a syndrome in which there is pronounced arterial hypoxaemia but the patient does not have proportionate signs and symptoms of respiratory distress¹⁸. These patients present late to hospital as they do not have any severe respiratory distress or dyspnoea despite low blood oxygenation.

High serum LDH levels were observed in 95% of patients, raised CRP levels in 83% and high levels of serum ferritin in 66%. About 31% had very high level of serum ferritin (levels

> 1,000 ng/ml). A study from Saudi Arabia noted that patients who died due to COVID-19 had high levels of ferritin, lactate dehydrogenase, D-dimer, and erythrocyte sedimentation rate at admission and 24 hours prior to death¹⁹. Thus, high LDH levels, D dimer, ferritin and CRP can be considered as poor prognostic markers.

Conclusion

The study concludes that maximum deaths were in first 24 - 72 hours of hospital admission. Thus, early admission and better management with ICU care during the initial period of disease is critical and may help in decreasing the mortality. There should be increased awareness about the need of early hospital care, as soon as there is fall in oxygen saturation. It may cause a rapid deterioration in clinical condition and a timely intervention can affect the course of disease. Raised CRP, high serum LDH and serum ferritin levels can be used as predictors of poor outcome.

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