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Original Research Article

Characteristics and risk factors associated with COVID-19 progression: Insights from a retrospective study in India ?

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ABSTRACT

Background: The COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has posed significant challenges worldwide, with India being one of the most affected countries. Understanding the clinical variables, complications, and laboratory markers associated with COVID-19 progression is crucial for effective management and reducing mortality.

Objective: This retrospective study aimed to analyze the clinical characteristics, complications, comorbidities, and laboratory markers associated with COVID-19 progression among patients admitted to SPM Hospital, India.

Material and Methods: Clinical data of 440 confirmed COVID-19 patients admitted between June and December 2020 were analyzed. Demographic characteristics, clinical symptoms, comorbidities, laboratory findings, and radiological manifestations were reviewed. Patients were categorized based on age, gender, comorbidities, and disease severity.

Results: The study cohort comprised mainly elderly patients, with more than half aged 50-80 years and a male predominance. Fever, cough, and sore throat were the most common symptoms, with a significant proportion of patients presenting with comorbidities such as diabetes mellitus and hypertension. Laboratory markers including interleukin-6 (IL-6), D-dimer, C-reactive protein (CRP), serum ferritin (S. ferritin), and lactate dehydrogenase (LDH) were elevated in severe cases, with higher levels observed in patients aged ≥50 years. Patients requiring oxygen supplementation had a higher mortality rate compared to those maintaining oxygen saturation on room air.

Conclusion: Age, gender, and comorbidities were identified as risk factors associated with COVID-19 severity and mortality. Elevated levels of IL-6, D-dimer, CRP, S. ferritin, and LDH were indicative of disease severity and poor prognosis. Early identification of high-risk patients and personalized management strategies are essential for improving clinical outcomes in COVID-19 patients.

1. Introduction

The COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in a global health emergency. India, as of September 1, 2023, has recorded the second-highest number of confirmed cases worldwide, totalling 44,996,963[1] infections, and the third-highest number of deaths, with 531,928[1] reported fatalities. The World Health Organization's estimation of approximately 4.7 million excess deaths in India by October 2021 underscores the profound impact of COVID-19 on mortality rates.

Effective risk assessment based on laboratory markers is crucial for early intervention and mortality reduction among COVID-19 patients. However, discrepancies exist in reported laboratory biomarkers associated with disease

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progression.[2–5] Variations in comorbidities among study cohorts contribute to the complexity of biomarker analysis,[6] as comorbid conditions often precipitate the transition to severe and critical cases in COVID-19 patients. Despite extensive documentation of clinical characteristics, the interpretation of laboratory indicators in specific subgroups remains challenging[7–9]

2. Aims and Objectives

1. To assess clinical variables, complications, comorbid conditions, duration of hospitalization, and ICU requirements among COVID-19 patients.
2. To investigate laboratory markers and CT findings to understand the progression of COVID-19 in patients with and without comorbidities.

3. Materials and Methods

The clinical records of patients diagnosed with COVID-19 at SPM Hospital, India, between June 28 and December 28, 2020, were subjected to a retrospective analysis. This involved consecutive admissions of patients who were medically ill enough to necessitate hospitalization due to confirmed infection with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), as determined by positive results on polymerase chain reaction (PCR) testing of nasopharyngeal samples.

Experienced clinicians meticulously reviewed and extracted clinical data, encompassing recent exposure history, symptoms, signs, comorbidities, and initial laboratory findings upon admission. The manifestations observed on chest radiographs or computed tomography (CT) scans were collated by integrating the documentation or descriptions provided in medical charts.

3.1. Inclusion criteria

Patients eligible for inclusion in the study were those who had been confirmed to have COVID-19 infection either through real-time reverse transcriptase polymerase chain reaction (RT-PCR) testing or chest computed tomography (CT). Additionally, included patients had available data regarding demographic characteristics, clinical features, and comorbidities.

3.2. Exclusion criteria

Patients were excluded if they exhibited symptoms but did not test positive on real-time reverse transcriptase polymerase chain reaction (RT-PCR) testing, or if their chest computed tomography (CT) results were negative.

3.3. Statistical analysis

Statistical significance was set at 95% confidence level (p- value of less than or equal to .05). Continuous data were summarized as mean ± SD while discrete data(categorical) in summarize, number and percentage. Continuous groups were compared by student's t test and categorical groups by Chi Square. Overall, these statistical methods provided a comprehensive analysis of the data, allowing for the assessment of associations and comparisons between different variables in your study.

4. Results

A total of 440 patients participated in the study, spanning ages from 18 to 80 years, with a mean age of 51.49 ± 16.51 years. More than half of the patients (59.78%) belonged to the 50-80 years age group, and the majority (66.82%) were male. Elderly patients exhibited a higher prevalence of one or more chronic diseases, notably Diabetes Mellitus and Hypertension (HTN) (Table 1).

Among the cohort, only 20 patients (4.55%) were asymptomatic, while the rest presented with various symptoms. The most prevalent symptoms included fever (91.82%), cough and sore throat (68.86%), dyspnea (16.59%), fatigue (14.55%), diarrhea with vomiting (2.04%), and burning micturition (0.91%) (Table 1).

Regarding oxygen saturation levels, 246 patients (55.91%) had levels between 95-100%, 105 patients had levels between 92-94%, and 89 patients (20.22%) had levels at or below 90% (Table 2). A minority, 37 patients (8.4%), required ventilator or BIPAP support, while 137 patients (31.14%) required high-flow oxygen. The remaining patients maintained adequate oxygen saturation on room air (Table 2).

Plasma concentrations of IL-6, D-DIMER, CRP, S. FERRITIN, and LDH were observed to be higher in ICU patients compared to non-ICU patients. The majority of severe cases displayed elevated levels of biomarkers associated with infection (S. ferritin, CRP, LDH) and inflammatory cytokines (IL6) (Table 3).

Among the patients, 424 were discharged after treatment, while 16 patients succumbed during treatment. Discharged patients had a mean age of 51.49 ± 16.51 years, whereas deceased patients had a mean age of 69.31 ± 10.35 years. Elderly patients with one or more comorbid conditions such as DM, HTN, and obesity showed a positive association with mortality (Table 4). Furthermore, patients requiring oxygen support, whether through HFC, BIPAP, or ventilator, also exhibited a positive association with mortality (Table 4).

Patients with elevated levels of IL-6, D-DIMER, CRP, S. FERRITIN, and LDH were significantly associated with mortality. Conversely, patients with normal or slightly elevated levels of these biomarkers recovered after treatment (Table 5).

Table 1: Baseline and clinical characteristics of the patients

N=440		N	%
Age	≤20 years	17	3.86
	21-30 years	25	5.68
	31-40 years	56	12.73
	41-50 years	79	17.95
	51-60 years	110	25.00
	61-70 years	93	21.14
	>70 years	60	13.64
Gender	Male	294	66.82
	Female	146	33.18
Co-morbidity	DM	143	32.50
	HTN	145	32.95
	Obesity	76	17.27
	Thyroid	35	7.95
	Artherities	6	1.36
	CAD	24	5.45
	COPD	17	3.86
	Hypothyroidism	14	3.18
	CKD	7	1.59
	Cancer	2	0.45
	TB	1	0.23
	CVA	2	0.45
	CABG	3	0.68
	Liver disease	2	0.45
Asymptomatic	-	20	4.55
Symptomatic	Breathlessness	73	16.59
	Sore throat with Cough& cold	303	68.86
	Fever	404	91.82
	Fatique	64	14.55
	Diarrhea with vomiting	9	2.04
	Burning micturition	4	0.91

Table 2: Details of SpO2 level in patients

		N	%
SpO2	<65	4	0.91
	65-79	9	2.05
	80-91	76	17.27
	92-94	105	23.86
	95-100	246	55.91
HFC	-	137	31.14
BIPAP	-	14	3.18
Ventilator	-	23	5.23

5. Discussion

In our investigation comprising 440 confirmed cases of COVID-19, we observed that a majority (59.78%) of patients belonged to the 50-80 years age bracket, indicating a heightened vulnerability among the elderly population compared to younger cohorts. Notably, severity of COVID-19 exhibited an age-related pattern, with younger individuals showing relatively better outcomes, possibly attributable to their stronger immune responses. Conversely, elderly patients demonstrated poorer survival rates, which may be linked to their compromised nutritional status and immune function. Such vulnerabilities could predispose them to severe pneumonia and elevate the risk of mortality.[10,11]

Although males exhibit similar susceptibility to SARS-CoV-2 as females, they are more prone to experiencing higher severity and mortality rates, akin to the SARS outbreak in 2003[12–15] Our analysis identified gender as an independent risk factor for COVID-19 mortality. Notably, levels of LDH, D-DIMER, S. FERRITIN, CRP, and IL-6 were significantly elevated in patients aged 50

Table 3: Details of clinical parameters

	Mean	Median	Std. Deviation	Minimum	Maximum	IQR	
						25	75
Hb	10.48	10.20	6.22	2.30	135.00	9.80	11.20
TLC	8916.66	8654.00	2405.18	15.23	29700.00	7600.00	9900.00
PC	1.94	2.00	0.60	0.62	3.00	1.38	2.34
SGOT	85.18	76.00	53.05	22.00	790.00	61.00	90.00
SGPT	77.22	73.00	43.71	22.00	803.00	60.00	83.00
S. CREATININE	1.40	0.90	5.98	0.60	126.00	0.80	1.50
IL6	42.37	11.60	122.43	0.12	1500.00	5.48	23.65
D. DIMER	5.70	0.46	53.05	0.00	710.00	0.30	1.31
CRP	21.35	2.32	98.95	0.00	1500.00	0.66	6.54
S. FERRITIN	272.31	129.90	636.07	0.21	7800.00	57.10	295.20
LDH	361.01	299.75	266.97	1.79	1538.00	153.05	511.90

Table 4: Association of baseline, Co-morbidity and clinical characteristics of the patients with discharge and death patients

		Discharge (424)		Death (n=16)		p-Value
		n	%	N	%	
Age	Mean ± SD	51.49±16.51		69.31±10.35		<0.001
Gender	Male	259	66.24	14	87.50	0.103
	Female	132	33.76	2	12.50	
Co-morbidity	DM	135	34.53	8	50.00	<0.001
	HTN	119	30.43	8	50.00	
	Obesity	121	30.95	6	37.50	
	Thyroid Disease	64	16.37	0	0.00	
	Arthritis	4	1.02	0	0.00	
	CAD	13	3.32	3	18.75	
	COPD	15	3.84	0	0.00	
	Hypothyroidism	6	1.53	1	6.25	
	CABG	1	0.26	1	6.25	
	CKD	5	1.28	2	12.50	
HFC		108	27.62	12	75.00	0.001
BIPAP		9	2.30	3	18.75	0.009
Ventilator		7	1.79	13	81.25	<0.001

Table 5: Association of different clinical parameters (investigation) of the patients with discharge and death patients

	Discharge (424)		Death (n=16)		p-Value
	Mean	±SD	Mean	±SD	
Hb	10.57	6.55	9.91	1.25	0.686
TLC	8949.13	2400.90	8885.14	3481.22	0.919
PC	1.93	0.60	1.95	0.69	0.891
SGOT	85.03	51.83	80.13	27.20	0.707
SGPT	77.72	45.19	72.44	22.47	0.642
Creatinine	1.39	6.34	1.71	1.04	0.841
IL6	32.29	82.96	134.85	203.21	<0.001
D. DIMER	3.86	39.92	47.73	176.67	0.002
CRP	16.73	60.84	17.34	47.80	0.002
S. FERRITIN	256.44	516.53	776.24	1957.60	0.003
LDH	350.62	246.27	548.20	451.25	0.004

years and above compared to those below 50 years, with females demonstrating a protective effect against COVID-19 mortality. However, the precise mechanisms underlying these gender disparities remain elusive. It is acknowledged that, generally, females display more robust innate and immune responses compared to males, who tend to express higher levels of proinflammatory cytokines and chemokines. Moreover, the heightened expression of the core cytokine storm mediator, IL-6 receptor, in lung epithelial cells in males suggests a heightened susceptibility to cytokine storms that may exacerbate COVID-19 progression.[16–18]

Comorbidity stands out as a significant risk factor for mortality among COVID-19 patients. Common comorbidities such as hypertension, diabetes, obesity, and chronic cardiovascular diseases have been identified among deceased individuals. COVID-19 patients with complications like diabetes and hypertension face a heightened risk of mortality. The state of hyperglycaemia and insulin resistance in diabetic patients may compromise the synthesis of pro-inflammatory cytokines such as interferon-γ and interleukin, rendering them more susceptible to SARS-CoV-2[12]. Additionally, viral infection can lead to sharp fluctuations in blood glucose levels, hindering patient recovery. The angiotensin-converting enzyme 2 (ACE2) serves as the receptor for SARS-CoV-2 entry into host cells[13]. Patients with at least one comorbidity are associated with poorer clinical outcomes, emphasizing the need to consider baseline comorbid diseases in comprehensive risk assessments for prognosis among COVID-19 patients.[14]

Laboratory tests in COVID-19 patients commonly reveal normal or decreased white blood cell counts, alongside increased levels of CRP, IL-6, S. FERRITIN, and LDH, sometimes accompanied by elevated liver enzymes. CRP, a key inflammatory marker, plays a critical role in combating pathogens and inflammation,[19] with higher levels correlating with adverse outcomes such as cardiac injury, ARDS, and mortality in COVID-19. Additionally, thrombocytopenia has been associated with increased mortality risk in pneumonia patients. Hence, assessing levels of LDH, IL-6, S. FERRITIN, CRP, and platelets can effectively gauge the severity of COVID-19, with CRP standing out as a reliable predictor of disease severity. These biomarkers offer valuable insights for evaluating the prognosis and severity of COVID-19 cases.[20–23]

Patients infected with COVID-19 typically exhibit one or more symptoms, with fever, dyspnoea, cough, fatigue, and gastrointestinal symptoms being the most common. Only a small percentage (4.55%) of COVID-19 positive patients remain asymptomatic. Those with severe disease often require supplemental oxygen and close monitoring for respiratory deterioration, as some may progress to acute respiratory distress syndrome (ARDS). Patients with mild disease generally do not require oxygen supplementation, maintaining adequate oxygen saturation on room air. Conversely, patients with severe disease may necessitate oxygen supplementation via high-flow oxygen, BIPAP, or ventilator support. Notably, this study highlights the correlation between hospitalization duration and the need for supplemental oxygen; longer hospital stays often coincide with increased oxygen therapy requirements. Furthermore, mortality rates are higher among patients requiring oxygen supplementation compared to those maintaining oxygen saturation on room air.

6. Limitation of the study

1. The sample does not reflect the actual demographic composition of the target population which also restricts the generalizability of the findings.
2. As the study populations included only the north Indian population, the recommendation of the results may not be applicable to the other zones of India and rest of the population group.

7. Conclusion

In conclusion, our study has identified three key risk factors—age, gender, and comorbidities—that are associated with the survival of COVID-19 patients. Understanding these risk factors can provide valuable insights into the underlying mechanisms of COVID-19 and assist clinicians in tailoring management and treatment strategies for patients. Our findings indicate that the majority of COVID-19 deaths occur in elderly men, with typical symptoms including fever, dyspnea, dry cough, and fatigue. Chronic underlying conditions such as hypertension, cardiovascular disease, and diabetes, along with associated laboratory abnormalities (low platelet count, increased CRP, ferritin, IL-6, and LDH), and complications such as ARDS and shock, are all significant risk factors for death in COVID-19 patients. It is crucial to closely monitor these risk factors and promptly identify critically ill patients. Personalized treatment approaches are essential to improving treatment efficacy and reducing the risk of COVID-19-related mortality.

8. Source of Funding

None.

9. Conflict of Interest

None.

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