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Outcome Prediction and Severity of Corona Virus Disease (COVID-19) on the Basis of Clinical and Laboratory Parameters

ABSTRACT

Background: Laboratory parameters play a key role in triaging, predicting disease course, severity and may determine prognosis COVID-19 patients.

Material and methods: Aim and Objectives: To study the relation of clinical and laboratory parameters (total WBC count, neutrophil: lymphocyte ratio, serum ferritin, serum D-dimer, serum LDH, CRP, ESR) with severity and outcome of Corona Virus Disease (COVID-19) confirmed by real-time RT-PCR. Sample size: It was a time-bound study conducted over 3 months (1st April to 30th June, 2020). A total of 206 patients were included in this study satisfying the inclusion criteria. Study design: This was a prospective, observational and non-interventional study conducted on patients with laboratory-confirmed COVID-19 admitted in a tertiary care teaching hospital. Statistical Analysis: Data was analyzed for mean, percentage, standard deviation, and chi-square test for quantitative data by using ap-

propriate statistical tests using INSTAT software version 8.0 (trial version) and p-value < 0.05 was considered statistically significant.

Results: Total of 206 patients of both genders were included in the present study. Total 141 (68.44%) patients were males and 65 (31.55%) patients were females (Chi Sq. 56.07; DF:1; p < 0.001). Among all the groups according to the severity of illness, 'D' group was the most common group (n = 99; 45.06%). Age > 60 years (17.48%), obesity (13.11%), hypertension (10.19%), COPD (5.83%), and diabetes mellitus (5.83%) were the most frequent risk factors or comorbidities associated with COVID-19 disease. Many patients had multiple risk factors in the present study. The majority (3/4th) of the patients were in C and D group (moderate) with co-morbidities and about 1/4th were in the severe group. Total 5 (2.43%) patients with COVID-19 patients succumbed to death with an overall case fatality rate of 2.43%. The case fatality rate was significantly higher among the patients with risk factors or comorbidities (p = 0.0124). Late presentation, associated comorbidity, advancing age, High level of ferritin, D-dimer, CRP, PaO₂/FiO₂ ratio less than 100 at the time of admission were associated with mortality. The terminal event in patients who have succumbed was bradycardia followed by cardiorespiratory arrest. The cause of death was ARDS with bilateral extensive pneumonia.

Conclusions: Late presentation, associated comorbidity like diabetes mellitus, advancing age, High level of

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ferritin, D-dimer, CRP, PaO₂/FiO₂ ratio less than 100 at the time of admission were associated with mortality. The terminal event in patients who have succumbed was bradycardia followed by cardiorespiratory arrest. The cause of death was ARDS with bilateral extensive pneumonia. (Clin Diabetol 2022, 11; 2: 107–118)

Keywords: laboratory parameters, COVID-19, diabetes mellitus, ARDS, bilateral extensive pneumonia

Introduction

Preexisting diabetes appears to be more vulnerable to developing severe COVID-19 virus. When people with diabetes develop a viral infection, it can be harder to treat due to variations in blood glucose and the existence of diabetes mellitus related complications. As the number of COVID-19 patients is dramatically increasing worldwide and treatment in intensive care units (ICU) has become a major challenge, early recognition of severe forms of COVID-19 is absolutely essential for timely triaging of patients. In December 2019, a cluster of patients with pneumonia of unknown cause was linked to a seafood wholesale market in Wuhan, China. A previously unknown betacoronavirus was discovered through the use of unbiased sequencing in samples from patients with pneumonia. Human airway epithelial cells were used to isolate a novel coronavirus, named 2019-nCoV, which formed a clade within the subgenus sarbecovirus, Orthocoronavirinae subfamily. Different from both MERS-CoV and SARS-CoV, 2019-nCoV is the seventh member of the family of coronaviruses that infect humans [1].

Material and methods

Aim and objectives

To study the relation of clinical and laboratory parameters [total WBC count, neutrophil: lymphocyte ratio, serum ferritin, serum D-dimer, serum LDH, CRP, ESR] with severity and outcome of Corona Virus Disease (COVID-19) confirmed by real-time RT-PCR.

Study design and setting

This was a prospective, observational and non-interventional study conducted on patients with laboratory-confirmed COVID-19 admitted in a tertiary care teaching hospital. The study was approved by the Institutional Ethical Committee (Ethical Committee (ICE) Protocol No. 375/2019-2020). The study was conducted over a period of three months, from 1st April to 30th June, 2020. The presence of 2019-nCoV in respiratory specimens was detected by next-generation sequencing or real-time RT-PCR methods [2]. Throat swab samples were collected for extracting 2019-nCoV RNA from

patients suspected of having 2019-nCoV infection and were placed into a collection tube containing a virus transport medium (VTM) for extraction of total RNA. This process was tried to be completed in the minimum possible time. The optimum amount of cell lysates were transferred into a collection tube and were later centrifugated. The suspension was used for RT-PCR assay of 2019-nCoV RNA. This diagnostic criterion was based on the recommendation by the National Institute of Virology. Various other laboratory methods that used were chemiluminescent immunoassay for serum ferritin, electro-chemiluminescent immunoassay for procalcitonin, and immunoturbidimetry for D-dimer.

Sample size

It was a time-bound study conducted over 3 months (1st April to 30th June, 2020). A total of 206 patients were included in this study satisfying the inclusion criteria. The appropriate written and informed consent was obtained from the participants of the study.

Inclusion criteria

All the patients with COVID-19 positive test by RT-PCR were included in the present study. All enrolled patients were undergone total WBC count, neutrophil: lymphocyte ratio, serum ferritin, serum D-dimer, serum LDH, CRP, ESR.

Exclusion criteria

Asymptomatic COVID-19 positive patients and mild symptoms without comorbidities were excluded from the study.

All the COVID-19 positive patients were grouped into various groups according to clinical and laboratory parameters.

- A. Mild (early infection) — Groups A: asymptomatic positive for COVID-19
- B. Groups B: symptomatic/URTI without comorbidity 3 out of 4 (fever, dry cough, shortness of breath, myalgia)
- C. Groups C: symptomatic/URTI with comorbidity (obesity, > 60 years, DM, HTN/IHD, COPD, immunocompromised state, immunosuppressive drugs, CKD, etc.)
Group 'A', 'B' and 'C' were excluded from the study
- A. Moderate (pulmonary involvement without hypoxia) — Group D: pneumonia (LRTI) without respiratory failure (PaO₂/FiO₂ > 300)
- B. Moderate (pulmonary involvement with hypoxia) — Group E: pneumonia (LRTI) with respiratory failure (PaO₂/FiO₂ < 300) and features of ARDS
- C. Severe (systemic hyper-inflammation with cytokine storm) — Group F: pneumonia (LRTI) with

Table 1. Mean and SD of the Numerical Variable of the Study Population

Variables	Mean	± SD	Variables	Mean	± SD
Age	36.69	17.84	Serum Creatinine	0.97	0.85
Symptom of onset	3.36	1.72	Ferritin	285.78	188.25
Hemoglobin	13.19	2.20	D-dimer	0.61	0.70
ESR	34.13	25.33	Procalcitonin	2.05	9.73
Total leucocytes count (TLC)	7545.91	3270.17	C-reactive protein	0.55	0.56
Neutrophil (N)	65.81	11.80	LDH	476.31	227.71
Lymphocyte count (L)	30.58	11.27	Triglycerides	108.16	31.68
N/L ratio	2.68	1.65	SpO ₂	94.48	7.00
Platelet count	182.33	4020.78	Pao ₂ /Fio ₂	428.31	91.35

ESR — erythrocyte sedimentation rate; SD — standard deviation

respiratory failure multi-organ dysfunction syndrome (MOD)

All patients were tested for CBC, LFT, RFT, RBS, Chest radiogram, ECG, ABG, ESR, CRP, S. Ferritin, D-dimer, LDH, S. Triglycerides, Troponin I, CPK-MB, Blood culture, procalcitonin, Neutrophil Lymphocyte ratio > 3.5, P:F ratio less than 300. Six-minute exercise-induced deoxygenation, Resting tachycardia, raised CRP/S. ferritin, D-dimer, LDH were considered as red flag signs. A real-time reverse transcription PCR (RT-PCR) assay was used to detect viral RNA by targeting a consensus RdRp region of pan β -CoV.

Statistical analysis

Data were analyzed for mean, percentage, standard deviation, and chi-square test for quantitative data by using appropriate statistical tests using INSTAT software version 8.0 (trial version) and p-value < 0.05 was considered statistically significant.

Results

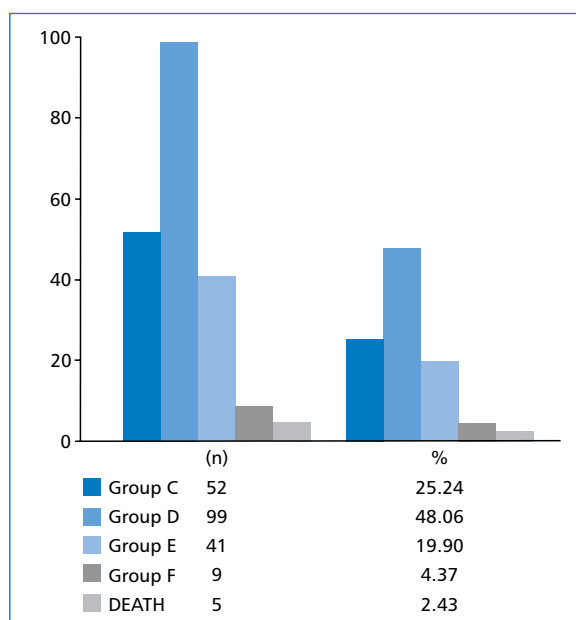
A total of 206 patients of both genders was included in the present study. Total 141 (68.44%) patients were males and 65 (31.55%) patients were females (Chi Sq. 56.07; DF:1; p < 0.001). The male population was outnumbered compared to the female population. The mean and SD of variables of the study population are shown in Table 1.

All the patients were grouped according to the severity of illness in to 'C, D, E, and F'. Among all the groups according to the severity of illness, 'D' group was the most common group (n = 99; 45.06%) (Tab. 2 and Fig. 1). Total 5 (2.43%) patients with COVID-19 succumbed to death with an overall case fatality rate of 2.43%.

The group 'C' is symptomatic COVID-19 with comorbidities, 'D' symptomatic COVID-19 with pneumonia without respiratory failure, 'E' symptomatic

Table 2. Distribution of Study Population with COVID-19 According to the Severity of Illness

Group	Male (n = 141) (68.44%)	%	Female (n = 65) (31.55%)	%	P value
C	31	59.62	21	40.38	< 0.05
D	69	69.70	30	30.30	< 0.034
E	29	70.73	12	29.27	< 0.031
F	12	85.71	2	14.28	< 0.01

**Figure 1. Distribution of Patients with COVID-19 According to the Severity of Illness (Groups)**

COVID-19 with pneumonia with respiratory failure, 'E' symptomatic COVID-19 with pneumonia with ARDS Group E and F (n = 55) were managed in an intensive care unit (Isolated COVID ICU) with Acute

Table 3. Relation of Laboratory Parameters with Various Groups of COVID-19

Variables	r	Variables	r
Age	0.52	Symptoms	0.82
ESR	0.15	LDH	0.30
TLC	0.08	TRG	0.40
N/L	-0.16	Procal	0.37
Ferritin	0.25	CXR	0.78
D-dimer	0.19	P/F ratio	-0.91
CRP	0.22	O2	0.77

CRP — C-reactive protein; CXR ESR — erythrocyte sedimentation rate; L — lymphocyte; LDH — lactate dehydrogenase; N — neutrophil; O2 — oxygen; TLC — total leucocytes count; TRG — triglycerides

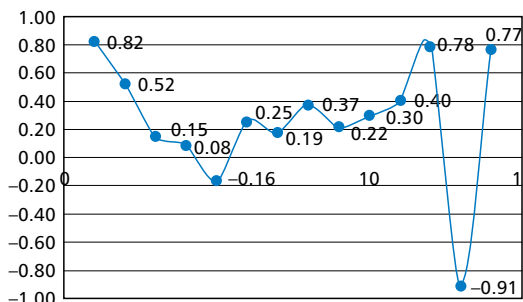


Table 4. Risk Factors and Comorbidities Associated with COVID-19

Risk factors	n	%
Age > 60 years	36	17.48
Obesity	27	13.11
Hypertension	21	10.19
Diabetes mellitus	12	5.83
COPD/asthma	12	5.83
IHD	11	5.34
Immunocompromised	4	1.94
ILD	2	0.97
CKD	6	2.91

CKD — chronic kidney disease; COPD — chronic obstructive pulmonary disease; IHD — ischaemic heart disease; ILD — interstitial lung disease

respiratory distress syndrome (ARDS), multi-organ-dysfunction (MOD), hypotension, sepsis, septic shock, etc. of them 7 patients received invasive ventilation with (Prone positioning), 36 patients received HFNO₂ and 12 patients received noninvasive ventilation (NIV) with CARP (COVID awake repositioning/proning) protocol.

Age, ESR, total leucocyte count, serum ferritin, D-dimer C-reactive protein, duration of onset of symptom, LDH, Triglyceride levels, Procalcitonin, involvement of lung by chest radiogram were positively correlated with severity group of COVID-19 disease and negatively correlated with Neutrophil to lymphocyte ratio and PaO₂ to FiO₂ ratio (Tab. 3).

Age > 60 years (17.48%), Obesity (13.11%), hypertension (10.19%) COPD (5.83%) and diabetes mellitus (5.83%) were the most frequent risk factors or comorbidities associated with COVID-19 disease. Many patients had multiple risk factors in the present study (Tab. 4).

The case fatality rate was significantly higher among the patients with risk factors or comorbidities (p = 0.0124)

Table 5. Relation of Case Fatality Rate with Risk Factor

Without risk factors/ /comorbidities	With risk factors/co-morbidities (n = 61)	Total deaths
1 (0.69%)	4 (6.56%)	5 (2.43%)

$\chi^2 = 6.24$ (DF:1) p = 0.0124

Two patients had an episode of ventricular tachycardia followed by ventricular fibrillation and was managed with an antiarrhythmic agent and defibrillation.

The majority (3/4th) of the patients were in C and D group (moderate) with co-morbidities and about 1/4th were in the severe group. The overall case-fatality rate was 2.43% in the present study. Late presentation, associated comorbidity, advancing age, High level of ferritin, D-dimer, CRP, PaO₂/FiO₂ ratio less than 100 at the time of admission were associated with mortality. The terminal event in patients who have succumbed was bradycardia followed by cardiorespiratory arrest. The cause of death was ARDS with bilateral extensive pneumonia. (Fig. 3). All patients received standard care of management as per Clinical management COVID-19 (interim guidance by WHO) in the form of oxygen (HFNO₂), Non-invasive Ventilation or Invasive ventilation antiviral (Remdesivir/ Favipiravir) Heparin/LMWH, Methylprednisolone among the moderate and severe group as per need and indication as per protocol. The use of off-label therapy or repurposed drugs with informed and written consent from patients or relatives as per protocol. The majority (3/4th) of the patients were in C and D group (moderate) with co-morbidities and about 1/4th were in the severe group. The overall case-fatality rate was 2.43% in the present study. Late presentation, associated comorbidity, advancing age, High level of ferritin, D-dimer, CRP, PaO₂/FiO₂ ratio less than 100 at the time of admission were associated with mortality. The terminal event in

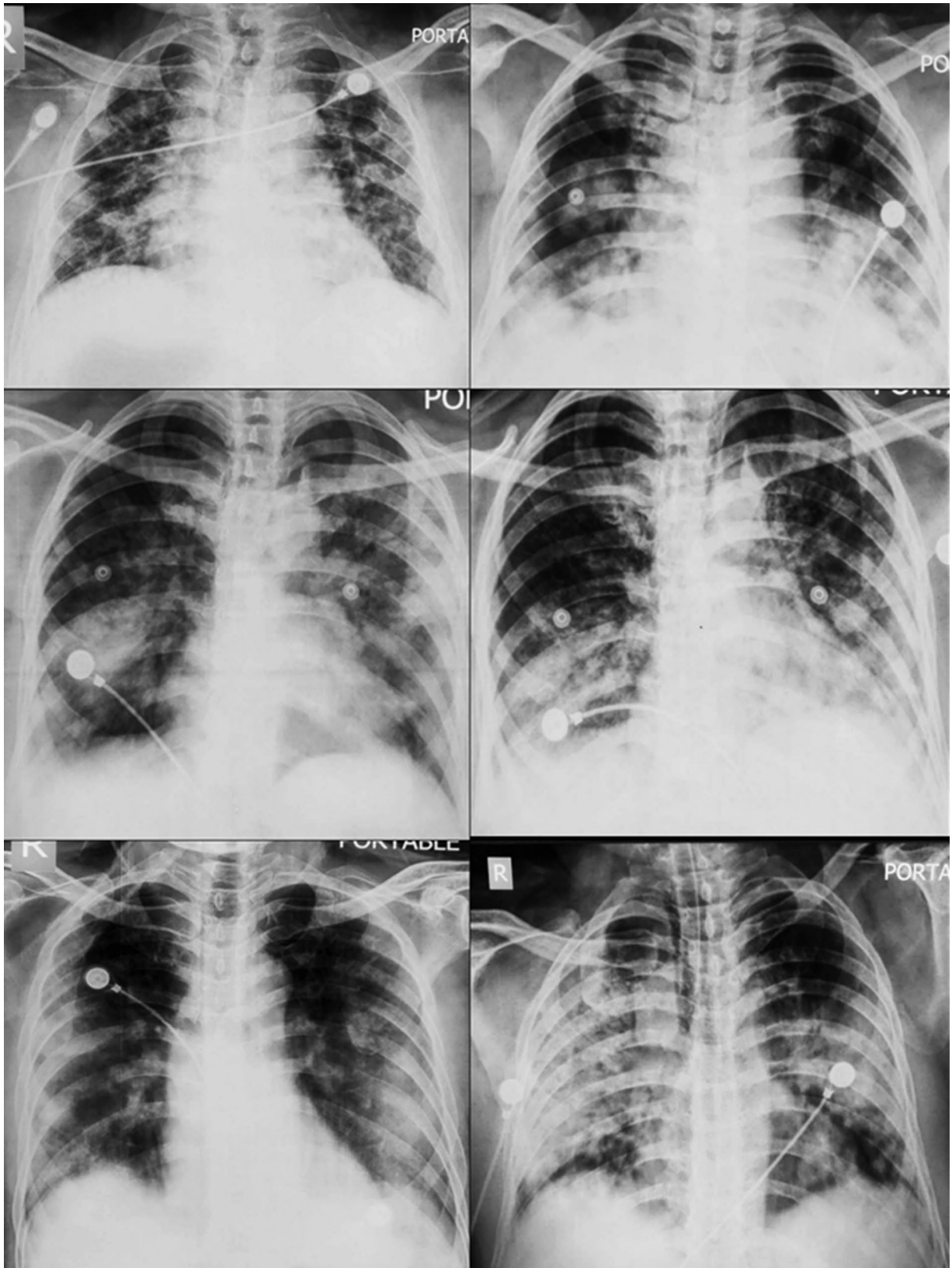


Figure 2. Chest Radiogram of Patients with COVID-19

patients who have succumbed was bradycardia followed by cardiorespiratory arrest. The cause of death was ARDS with bilateral extensive pneumonia. The chest radiogram

and HRCT (ground-glass opacity, with consolidation and sub-pleural location) images showed evidence of bilateral pneumonia.



Figure 3. HRCT Imaging of COVID-19 Patients
HRCT — high resolution computed tomography

Discussion

On March 11, 2020, the World Health Organization declared the worldwide spread of the infectious disease COVID-19, caused by a new strain of coronavirus, SARS-CoV-2, as a pandemic. Like in all other infectious diseases, the host immune system plays a key role in our defense against SARS-CoV-2 infection. However, viruses are able to evade the immune attack and proliferate and, in susceptible individuals, cause severe inflammatory response known as cytokine storm, particularly in the lungs [3]. Coronavirus disease 2019 (COVID-19) causes serious respiratory illnesses such as pneumonia and respiratory failure. The etiological agent of COVID-19 has been confirmed as a novel coronavirus, now known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is most likely originated from zoonotic coronaviruses, SARS-CoV-2 had spread across China and worldwide, reaching a pandemic level. COVID-19 has triggered huge human casualties and grave economic loss posing a global threat. Currently, several repurposing therapeutics for COVID-19 have shown to be clinically effective. In addition, global institutions have begun to develop

vaccines for the prevention of COVID-19 [4]. Since the outbreak of novel coronavirus pneumonia (coronavirus disease 2019 [COVID-19]) in December 2019. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a member of coronaviruses known to cause common colds and severe illnesses, is the cause of COVID-19. The World Health Organization has raised the COVID-19 outbreak risk to “very high”, and SARS-CoV-2 infection has become a serious threat to public health [5].

Demographic profile

Zhe-Feng Zhong et al. (2020) reported 48 cases of COVID-19, of which 1 was mild, 38 were moderate, and 9 were severe. It was unveiled that there were 31 (64.6%) male patients and 17 (35.4%) female patients, with a female-to-male ratio of 1.82:1 [6]. Similarly in present study, total 141 (68.44%) patients were males and 65 (31.55%) patients were females ($p < 0.001$). The male population was outnumbered compared to the female population. Total 1/4th were the mild group and severe group and half were the moderate group. Sudhir Bhandari et al. (2020) in their study observed that the male patients constituted 66.66% of total

patients and the majority of the patients (80.90%) were below 60 years of age [7]. Tao Chen et al. (2020) in their retrospective case series from Wuhan, China reported median age of deceased patients (68 years) was significantly older than recovered patients (51 years). Male sex was more predominant in deceased patients (83; 73%) [8]. In the present study overall case fatality rate was 2.43%. Late presentation, associated comorbidity, advancing age, High level of ferritin, D-dimer, CRP, PaO₂/FiO₂ ratio less than 100 at the time of admission were associated with mortality.

Imaging

Wenbin Hu et al. 2020 On admission, abnormalities in computed tomography (CT) or chest X-ray images were revealed among all patients, and 11 (68.8%) of 16 patients had bilateral involvement [9]. Sheng Yin et al. (2020) CT images of these patients showed bilateral multiple plaques or nodular ground-glass opacities (68.4 %) [10]. Similarly, bilateral involvement in chest radiogram had a longer duration of stay and mortality in the present study. Tie Long Chen et al. (2020) studied a retrospective investigation of hospitalized older patients with confirmed COVID-19 at Wuhan University. In total, 203 patients were diagnosed with COVID-19, with a median age of 54 years. Men accounted for 108 (53.2%) of the cases, and 55 patients (27.1%) were > 65 years of age [11].

Oxygen therapy

In the present study, groups E and F (n = 55) were managed in an intensive care unit (isolated COVID ICU) with acute respiratory distress syndrome (ARDS), multi-organ-dysfunction (MOD), hypotension, sepsis, septic shock, etc. of them 7 patients received invasive ventilation with (prone positioning), 36 patients received HFNO₂ and 12 patients received noninvasive ventilation (NIV) with CARP (COVID awake repositioning/proning) protocol with In overall case fatality rate of 2.43%. Similarly in other studies, 11.1% received high-flow oxygen therapy, 41.7% received noninvasive ventilation, and 47.2% received invasive ventilation (overall mortality: 4.3%) [12–14].

Clinical and biochemical profile

In the present study the age, ESR, total leucocyte count, serum ferritin, D- dimer C-reactive protein, duration of onset of symptom, LDH, Triglyceride levels, Procalcitonin, involvement of lung by chest radiogram were positively correlated with the severity group of COVID-19 disease and negatively correlated with Neutrophil to lymphocyte ratio and PaO₂ to FiO₂ ratio. Age > 60 years (17.48%), Obesity (13.11%), hypertension

(10.19%) COPD (5.83%) and diabetes mellitus (5.83%) were the most frequent risk factors or comorbidities associated with COVID-19 disease. Dawei Wang et al. (2020) reported a fever (98.6%) and dry cough (59.4%). Lymphopenia occurred in 97 patients (70.3%), and elevated lactate dehydrogenase (39.9%). Acute respiratory distress syndrome 61.1%, arrhythmia 44.4%, and shock 30.6% [14]. Jui-Yao Liu et al. (2020) quoted 73% of the cases with COVID-19 had respiratory symptoms and some cases had flu-like symptoms. A proportion of the cases (13%) had the neurological symptoms of loss of smell or taste. Few of the cases (8%) had gastrointestinal symptoms, specifically diarrhea (7.2%). Eleven cases (3.4%) did not have any symptoms [15]. Jiao Gong et al. (2019) reported that among all cases 19.4% of patients developed severe COVID-19. Older age; higher serum lactate dehydrogenase, C-reactive protein, blood urea nitrogen, direct bilirubin; and lower albumin were associated with severe COVID-19 [16]. Wenbin Hu et al. (2020) The average age of the patients was 44.1 (16.5) years, and there were 10 women (62.5%) and 6 men (37.5%). More than half had chronic diseases [9 (56.3%)]. The most common symptoms at onset of COVID-19 infection were fever [12 (75%)] and cough [8 (50%)]; 11 (68.8%) patients had lymphopenia, and 12 (75%) had elevated C-reactive protein [9]. Manoj Saluja et al. (2020) reported, lymphocytosis, raised LDH were common and patients over the age of 60 had a severe illness and more complications [18]. Sheng Yin et al. (2020) reported a significant reduction in lymphocytes (61%). Procalcitonin did not increase and D-dimer increased slightly. Lactate dehydrogenase (LDH) levels have elevated in most patients [10]. Sudhir Bhandari et al. (2020) quoted 52.38% had lymphopenia 19.04% thrombocytopenia and patients in the severe category had raised FDP, D-Dimer procalcitonin levels, serum ferritin levels, and LDH levels, deranged liver functions, and needed oxygen support. Sudhir Bhandari et al. (2020) quoted that the initial COVID-19 patients in the Indian subcontinent revealed lymphopenia. The numbers of peripheral blood leukocytes, lymphocytes, and eosinophils were significantly reduced in the majority of the patients. The levels of C-reactive protein, fibrinogen, blood glucose, lactate dehydrogenase, and D-dimer, (ALT) were remarkably increased in severe patients [7]. Tao Chen et al. (2020) in their study reported that chronic hypertension and other cardiovascular comorbidities were more frequent among deceased patients (48%) and (14%) and Leukocytosis was present in 56 (50%) patients who died, and lymphopenia was present in 91% and 47% respectively. Concentrations of SGOT, SGPT, creatinine, creatine kinase, LDH, cardiac troponin I, N-terminal pro-

brain natriuretic peptide, and D-dimer were markedly higher in deceased patients than in recovered patients [8]. Tie Long Chen et al. (2020) reported common symptoms of older patients with COVID-19 included fever (94.5%), dry cough (69.1%), and chest distress (63.6%). Compared with young patients, older patients had more laboratory abnormalities and comorbidities [11]. Bicheng Zhang et al. (2020) quoted 94.5% had a high neutrophil-to-lymphocyte ratio of > 5 , high systemic immune-inflammation index of > 500 (89.2%), and increased C-reactive protein (100%), lactate dehydrogenase (93.2%), and D-dimer (97.1%) levels. A high level of IL-6 (> 10 pg/mL) was observed in all detected patients [12]. Dawei Wang et al. (2020) quoted the tri-phasic pattern of the clinical course of COVID-19. Week 1 after illness onset was characterized by fever, cough, dyspnea, lymphopenia, and radiological multilobar pulmonary infiltrates. In severe cases showed persistent lymphopenia, severe acute respiratory distress syndrome, refractory shock, anuric acute kidney injury, coagulopathy, thrombocytopenia, and death. Older age and male sex were independent risk factors for the poor outcome of the illness. A period of 7–13 days after illness onset is the critical stage in the COVID-19 course [14]. Nanshan Chen et al. (2020) quoted mean age of the patients was 55.5 years, including 67 men and 32 women, with 51% of patients having chronic diseases. According to imaging examination, 75% of patients showed bilateral pneumonia, 14% showed multiple mottling and ground-glass opacity, 17% developed acute respiratory distress syndrome [17]. Chaolin Huang et al. (2020) quoted predominance of men (73%) with less than half had underlying diseases (32%), including diabetes (20%), hypertension (15%), and cardiovascular disease (15%). Common symptoms at the onset of illness were fever (98%) cough (31%), and myalgia or fatigue (44%). Dyspnoea developed in 55%, 63% of patients had lymphopenia. Complications included acute respiratory distress syndrome (29%), 12% acute cardiac injury, 32% of patients were admitted to an ICU [19]. Risk factors: Age > 60 years (17.48%), Obesity (13.11%), hypertension (10.19%) COPD (5.83%), and diabetes mellitus (5.83%) were the most frequent risk factors or comorbidities associated with COVID-19 disease in the present study. Many patients had multiple risk factors in the present study. The majority (3/4th) of the patients were in C and D group (moderate) with co-morbidities and about 1/4th were in the severe group. Male gender, late presentation, associated comorbidity, advancing age, High level of ferritin, D-dimer, CRP, PaO₂/FiO₂ ratio less than 100 at the time of admission were associated with mortality. Manoj Saluja et al. (2020) Poor prognosis

was noted in the elderly, especially those with comorbidities. Though the disease has a relatively mild course in this part of the subcontinent, patients aged ≥ 60 are at significant risk for morbidity and mortality [18]. Bicheng Zhang et al. (2020) More than half of the patients who died were older than 60 years (80.5%). The bulk of the patients who died had comorbidities (76.8%), including hypertension (56.1%), heart disease (20.7%), diabetes (18.3%), cerebrovascular disease (12.2%), and cancer (7.3%) [12]. Sudhir Bhandari et al. (2020) Three patients (14.28%) had underlying comorbidity in the form of hypertension, diabetes mellitus, hypothyroidism, chronic kidney disease or coronary artery disease [7]. Sudhir Bhandari et al. (2020) Patients with older age and associated comorbid conditions (COPD and diabetes) seem to have a greater risk for lung injury thereby requiring oxygen support during the course of disease [7]. Outcome complications and Mortality: The overall case fatality rate was 2.43% in the present study. Late presentation, associated comorbidity, advancing age, High level of ferritin, D-dimer, CRP, PaO₂/FiO₂ ratio less than 100 at the time of admission were associated with mortality. Similarly, Nanshan Chen et al. quoted 11% of patients worsened in a short period of time and died of multiple organ failure. The terminal event in patients who have succumbed was bradycardia followed by cardiorespiratory arrest. The cause of death was ARDS with bilateral extensive pneumonia in the present study [17]. Tie Long Chen et al. (2020) quoted that, older patients, males, comorbidities, time from disease onset to hospitalization, abnormal kidney function, and elevated procalcitonin levels were all significantly associated with death. Among patients who were 65 years and older, the mortality rate was 34.5%, which was significantly higher than that of younger patients at 4.7% [11]. Common complications observed more frequently in deceased patients included acute respiratory distress syndrome, sepsis, acute cardiac injury, heart failure, alkalosis, hyperkalemia, acute kidney injury, and hypoxic encephalopathy. Patients with cardiovascular comorbidity were more likely to develop cardiac complications. Regardless of the history of cardiovascular disease, acute cardiac injury and heart failure were more common in deceased patients [8]. Bicheng Zhang et al. (2020) reported that respiratory failure remained the leading cause of death (69.5%), followed by sepsis/MOF (28.0%), cardiac failure (14.6%), hemorrhage (6.1%), and renal failure (3.7%). The lymphopenia (89.2%), neutrophilia (74.3%), and thrombocytopenia (24.3%) were usually observed [12]. Chaolin Huang et al. (2020) quoted a mortality of 15% [19]. Bicheng Zhang et al. (2020) Older males with comorbidities are

Table 6. Comparison of Various Studies with the Present Study

Study author	Study design	Symptomatology, risk factors, and markers	Outcome
Wenbin Hu (2020) [9]	Retrospective, single-center, study (Shaoxing University)	Mean age: 44.1 (16.5) years Women were 62.5% and men 37.5%. Fever 75% and cough (50%) (68.8%) patients had lymphopenia, and 75% had elevated C-reactive protein	11 (68.8%) of 16 patients had bilateral involvement with no mortality.
Tao Chen 2020 [8]	Wuhan, China of (n=799) patients. [113 who died and 161 who recovered with a diagnosis of covid-19 were studied]	Male sex was more predominant (73%) hypertension and CAD were more frequent among deceased patients (48%). Leukocytosis was present in 50% of patients who died, and lymphopenia was present in 91%. SGPT, SGOT, creatinine, creatine kinase, LDH, troponin I, and D-dimer were markedly higher in deceased patients	Common complications in deceased patients included acute respiratory distress syndrome (100%), type I respiratory failure (51%), sepsis (100%), acute cardiac injury (77%), heart failure (49%), alkalosis (40%), hyperkalemia (37%), acute kidney injury (25%), and hypoxic encephalopathy (20%)
Pingzheng Mo et al. 2020 [21]	Retrospective single-center study, (n= 155)	Risk factors: old age were 45.2%, male sex, comorbidities	High levels of neutrophil, AST, LDH and C-reactive protein, lower levels of platelets and albumin, and higher incidence of bilateral pneumonia associated with poor outcome
Zhe-Feng Zhong 2020 [6]	(n=48) Cross sectional, observational	Lymphocytes, and eosinophils were significantly reduced. The levels of CRP, fibrinogen, blood glucose, LDH, D-dimer, SGOT, SGPT, and creatinine kinase (CK) were increased in severe patients	The patients with COVID-19 often have multiple organ dysfunction or damage
Dawei Wang et al. (2020) [14]	Retrospective case series of 107 discharged	A period of 7–13 days after illness onset is the critical stage in the COVID-19 course. Older age and male sex were independent risk factors for poor outcomes.	Severe cases showed persistent lymphopenia, severe ARDS, refractory shock, anuric AKI, coagulopathy, thrombocytopenia, and death.
Sheng Yin (2020) [10]	Retrospective (n=33) COVID-19 patients (16 male, 17 female) median age was 46 years	most common symptoms were fever (70%) and cough (39%) WBC counts are normal, while they manifest as significant reduction in lymphocytes (61%). The levels of c-reactive protein and ESR suggest a typical viral infection. D-dimer increased slightly	Reduced whole blood lymph count can be used as an adjuvant diagnosis of early SARS-CoV-2 infection. (LDH) levels have elevated in most patients. CT images of these patients showed bilateral multiple plaques or nodular ground-glass opacities (68.4%)
Manoj Saluja 2020 [18]	Cross-sectional, observational study	Thrombocytopenia, lymphocytosis, raised LDH was common (> 35%, p < 0.05). Patients over the age of 60 were the ones having severe illness and more complications (p < 0.05)	Radiographic abnormality was frequently associated irrespective of clinical presentation and its severity. Poor prognosis was noted in the elderly, especially those with comorbidities
Jiao Gong et al. (2019) [15]	Retrospective multicenter study, (n = 372) COVID19.	Older age; higher LDH, CRP, blood urea nitrogen, and direct bilirubin; and lower albumin were associated with severe COVID-19.	Among all cases 19.4% patients developed severe COVID-19

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Table 6 (cont.). Comparison of Various Studies with the Present Study

Study author	Study design	Symptomatology, risk factors, and markers	Outcome
Bicheng Zhang et al. (2020) [12]	(n = 82) death patients	80.5% who died were > 60 years. The patients who died had comorbidities (76.8%), hypertension (56.1%), CAD (20.7%), diabetes (18.3%), CVA (12.2%), and cancer (7.3%). The lymphopenia (89.2%), and thrombocytopenia (24.3%).	High neutrophil-to-lymphocyte ratio of > 5 (94.5%) and increased CRP (100%), LDH (93.2%), and D-dimer (97.1%) levels. Respiratory failure remained the leading cause of death (69.5%), followed by sepsis/MOF (28.0%)
Tie Long Chen et al. (2020) [11]	Retrospective (n = 203)	Men accounted for 108 (53.2%) Among patients who were 65 years and older, the mortality rate was 34.5%, which was significantly higher than that of younger patients at 4.7% (7/148)	The patients aged 65 and older had greater initial comorbidities, more severe symptoms, and were more likely to experience multi-organ involvement and death, as compared with younger patients
Fei Zhou et al. (2020) [20]	Retrospective, multicentre cohort study (n = 191)	91 (48%) patients had a comorbidity, with hypertension being the most common (58 [30%] patients), followed by diabetes (36 [19%] patients) and CAD (15 [8%] patients)	The potential risk factors of older age, high SOFA score, and d-dimer greater than 1 µg/mL could help clinicians to identify patients with poor prognoses at an early stage. The case fatality rate was 28.27%
Dawei Wang et al. (2020) [13]	Retrospective, single-center case series (n = 138)	Fever (98.6%), and dry cough (59.4%). Lymphopenia occurred in 97 patients (70.3%), and elevated LDH 55 patients (39.9%). Chest computed tomographic scans showed bilateral patchy shadows or ground-glass opacity in the lungs.	Patients treated in the ICU were more likely to have underlying comorbidities. Of the 26.1% cases in the ICU, 11.1% received high-flow oxygen therapy, 41.7% received noninvasive ventilation, and 47.2% received invasive ventilation. Overall mortality 4.3% Interim analysis
Mahajan NN et al. (2020) [22] Mumbai, India	Retrospective (n = 3711) HCWs	Quoted 11% prevalence of SARS-CoV-2 comorbidities were reported in 19% of HCWs with COVID-19	Hypertension and diabetes mellitus were the most common co-morbidities reported
Present study	Prospective and observational study (n = 206)	Total 141 (68.44%) patients were males and 65 (31.55%) patients were females (p < 0.001). Among all the groups according to the severity of illness 'D' group was the most common group (n = 99; 45.06%). Age > 60 years (17.48%), Obesity (13.11%), hypertension (10.19%) COPD (5.83%) and diabetes mellitus (5.83%) were the most frequent risk factors associated with COVID-19 disease. Many patients had multiple risk factors in the present study. The overall case fatality rate of 2.43%	Late presentation, associated comorbidity like diabetes mellitus, advancing age, high level of ferritin, D-dimer, CRP, PaO ₂ /FiO ₂ ratio less than 100 at the time of admission were associated with mortality

AKI — acute kidney injury; ARDS — acute respiratory distress syndrome; AST — aspartate aminotransferase; CAD — coronary artery disease; CK — creatinine kinase; COPD — chronic obstructive pulmonary disease; CRP — C-reactive protein; ESR — erythrocyte sedimentation rate; ICU — intensive care unit; HCWLDH — lactate dehydrogenase; SGOT — serum glutamic-oxaloacetic transaminase; SGPT — serum glutamic-pyruvic transaminase; WBC — white blood cell

more likely to develop severe disease and even die from SARS-CoV-2 infection. Respiratory failure, cytokine release syndrome-mediated damage to other organs, including cardiac, renal, hepatic, and hemorrhagic damage is the main cause of COVID-19 [12]. Dawei Wang et al. (2020) advancing age and male gender were independent risk factors for death of COVID-19 [13]. Fei Zhou et al. (2020) observed 48% of patients had a comorbidity, with hypertension being the most common (30%), followed by diabetes (19%) and coronary heart disease (8%). The potential risk factors of older age, high SOFA score, and D-dimer greater than 1 $\mu\text{g}/\text{mL}$ could help clinicians to identify patients with poor prognosis at an early stage [20]. Pingzheng Mo et al. (2020) in their single-center study, quoted that the Old age, male gender, comorbidities, higher incidence of breath shortness and anorexia, severer disease assessment on admission, high levels of neutrophil, aspartate aminotransferase (AST), lactate dehydrogenase (LDH) and C-reactive protein, lower levels of platelets and albumin, and higher incidence of bilateral pneumonia associated with poor outcome [21].²¹ Mahajan NN et al. (2020) quoted 11% prevalence of SARS-CoV-2 and comorbidities were reported in 19% of HCWs with COVID-19. Hypertension and Diabetes Mellitus were the most common co-morbidities reported [22]. The comparison of various studies is shown in Table 6.

Conclusions

All enrolled moderate to severe COVID had pneumonia and therefore were aggressively managed with a multidisciplinary and personalized therapeutic approach that included nutritional support, antiviral pharmacotherapy, active control of comorbidities, and prevention of complications, as and when required steroids and low molecular weight heparin (LMWH) and psychological intervention. Late presentation, associated comorbidity like diabetes mellitus, advancing age, High level of ferritin, D-dimer, CRP, $\text{PaO}_2/\text{FiO}_2$ ratio less than 100 at the time of admission were associated with mortality with COVID-19. Our experience highlights the importance of the use of a multidisciplinary therapeutic approach that tailors to the specific condition of the patient in achieving a favorable clinical outcome. Proper triaging of patients, identifying risk factors and comorbidities and their control is important for COVID-19. Adequate and timely treatment of hypoxia by HFNO₂, non-invasive ventilation (NIV) and timely intubation were the most important factors observed in the present study for a better outcome of COVID-19. Judicious use of repurposed drugs (Remdesivir, Favipiravir LMWH, Steroids and Tocilizumab) plays as a compassionate

role in the management of COVID-19. There should be a global effort and strategy, to reduce the risk for people with diabetes during the COVID-19 pandemic.

Conflict of interest

None declared.

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