How to Cite:
Parashar, B., Pathak, M., & Ahmad, A. (2021). Laboratory analysis of patients with SARS-CoV-2 Infection in a semi-urban COVID-19 center of Lucknow, India. *International Journal of Health Sciences*, *5*(S2), 431–443. https://doi.org/10.53730/ijhs.v5nS2.5865

Laboratory analysis of patients with SARS-CoV-2 Infection in a semi-urban COVID-19 center of Lucknow, India

Bharti Parashar
Assistant Professor, Department of Pathology, Career Institute of Medical Sciences and Hospital, Lucknow-226020, Uttar Pradesh, India

Meeta Pathak
Professor, Department of Pathology, Career Institute of Medical Sciences and Hospital, Lucknow-226020, Uttar Pradesh, India

Absar Ahmad
Assistant Professor, Department of Community Medicine, Manipal Tata Medical College, Manipal Academy of Higher Education, Jamshedpur-831017, India

***Abstract*---**Timely analysis of the laboratory characteristics associated with 2019 novel coronavirus infection (COVID-19) can assist with clinical diagnosis and prognosis. This study is a collection of clinical data from 100 hospitalized patients diagnosed with COVID-19 in a dedicated COVID- 19 health center located in a semi-urban area from July to September, 2020. The average age of the patients was 50 years. The proportion of patients with comorbidities was 59%. Lymphocyte counts were reduced in the routine blood-work for all patients, but significantly lower in L2-type patients. Elevation of D-Dimer with near normal PT and APTT were detected in coagulation function tests, and more significant changes were observed in L2-type patients compared to L1-type patients. Serum ferritin levels were sensitive to SARS-CoV (severe acute respiratory syndrome coronavirus-2) infection and found to rise in L2-type patients more than L1-type patients. Inflammatory markers, CRP and Interleukin-6 (IL-6) were significantly increased in all patients, but higher in L2-type patients compared to L1-type patients. Coming to organ damage, kidney injury was the most common organ affected by COVID-19 followed by heart and liver. Kidney and heart injury were more severe in L2-type patients in contrast to L1-type patients. 99% of the patients recovered from the SARS-CoV-2 infection. Only one patient died from the L2 category.

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2021.
***Corresponding author**: Parashar, B.; Email: bharti.parashar@gmail.com*
Manuscript submitted: 18 Sept 2021, Manuscript revised: 9 Nov 2021, Accepted for publication: 12 Dec 2021

***Keywords*---**SARS-CoV-2, COVID-19, biochemical biomarker, hematological biomarker, immunological biomarker.

Introduction

SARS-COV-2 is highly pathogenic and transmissible among other corona viruses that emerged as a novel pneumonia and surfaced in Wuhan, Hubei Province, China, in December, 2019 [1]. On March 11, 2020, the World Health Organization (WHO) declared this epidemic outbreak into a pandemic situation [2]. Since its first report of a novel pneumonia outbreak in 2019, it spread throughout the world at a very fast pace due to its high transmissibility, resulting in widespread morbidity and mortality [3]. SARS-CoV-2 causes an acute respiratory syndrome called coronavirus disease (COVID-19) [4]. The clinical manifestations of SARS-CoV-2 infection differ from asymptomatic to mild-flu like (symptomatic), acute respiratory distress (ARD) and septic shock to the demise of individuals in more serious cases. Extended complications including pulmonary, cardiological and neurological have been detected in the cases of COVID-19 patients. The reproductive number of SARS-CoV-2 ranged from 2.2 to 3 which is significantly greater than Spanish flu [5]. SARS-CoV-2 infection can spread easily because it also spreads during the pauci-symptomatic or pre-symptomatic condition. The fundamental basis of management of SARS-CoV-2 infection is early detection of the virus in the respiratory specimens like nasopharyngeal swabs from the patients that manifest the clinical features like dry cough, fever and shortness of breath. The standard method for the detection of the SARS- CoV-2 infection is real time-polymerase chain reactions (RT-PCR) of throat and nasal secretions. Still, there is a need to explore the diagnosis, prognosis and therapeutic indicators for the early detection of the SARS-CoV-2 infection. A large number of epidemiological studies are available on clinical diagnosis and prognosis [6,7]. In India, the first case was observed in a female candidate of Kerala province on January 27, 2020 [8]. Only few studies are available on the clinical diagnosis and prognosis in Indian populations. Hence, the goal of this study is to analyze the biochemical, hematological and immunological biomarkers in various stages of SARS-CoV-2 patients, to help predicting the prognosis and guiding the management of patients.

Materials and Methods

Study population and patients

The current retrospective study was carried out at Altis Hospital, Mutakkipur, Lucknow which was a dedicated COVID-19 care center from July to September, 2020. A total of 100 patients (4 children and 96 adults) were diagnosed with COVID-19 infection. The standard procedure for diagnosis, clinical classification, and treatment of COVID-19 was done by following the guidelines approved by ICMR [9]. All patients were positive for SARS-CoV-2 infection as analyzed by RT-PCR by using nasal and throat samples. All tests were done at NABL accredited ICMR approved laboratories. Most of the patients were admitted with fever and respiratory symptoms, some of the patients were diagnosed with pneumonia after chest X-ray. The symptoms were categorized as: 1) Asymptomatic: when SP_{O2}

>94% in room air and respiratory rate (RR) <24 min with chest clear on imaging 2) Moderate (L1): when SP_{O2} being 90-94% in room air, RR=24-30/min with pneumonia (+) and 3) Severe form of infection (L2): when SP_{O2}<90% in room air, RR >30/min with pneumonia (++) [10]. Recovery was also defined as per ICMR guidelines including the disappearance of clinical symptoms, one consecutive negative nucleic acid tests for SARS-CoV-2 and absence of viral pneumonia [9].

Data collection

The clinical data of the patient were extracted through a medical record system available at the hospital including general personal information, previous medical history and laboratory testing. Routine blood investigations including coagulation function, serum biochemistry, and measurement of inflammatory markers were performed within 24 hours of admission followed on day 3rd and day 5th. Patients who continued their treatment post day 5 were investigated for further analysis. But, we limited our study up to investigations done in five first days of admission. Pulse oxygen saturation data were collected immediately upon admission.

Statistical analysis

The results were analyzed by using a SPSS Statistics software version 25.0. The data with a normal distribution were expressed as mean ± standard deviation (SD) and assessed by T test. The data were expressed as a percentage and compared by Chi-square test. Wilcoxon signed-rank test is used which is the nonparametric test equivalent to paired T test to understand whether there were any differences in inflammatory markers in COVID19 patients on day1 and day5. A value of $P<0.05$ was considered as statistically significant.

Results

A total of 100 patients were included in this study, categorized into three groups; i) Asymptomatic: 19 patients, ii) L1: 68 patients and iii) L2: 13 patients. The mean age of the enrolled patients was 50 year ranged from 7-85 years. The mean age in asymptomatic, L1 and L2 categories were 36.6(±17.2), 51.6(±13.4) and 62.3(±14.4) years respectively. The age groups were statistically associated with the category of the patients (p=0.001). There were 72 males and 28 females. Among males, 39 males had co morbidities while among females, 20 females had co morbidities. A total of 84 patients had co-morbidities, including hypertension (38), diabetes (42) and coronary artery heart disease (4). The patient classification was associated with diabetes (p=0.003), hypertension (p=0.028) and cardiovascular disease (0.014). The average number of co-morbidities varies among the three groups and were 0.42(±0.77), 0.79(±0.87), and 1.69(±0.48), further significantly associated (p=0.01) in contrast to asymptomatic COVID-19 patients. Oxygen support (p<0.001), fever (p<0.001), chest X-ray (p<0.001) at the time of admission were associated with classification of COVID-19 patients (Table-1). At follow-up, 99 of 100 patients completely recovered and one patient died from L2 category.

(Table-2) Analysis showed a statistically significant change in the N/L (Neutrophil/Lymphocyte) ratio in individuals with asymptomatic COVID ($Z = -2.254$, $p = 0.024$) from day1 to day 5. The median N/L ratio among asymptomatic

COVID patients was 1.96 and 2.16 on day1 and 5. However, for L1 and L2 patients, the N/L ratio was not significantly changed from day1 to day5. Absolute Eosinophil count (AEC) show significant changes (Z=-2.039, p=0.041) among L1 patients from day1 to day5 but insignificant among asymptomatic and L2 COVID patients. Median AEC among 69 to 98 among L1 patients from day1 to day5. However, median ESR values among asymptomatic were 36 to 30, among L1, 38 to 35, and L2 from 45 to 40, respectively. Erythrocyte sedimentation rate (ESR) was found significant changes among all three categories asymptomatic (Z=-2.20, p=0.028), L1(Z=-2.25, p=0.024), and L2(Z=-2.40, p=0.016) from day1 to day 5. Prothrombin time test or PT test were not found significant among all categories of COVID patients from day 1 to day 5. The median value of D-Dimer (reference value <500 ng/ml) was 718.75 to 567.25 for the L1 category of COVID patients, and the changes were also statistically significant (Z=-2.977, p=0.003).

Tables 3 presents the biochemical parameters of COVID19 patients of all the categories. Among biochemical parameters, SGOT and SGPT were not statistically significant for all COVID patients for day1 to day 5. However, ALP (reference range 108-306 IU/L) was statistically significant for asymptomatic (Z=-3.823, p=0.000) as well as for L1(Z=-2.226, p=0.026) category patients for day1 to day5. The median values for asymptomatic were from day1 to day five were 218 to 168. Whereas for the L1 patient, it was 146.5 to 148.5. The normal range for urea nitrogen in blood or serum is 10-40 mg/dl. The changes from day1 to day5 of Urea were significant among asymptomatic (Z=-2.276, p=0.023) COVID patients. The median value of Urea for day1 to day 5 was 26.13 to 28.6. The normal range of Creatinine in the blood is around 0.4-1.5 mg/dl. Analysis showed that changes in Creatinine were significant only for L2(Z=-2.671, p=0.008) category patients. The median value of L2 COVID patients from day1 to Day5 were 1.4 to 1.05.

The immunological biomarkers are represented in Table-4. Among asymptomatic (Z=-3.200, p=0.001) and L1(Z=-3.962, p=0.000) patients, changes in CRP tests were found significant from day1 to day5. The median value from day1 to day5 among asymptomatic patients were 2.4 to 1.5. However, the median value among L1 patients from day1 to day5 was 2.95 to 1.55. Lactic acid dehydrogenase (LDH) is an enzyme that has an important role in cellular respiration and is highly expressed in body tissues such as heart muscles and blood cells. The range of normal LDH levels is 114 U/L (units/liter) to 240 U/L. The changes in LDH from day to day5 among asymptomatic (Z=-3.158, p=0.002), L1(Z=-5.903, p=0.000) and L2(Z=-2.040, p=0.041) were significant. The median value of LDH for asymptomatic, L1, and L2 for day1 and day 5 were 346-290,299-210 and 414-295.5. Normal ferritin level ranges from 70-435 µg/l for men while 10-280µg/l for women. The changes in Ferritin level from day1 to day five were found significant among L1(Z=-3.034, p=0.002) COVID patients only. The median value of Ferritin for day1 was 220.25, and for day five were 159. Interleukin-6 (IL-6) is an interleukin protein produced by various cells and acts as anti-inflammatory myokines and pro-inflammatory cytokines. IL6 is involved in regulating immune responses and acts as a potential marker of immune system activation. The level of IL-6 is enhanced in the cases of inflammation, infection, autoimmune disorders, cardiovascular diseases, and some cancers. The normal range of IL-6 is 0-7 pg/ml. The changes in IL6 level from day 1 to day5 were found significant in asymptomatic (Z=-3.829, p=0.000), L1(Z=-6.418, p=0.000) and L2(Z=-3.062,

p=0.002) COVID patients. The median value of IL6 from day 1 to day five among asymptomatic (11-4), L1(18.5-6.5), and L2(23-11.5).

Discussion

SARS-CoV-2 is a newly emerged form of coronavirus that causes novel pneumonia which is responsible for the current pandemic and declared as global public health concern [16]. SARS-CoV-2 engulfed so many lives in the whole world and it is highly transmissible in nature in contrast to other β-coronavirus. Infection of SARS-CoV-2 may lead to asymptomatic or symptomatic or severe respiratory distress. The fundamental basis for the management of SARS-CoV-2 infection is the early detection, for which the gold standard is the RT-PCR test. Several epidemiological studies are available on clinical diagnosis and prognosis for SARS-CoV-2 [6,7] while only few studies are available on the clinical diagnosis and prognosis especially on the Indian populations. Hence, the goal of this study is to analyze the biochemical, hematological and immunological biomarkers in various stages of SARS-CoV-2 patients, in the semi-urban regions in Lucknow. Recent findings observed that the age of majority of patients belongs to 20-59 years [11,12]. In this current report, among the asymptomatic, L1 and L2 category patients, the average age was 50 years, with the predominant population in the age group of 41 to 60 years. One of the previous studies demonstrated the correlation between age and severity of COVID-19 disease [12]. A meta-analysis conducted, showed the correlation between age, severity of disease and comorbidities and reported these conditions mostly associated with older patients owing to weakened immune system [13]. Several lines of evidence demonstrated that the patients with hypertension, diabetes are more prone to COVID-19 infection [14,15]. In this study, people with comorbidities, such as hypertension, diabetes, coronary heart disease, and the older patients, appear to have a higher risk for COVID-19.

Several previous studies showed that lymphocyte counts are decreased in case of COVID-19 infections [16,17]. A recent study conducted by Wu et al., [18] found that counts of the lymphocyte subset changed more rapidly in contrast to their proportions. In this present study, all COVID-19 patients had mild reductions in lymphocyte counts, interestingly patients from L3 category had lower lymphocyte counts compared with the patients from the L2 category. This decrease in lymphocytes counts in peripheral blood may be due to apoptosis and phagocytosis by immune cells induced by SARS-CoV-2 infection. Shreds of evidence demonstrated the increase in neutrophil counts in patients with COVID-19 infections [19,20]. We also observed an increase in neutrophil counts that were observed in the patients with SARS-CoV-2 infection which were higher in L2 patients in contrast to L1 patients. Bacterial co- infections are one of the explanations for the L2 patients having higher neutrophilic counts.

Prolongation of PT, APTT and elevation of D-Dimer are the main manifestations of abnormal coagulation. Several past studies reported the prolongation of PT, elevation of D-Dimer in patients with COVID-19 infection [21,22]. In this present study, we found the prolongation of PT and elevation of D-Dimer in patients with COVID-19 infection. Several lines of evidence reported the alteration in the APTT in case of COVID-19 infection [23]. In this report, we did not observe significant

changes in the APTT in patients with COVID-19 infection. Enhanced level of serum ferritin is associated with severity of lung infection and inflammation. Several recent studies showed that the level of serum ferritin is increased in COVID-19 infection [24,25]. The present study also found the enhanced level of serum ferritin in L1/L2 patients COVID- 19 patients and was the last laboratory value to return to normal. However, CRP, an acute phase protein, returned to normal levels 5 days before in contrast to ferritin. On entry of the virus, host immune cells release the cytokines which transform into the 'cytokine storm' if the infection is persistent that leads to multiple organ failure and damage. Recent findings on SARS-CoV-2 demonstrated that cytokine storms are linked with SARS-CoV-2 infections [26]. A recent study performed by Santa Cruz et al., [27] reported that IL-6 is the potential biomarker for the development of fatal novel pneumonia. In this current study, we also observed the elevated level of IL-6 in the sera of L1 and L2 patients of COVID-19 patients.

Several recent reports showed that SARS-Cov-2 caused a kidney injury and they detected the SARS-CoV-2 in distal convoluted renal tubules [28] and liver [29]. In this present study, we observed that the kidney injury was the most common injury followed by the heart injury and the liver injury. The Urea, Creatinine, SGOT, SGPT and LDH levels were more deranged in L2 patients as compared to L1 patients suggesting that L2 patients are more prone to multiple organ injuries. The patients from L1 category have a better prognosis and a high rate of recovery because in contrast to L2 patients as they exhibit high pulse oxygen saturation which do not require noninvasive ventilation (NIV) or invasive mechanical ventilation (IMV), and also experience a less intense inflammatory cytokine storms as well as less prone to organ damage.

These above results suggest that SARS-CoV-2 infection can cause tissue damage resulting in the release of tissue factors that leads to stimulation of the exogenous coagulation pathway which eventually culminates with prolonged PT. Enhanced level of D-Dimer indicated that a patient is in a state of secondary fibrinolysis hyperactivity. SARS-CoV-2 infection can lead to partial vascular endothelial shedding and thrombosis. Thrombosis may also cause a secondary increased fibrinolysis activity as well as increased D-Dimer. Additionally, SARS-CoV-2 enhanced the level of serum ferritin which did not returned back to the normal level even after the recovery of the patients from infection. Hence, serum ferritin cannot be employed for the assessment of the disease.

Conclusion

SARS-CoV-2 engulfed a large number of lives in the whole world which is a matter of global concern. We observed that enhanced level of lymphocyte counts, elevated PT, secondary increase in fibrinolytic activity and increased IL-6 are the typical manifestations of COVID-19 that are associated with severity of disease. However, still further studies are required to unravel the specific molecular mechanisms behind this rise in different biomarkers. Additionally, a multicentric randomized control study is needed to validate the data at the national level and global level for timely analysis as well as to prevent the infection of SARS-CoV-2 infection.

Table 1
Characteristics of patients with COVID-19

Variable	Subcategories	Asymptomatic (19)	L1 (68)	L2 (13)	Total patients	P value
Age, n(%)	<20 years	4(21.1)	1(1.5)	0(0.0)	5	
	21 to 40	8(42.1)	15(22.1)	0(0.0)	23	
	41 to 60	5(26.3)	33(48.5)	7(53.8)	45	
	60+	2(10.5)	19(27.9)	6(46.2)	27	0.001#
	Mean(SD)	36.6(17.2)	51.6(13.4)	62.3(14.4)	100	
Gender, n(%)	Female	3(15.8)	21(30.9)	4(30.8)	28	
	Male	16(84.2)	47(69.1)	9(69.2)	72	0.434
Co-Morbidities, n(%)	Diabetes	5(11.9)	26(61.9)	11(26.2)	42	0.003#
	Hypertension	3(7.9)	27(71.1)	8(21.1)	38	0.028#
	CVD	0(0.0)	1(25.0)	3(75.0)	4	0.014#
Number of Co-morbidities	Mean(SD)	0.42(0.77)	0.79(0.87)	1.69(0.48)	100	<0.01#
Signs and symptom						
	Dyspnea/ O2 support	0(0.0)	1(7.1)	13(92.9)	14	<0.001#
	Gastrointestinal Disorders	3(23.1)	6(46.2)	30.8)	13	0.058
	Fever	0(0.0)	68(84.0)	13(16.0)	81	<0.001#
Chest X ray	B/L chest clear	16(84.2)	43(63.2)	0(0.0)	59	
	B/L chest congestion	1(5.3)	1(1.5)	2(15.4)	4	
	B/L chest Pneumonia	0(0.0)	15(22.1)	8(61.5)	23	
	Left side Pneumonia	0(0.0)	1(1.5)	0(0.0)	1	
	Right side Pneumonia	2(10.5)	8(11.8)	3(23.1)	13	<0.001#
Outcomes	Recovery	19	68	12	99	

	Death	0	0	1	1	

n-number of patients, Continuous variable expressed as mean and standard deviation., Fisher's Exact test, # Significant at 5% level of significance

Table 2
Hematological parameters of Asymptomatic, L1 and L2 COVID patients

	Asymptomatic		L1		L2	
Hematological parameters	Median(Min-Max)	n	Median(Min-Max)	n	Median(Min-Max)	N
N/L Ratio(1-3)						
Day1	1.96(0.71-4.47)	19	2.48(0.53-18.6)	68	3.89(1.06-23.5)	13
Day3	2.23(0.74-5.0)	19	2.94(0.73-31.670	68	4.45(1.94-12.86)	12#
Day5	2.16(1.09-5.47)	19	2.59(0.82-18.20)	66*	5.20(1.33-47.5)	12
Z, P-value $	*-2.254,* ***0.024***		*-1.889, 0.059*		*-1.804, 0.071*	
AEC (20-500/µl)						
Day1	130(43-680)	19	69(0-620)	68	58(0-1749)	13
Day3	97(44-228)	19	87(0-480)	68	86(31-190)	12
Day5	108(48-208)	19	98(0-498)	66	123(42-228)	12
Z, P-value $	*-1.59,0.112*		*-2.039,* ***0.041***		*-1.156,0.248*	
ESR (male 0-22 and female 0-29)						
Day 1	36(12-54)	19	38(14-55)	68	45(36-58)	13
Day 3	35(16-49)	19	38(16-52)	68	42.5(34-53)	12
Day 5	30(18-42)	19	35(19-52)	66	40(28-48)	12
Z, P-value $	*-2.20,* ***0.028***		*-2.25,* ***0.024***		*-2.40,* ***0.016***	
PT (<15 sec)						
Day1	13.8(12-17)	19	14(9.9-18.0)	68	16(10.6-21.8)	13
Day3	14(12.7-17)	19	14(9.5-17.9)	68	15(13.1-17.4)	12
Day5	14(13-16.6)	19	14(12.5-17.5)	66	14(10.6-18.2)	12
Z, P-value $	*-1.134,0.257*		*-0.824,0.410*		*-1.890,0.059*	
D-DIMER <500 ng/ml						
Day1	230(100-7500)	19	718.75(41.7-10000)	68	900(100-8693.8)	13

Day3	419(120-2239)	19	658.5(135.12-10000)	68	1250(330-10000)	12
Day5	410(100-1121)	19	567.25(245-4700)	66	710(280-2200)	12
Z, P-value $)	*-0.282,0.778*		*-2.977,**0.003***		*-1.020,0.308*	

Note: # 1 death, *$Day5 to Day1*
* 2 Leave against medical advice (LAMA)

Table 3
Biochemical Parameter for Organ damage in asymptomatic, L1 and L2 COVID patients

Biochemical Parameter	Asymptomatic		L1		L3	
	Median(Min-Max)	n	Median(Min-Max)	n	Median(Min-Max)	N
SGOT (5 to 45 units/liter)						
Day1	37.1(26.18-120)	19	52.7(24-188.5)	68	59(35-1230)	13
Day3	48.0(27.0-170.0)	19	49.0(26-1113)	68	59(32.6-246)	12 #
Day5	45.0(31-190)	19	48.5(25-142)	66*	51.15(30-171)	12
Z, P-value $	*-1.529,0.126*		*-1.495,0.135*		*-0.941,0.347*	
SGPT (0-35 units/liter)						
Day1	35.3(23.91-129)	19	42.7(17-176)	68	49.0(30.5-681)	13
Day3	42.2(24.7-187.4)	19	43.5(21.2-189.0)	68	42.35(28.2-129)	12
Day5	39.0(27-178)	19	41.5(21.2-198.0)	66	44.1(37.0-126)	12
Z, P-value $	*-0.805,0.421*		*-0.217,0.828*		*-0.756,0.449*	
ALP (108-306 IU/liter)						
Day1	218(102-540)	19	146.5(68-512.3)	68	110.5(60.0-470)	13
Day3	189(78-380)	19	155(69-511.4)	68	97.5(78-452)	12
Day5	168(85-390)	19	148.5(74-502)	66	101(76-453)	12
Z, P-value $	***-3.823,0.000***		***-2.226,0.026***		*-1.020,0.308*	
Urea (10-40 mg/dl)						
Day1	26.13(17.7-35.9)	19	31.65(21.3-160)	68	48(22-141.5)	13

Day3	26(19-38)	19	31.85(18-86)	68	34(20.26-70)	12
Day5	28.6(21-38)	19	32(21-80)	66	40(21-64)	12
Z, P-value $	***-2.276,0.023***		*-0.657,0.511*		*-1.845,0.065*	
Creatinine(0.4-1.5 mg/dl)						
Day1	0.8(0.49-1.2)	19	1.0(0.6-3.9)	68	1.4(0.7-2.9)	13
Day3	0.8(0.6-1.2)	19	1.0(0.7-3.4)	68	1.15(0.65-2.30)	12
Day5	0.9(0.7-1.1)	19	1.0(0.6-3.0)	66	1.05(0.6-2.2)	12
Z, P-value $	*-1.893,0.058*		*-1.364,0.173*		***-2.671,0.008***	

Note: # 1 death, $*Day5 to Day1*
* 2 Leave against medical advice (LAMA)

Table 4
Inflammatory markers among COVID patient of asymptomatic, L1 and L2 category

Inflammatory markers	Asymptomatic		L1		L2	
	Median(Min-Max)	n	Median(Min-Max)	n	Median(Min-Max)	n
CRP test (< 1mg/dl)						
Day1	2.4(1-18)	19	2.95(0.4-157)	68	5.0(1.1-13.3)	13
Day3	1.9(0.5-9)	19	2.2(0.37-14.6)	68	6.25(2-14)	12 #
Day5	1.5(0.4-9.3)	19	1.55(0.3-38.0)	66*	3.0(1.1-10.0)	12
Z, P-value $	***-3.200,0.001***		***-3.962,0.000***		*-1.956,0.050*	
LDH test (114 -240 U/L)						
Day1	346(190-650)	19	299(90.8-850)	68	414(189-1289)	13
Day3	340(190-650)	19	272(120-731)	68	450(229-892)	12
Day5	290(167-453)	19	210(112-520)	66	295.5(119-550)	12
Z, P-value $	***-3.158,0.002***		***-5.903,0.000***		***-2.040,0.041***	
FERRITIN (70-435 µg/l men ,10-280µg/l						

women)						
Day1	176(13.2-1250)	19	220.25(20-1199)	68	319.8(49.3-1500)	13
Day3	258(38-1650)	19	212.5(29.7-1500)	68	354(45.8-845)	12
Day5	210(27-760)	19	159(30-919)	66	318(89-801)	12
Z, P-value [$]	*-1.288,0.198*		***-3.034,0.002***		*-0.078,0.937*	
IL-6 (0-7 pg/ml)						
Day1	11(4-267)	19	18.5(3-1500)	68	23(3-136)	13
Day3	8(3-57)	19	12(1-414)	68	15.5(1-76)	12
Day5	4(1-11)	19	6.5(1-53.6)	66	11.5(2-23)	12
Z, P-value [$]	***-3.829,0.000***		***-6.418,0.000***		***-3.062,0.002***	

Note: [#] 1 death, [$]*Day5 to Day1*
* 2 Leave against medical advice (LAMA)

References

1. Li Y, Tenchov R, Smoot J, Liu C, Watkins S, Zhou Q: A Comprehensive Review of the Global Efforts on COVID-19 Vaccine Development. ACS Central Science. 2021 Mar 29;7512-33. 10.1021/acscentsci.1c00120
2. Belete TM. Review on up-to-date status of candidate vaccines for COVID-19 disease. Infection and drug resistance. 2021;14:151. 10.2147/IDR.S288877
3. Wang L, Didelot X, Yang J, Wong G, Shi Y, Liu W, Gao GF, Bi Y. Inference of person- to-person transmission of COVID-19 reveals hidden super-spreading events during the early outbreak phase. Nature communications. 2020 Oct 6;11(1):1-6. 10.1038/s41467-020-18836-
4. World Health Organization. Naming the coronavirus disease (COVID-19) and the virus that causes it. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it.
5. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med. 2020;382(13):1199–207. 10.1056/nejmoa2001316
6. Kolifarhood G, Aghaali M, Saadati HM, Taherpour N, Rahimi S, Izadi N, Nazari SS. Epidemiological and clinical aspects of COVID-19; a narrative review. Archives of academic emergency medicine. 2020;8(1).e41.1-9. PMC7117787
7. Adhikari SP, Meng S, Wu YJ, Mao YP, Ye RX, Wang QZ, Sun C, Sylvia S, Rozelle S, Raat H, Zhou H. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. Infectious diseases of poverty. 2020 Dec;9(1):1-2.10.1186/s40249-020-00646-x

8. Andrews MA, Areekal B, Rajesh KR, Krishnan J, Suryakala R, Krishnan B, Muraly CP, Santhosh PV. First confirmed case of COVID-19 infection in India: A case report. The Indian journal of medical research. 2020 May;151(5):490. 10.4103/ijmr.IJMR_2131_20.
9. Mathur R. ICMR Consensus Guidelines on 'Do not attempt resuscitation'. Indian Journal of Medical Research. 2020 Apr 1;151(4):303. 10.4103/ijmr.IJMR_395_20.
10. Thevarajan I, Buising KL, Cowie BC. Clinical presentation and management of COVID- 19. Med J Aust. 2020 Aug 1;213(3):134-9. 10.5694/mja2.50698
11. Malhotra S, Rahi M, Das P, Chaturvedi R, Chhibber-Goel J, Anvikar A, Shankar H, Yadav CP, Meena J, Tewari S, Gopinath SV. Epidemiological profiles and associated risk factors of SARS-CoV-2 positive patients based on a high-throughput testing facility in India. Open biology. 2021 Jun 2;11(6):200288. 10.1098/rsob.200288
12. Bajaj V, Gadi N, Spihlman AP, Wu SC, Choi CH, Moulton VR. Aging, immunity, and COVID-19: how age influences the host immune response to coronavirus infections? Frontiers in Physiology. 2021 Jan 12;11:1793. 10.3389/fphys.2020.571416
13. Biswas M, Rahaman S, Biswas TK, Haque Z, Ibrahim B. Association of sex, age, and comorbidities with mortality in COVID-19 patients: a systematic review and meta- analysis. Intervirology. 2021;64(1):36-47. 10.1159/000512592.
14. Sanyaolu A, Okorie C, Marinkovic A, Patidar R, Younis K, Desai P, Hosein Z, Padda I, Mangat J, Altaf M. Comorbidity and its impact on patients with COVID-19. SN comprehensive clinical medicine. 2020 Jun 25:1-8. 10.1007/s42399-020-00363-4
15. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, Liu XQ, Chen RC, Tang CL, Wang T, Ou CQ. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. European Respiratory Journal. 2020 May 1;55(5).10.1183/13993003.00547-2020Huang I, Pranata R. Lymphopenia in severe coronavirus disease-2019 (COVID-19): systematic review and meta-analysis. Journal of intensive care. 2020 Dec;8:1-0. 10.1186/s40560-020-00453-4
16. Diao B, Wang C, Tan Y, Chen X, Liu Y, Ning L, Chen L, Li M, Liu Y, Wang G, Yuan Z. Reduction and functional exhaustion of T cells in patients with coronavirus disease 2019 (COVID-19). Frontiers in immunology. 2020 May 1;11:827. 10.3389/fimmu.2020.00827
17. Wu D, Wu X, Huang J, Rao Q, Zhang Q, Zhang W. Lymphocyte subset alterations with disease severity, imaging manifestation, and delayed hospitalization in COVID-19 patients. BMC Infectious Diseases. 2021 Dec;21(1):1-2. 10.1186/s12879-021-06354-7.
18. Wang J, Li Q, Yin Y, Zhang Y, Cao Y, Lin X, Huang L, Hoffmann D, Lu M, Qiu Y. Excessive neutrophils and neutrophil extracellular traps in COVID-19. Frontiers in immunology. 2020 Aug 18;11:2063. 10.3389/fimmu.2020.02063.
19. Borges L, Pithon-Curi TC, Curi R, Hatanaka E. COVID-19 and neutrophils: the relationship between hyperinflammation and neutrophil extracellular traps. Mediators of Inflammation. 2020 Dec 2;2020. 10.1155/2020/8829674.
20. Long H, Nie L, Xiang X, Li H, Zhang X, Fu X, Ren H, Liu W, Wang Q, Wu Q. D-dimer and prothrombin time are the significant indicators of severe

COVID-19 and poor prognosis. BioMed research international. 2020 Oct;2020.10.1155/2020/61597. Wang L, He WB, Yu XM, Hu DL, Jiang H. Prolonged prothrombin time at admission predicts poor clinical outcome in COVID-19 patients. World Journal of Clinical Cases. 2020 Oct 6;8(19):4370. 10.12998/wjcc.v8.i19.4370 .

21. Wang L, He WB, Yu XM, Hu DL, Jiang H. Prolonged prothrombin time at admission predicts poor clinical outcome in COVID-19 patients. World Journal of Clinical Cases. 2020 Oct 6;8(19):4370.
22. Shimura T, Kurano M, Kanno Y, Ikeda M, Okamoto K, Jubishi D, Harada S, Okugawa S, Moriya K, Yatomi Y. Clot waveform of APTT has abnormal patterns in subjects with COVID-19. Scientific reports. 2021 Mar 4;11(1):1-1. 10.1038/s41598-021-84776-8
23. Carubbi F, Salvati L, Alunno A, Maggi F, Borghi E, Mariani R, Mai F, Paoloni M, Ferri C, Desideri G, Cicogna S. Ferritin is associated with the severity of lung involvement but not with worse prognosis in patients with COVID-19: data from two Italian COVID-19 units. Scientific Reports. 2021 Mar 1;11(1):1-1. 10.1038/s41598-021-83831-8
24. Banchini F, Cattaneo GM, Capelli P. Serum ferritin levels in inflammation: a retrospective comparative analysis between COVID-19 and emergency surgical non- COVID-19 patients. World Journal of Emergency Surgery. 2021 Dec;16(1):1-7. 10.1186/s13017-021-00354-3

25. Sinha P, Matthay MA, Calfee CS. Is a ―cytokine storm‖ relevant to COVID-19?. JAMA internal medicine. 2020 Sep 1;180(9):1152-4. 10.1001/jamainternmed.2020.3313.
26. Santa Cruz A, Mendes-Frias A, Oliveira AI, Dias L, Matos AR, Carvalho A, Capela C, Pedrosa J, Castro AG, Silvestre R. IL-6 is a biomarker for the development of fatal SARS-CoV-2 pneumonia. Frontiers in immunology. 2021;12:263. 10.3389/fimmu.2021.613422
27. Chen Z, Hu J, Liu L, Chen R, Wang M, Xiong M, Li ZQ, Zhao Y, Li H, Guan C, Zhang J. SARS-CoV-2 Causes Acute Kidney Injury by Directly Infecting Renal Tubules. Frontiers in cell and developmental biology. 2021 May 31;9:1245. 10.3389/fcell.2021.664868
28. Anastasiou OE, Korth J, Herbstreit F, Witzke O, Lange CM. Mild versus severe liver injury in SARS-CoV-2 infection. Digestive Diseases. 2021;39(1):52-7.10.1159/000510758