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Original Article

Pathology Section

Haematological, Clinical and Radiological Prognostic Markers in Young COVID-19 Patients during the Second Wave: A Prospective Cohort Study

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ABSTRACT

Introduction: The devastating outbreak of the second wave of Coronavirus Disease-2019 (COVID-19), resulting in numerous deaths among young individuals, has been the deadliest pandemic witnessed in this century. It caught us off guard by affecting young people and those without any underlying health conditions, leaving profound psychological and economic scars.

Aim: To investigate various prognostic markers (haematological and clinicoradiological) in young COVID-19 patients during the second wave.

Materials and Methods: This prospective, cohort study was conducted at a tertiary care centre in Karnataka, India from May 1st, 2021, to June 30th, 2021. All COVID-19 patients between the ages of 18 and 45, regardless of their pre-existing health status, who tested positive on Real-time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR)/Rapid Antigen Test (RAT) or showed typical Computed Tomography (CT) changes, were included. Patients with COVID-19 symptoms but negative RT-PCR/RAT results and without typical CT changes were excluded. Clinical, haematological, and radiological parameters were compared between the survivor group and non survivor group, and the results were analysed using measures of central tendency (mean, median, and mode), Chi-square test, and Independent t-test Statistical Package for Social Sciences (SPSS) version 21.0.

Results: A total of 624 cases aged between 18 and 45 were included in the study. Among them, 481 (77.08%) patients survived, while 143 (22.92%) patients were dead. Of the 624 cases, 376 (60.26%) were males, 247 (39.58%) were females, and 1 (0.16%) was transgender. Factors associated with increased mortality included older age (>40 years), presentation with cough (119 patients, 83.2%) and dyspnoea (120 patients, 83.9%), asthma (7 patients, 1.1%), clinical classification based on respiratory rate, oxygen saturation, CT changes, and requirement for mechanical ventilation (78 patients, 54.5% in the Severe category and 54 patients, 37.8% in the Critical category), increased white blood cell count (mean μ=9685.8±5470.9), increased neutrophils (μ=8216±4986.9), elevated levels of CRP (μ=96.7±65.84 mg/dL), serum ferritin (μ=571.4±353.15 ng/mL), LDH (μ=1268.7±835 U/L), D-dimer (μ=74.87±527), serum globulin, ALT (μ=67.6±58.5 U/L), AST (μ=76.4±62 U/L), ALP (μ=120±89 U/L), urea, creatinine, decreased levels of albumin, total protein, haemoglobin, and lymphopenia (μ=1096.1±795.9). Additionally, a CT score >15 was associated with increased mortality.

Conclusion: The aforementioned clinical, haematological, and radiological predictive biomarkers were associated with poor outcomes in young COVID-19 patients. Therefore, prompt and intensive management should be implemented to improve the prognosis of these patients.

Keywords: Biomarkers, Cough, Dyspnoea, Ferritin, Lymphopenia, Mortality

INTRODUCTION

According to the World Health Organisation (WHO), as of April 2023, India had the third-highest number of confirmed COVID-19 cases in the world, with a cumulative caseload of 44,834,859 cases. It ranks below the USA and China. India also stands third in terms of the highest number of COVID-19 deaths, with a cumulative death toll of 531,152 cases. It follows the USA and Brazil [1]. The first wave of COVID-19 lasted approximately from August 15, 2020, to January 17, 2021, while the second wave lasted from March 13, 2021, to June 19, 2021 [2]. Even today, deaths are being reported due to COVID-19 globally and in India. However, the second wave of COVID-19 has deeply impacted the nation, causing an explosive increase in the number of cases, shortage of hospital beds, oxygen supply, vaccines, and unfortunately, preventable young deaths.

Two years ago, on April 30, 2021, India led the world with the highest number of new and active cases, with over 400,000 new cases reported within a 24-hour period [3]. This unprecedented outbreak was so unpredictable and different from the first wave that many young, healthy individuals without any co-morbidities were dying. This was due to virus mutations that showed a predilection for that age group, and partly because older individuals were given priority in vaccination.

During the first wave, extensive studies were conducted on mortality, morbidity, and prognostic markers in the elderly. However, little was known about how the immune system reacted in younger patients and how CT and haematological markers were affected in these individuals. This study was conducted during the second wave of COVID-19 at the Shimoga Institute of Medical Sciences (SIMS) in Karnataka, India. Its aim was to examine various prognostic markers (haematological and radiological) in young COVID-19 patients and compare their ability to predict severity and death.

MATERIALS AND METHODS

This prospective, time-bound cohort study was conducted at SIMS, Shimoga, Karnataka, from May 1st, 2021, to June 30th, 2021, following Institutional Ethical Clearance (IEC) (SIMS/IEC/576/2021-22).

Inclusion criteria: All RT-PCR/RAT-positive COVID-19 patients admitted at SIMS, Karnataka, within the age group of 18-45 years, regardless of their pre-existing health status. RT-PCR/RAT-negative patients with CT scan changes suggestive of COVID-19 pneumonia

within the mentioned age group were also included, regardless of the outcome.

Exclusion criteria: Patients with COVID-19 symptoms, negative RT-PCR/RAT reports, and/or without typical CT changes were excluded. Patients who died shortly after admission and couldn't undergo haematological and radiological evaluations were also excluded.

Basic identification details of the patients, including age, detailed history, presenting complaints, vaccination status, co-morbidities, vitals, and haematological and radiological details, were collected from all patients who met the inclusion criteria. This information was obtained by reviewing the case sheets and interviewing the patients.

Patients who presented with clinical symptoms but without changes in CT chest were categorised as 'Mild.' Patients with respiratory symptoms, oxygen saturation >93%, and associated CT changes were categorised as 'Moderate.' Patients with a respiratory rate >30/min or oxygen saturation <93% were categorised as 'Severe.' Patients who presented with respiratory failure, required mechanical ventilation on admission, or had sepsis/organ dysfunction were classified as 'Critical' [4].

STATISTICAL ANALYSIS

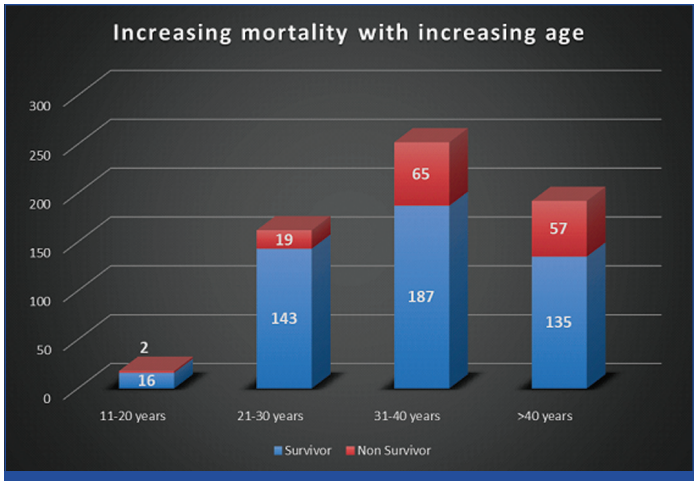
The data were collected using Google Forms and tabulated in an Excel sheet. Information that could not be collected in the wards or missed follow-up in the wards was retrieved from the records department by accessing the case sheets. Cases without relevant information were excluded from the study. The data were analysed using SPSS software version 21.0, and a significance level of $p<0.05$ was considered statistically significant. The Chi-square test and Independent t-test were used for comparison of means and measures of central tendency like mean, median, and standard deviation. The study did not require any changes in the existing dosage of drugs used on the patients or the usage of newer drugs.

RESULTS

After applying the inclusion and exclusion criteria, a total of 624 cases aged 18-45 years diagnosed with COVID-19 were included in the study. Among them, 481 (77.08%) patients survived, and 143 (22.92%) patients did not survive.

Epidemiological Findings

Of the total 624 cases, the mean age was 35.5±8.48 years, with a median of 36 years. There were 18 (2.8%) cases below 20 years of age, 162 (26%) cases within the age group of 21-30 years, 252 (40.4%) cases within the age group of 31-40 years, and 192 (30.8%) cases above 40 years of age. There was a statistically significant increase in the number of non survivors with increasing age (p-value=0.001), as shown in [Table/Fig-1].



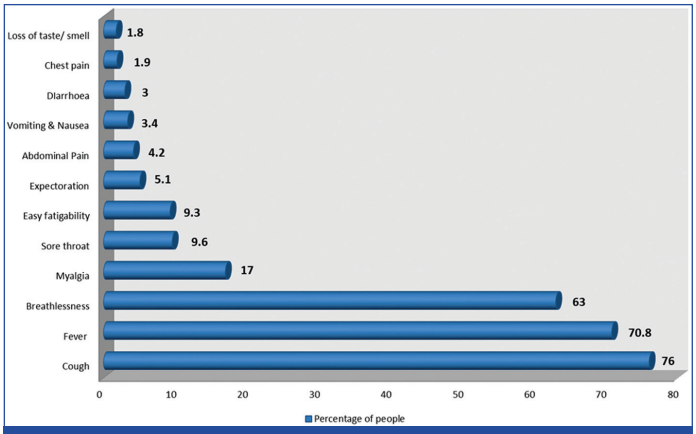
[Table/Fig-1]: Shows the age-wise distribution of survivors and non survivors.

Out of the 624 cases, 376 (60.26%) were males, 247 (39.58%) were females, and 1 (0.16%) was transgender. Although deaths were higher in males, with 89 (62.2%) cases compared to females with 53 (37.1%) deaths and transgender with 1 (0.7%) deaths, the difference was not statistically significant (p-value=0.151). The majority of the people included in the study, 598 (95.8%) cases, were not vaccinated as the vaccination during that time period was primarily given to healthcare workers, the elderly, and people over 45 years with co-morbidities.

A total of 18 (2.9%) were vaccinated with Covaxin and 8 (1.3%) were vaccinated with Covishield. One (0.7% of dead) of the 18 cases who were vaccinated with Covaxin did not survive. While two (1.4% of dead) of the eight cases vaccinated with Covishield were dead. Of the 26 cases who had taken vaccination, 11 (1.8%) cases had taken a single shot while 15 (2.4%) cases had taken both doses. But none of these differences were statistically significant and considering the smaller proportion of people with vaccination, the results cannot be generalised to the general population.

Of the 624 cases, 33 (5.3%) were healthcare workers and all the healthcare workers survived as compared to 143 deaths (100%) in the non healthcare worker group which was statistically significant (p-value=0.0001).

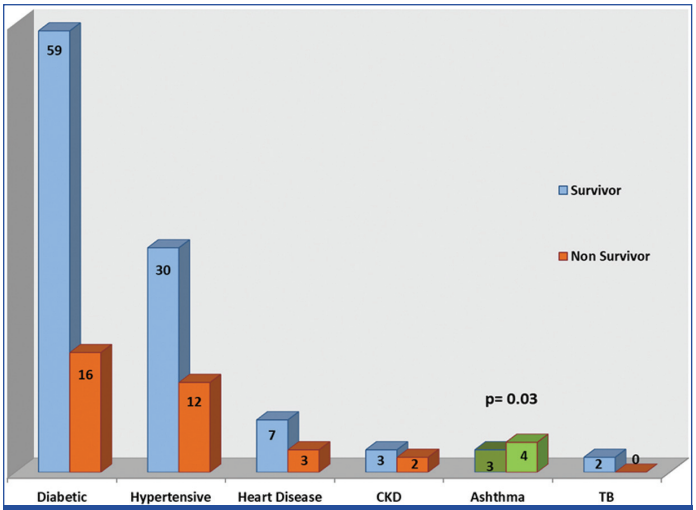
Presenting symptoms: Most of the patients presented with fever, cough, breathlessness, and myalgia. However, fewer common presentations were easy fatigability, sore throat, expectoration, abdominal pain, vomiting, nausea, chest pain, and oedema. [Table/Fig-2] shows the percentage comparison of the presenting complaints in the study. Cough was the presenting feature in 119 patients (83.2%) among the non survivors as compared to 357 cases (74.2%) among the survivors which were statistically significant (p-value=0.026). Breathlessness was the presenting symptom in 120 (83.9%) cases of the deceased group as compared to 275 (57.2%) of the survivors and this difference was statistically significant (p-value <0.001). Whereas, myalgia was the presenting symptom in 93 (19.3%) cases of survivors as compared to 14 (9.8%) cases of non survivors and this difference was statistically significant (p-value=0.008). Easy fatigability was the presenting symptom in 51 (10.6%) survivors as compared to 7 (4.9%) cases amongst non survivors, which was statistically significant (p-value=0.039).



[Table/Fig-2]: Shows the presenting symptoms of the patients in this study. Most of the patients had cough, fever and breathlessness as the presenting symptoms.

Co-morbidities: Of the 624 cases, 139 cases (22.3%) had associated co-morbidities. Of these, the majority had a history of diabetes with 75 (12%) cases followed by hypertension with 42 cases (6.7%), heart disease with 10 (1.6%) cases, Bronchial Asthma with 7 (1.1%) cases, Hypothyroidism with 7 (1.1%) cases, obesity with 6 (1%) cases, Chronic kidney disease with 5 (0.8%) cases, Tuberculosis with 2 (0.3%) cases and other less frequent ailments like Chronic Obstructive Pulmonary Disease (COPD) (two cases), Cerebrovascular Disease (two cases), and one case each of chronic liver disease, epilepsy, HIV, hypocalcaemia, psoriasis,

thyroiditis, and Wilson's disease. Unlike the observation among the old with COVID-19, none of the co-morbidities were significantly associated with fatalities except asthma. Asthmatics reported more deaths {4 (2.8% of the dead)} which was statistically significant (p-value=0.03 [Table/Fig-3].



[Table/Fig-3]: Shows the comorbidities encountered in the patients in the study and the comparison of the same between the survivors and non survivors.

Clinical severity: The cases were categorised as mild, moderate, severe, and critical based on their presentation to the hospital. The 'mild' category constituted 131 (21%) cases, and out of these, 2 (1.4%) cases resulted in death. The 'moderate' category constituted 179 (28.7%) cases, and out of these, nine (6.3%) cases resulted in death. The 'severe' category constituted 258 (41.3%) cases, and out of these, 78 (54.5%) cases resulted in death. The 'critical' category constituted 56 (9%) cases, and out of these, 54 (37.8%) patients succumbed to the disease [Table/Fig-4].

Clinical classification of severity [4]	Total number	Survivors (%)	Non-survivors (%)	Chi-square	p-value
Critical (Mechanical Ventilation due to Respiratory failure, Sepsis, or Organ dysfunction)	56	2 (0.4)	54 (37.8)	245.487	<0.001
Mild (Clinical Symptoms+ No changes in CT Chest)	131	129 (26.8)	2 (1.4)		
Moderate (Respiratory symptoms with CT changes)	179	170 (35.3)	9 (6.3)		
Severe (RR >30/Min or SpO_2 <93%)	258	180 (37.4)	78 (54.5)		

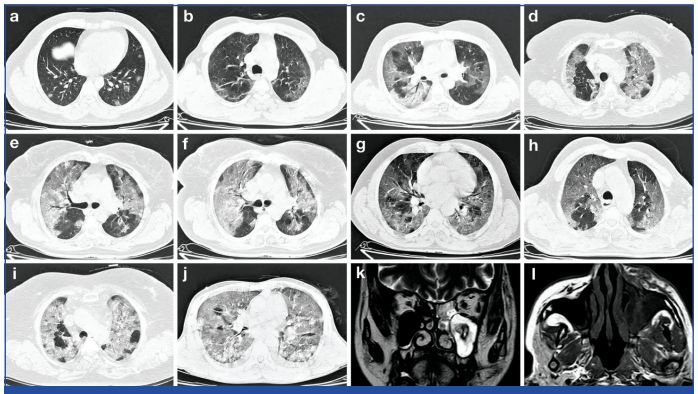
[Table/Fig-4]: Shows the categorisation of the patients based on the severity and the comparison of the individual categories between the survivors and non-survivors.

Prognostic biomarkers and CT score: The various blood investigations were analysed, and it was observed that increased WBC count, increased neutrophil percentage, increased absolute neutrophil count, decreased lymphocyte percentage, decreased lymphocyte count, increased CRP, ferritin, LDH, low protein, increased ALP, ALT, AST, increased urea, creatinine, and CT score were significantly associated with a fatal outcome. The individual data is shown in [Table/Fig-5]. [Table/Fig-6] shows the various grades of CT changes in different clinical grades of COVID-19 pneumonia, ranging from focal consolidation, Ground Glass Opacities (GGO), and crazy pavement pattern. The mean CT score in the survivor group was 9.28±5.97, while in the non survivor group, it was 16.52±4.42 (p-value <0.001), indicating a significant increase in the CT score in the non survivor group. The CT scan was normal without any changes suggestive of COVID-19 in 79 (12.7%) cases. The mild category with a CT score of less than eight constituted 140 (22.4%) cases, while the moderate category (CT score 9-15)

Variables	Categories	N (Total-624)	Outcome		Chi-square	p-value
			Survivor (N (%))	Non survivor (N (%))		
WBC count	Decreased	57	42 (8.7)	15 (10.5)	12.754	**0.002**
	Increased	176	120 (24.9)	56 (39.2)		
	Normal	391	319 (66.3)	72 (50.3)		
Absolute neutrophil count	Decreased	14	9 (1.9)	5 (3.5)	20.732	**<0.001**
	Increased	223	160 (33.3)	63 (44.1)		
	Normal	387	312 (64.9)	75 (52.4)		
Lymphocyte count	Decreased	209	132 (27.4)	77 (53.8)	40.841	**<0.001**
	Increased	5	2 (0.4)	3 (2.1)		
	Normal	410	347 (72.1)	63 (44.1)		
Platelet count	Decreased	120	84 (17.5)	36 (25.2)	4.225	**0.121**
	Increased	9	7 (1.5)	2 (1.4)		
	Normal	495	390 (81.1)	105 (73.4)		
Haemoglobin	Decreased	120	79 (16.4)	41 (28.7)	18.372	**<0.001**
	Increased	13	11 (2.3)	2 (1.4)		
	Normal	491	391 (81.3)	100 (69.9)		
CRP	Increased	480	347 (72.1)	133 (93)	27.035	**<0.001**
	Within limits	144	134 (27.9)	10 (7)		
S.Ferritin	Increased	253	146 (30.4)	107 (74.8)	90.651	**<0.001**
	Decreased	4	4 (0.8)	0 (0)		
	Within limits	367	331 (68.8)	36 (25.2)		
LDH	Increased	511	371 (77.1)	140 (97.9)	32.077	**<0.001**
	Decreased	2	2 (0.4)	0 (0)		
	Within limits	111	108 (22.5)	3 (2.1)		
D-Dimer	Increased	128	68 (14.1)	60 (42)	52.484	**<0.001**
	Decreased	1	1 (0.2)	0 (0)		
	Within limits	495	412 (85.7)	83 (58)		
Albumin	Increased	3	2 (0.4)	1 (0.7)	23.799	**<0.001**
	Decreased	259	175 (36.4)	84 (58.7)		
	Within limits	362	304 (63.2)	58 (40.6)		
Globulin	Increased	172	124 (25.8)	48 (33.6)	12.453	**0.002**
	Decreased	72	47 (9.8)	25 (17.5)		
	Within limits	380	310 (64.4)	70 (49)		
ALT	Increased	312	212 (44.1)	100 (69.9)	32.423	**<0.001**
	Decreased	3	3 (0.6)	0 (0)		
	Within limits	309	266 (55.3)	43 (30.1)		
AST	Increased	336	230 (47.8)	105 (74)	33.549	**<0.001**
	Decreased	2	2 (0.4)	0 (0)		
	Within limits	286	249 (51.8)	37 (25.9)		
Total protein	Increased	4	3 (0.6)	1 (0.7)	12.435	**0.002**
	Decreased	157	105 (21.8)	52 (36.4)		
	Within limits	463	373 (77.5)	90 (62.9)		
ALP	Increased	127	73 (15.2)	54 (37.8)	35.604	**<0.001**
	Decreased	5	5 (1)	0 (0)		
	Within limits	492	403 (83.8)	89 (62.2)		
Urea	Increased	62	26 (5.4)	36 (25.2)	49.255	**<0.001**
	Decreased	13	11 (2.3)	2 (1.4)		
	Within limits	549	444 (92.3)	105 (73.4)		
Creatinine	Increased	30	12 (2.5)	18 (12.6)	24.534	**<0.001**
	Within limits	594	469 (97.5)	125 (87.4)		
Sodium	Increased	5	4 (0.8)	1 (0.7)	0.666	0.717
	Decreased	55	40 (8.3)	15 (10.5)		
	Within limits	564	437 (90.9)	127 (88.8)		

RBS (on admission)	<99 mg/dL	62	52 (10.8)	10 (7)	12.493	**0.029**
	>401 mg/dL	16	12 (2.5)	4 (2.8)		
	100-200 mg/dL	414	328 (68.2)	86 (60.1)		
	201-300 mg/dL	105	70 (14.6)	35 (24.5)		
	301-400 mg/dL	24	18 (3.7)	6 (4.2)		
	Not checked	3	1 (0.2)	2 (1.4)		

[Table/Fig-5]: Shows the comparison of high, normal, and low values among survivors and non survivors.



[Table/Fig-6]: a-j) Shows the different levels of lung involvement in COVID-19 patients in the study. k-l) Shows a case of mucormycosis – Right maxillary and ethmoid sinus in a COVID-19 patient in the study.

constituted 237 (38%) cases. The severe category with a CT score >15 constituted 168 (27%) cases.

Treatment factors: The average number of vaccine doses administered was 0.08±0.36, which was higher than that of the non survivors, which was 0.03±0.2 doses, and this difference was statistically significant (p-value=0.039). The mean duration of symptoms before hospitalisation was 3.9±1.6 days among survivors, compared to 4.08±1.6 days among non survivors; however, this difference was not statistically significant. The oxygen saturation at admission was higher in the survivor group compared to the non survivors, and this difference was statistically significant. The mean day of starting Remdesivir post-hospitalisation was 2.22±2.83 in the survivor group, which was earlier compared to that in the non survivor group, which was 3.15±3.01 days, and this difference was statistically significant (p-value=0.001). However, 92 (64.3% of the deceased) cases had taken Remdesivir compared to 51 (35.7% of the deceased) cases who had not taken Remdesivir, and this difference was statistically significant (p-value <0.00001). The average day of starting steroid post-hospitalisation among the survivors was 4.04±2.27 days compared to the non survivors, which was 4.35±1.99 days; however, this difference is not statistically significant.

DISCUSSION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), commonly known as the Novel Coronavirus 19 virus, has four different genera: α-CoV, β-CoV, γ-CoV, and δ-CoV [5]. The α- and β-CoV cause infection in mammals, while γ- and δ-CoV infect birds [5]. It has been found that SARS-CoV-2 uses a host protein named Angiotensin-Converting Enzyme 2 (ACE2) and CD 147 to infect humans [5]. The second wave of COVID-19 surprised the world by causing a sudden increase in young COVID-19 deaths, which was not seen in the previous wave [6]. Additionally, there was a sudden reduction in oxygen saturation in these individuals, making the disease course unpredictable, especially when there were limited resources like oxygen cylinders and mechanical ventilators. These factors could possibly be due to mutations in the virus and new variants [6]. Little was known about the prognostic factors in a relatively younger population.

In present study, out of the 624 cases, 481 (77.08%) patients survived, and 143 (22.92%) patients died. This mortality rate was comparable to another study with a rate of 25.5% [7]. A meta-analysis by Tian W et al., showed that male sex was significantly associated with adverse outcomes [7]. Although 83 cases (62.2% of the deceased) were male in present study, the increase was not statistically significant. Tian W et al., also established that older age was associated with a higher risk of death, which was comparable to present study (p-value=0.001). The good outcomes for healthcare workers in this study could be due to awareness, early attention, and preferential vaccination.

The mean incubation period (the time from exposure to symptom onset) of COVID-19 is approximately five days (95% Confidence Interval [CI], 4.1-7.0 days), and it takes around eight days to develop pneumonia [8]. The virus is transmitted through air, direct or indirect contact. In present study, the mean number of days from symptom onset to hospital presentation was 3.95±1.6 days (Median=4; Range=1-10 days), which was comparable to the study by Kim L et al., [9].

COVID-19 patients often present with mild symptoms such as fever, cough, myalgia, and fatigue, and generally have a good prognosis [9]. However, a proportion of cases can rapidly progress to severe types, especially among older men with underlying diseases, and can present with shock, dyspnoea, Acute Respiratory Distress Syndrome (ARDS), cardiac impairment, coagulation abnormalities, and death [10]. In present study, most patients presented with cough (476 cases, 76.3%), fever (442 cases, 70.8%), and breathlessness (395 cases, 63.3%) as shown in [Table/Fig-2]. Patients who presented with early lung involvement, characterised by cough and breathlessness, had a significantly increased mortality rate (p-value <0.05). Breathlessness was the presenting symptom in 120 (83.9%) cases of the deceased group, compared to 275 (57.2%) of the survivors, and this difference was statistically significant (p-value <0.001). The increased fatality in patients presenting with cough and breathlessness could be due to early lung involvement by a virulent strain. A meta-analysis showed that anosmia or hyposmia is significantly associated with positive COVID-19 infections [11]. However, in present study, only 11 (1.8%) cases presented with loss of taste or smell. This could be due to differences in the strain of the virus in the region. Easy fatigability was the presenting symptom in 51 (10.6%) survivors, compared to 7 (4.9%) cases among non survivors, and this difference was statistically significant (p-value=0.039). This could also possibly be due to the difference in the strain of COVID-19, with a milder variant presenting with myalgia and easy fatigability. Most studies have shown that mortality increases with the presence of co-morbidities. However, in present study, only asthmatic patients had increased mortality. This could be due to the exclusion of the older population in this study [12-16].

The fusion between the viral envelope and endosomal membrane induces the release of the viral genome into the cell, which can be identified by Pattern Recognition Receptors (PRRs) in the cytosol, such as MDA-5 or RIG-1 [17]. These PRRs also trigger the activation of Nuclear Factor kappa Beta (NF-κB) through a different signaling pathway [18], resulting in a cytokine storm. Increased levels of several cytokines have been reported in patients with severe COVID-19, including Interleukin (IL)-1β, IL-2, IL-6, IL-7, IL-8, IL-10, IL-17, IFN-γ, IFN-γ-inducible protein 10, MCP-1, G-CSF, MIP-1α, and TNF-α [19].

Cytokine storm, a pathological overproduction of cytokines that leads to a systemic inflammatory response affecting several organs such as the heart, liver, and kidney, is the leading cause of death in COVID-19 patients. The presenting symptoms and clinical presentations, such as increased respiratory rate, decreased oxygen saturation, and other signs and symptoms of lung involvement, are associated with poor survival in this study, as established in several meta-analyses

Variables	A study done at the institute in the First wave (Mahendra M et al.,) [15]				A study done in second wave (18-45 years) Pandey A et al.,			
	Total (n=560)	Survived (n=254)	Death (n=306)	p-value	Total (n=624)	Survived (n=481)	Dead (n=143)	p-value
Age in years, Mean±SD	57.75±13.96	54.39±14.99	60.54±12.39	0.004	35.5±8.48	34.7±8.65	38.04±7.37	<0.001
Male gender	365 (65.17%)	166 (65.35%)	199 (65.03%)	0.840	376 (60.3%)	287 (59.7%)	89 (62.2%)	0.151
Cough	262 (46.78%)	131 (51.57%)	131 (42.95%)	0.083	476 (76.3%)	357 (74.2%)	119 (83.2%)	0.026
Breathlessness	389 (69.46%)	140 (55.12%)	249 (81.37%)	0.001	395 (63.3%)	275 (57.2%)	120 (83.9%)	<0.001
Myalgia	61 (10.89%)	41 (16.14%)	20 (6.54%)	0.315	107 (17.2%)	93 (19.3%)	14 (9.8%)	0.008
Duration of symptoms before admission, mean±SD (in days)	4.11±2.09	3.27±1.92	4.79±1.98	0.0001	3.95±1.6	3.9±1.6	4.08±1.6	0.239
Co-morbidities, n (%)	343 (61.25%)	115 (45.28%)	228 (74.51%)	0.0001	139 (22.3%)	103 (21.4%)	36 (25.2%)	0.343
Diabetes, n (%)	230 (41%)	80 (31.50%)	150 (49.02%)	0.016	75 (12%)	59 (12.3%)	16 (11.2%)	0.728
Hypertension, n (%)	231 (41.25%)	72 (28.35%)	159 (51.96 %)	0.009	42 (6.7%)	30 (6.2)	12 (8.4)	0.367
Laboratory findings at the time of admission, mean±SD								
Total White blood cell count (cells×10^9/L)	9.87±6.5	9.04±4.59	10.56±7.74	0.071	8.9±4.4	8.657±3.9	9.68±5. 47	0.038
Platelet count (lac/mm^3)	2.10±0.93	2.24±0.87	2.03±0.86	0.081	2.05±0. 89	2.11±0. 88	1.84±0. 88	0.002
Serum ferritin (µg/L)	539.66±381.78	367.2±308.63	632.29±385.61	0.0001	343.52±332	275.8±293	571.4±353	<0.001
Serum LDH (U/L)	845.73±593.51	788.1±681.62	866.39±558.5	0.160	841.89±574	715±390.12	1268.7±835	<0.001
Serum creatinine (mg/dL)	1.66±2.08	1.24±1.33	1.94±2.51	0.002	0.72±0.69	0.66±0.42	0.92±1.18	0.01
Remdesivir usage n (%)	298 (53.21%)	165 (64.96%)	133 (43.46%)	0.019	316 (50.6%)	224 (46.6%)	93 (64.3%)	<0.001
First dose of Remdesivir after symptoms onset	5.58±2.78	5.06±3.12	6.01±2.37	0.0001	2.43±2.89	2.22±2.83	3.15±3.01	0.001
First dose of steroid after admission (in days)	1.22±1.19	1.19±1.25	1.24±1.03	0.931	4.1±2.22	4.04±2.27	4.35±1.99	0.207

[Table/Fig-7]: Shows the comparison of various mortality predictors between first wave and second wave in the same institute [16].

[12-16]. This study was conducted in a tertiary care referral centre, which probably explains the relatively larger proportion of severe and critical cases. The deaths increased with increasing severity, with the highest adverse outcomes reported in the 'severe' category, followed by the 'critical' category, and were significantly higher than mild and moderate cases (p-value <0.001). The preferential treatment of critical cases, with the availability of ventilators and Intensive Care Unit (ICU) services upon admission, could possibly be the reason for lower mortality in these cases compared to cases categorised as 'severe'. The haematological and biochemical parameters, as well as CT findings, and their relation to the outcome in this study, are shown in [Table/Fig-5,6]. [Table/Fig-7] compares the findings of this study with a similar study conducted during the first wave in the same institute [16]. In the initial days of the first wave, various antiviral drugs developed for influenza virus, Human Immunodeficiency Virus (HIV), and SARS-CoV/MERS-CoV viruses, as well as antibiotics, antiprotozoals, anthelmintic drugs, and convalescent plasma, were tried in vain. The National Institute of Health (NIH) recommends the use of corticosteroids (dexamethasone), IL-6 inhibitors (tocilizumab or sarilumab), and JAK inhibitors (baricitinib or tofacitinib) for treating COVID-19 [20]. Remdesivir is a prodrug that has shown antiviral activity against various viruses, including SARS-CoV, in-vitro [21]. In this study, there was a significant increase in deaths in patients who had been started on Remdesivir. This could be due to the preference of severe and critical patients only for Remdesivir in a resource-limited setting. However, Remdesivir was started earlier in patients who had survived, which was statistically significant. This indicates the increased chances of survival with early administration of Remdesivir.

Limitation(s)

Limited follow-up of these patients to comment on the long-term effects of this viral infection/disease. The study was conducted during the initial vaccination phase in India, so the effect of vaccines on the disease outcome could not be fully studied. Since the study was conducted in a tertiary care centre, the number of patients with severe disease was relatively higher, and mild cases were treated symptomatically without admission, so the data cannot be generalised.

CONCLUSION(S)

The young population showed a different response to COVID-19 compared to older individuals, especially those with associated co-morbidities. The prognosis worsened with increasing age, even among the young. Severe/critical clinical grade, higher CT score, increased WBC, neutrophil, CRP, D-dimer, LDH, ferritin, and decreased lymphocyte count, haemoglobin, total protein, and albumin were associated with poor outcomes in young COVID-19 patients, and prompt and vigorous management should be implemented to salvage these patients.

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