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Original Article

Biochemistry Section

Clinical Characteristics and Risk Factors for Mortality in COVID-19 Patients at a Tertiary Care Centre in Southern Assam, India: A Retrospective Study

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ABSTRACT

Introduction: Coronavirus Disease-2019 (COVID-19) infection can cause a wide range of symptoms, from asymptomatic infection and mild upper respiratory tract disease to severe viral pneumonia with respiratory failure and multiorgan malfunction. Through this study, effort was put forward to know the COVID-19 in terms of clinical characteristics, risk factors and laboratory parameters which in turn may serve as predictors of severe sickness and negative outcomes of COVID-19.

Aim: To study the clinical characteristics, risk factors and laboratory parameters of COVID-19 patients in a part of North Eastern India, and also to compare these parameters between survivors and non survivors.

Materials and Methods: This retrospective study was conducted in Silchar Medical College and Hospital, Silchar, Assam, India. Study included all patients of COVID-19 diagnosed by Reverse Transcriptase Polymerase Chain Reaction (RTPCR) or Rapid Antigen Test (RAT) admitted from 1st July, 2020 to 31st December, 2020. The data included demographic parameters, presenting symptoms, significant medical, surgical or drug history etc., and laboratory parameters including complete blood count, Random Blood Sugar (RBS), chest x-ray, renal and liver function test, C-reactive protein, Lactate Dehydrogenase (LDH), serum ferritin, troponin I etc. Data were statistically analysed by unpaired t-test for continuous variables and chi-square test was used for comparing proportions.

Results: Out of a total 2262 study subjects, 2066 (91.34%) were discharged from the hospital after recovery and 196 (8.66%) had expired. The various parameters contributing significantly to mortality were male gender, age >60 years, various co-morbid conditions like diabetes mellitus, hypertension and cardiac illness. The laboratory parameters observed to be significantly associated with mortality were thrombocytopenia, leucocytosis, hyperglycaemia, raised value of lactate dehydrogenase, creatinine, D-dimer, ferritin, C-reactive protein. Radiological findings including ground glass opacities and pleural effusion also were more common in the non survivor group as compared to the survivor group.

Conclusion: More than half of the deceased patients were older than 60 years of age. The prevalence of co-morbidities and mean level of laboratory parameters were significantly high among non survivors as compared to those who recovered.

Keywords: Coronavirus disease-2019, Laboratory parameters, Rapid antigen test, Respiratory tract disease

INTRODUCTION

The Severe Acute Respiratory Syndrome (SARS) Coronavirus-2, which belongs to Corona viridae family, has resulted the frightening outbreak of acute atypical respiratory infections that began in Wuhan, China [1]. The COVID-19 is thought to have spread throughout the world by zoonotic transmission from a Chinese seafood market, and subsequent human-to-human transmission. On March 11, 2020, the World Health Organisation (WHO) labelled it a pandemic [1].

The COVID-19 infection can cause a wide range of symptoms, from asymptomatic infection and mild upper respiratory tract disease to severe viral pneumonia with respiratory failure and multiorgan malfunction, which can lead to death [2]. The intensity of disease is determined not only by the virus's virulence, but also by the host's immune response to the infecting agent [2].

Hypertension (HTN), Diabetes Mellitus (DM), age >60 years, Chronic Obstructive Pulmonary Disease (COPD), cancer, alcohol intake, smoking and others are considered as risk factors for COVID-19 infection [3]. Several laboratory indicators that could aid in predicting the severity of disease include d-dimer levels greater than 1 µg/mL and higher Sequential Organ Failure Assessment (SOFA) score on admission, high sensitivity cardiac troponin I, elevated levels of blood Interleukin (IL)-6, and lactate dehydrogenase, higher white blood cell and neutrophil counts, lymphopenia, thrombocytopenia, Alanine Transaminase (ALT), Aspartate Transaminase (AST), total bilirubin, serum creatinine etc [2,3,4].

Silchar Medical College and Hospital, a tertiary care hospital, in Southern Assam, stands as one of the most equipped hospital covering not only the entire Barak Valley of North-eastern India, but also for the nearby states viz Tripura, Manipur and Mizoram, thus broadening the scope of getting patients having different ethnic and social and cultural background. The goal of the research was to discover the clinical characteristics, risk factors and laboratory parameters of COVID-19 patients of this part of North-eastern India. Being a new infection that gained public importance in a short span of time, related studies from this part of Assam was scarce.

In the pioneer work of Patgiri PR et al., [4], the focus was mainly to analyse the demographic, clinical characteristics and outcome among the COVID-19 infected elderly patients. In the present research work, along with the elderly, the young subjects were also included for indepth understanding of the disease pathogenesis and outcome. Identifying the various factors associated with adverse outcome of the disease would help in proper resource allocation and planning and help prioritise patients for timely care and intervention as well as educating the mass in general.

Hence; present study was conducted to analyse the clinical characteristics, risk factors and laboratory parameters of COVID-19 patients of this part of North East India.

MATERIALS AND METHODS

This retrospective study was conducted from 1st July 2020 to 31st December 2020 for a period of six months, in Silchar Medical College and Hospital and the data was analysed from 1st August 2021 to 30th August 2021. The study was approved by Institutional Ethics Committee with issue no. [SMC/680 dated 09/02/2021].

Inclusion criteria: All patients aged >12 years, who tested positive for COVID-19 by Reverse Transcriptase Polymerase Chain Reaction (RTPCR) or rapid antigen test (RAT) and symptomatic for the disease (fever, cough, dyspnea, myalgia, etc) were included irrespective of severity of disease.

Exclusion criteria: Patients less than 12 years of age and patients who tested positive for COVID-19 infection but were brought dead to the hospital.

The data of all patients (2262) admitted between 1st July 2020 to 31st December, 2020 in COVID ward and covid Intensive Care Unit (ICU) of Silchar Medical College and Hospital with COVID-19 infection was taken for the study from the hospital data base.

Study Procedure

The data included were demographic parameters (like age, gender), presenting symptoms (like fever, cough, headache, dysnea, myalgia etc.), surgical history, medical history including diabetes mellitus, hypertension, malignancy, Chronic Obstructive Airway Disease (COAD), Chronic Kidney Disease (CKD), Chronic Liver Disease (CLD), or drug history such as immunosuppressive medications etc., and laboratory parameters including complete blood count, RBS, renal and liver function test, C-reactive protein, LDH, serum ferritin, troponin I etc, chest x-ray. The clinical profile, laboratory parameters and outcome during in-hospital stay were compared between those who survived and those who succumbed to the infection. The data obtained were recorded as per preformed proforma.

STATISTICAL ANALYSIS

Statistical analysis was done using Microsoft Excel 2016 and Statistical Package for the Social Sciences (SPSS) version 21.0. The discrete data were represented as number and percentage whereas continuous variables were represented as mean±Standard Deviation (SD). The p-value was calculated by unpaired t-test for continuous variables and chi-square test was used for comparing proportions. A p-value <0.05 was taken as statistically significant.

RESULTS

A total of 2262 patients were admitted out of which, 1546 (68.35%) were males and 716 (31.65%) were females. Mean age of the study subjects was 51.6±17.68 years. The mean age among the non-survivor group was 62.67±3.94 years which was significantly higher than the survivor group (44.82±7.92 years, p<0.001). Among the deceased patients, 104 (53.06%) were aged >60 years. The mortality among other age groups were 43 (21.94%) in 51-60 years, 25 (12.76%) in 41-50 years, 17 (8.67%) in 31-40 years, 2 (1.02%) in 21-30 years and 5 (2.55%) in <20 years age group. The recovery rate was highest 623 (30.15%) in 41-50 years age group followed by 504 (24.39%) in 31-40 years age group [Table/Fig-1].

After assessing clinically, it was found that out of total 2262 patients, 1102 (48.72%) were with mild, 875 (38.68%) with moderate and 285 (12.6%) were admitted with severe COVID-19. Also, while taking the drug history, no patients were found to be on immunosuppressive medications.

A total of 2066 (91.34%) patients were discharged from the hospital after recovery and 196 (8.66%) expired. Death was more among male subjects 140 (71.43%) as compared to females 56 (28.57%). Male population1406 (68.05%) also outnumbered female population 660 (31.95%) in terms of survival [Table/Fig-2].

Age distribution	Survivors	Non survivors	p-value
≤20	108 (5.23%)	5 (2.55%)	0.100
21-30	250 (12.10%)	2 (1.02%)	<0.001
31-40	504 (24.39%)	17 (8.67%)	<0.001
41-50	623 (30.15%)	25 (12.76%)	<0.00001
51-60	301 (14.57%)	43 (21.94%)	0.006
>60	280 (13.55%)	104 (53.06%)	<0.001

[Table/Fig-1]: Age distribution of survivors and non survivors among COVID-19 patients.
p-value through chi-square test

Gender	Survivors	Non survivors	p-value
Male	1406 (68.05%)	140 (71.43%)	331
Female	660 (31.95%)	56 (28.57%)	
Total	2066 (91.34%)	196 (8.66%)	

[Table/Fig-2]: Mortality and gender distribution among COVID-19 patients.

The most common clinical presentations among those who recovered were myalgia 1360 (65.83%), anosmia 1265 (61.23%), fever 1244 (60.21%) and cough 1104 (53.43%). The most common presentation among the death cohort were shortness of breath 155(79.08%) and cough 132 (67.35%). The other presentation among the deceased were fever 126 (64.29%), myalgia 69 (35.20%), diarrhoea 45 (22.96%) and anosmia 32 (16.33%) [Table/Fig-3]. In the present study it was observed that mortality from COVID-19 infection was more in the presence of associated co-morbid condition. Among the study population, the prevalence of diabetes mellitus, hypertension, cardiac illness and chronic kidney disease were significantly high among those who succumbed to the death as compared to those who recovered. Although the prevalence of malignancy, CLD, COAD, surgery was found to be higher among survivors than that of non survivors, but it was not statistically significant [Table/Fig-3].

Variables	Factors	Survivors	Non survivors	p-value
Clinical presentations	Fever	1244 (60.21%)	126 (64.29%)	0.264
	Myalgia	1360 (65.83%)	69 (35.20%)	<0.001
	Diarrhoea	610 (29.53%)	45 (22.96%)	0.527
	Anosmia	1265 (61.23%)	32 (16.33%)	<0.001
	Cough	1104 (53.43%)	132 (67.35%)	0.001
	Shortness of breath	500 (24.20%)	155 (79.08%)	<0.001
Co-morbidities	DM	323 (15.63%)	70 (35.71%)	<0.001
	HTN	381 (18.44%)	99 (50.51%)	<0.001
	Cardiac Illness	43 (2.08%)	22 (11.22%)	<0.001
	Malignancy	12 (0.58%)	1 (0.51%)	0.900
	CKD	92 (4.45%)	15 (7.65%)	0.043
	COAD	63 (3.04%)	5 (2.55%)	0.696
	CLD	45 (2.18%)	3 (1.53%)	0.547
Surgery		10 (0.48%)	3(1.53%)	0.063

[Table/Fig-3]: Comparison of clinical presentations and co-morbidities among survivors and non survivors of COVID-19.

The mean level of White Blood Cell (WBC) count, RBS, LDH, creatinine, d-dimer, ferritin and CRP were significantly high among the non survivors. Various other markers including ALT, troponin I, though high among the non survivors, did not reach the level of statistical significance [Table/Fig 4].

In the study population chest x-ray was found to be normal in 410 (19.84%) among the survivors when compared to non survivors 5 (2.55%). The various abnormalities observed in chest x-ray among those who recovered were ground glass opacity (1018, 49.27%),

Laboratory parameters	Survivors	Non survivors	p-value
Haemoglobin	12.4±1.42 g/dL	11.5±1.18 g/dL	0.062
Platelet count	1.75±0.57 lakhs/cmm	1.22±0.43 lakhs/cmm	0.013
WBC	9760±2354.51/ cmm	15700±4073.08/ cmm	<0.001
RBS	180±38.57 mg/dL	283.6±70.15 mg/dL	<0.001
LDH	213±12.51 U/L	477±44.37 U/L	0.003
ALT	44.2±12.26 U/L	68.8±14.58 U/L	0.058
Serum creatinine	0.6±0.34 mg/dL	6.24±4.84 mg/dL	<0.001
D-dimer	0.39±0.22 mcg/mL	2.82±0.86 mcg/mL	0.026
Ferritin	174.2±10.15 ng/dL	341.4±37.43 ng/dL	0.028
Troponin I	0.01±0.004 ng/mL	0.06±0.04 ng/mL	0.121
CRP	0.96±0.21 mg/dL	1.72±0.73 mg/dL	<0.001

[Table/Fig-4]: Comparison of laboratory parameters among survivors and non survivors of COVID-19.
p-value-unpaired t-test

consolidation in 620 (30.01%) and pleural effusion in 18 (0.87%). Among the non-survivor group, most common abnormality was observed to be ground glass opacity 111 (56.63%) followed by consolidation 63 (32.14%) and pleural effusion 17 (8.24%). Ground glass opacity and pleural effusion were significantly high among those who succumbed to the infection compared to those who recovered (p=0.048, p <0.001) [Table/Fig-5].

Chest x-ray findings	Survivors	Non survivors	p-value
Normal	410 (19.84%)	5 (2.55%)	<0.001
Consolidation	620 (30.01%)	63 (32.14%)	0.535
Ground glass opacity	1018 (49.27%)	111 (56.63%)	0.049
Pleural effusion	18 (0.87%)	17 (8.24%)	<0.001

[Table/Fig-5]: Comparison of chest x-ray among survivors and non survivors of COVID-19.
p-value using chi-square test

DISCUSSION

The COVID-19 infection spread throughout the world, causing serious morbidity and mortality among humans [1]. Acute respiratory distress syndrome and a number of serious complications can occur, leading to multiorgan failure and death. It emphasises the importance of early diagnosis and categorisation of cases in order to provide suitable and timely treatment.

In the present study out of 2262 patients admitted, in hospital mortality was observed to be 8.66%. The mortality was lower when compared to the multicentric study conducted in Wuhan by Li M et al., [3] where it was found to be 9.4%. Surendra H et al., [5] observed a mortality rate of 12% in their study conducted in Indonesia.

In the present study, death was more among male subjects as compared to females (female 28.57% and male 71.43%). The findings in the present study were similar to the observations made by Zhou F et al., [2] (male 70% and female 30%) and Li M et al., [3] (male 78.3% in the non-survivor group).

Age is an important risk factor for respiratory diseases including COVID-19 pneumonia and declining immune function associated with advancing age remains a major cause of adverse outcome due to severe pneumonia [6,7]. Elderly subjects aged > 60 years contributed significantly to mortality in the present study. The mean age among the non-survivor group was 62.67±3.94 years that was significantly higher than the survivor group (44.82±7.92 years, p=0.000102). In another pioneer study conducted by Iftimie S et al., [8], it was observed that the deceased patients were significantly older than the patients who recovered from the infection (77±13.1 vs 62.8±18.4 years, p<0.001). Older age also contributed to the majority among the non survivors in study conducted by Zhou F et al., [2].

Among the various clinical presentations, cough and shortness of breath were significantly high among the deceased population whereas diarrhoea, myalgia and anosmia were more common among those who recovered. Fever was comparable among both the groups. In other studies by Surendra H et al., [5] and Jain S et al., [9], the most common symptoms among the deceased were fever, cough and shortness of breath [Table/Fig-6] [5,9].

Symptomatology	Present Study	Shikha Jain et al., [9] (India, 2022)	Iqbal HS et al., [5] (Indonesia, 2021)
Fever	126 (64.29%)	496 (64.83%)	303 (63%)
Myalgia	69 (35.20%)	-	100 (22%)
Diarrhoea/ GI symptoms	45 (22.96%)	87 (11.37%)	53 (12%)
Anosmia	32 (16.33%)	-	-
Cough	132 (67.35%)	380 (49.67%)	372 (76%)
Shortness of breath	155 (79.08%)	633 (83.74%)	348 (71%)

[Table/Fig-6]: Clinical presentation among non- survivors and comparison with other studies [5,9].
GI: Gastro-intestinal

The various co-morbid conditions that contributed significantly to mortality in this study were DM, HTN and cardiac illness. The prevalence of COPD, CLD and CKD was also high in the mortality group as compared to those who survived although it did not reach statistical significance. Similarly, in the research work conducted by Zhou F [2], the various co-morbid conditions contributing significantly to mortality were DM, HTN, COPD, CKD and chronic heart disease. In another pioneer work by Henry Surendra Iqbal et al., [5], the prevalence of DM, HTN, cardiac illness, CKD and liver disease were significantly high in the deceased group [Table/Fig-7].

Co-morbidities among non survivors	Present study	Zhou F [2] (china, 2020)	Iqbal HS et al., [5] (Indonesia, 2021)
DM	70 (35.71%)	17 (31%)	201 (42%)
HTN	99 (50.51%)	26 (48%)	142 (29%)
Cardiac Illness	22 (11.22%)	13 (24%)	105 (22%)
Malignancy	1 (0.51%)	0	2 (0.4%)
CKD	15 (7.65%)	2 (4%)	45 (9%)
COPD	5 (2.55%)	4 (7%)	28 (6%)
CLD	3 (1.53%)	Others 11 (20%)	7 (2%)
Surgery	3(1.53%)	-	-

[Table/Fig-7]: Co-morbidities among non survivors and comparison with other studies.

In the present study, it was observed that high WBC count (p=0.000098), low haemoglobin concentration (p=0.062) and low platelet count (p=0.013) were associated with adverse outcome and the findings were comparable to that of Bairwa M et al., [10] where death cohort had higher WBC count (p=0.003) and lower haemoglobin concentration (p=0.001) and platelet count (0.069) as compared to those who recovered. In the present study RBS was significantly high among the non-survivor group (p=0.000074). Similar observations were made by Gao Y et al., [11] where a higher mean serum glucose was associated with more severe disease when compared to those with mild covid (p=0.022).

In the present study, the mean level of serum LDH was significantly high in the deceased group (p=0.003611) and the findings corroborated with that of Cekerevac I et al., [12] where a higher level of LDH was associated with more severe disease (p=0.003). Disease severity and adverse outcome in the study population were observed to be high in patients with higher level of D-dimer (p=0.026037) and similar observation were made by Yao Y et al., [13]. Ferritin is an acute phase reactant and is elevated in myriad of inflammatory responses [14]. Mean level of serum ferritin was significantly high among patients who succumb to the infection as compared to those who recovered (p=0.029). This finding was comparable to the eminent study by Lino K et al., [14] where it was observed that higher level of serum ferritin among the COVID-19 infected patients was associated with adverse outcome.

Troponin I elevation is common in patients with severe COVID and may relate to viral myocarditis, cytokine-driven myocardial damage, microangiopathy [15]. The mean level of troponin I was higher in the deceased group as compared to those who recovered but it was statistically not significant at p=0.121. But in the pioneer work by Abbasi BAL et al., [15], elevated troponin was seen in 66% of the subjects in non-survivor group as compared to 17% in the survivor group and was statistically significant (p<0.0001).

The mean level of ALT in the present study was 44.2±12.26 U/L in the survivor group and 68.8±14.58 U/L in the non-survivor group. Although it was high in the non- survivor group it was statistically not significant (p=0.0588). similarly in another study by Padmaprakash KV et al., [16], although a higher percentage of patients in the death cohort had ALT more than the upper limit of normal as compared to that of the survival cohort, the result didn't reach the value of statistical significance, (84.38% vs 79.57%, p=0.335). In the present study a significantly higher value of mean serum creatinine and CRP was observed in the death cohort compared to those who recovered. Similarly, Salinas M et al., [17] observed that pathological values of creatinine, LDH, CRP, D-dimer, albumin etc were significantly high in the deceased group.

In the present study, chest x-ray was found to be normal in a significant proportion among the survivors when compared to the non survivors (19.84% vs 2.55%, p<0.00001). Among the non-survivor group, most common abnormality was observed to be ground glass opacity (56.63%). Ground glass opacity and pleural effusion were significantly high among those who succumbed to the infection compared to those who recovered (p=0.048, p<0.001). Similar findings were observed in the research work of Colman J et al., [18] where the most common abnormal chest x-ray finding among the non survivors were ground glass opacity (76.7%). Although the proportion of ground glass opacity and consolidation was higher among the death cohort, it was statistically not significant. A significant proportion of study subjects were found to have pleural effusion (16.3%) in the non- survivor group.

Limitation(s)

This study did not consider the patients with covid infection treated at other hospitals in the region. Also, being a retrospective study, it did not consider the duration of various co-morbid conditions that might influence the immune status of a patient. So, a multicentered, prospective study would have been more beneficial for drawing the inferences.

CONCLUSION(S)

In present study, it was observed that in Southern Assam, more than half of the deceased COVID-19 patients were older than 60 years of age. In addition, most common presentation among the deceased COVID-19 patients were observed to be shortness of breath and cough. Diabetes mellitus, hypertension and chronic kidney disease were found to be high among non survivors than survivors. Laboratory parameters were also found to be higher among non survivors except heamoglobin concentration and platelet count. In chest X-ray, most common abnormality among non-survivor group was observed to be ground glass opacity. These findings are useful for future studies with the population of this part of North East India.

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