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CLINICAL AND EPIDEMIOLOGICAL PROFILE OF COVID-19 PATIENTS ADMITTED AT A TERTIARY CARE CENTRE OF NORTH INDIA

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Abstract:

Background & objectives: The COVID-19 pandemic emerged as a major public health emergency affecting the healthcare services all over the world. It is essential to analyse the epidemiologicalandclinicalcharacteristicsofpatientswithCOVID19indifferentpartsofourcountry.This study highlights clinical experience in managing patients with COVID-19 at a tertiary care centre in northernIndia.

Methods:Clinicalcharacteristicsandoutcomesofconsecutiveadultpatientsadmittedtoatertiarycare hospitalatAll India Institute of medical Sciences, Patna, Bihar,India,from August12020 toJanuary 31,2021werestudied.ThediagnosisofSARS-CoV-2 infection was confirmed by real-time reverse transcriptase polymerase chain reaction (RT-PCR) on throat and/or nasopharyngeal swabs. All patients were managed according to the institute's consensus protocol and in accordance with Indian Council of Medical Researchguidelines.

Results: During the study period, 283 patients with SARS-CoV-2 infection were admitted. The history of contact with COVID-19-affected individuals was available in only29 patients. The median age of the patients was 53.85 years (15-95 years), and there were 217 (76.67 %) males. Of the total enrolled patients, only 19 patients (7%)were asymptomatic and rest 264 patients (93%) were symptomatic.Thecommonpresentingcomplaintswerefever in 231 patients(81 %),cough in 217 patients(76 %) and shortness of breath in 204 patients (72%). Out of 283 patients enrolled for the study, 113 patients (39%) had Hypertension as an accompanying comorbid illness, 122 (43%) had Diabetes mellitus, CKD and Hypothyroidism each in 8% of patients, CAD & COPD in 7% and 6% patients respectively. Agemorethan60yearsandpresenceofdiabetesandhypertensionweresignificantlyassociatedwith severeCOVID-19disease.Mortalityof 65 patients (23%) wasobserved.

Interpretation&conclusions:MajorityofthepatientswithCOVID-19infectionpresentingtoourhospital were elderly and symptomatic. Fever was noted only in three-fourth of the patients and respiratory symptoms in more than half of the enrolled patients. Patients with comorbidities were more vulnerable to complications. Certain Inflammatory markers like serum CRP, Ferritin, LDH, & D-Dimer have define prognostic value. Triaged classificationofpatientsandprotocol-basedtreatmentresultedingoodoutcomesandlowcasefatality.

Key words - comorbidities - COVID-19 - hypoxia - India - pandemic – pneumonia-Inflammatory marker

Introduction:

The World Health Organization (WHO) reported more than 179 million confirmed cases of SARS-CoV-2 infection and more than Threemillion deaths globally[3], with India contributing to more than 29 million confirmed patients and more than Three Lakhs deaths until June 22, 2021[4]. The first patientinIndiawasreportedfromKerala,andgradually COVID-19hasengulfedtheentirecountry.Patientswith SARS-CoV-2infectionmayhavemild-to-asymptomatic illness, but some rapidly progress to acute respiratory distress syndrome (ARDS), multi-organ dysfunction syndrome (MODS) anddeath. Coronaviruses (CoVs) is accountable for mixture of ailments in human and animals that include respiratory, enteric, renal, and neurological diseases [1].Combined, animal and human coronaviruses fall into four genera namely alpha coronavirus, beta coronavirus, gamma coronavirus, and delta coronavirus genus. The Middle East respiratory syn- drome (MERS), Severe acute respiratory syndrome (SARS), and SARS-CoV-2 all three belong to beta coronavirusgenus.[2].There have already been three zoonotic outbreaks in this century. Severe acute respiratory syndrome coronavirus (SARS-CoV) with about 10% case fatality rate (CFR) was initially witnessed from China in 2002, while Middle East respiratory syndrome coronavirus (MERS-CoV) infection with about 34.4% CFR was originally detailed from Saudi Arabia in June 2012[2].The third outbreak coronavirus disease 19 (COVID-19) is indisputably the most frightening compared to the previous epidemics, which has spread from a marketplace inWuhan, China in December 2019 to more than 213 countries and territories, infecting more than 1.5 crore people with death toll more than 6 lakhs of the world within nine months. With nearly 4% CFR, we have never thought anything like this highly contagious and pathogenic COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

It is pertinent to identify the clinical and demographic characteristics of patients considering the novelty and substantial heterogeneity of the illness across the world, particularly in countries like China and India[5.6.7.8]. This study describes the demographic characteristics, comorbid conditions, baseline laboratory findings, clinical course and outcomes among COVID-19 patients admitted at All India Institute of Medical Sciences, Patna, a dedicated COVID hospital in North India.

Material & Methods:

Study population and settings: The study was conducted at All India Institute of Medical Sciences, Patna, Bihar, a dedicated covid hospital in North India, from 1st August 2020 to 31st January 2021. Individuals with influenza-like illness who fulfilled the ICMR screening criteria (dated May 18, 2020). Consecutive adult patients (>14 yrs.) who tested positive on real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay for SARS-CoV-2 on a throat and/or a nasopharyngeal swab were admitted and included in the study. Pregnant women and children were excluded. The study was approved by the Institutional Research Committee & Institutional Ethics Committee.

Data collection: Awritten informed consent was taken in person from patients by the treating team while a telephonic consent was obtained from the quarantined immediate family members in case the patient was unable to consent himself/herself. Demographic details, medical history including comorbidities, history of exposure to COVID-19 and vitalparameters were recorded at admission to the hospital. Baseline laboratory parameters, treatment details and clinical outcomes were alsocollected.

Casedefinitionsandclassification: Astandardprotocol which included case definitions for categorization of SARS-CoV-2 infection, detailed management plan, baseline and follow up investigations and treatment according to clinical severity was devised by a group of experts from various specialties of the AIIMS/PATNA. This consensus treatment algorithm was developed after reviewing the guidelines of various international societies and revised national clinical management guidelinesforCOVID-19bytheMOHFW,Government ofIndia,datedMarch31,2020[10].Symptomaticpatients were categorized to have mild, moderate or severe disease. Patients with uncomplicated upper respiratory tract infection or non-specific symptoms such asfever, cough, sore throat, nasal congestion, malaise and headachewereclassifiedtohavemilddisease.Patients with radiologically proven pneumonia but without the signs of severe pneumonia were categorized as moderatedisease. Patients of disease severity Mild & Moderate were taken as Non-Severe in our analysis while Severepneumoniaincludedapatient withfever,plusoneofthefollowing:respiratoryrate>30 breaths/min, severe respiratory distress and SpO_2<90%

on room air. Standard criteria for defining ARDS and MODS were used[68,69]. Critically ill patients included those who had severe pneumonia, shock and organ dysfunction syndrome at admission or during hospital stay. All stable patients irrespective of symptoms were treated in isolation rooms, while those with critical illness were admitted in the intensive care unit (ICU). Standard organ-specific supportive care was provided when clinically indicated.

Specimen collection, laboratory test and discharge policy: Throat and/or nasopharyngeal specimens were obtained using standard techniques. The nasopharyngeal samples were tested using the National Institute of Virology (NIV), Pune-developed kits as per the ICMR recommendations[11]. The ICMR guidelines were followed to discharge the patients from the hospital[12,13]. Initially, till May 8, 2020, all the admitted patients were discharged only after two consecutive nasopharyngeal swabs (done after 14th day of stay) tested negative on RT-PCR. After May 8, 2020, with a change in the national guidelines, asymptomatic and mild patients weredischargedafter10daysofsymptomonset and being afebrile for three consecutive days. The discharge guidelines for severe pneumonia were also revised and mandated oxygen-free period of three days and a negative RT-PCR result as against the two samplespreviously[12,13].

Statistical analysis: Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA, version 23.0 for Windows) and Microsoft Excel 2016. All quantitative data such as age, weight, hemodynamic parameters and laboratory values were estimated using measures of central location (mean). Qualitative or categorical variables were described as proportions. For normally distributed data, means were compared using independent *t* test. Mann-Whitney U-test was applied for statistical analysis of skewed continuous variables and ordered categorical variables. .

Results :

Demographics and baseline clinical characteristics: During the study period, 283 patients were diagnosed tohaveCOVID-19andwereincludedinthestudy.The baseline demographic and clinical characteristics of these patients are summarized in Table I. The median age of the patients was found to be 53.85 yrs. (SD: 15.85, range: 15-95 yrs.) and out of 283(n=283), 217 (76.67%) were Males and 66(33.33%) were females. Out of total 283 patients, 28 (9.89%) were in age group of 15-30 years, 52 (18.37%) in 31-45 years, 90 (31.80%) in 46-60 years and 113 (about 40%) were in age group of more than 60 years. Among the symptomatic patients(n=283), total 218 (77%) patients were discharged from the hospital while 65 (23%) patients succumbed to covid-19.out of 217 male patients, 167 (77%) were survivors while 50 male patients (23%) succumbed to covid-19. Out of total 66 female patients 51 (77%) were survivors while 15(23 %) were non-survivors. Out of total 65 Deaths of covid-19 patients out of 283 patients admitted during the study period, 50 (about 80%) were males while only 15 (about 20%) were females. In the age group of 15-30 years, there was not a single mortality during the study period. While mortality (n=65) was 9 (14%) in age group of 16-30 years, 20 (about 33%) in age group of 46-60 years and 36(about 53%) deaths were in elderly population (age more than 60 years).

Out of 283 patients (n=283), 231(81%) patients were having history of fever, which was the most common symptom. Second most common symptom was cough which was present in 217 (76%) patients. Out of that only 6 patients had history of sputum production. 204 (72%) patients had history of dyspnea and in all the patients who succumbed to death had , history of dyspnea. 92 (32%) patients had complaints of headache. Other symptoms were fatigue in 50(17%), sore throat in 36(12%), and nasal congestion in 3(1%). Around 12(4%) patients had history of diarrhoea and only 3 (1%) patients had history of nausea and vomiting. 19 (6%) patients were asymptomatic and there was no mortality in these 19 patients.

Out of 283 patients (n=283),104(36%) patients were having history of smoking, and they were mostly males. Out of 104 smokers (n=104), 36(34%) patients died and rest 68(66%) survived. 29(10%) patients had history of contact to covid-19 patients. Only 4 patients had history of travel in last 14 days of onset of symptoms.

Table No. 1 Demographic profile of Covid-19 patients in Survivors &Non Survivors

	Total cases(n)=283	**Survivors=218**	**Non-survivors=65**
AGE(yrs)			

15-30	28	28	0
31-45	52	43	9
46-60	90	70	20
>60	113	77	36
MALE	**217**	**167**	**50**
FEMALE	**66**	**51**	**15**
COMORBIDITY			
HTN	**113**	**75**	**38**
T2DM	**122**	**88**	**34**
COPD	17	16	1
CAD/CVS	21	13	8
HYPOTHYROID	23	17	6
CKD	24	14	10
ABSENT	100	85	15
Hepatitis B/C	3	2	1
Hematological malignancy	1	1	0
COMPLICATION			
Septic shock	44	8	36
ARDS	61	5	56
AKI	17	7	10
PNEUMONIA	64	55	9
ABSENT	150	148	2
SYMPTOMS			
Fever	230	169	61
Headache	92	59	33
Cough	217	157	60
Dyspnea	204	139	65
Sputum production	6	6	0
Nasal congestion	3	3	0
Sore throat	36	30	6
Hemoptysis	0	0	0
Fatigue	50	36	14
Nausea/vomiting	3	3	0
Diarrhea	12	10	2
Myalgia/arthralgia	7	6	1
chills	1	0	1
Asymptomatic	19	19	0
Smoker	104	68	36
Non-smoker	179	150	29
Migrant	4	4	0
Non-migrant	279	214	65
Exposed within 14 days	29	29	0
Not exposed	250	186	64
Not sure about exposure	4	3	1
Markers			
LDH increased(0-460)	251	186	65
Ferritin increased(0-291)	186	126	60
CRP increased(0-10)	231	178	53
d-dimer increased(0-0.5)	204	144	60

Clinical characteristics of patients with comorbid illness: As far as associated comorbidities is concerned, (n=283), 113 (39%) patients were Hypertensives, 122 (43%) were having Diabetes mellitus, 17(6%) were having COPD as comorbidity, 21(7%) were having Coronary artery disease, 23(8%) with hypothyroidism, 24(8%)were having Chronic Kidney disease, 3(1%) with Hepatitis B/C and 1(0.35%) with hematological malignancy.. Out of 283 patients studied 100 were free from any comorbidities. Out of 113 hypertensives (n=113), mortality was 38 (33%) while 75(66%) survived and were discharged. Out of 122 patients with Diabetes mellitus (n=122), mortality was 34(27%) while 88(73%) survived. Out of 17 COPD patients with covid-19, only one (6%) succumbed to covid-19 and 16 (94%) were discharged. Out of 24 CKD patients with covid-19, 14 (58%)survived while mortality was 10(42%). In covid patients with hypothyroidism as comorbidity(n=23), 17 (73%) survived while 6 (27%) patients succumbed to the disease.

Figure No.1 Number of Survivors & Non-Survivors in different age groups

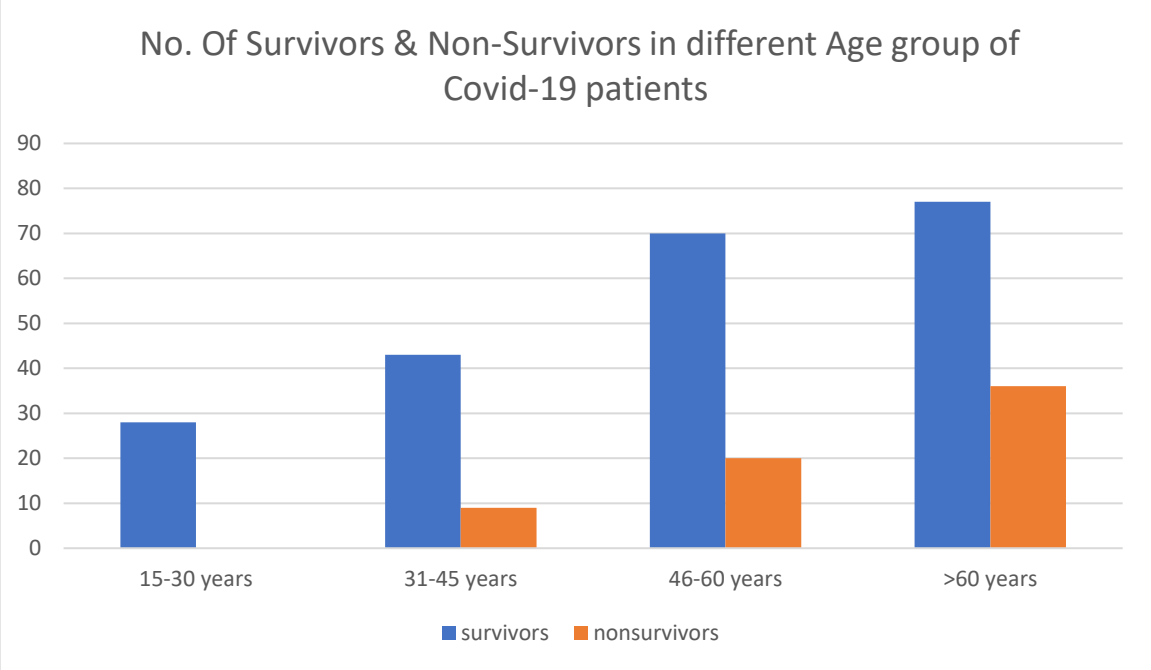
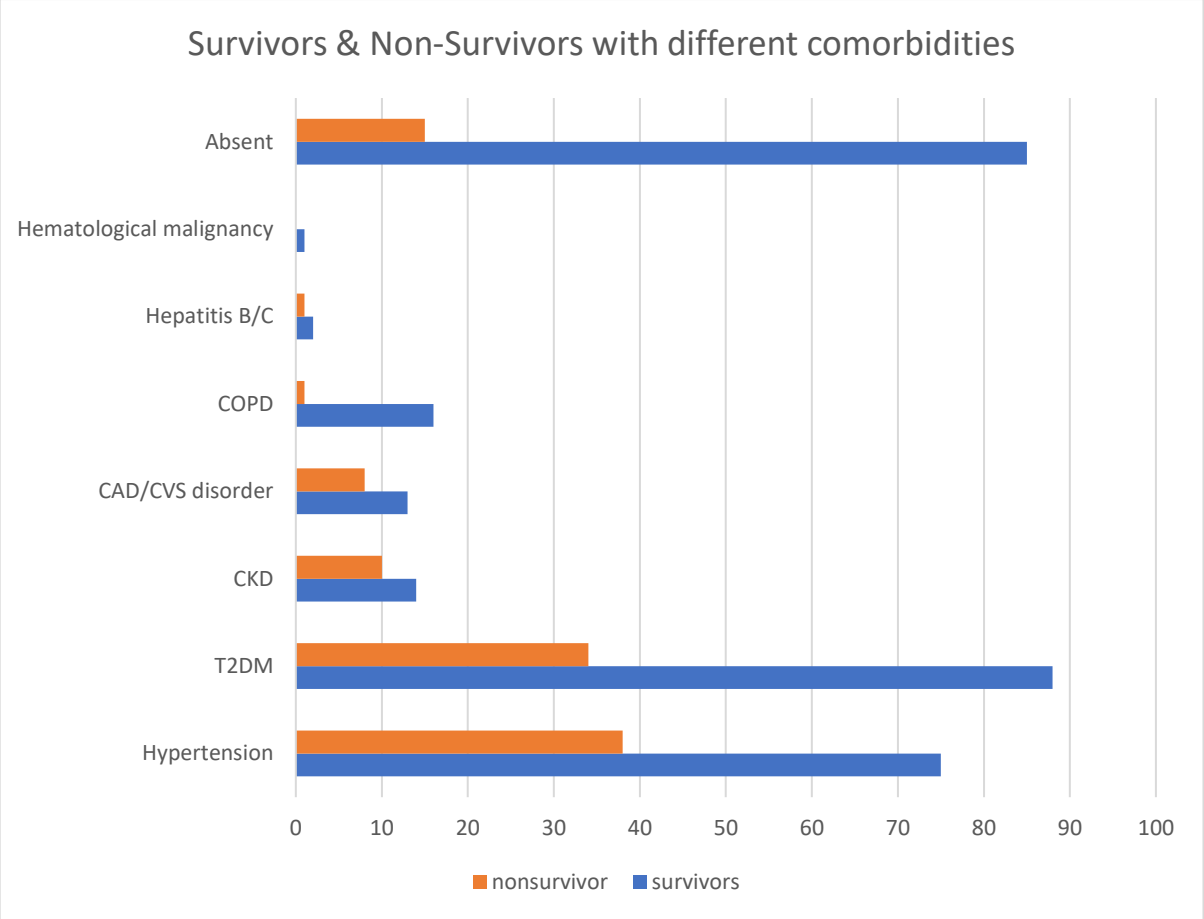


Figure No. 2 Number of Survivors & Non-Survivors with different comorbidity



Clinical characteristics of patients with complications: Out of 283 patients(n=283), 150 (53%) patients didn't develop any complication while 64 (22%)developed pneumonia, 61 (21%) developed ARDS, 44 (15%) developed septic shock and 17 (6%) developed Acute Kidney Injury during the course of hospital stay. Out of total 64 patients (n=64) who developed pneumonia, most of them 55 (85%) recovered well and discharged from the hospital while 9 (15%) out of 64 died due to that complication. Out of 61 patients (n=61) who developed ARDS as complication, only 5 (8%) survived while 56 (92%) succumbed to the disease. Out of 44 patients who develop septic shock(n=44), only 8 (18%) patients survived and rest 36(82%) died. Out of 17 patients (n=17), who developed AKI, only 7(41%) survived while death was there in rest 10 (59%) patients. Out of 150 patients who had not developed any complications, mortality was only 2 (1.5%) while rest 148(98.5%) survived.

Figure No. 3 Number of Survivors & Non-Survivors with different complications

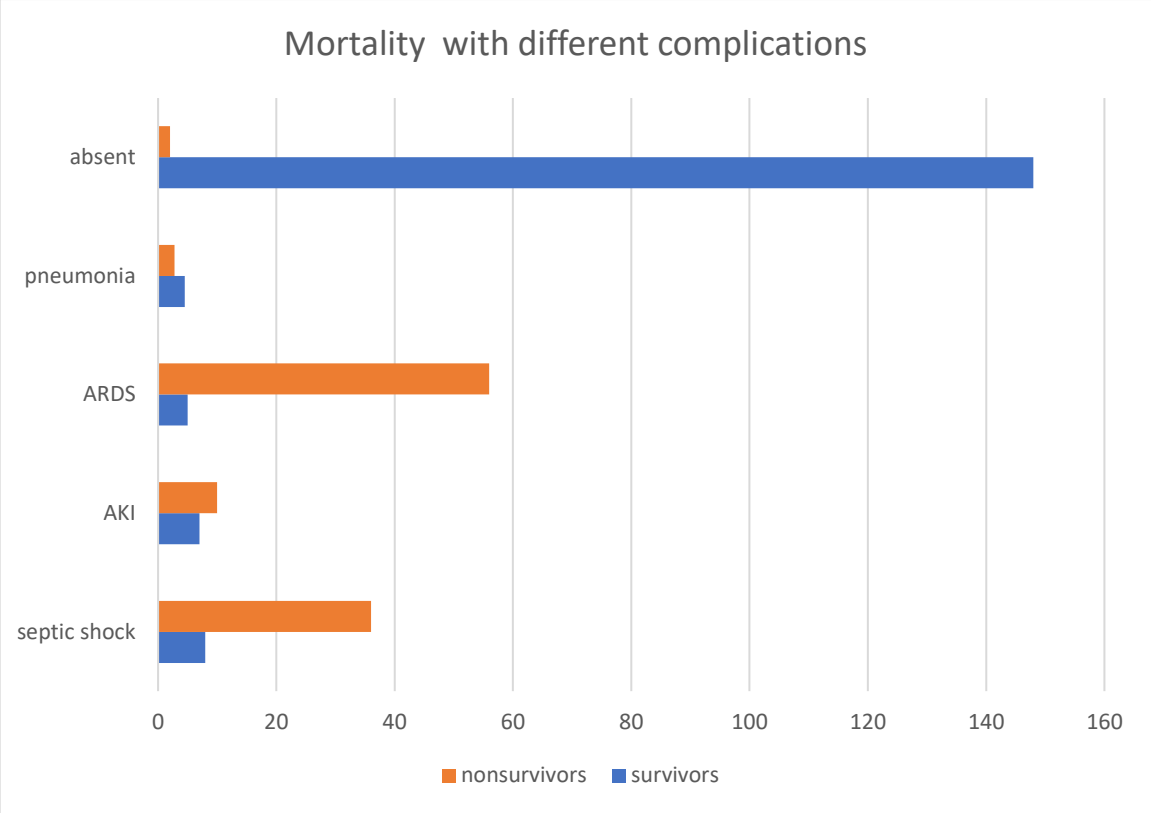


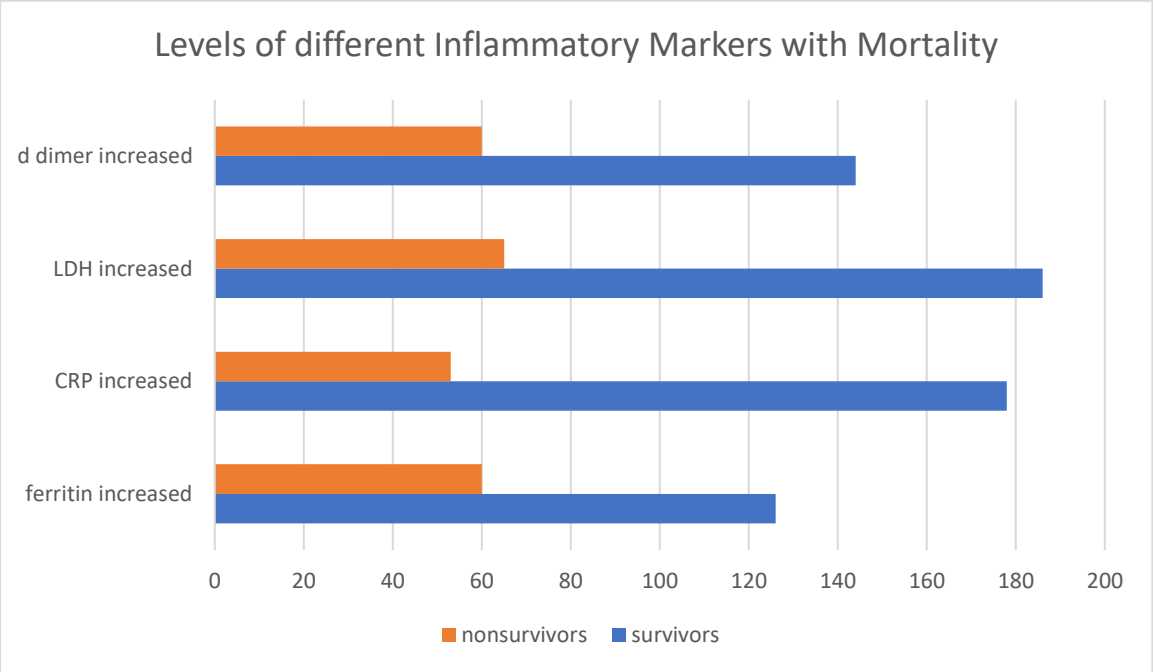
Table No. 2 Demographic profile of patients with Severe & No severe Covid-19

	Total cases=283	Severe=84	Non-severe=199
Age			
15-30	28	0	28
31-45	52	12	40
46-60	90	27	63
>60	113	45	68
Male	217	63	154
Female	66	21	45
Comorbidity			
HTN	113	48	65
T2DM	122	46	76
COPD	17	5	12
CAD	21	6	15
CKD	24	12	12
HYPOTHYROID	23	7	16
ABSENT	100	20	80
Symptoms			
Fever	230	78	152
Headache	92	37	55
Cough	217	75	142
Dyspnea	204	82	122
Sputum production	6	0	6
Nasal congestion	3	0	3
Sore throat	36	10	26
Hemoptysis	0	0	0
Fatigue	50	15	35
Nausea/vomiting	3	1	2
Diarrhea	12	2	10
Myalgia/arthralgia	7	1	6

chills	1	1	0
Asymptomatic	19	0	19
Hep B/C	3	1	2
Hematological malignancy	1	0	1
Complication			
Septic shock	44	35	9
AKI	17	11	6
ARDS	61	52	9
Pneumonia	64	26	38
Absent	150	13	237
Smoker	104	35	69
Non-smoker	179	49	130
Migrant	4	0	4
Non-migrant	279	84	195
Exposed within 14 days	29	1	28
Not exposed	250	81	169
Not sure about exposure	4	2	2
LDH increased	251	84	167
Ferritin increased	186	73	113
CRP increased	231	68	163
d-dimer increased	204	74	130

Clinical correlation of various inflammatory markers in disease severity: Out of all the inflammatory markers, serum LDH, Ferritin, CRP, and D-Dimer was significantly increased in (n=283) 251(88%) patients, 186(65%) patients, 231(81%) patients and 204(72%) respectively. Out of 251 patients with raised serum LDH level 186 (74%) survived while 65(26%) died. Similarly Out of 186 patients with raised serum Ferritin level 126 (67%) survived while 60 (33%) died. Out of 231 patients with raised serum CRP level 178 (77%) survived while 53(23%) died. While Out of 204 patients with raised serum D-Dimer level 144 (70%) survived while 60(30%) succumbed to covid-19.

Figure No. 4Different Inflammatory Markers with Mortality



Clinical characteristics of critically ill patients: Presence of comorbidities such as hypertension and diabetes, increased serum levels of inflammatory biomarkers (CRP, ferritin and LDH) and renal dysfunction/high creatinine atadmission were significantly higher among critically ill patients. (P<0.05). High D-dimers and fibrinogen levels were also observed among these patients.

Table No. 3:Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age of COVID 19 patients	283	15.00	95.00	53.8516	15.85258
LDH level at the time of admission	283	271.00	3912.00	974.2185	560.67724
Ferritin level at the time of admission	283	5.70	4416.00	728.5334	643.59163
CRP level at the time of admission	283	1.80	354.36	78.8852	87.12769
D-dimer level at the time of admission	283	.15	20.00	3.0180	4.57020
Valid N (listwise)	283				

As the P-P plots and Shapiro-Wilk test shows that biochemical markers data was not normally distributed so it is represented as Median (IQR) / Boxplot and tested using Mann-Whitney U test.

Table No. 4:Descriptive Statistics

		LDH level at the time of admission	Ferritin level at the time of admission	CRP level at the time of admission	D-dimer level at the time of admission
N	Valid	283	283	283	283
	Missing	0	0	0	0
Median		837.0000	551.0000	43.0000	1.1100
Percentiles	25	590.0000	198.0000	12.4500	.5000
	50	837.0000	551.0000	43.0000	1.1100
	75	1167.0000	1185.0000	114.0000	2.9000

Correlation of various inflammatory markers with mortality of covid-19 patients:
we have framed null hypothesis assuming that not a single inflammatory marker is strongly correlating with the mortality of covid 19 patients and the hypothesis test summary is described in Table No.5.Based on statistical analysis, by using Independent samples Mann whitney U test, we have rejected the null hypothesis and it has been inferred that inflammatory markers serum LDH, Serum Ferritin, serum CRP & serum D-Dimer levels are strongly related with severity of the disease and are related with mortality of the patients. These markers have definite prognostic value in covid-19.

Discussion:SARS-CoV-2 is one of the most virulent pathogens causing severe acute respiratory illness along with MERS and swine flu in humans. Initial case studies from China demonstrated COVID-19 to be a respiratory illness with a spectrum ranging from mild illness (81%), severe respiratory distress (14%) and critical illness in five per cent with a case fatality rate of around 2.4 per cent[14]. Considerable disparitiesin demographic and clinical patterns have been observed between countries across different continents. This prospective study demonstrated the clinical profileand outcomes of initial COVID-19 patients from northern India. These patients were well categorizedaccording to severity and managed using standard protocols for investigations and treatment.

Patients in our study were almost of similar age group (median age– 53.85 yrs.) as compared to those in China (median age – 56 yrs.)[15], New York (median age – 63 yrs.)[16] or Italy(median age – 63 yrs.)[17]. The Covid-19 virus affects the older population more commonly. Males are more commonly affected than the females. Mortality in younger population were less than the older population. T2DM and Hypertension were the most common co-morbidities associated with this disease. Another observation was an increased incidence of severe COVID-19 disease manifestations in patients with underlying chronic diseases (hypertension 16.6% and diabetes 14.9%). Similar findings have been reported from various studies across theworld [18,19,20].

As per our institutional protocol, early institution of heparin therapy based on D-dimerslevelswasstrictlyfollowed..Tang *et al* [21]also observed beneficial effects of early initiation of low molecular weight heparin among the 449 severe COVID-19 patients with markedly elevated D-dimers with a significantly improved 28 day overall survival (*P*=0.017 and *P*=0.029, respectively) among the users versus non-users.

Thecasefatalityrateinourstudywas23percent. Higher mortality in our study has been observed as most of the patients admitted to our centre are symptomatic and having severe disease.

To conclude, in our study out of 283 patients enrolled, severe illness was seen in 29% per cent patients only. Fever was noted in 80% of the patients and respiratory symptoms in more than half of them. High inflammatory parameters and deranged creatinine predicted severe COVID-19 illness. Older patients with diabetes and hypertension were significantly associated with severedisease. the inflammatory markers like CRP, Ferritin, D-Dimer and LDH have definite value in guiding the mode of treatment and outcome of the disease. These inflammatory markers are taken as prognostic markers of the disease. Themanagement teamconsistingofphysiciansfromdifferentspecialties andtriagedclassificationofpatientsandprotocol-based managementalgorithmsresultedingoodoutcomesand low casefatality.

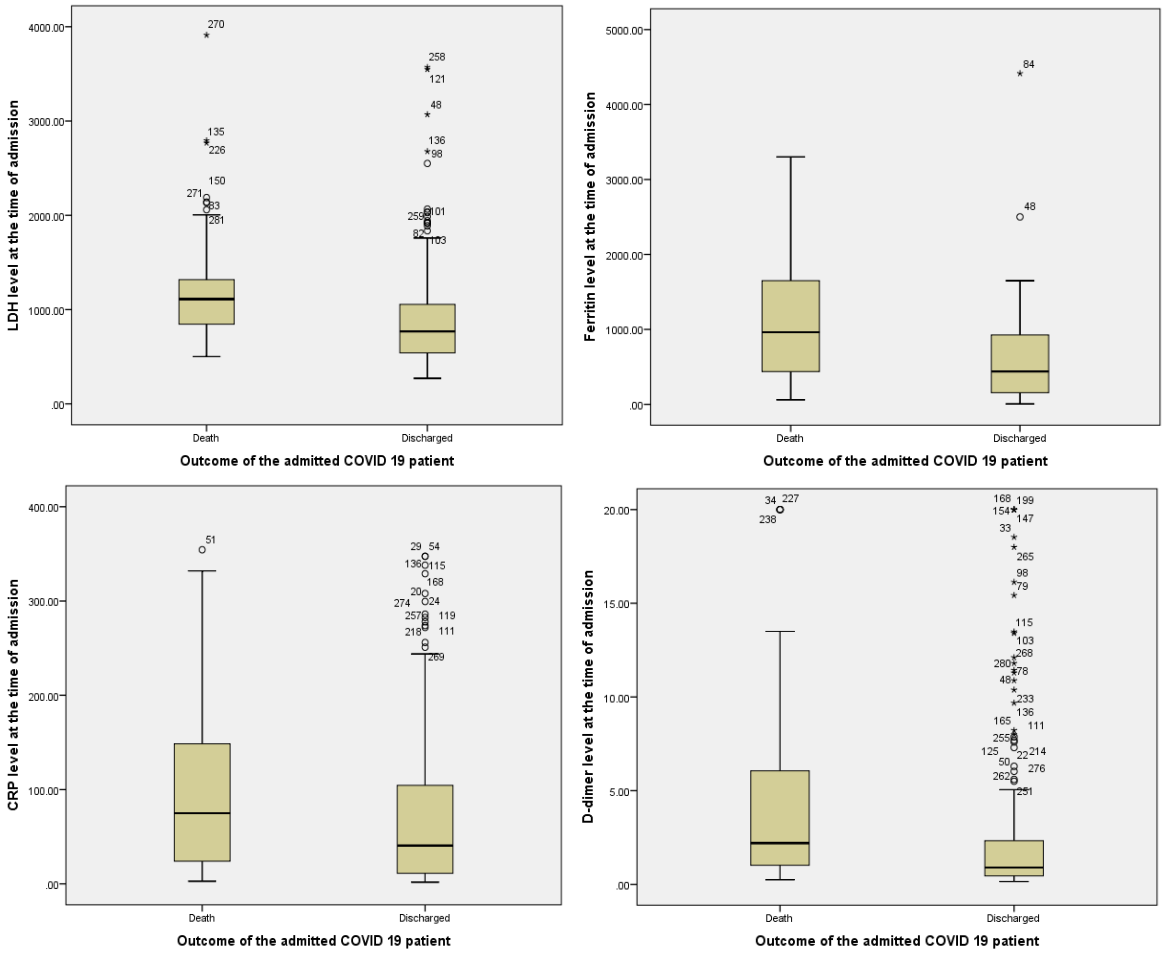


Table No. 5:Hypothesis test summary

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of LDH level at the time of admission is the same across categories of Outcome of the admitted COVID 19 patient.	Independent-Samples Mann-Whitney U Test	.000	Reject the null hypothesis.
2	The distribution of Ferritin level at the time of admission is the same across categories of Outcome of the admitted COVID 19 patient.	Independent-Samples Mann-Whitney U Test	.000	Reject the null hypothesis.
3	The distribution of CRP level at the time of admission is the same across categories of Outcome of the admitted COVID 19 patient.	Independent-Samples Mann-Whitney U Test	.011	Reject the null hypothesis.
4	The distribution of D-dimer level at the time of admission is the same across categories of Outcome of the admitted COVID 19 patient.	Independent-Samples Mann-Whitney U Test	.000	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

Conclusion: The study showed variable range of presentations with fever, cough and dyspnea as the most common presenting symptoms. The inflammatory markers like serum CRP, LDH, Ferritin & D-Dimer have significant prognostic value and can be considered as mortality indicators in patients of Covid-19. Old age and co morbidity like CKD, CAD, Diabetes Mellitus and Hypertension are associated with poor prognosis.

Limitations of the study: The samples were collected from a particular geographical location , so it may not represent the population from other geographical area.

Financial support & sponsorship: None.

Conflict of Interest: None of the authors have conflict of interest.

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