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Retrospective comparative study of laboratory parameters in Covid-19 positive deceased and non-deceased cases

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ABSTRACT

Background: Covid 19 infection came into existence in 2019 and hence the name. It started from a city in China named Wuhan. It continued to affect the whole world, so in 2020 it was declared as a pandemic outbreak and is prevalent worldwide till date. India is still suffering and struggling through its dreadful impact. The objective of this retrospective study is to analyze the laboratory parameters and to predict the severity/mortality related to the infection.

Materials and Methods: A total of 312 hospitalized COVID-19 RTPCR positive patients from 1st April - 15^{th} May 2021 were enrolled. Patients were categorized into deceased and non-deceased groups and their demographic as well as laboratory parameters were collected and compared.

Results: Out of 312 patients, 100 succumbed to disease. Majorities were males between 55 to 60 years. The laboratory values of TLC ($p<0.0001$), Neutrophil count ($p<0.0001$), Lymphocyte count ($p<0.0001$), Platelet count ($p<0.0001$), Neutrophil to Lymphocyte Ratio(NLR) ($p<0.0001$), plasma D-dimer($p=0.007717$), serum CRP level ($p=0.000174$), serum Lactate dehydrogenase(LDH) level ($p<0.0001$), serum SGOT ($p<0.0001$), serum Ferritin ($p=0.000085$) were statistically significant for deceased as compared to non-deceased group. Serum SGPT was statistically insignificant.

Conclusion: The attained results showed deranged laboratory parameters among COVID-19 positive patients. The mortality rate was found to be higher in elderly males as compared to females of same age group. There was significant correlation between the markedly abnormal laboratory values and severity/mortality of the COVID-19 infection, which could help in predicting the outcome of the disease in patients admitted to the hospitals.

1. Introduction

Covid 19 started its journey from a small city Wuhan in China, from December last week 2019. This disease, COVID-19 spread to different continents of this Globe, which compelled WHO to recognize this Outbreak as a pandemic, SARS-CoV-2 on 11th March 2020.[1] The three most affected countries by Covid 19 are United States of America, India and Brazil with total cases as of on May 16, 2021, being 33,747,439 in USA, 25,227,970 in India and 15,661,106 in Brazil. The Chinese Center for Disease Control and Prevention then confirmed, after studying throat cultures from patients that these cases were caused by a new type of beta-corona virus.[2] Corona viruses are enveloped positive sense RNA viruses ranging from 60 nm to 140 nm in diameter with spike like projections on its surface giving it a crown like appearance under the electron microscope; hence the name corona virus.[3]Human-to-human transmission of COVID-19 occurs among close contacts, mostly between family members and friends, either via direct contact or through droplets. The common clinical manifestations of

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the disease can be listed as fever, dry cough, fatigue, sputum production, dyspnea, sore throat, and headache.[4,5] Despite the documentation that showed that SARS-CoV-2 manifested as a respiratory infection in the first place, but new data indicated that it must be regarded as a systemic disease infecting numerous systems, such as; gastrointestinal, immune, respiratory, hematopoietic, and cardiovascular system.[6,7]Those people with advancing age, male sex and other Comorbities like Diabetes, Hypertension, Cardiovascular disease, Chronic obstructive pulmonary disease, and other Immunosuppressive state have been considered to be at a higher risk than others. Early identification of severe illness risk factors can help clinicians facilitate appropriate remedial measures and help control mortality.[8] Widely-used techniques, such as serum biochemical and hemogram analysis, might be faster, easy-to-measure, routine, and low-cost techniques facilitating the diagnosis and prognosis of this disease.[9] Few important and independent predictors for prognosis are the inflammatory markers from blood like White blood cell (WBC) count, Neutrophil-to-Lymphocyte ratio (NLR), Platelet-to-Lymphocyte ratio (PLR), LDH and serum C-reactive protein (CRP) levels. Recent studies have suggested that elevated NLR and LDH can be considered independent biomarkers for indicating poor clinical outcomes, while elevated LDH values were associated with the severity of COVID-19 disease.[10,11] Increased White blood cell count, raised Neutrophil to lymphocyte ratio (NLR) and Neutrophil to Lymphocyte ratio (NLR) project not only to the severity of disease but are also considered to be associated with poor prognosis and high mortality rates. D-dimer has also been considered as one of the important diagnostic tool of severity particularly in patients suffering from chronic obstructive pulmonary disease and severe community-acquired pneumonia. Coagulopathy is present in COVID-19, and 81% of non surviving patients have been reported to have D-dimer levels higher than 1ng/ml.[12]

Our study was done on 312 Covid-19 RTPCR confirmed cases admitted to our hospital. The objective of this study is to analyze the laboratory parameters (hematological and biochemical) and to predict the severity/mortality related to the infection. This would guide clinicians to group patients according to severity and also predict the outcome of disease. The biomarkers taken include Total Leukocyte count (TLC), Neutrophil Count, Lymphocyte Count, Platelet count, Neutrophil-to-Lymphocyte ratio (NLR), C-reactive protein (CRP), Lactate dehydrogenase (LDH), SGPT, SGOT, Ferritin and D-dimer. Demographic characteristics like advanced age, male sex were also taken into consideration for predicting the severity of the disease.

2. Materials and Methods

This is a single-center, retrospective, observational study conducted between 1^{st} April to15^{th} May 2021 at Mayo Institute of Medical Sciences Barabanki U.P, India. A total of 312 adult COVID-19 positive patients were enrolled in this study. The study was approved by the institutional scientific and ethical committees.

2.1. Inclusion criteria

RTPCR Positive Adults admitted to the institute.

2.2. Exclusion criteria

Patient below 18 years.

2.3. Case definition

A COVID-19 positive case was defined as those patients who had positive result on a Reverse-transcriptase polymerase chain reaction assay using a nasopharyngeal and oral swab specimen as per ICMR /National guideline.

2.4. Data collection

The demographic characteristics, hematological and biochemical findings of COVID-19 positive cases were recorded at the time of admission. The data of Non Deceased and Deceased cases were collected from medical record department.

2.5. Statistical analysis

The Laboratory parameters of TLC, Neutrophil count, Lymphocyte count, Platelet count, Neutrophil-to-Lymphocyte ratio (NLR), D-dimer, C-reactive protein (CRP), Lactate dehydrogenase (LDH), SGPT, SGOT, and Ferritin were collected using institutional software. The collected data was transferred into a Microsoft Excel spreadsheet and was analyzed using Statistical Package for Social Sciences (SPSS). Mean, Standard deviations, Median, Interquartile range (IQR) and Variance was used to present the findings. All continuous variables were described as both mean & standard deviation as well as median & interquartile range. The Fisher exact test was used to compare demographic distribution. Independent sample –t-test was applied to compare age, biochemical and hematological findings of deceased and non deceased in COVID-19 patients. The level of significance was $p < 0.05$.

3. Results

The demographic distribution of all the 312 patients is shown in Table 1. The mean age in Non-deceased group (n=212) was 50.83±14.92 years and in deceased group (n =100) it was 56.45± 14.24 years with significant p-value (0.00316). In non-deceased group 40.1% (n=85) of the patients were less than or equal to 45 years and 59.9% (n=127) of the patients were more than 45 years of age. In the deceased group, 23% (n=23) cases were

less than or equal to 45 years and 77% (n=77) cases were more than 45 years of age with significant p-value (0.003) (Table 2). The sex distribution pattern depicts that among the non-deceased, males were 68.8%(n=146) and females were 31.2%(n=66) while in deceased category, males were 65%(n=65) and females were 35% (n=35)(Table 3).

Value of the laboratory parameters among non-deceased and deceased group is depicted in the form of mean ± standard deviation, median (inter-quartile range) and variance inTables 4 and 5.

At the time of hospitalization, various laboratory parameters like TLC, Neutrophil count, NLR, D-dimer, CRP, LDH, SGOT and Ferritin were significantly high (p-value <0.00001, < 0.00001, < 0.00001, 0.007717, 0.000174, < 0.00001, < 0.00001 and 0.000085 respectively) in patients who succumbed later (deceased group). Parameters like Lymphocyte count, platelet count and SGPT were higher (p-value <0.00001< 0.00001 and 0.240791 respectively) in non-deceased cases as compared to deceased cases (Table 6).

We found a statistically significant correlation of various above mentioned laboratory parameters between succumbed and survived cases except for SGPT.

Table 1: Showing Demographic distribution of patients.

Characteristics	Non Deceased	Deceased
Total No. of Cases	212	100
Median Age in Years	51.5	55.5
Mean Age in Years	50.83	56.45
Total Male Patients	146 (68.8%)	65 (65%)
Total Female Patients	66 (31.2%)	35 (35%)

Table 2: Showing Age distribution between Non deceased and Deceased

Age	Non Deceased (n=212)	Deceased (n=100)	p-value
≤ 45 Years (n=108)	85 (40.1%)	23 (23%)	0.0033*
>45 Years (n=204)	127 (59.9%)	77 (77%)	

*significant p-value

Table 3: Showing Sex distribution between Non deceased and Deceased

Sex	Non Deceased (n=212)	Deceased (n=100)	p-value
Male (n=211)	146 (68.8%)	65 (65%)	0.518
Female (n=101)	66 (31.2%)	35 (35%)	

4. Discussion

Every COVID19 surge brings new impacts to human life. COVID19 disease is affecting each and almost every organ of the body but we are still at very early stage to completely understand or predict the course of the disease. So far, several studies have been conducted worldwide and have suggested different speculations of COVID19 effect on humans. This retrospective study was conducted on 312 COVID19 positive patients and a comparative analysis of various hematological and biochemical parameters were made to show any significant correlation between deceased and survived cohorts. We have analyzed the data to summarize its usefulness in early detection of severity so that the clinician can take early interventions to improve the disease outcome.

In this study we found that mean age of deceased patients was more as compared to the non-deceased group and this finding has been mentioned in several previous studies.[13,14] This finding is implicated to presence of co-morbidity, reduced immunity, decreased functional capacity of various organs like liver, heart and kidney in older age group.

Our study showed higher WBC count, Neutrophil count, Neutrophil-Lymphocyte ratio and D-dimer in deceased group as compared to non-deceased group and this finding is in agreement with the previous similar studies.[13,15,16] These findings can be due to other super added infections, associated sepsis and DIC. The lymphocyte count and platelet count was significantly higher in survived group of this study. Reduced platelet count is also related to disease severity and is assumed to be due to immune-mediated destruction and excessive consumption. Correlation of decreased platelet count with COVID19 disease severity in this study is in agreement with the previous studies.[17,18] In view of these hematological parameters, it can be suggested to the clinicians to observe and follow-up the COVID19 patients thoroughly. During the course of the disease, increasing trend in WBC count, Neutrophil count and NLR while decrease in platelet count and lymphopenia are seen to be critical and require prompt intervention accordingly.

In the present study, serum levels of various biochemical parameters like C-reactive protein, Lactate dehydrogenase, SGOT and Ferritin were significantly higher in deceased group as compared to non-deceased group. This finding also matches with the previously conducted studies.[13,19,20] No significant difference in serum SGPT level was found among survived and deceased group which is not in agreement with some previous studies.[21] The difference can be attributed to lack of data or less number of cases.

Higher levels of SGOT and LDH indicate damage to liver and myocardium. Increased levels of CRP and Ferritin indicate active inflammation. This study showed comparatively higher values of SGOT and LDH in deceased cohort which indicates the degree of organ damage was

Table 4: Showing laboratory parameters of Non-deceased cases (n=212) at the time of hospital admission

S.No.	Parameters	Mean ± SD	Median	IQR	Variance
1	Age (Years)	50.83 ±14.92	51.5	22	222.6
2	TLC (cells/cumm)	8785±4521.19	7700	5000	21852
3	Neutrophil count (%)	75.73±13.38	78.5	16.75	179
4	Lymphocyte count (%)	19.80±12.3478	16.5	16	152.4
5	Platelet count (cells/cumm)	2.08±0.91	1.8	0.915	0.8368
6	N.L.R.	6.58±6.34	4.51	5.95	40.209
7	D-dimer (ng/ml)	2322.84±7319.55	685.2	1144.9	53575911
8	CRP (mg/L)	32.42±23.62	30.7	41.95	558.32
9	LDH (U/L)	419.39±237.89	357.5	236.75	56591.7
10	SGPT (IU/L)	49.69±73.44	55	64.5	5394.14
11	SGOT (IU/L)	58.75±40.65	47	42.5	1652.68
12	Ferritin (ng/ml)	591.03±644.44	461	518.2	415305.69

CRP: C-reactive protein, IQR: Interquartile range, LDH: Lactate dehydrogenase, NLR: Neutrophil-to-lymphocyte ratio, SD: Standard deviation, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic-pyruvic transaminase TLC: Total Leucocyte count

Table 5: Showing laboratory parameters of Deceased cases (n=100) at the time of hospital admission

S.No.	Parameters	Mean ± SD	Median	IQR	Variance
1.	Age (Years)	55.30±14.24	55.5	20.75	200.82
2.	TLC (cells/cumm)	13987±7489.24	11350	9900	55527931
3.	Neutrophil count (%)	85.43±7.80	87	8.75	60.3251
4.	Lymphocyte count (%)	11.39±6.63	10	6.75	43.57
5.	Platelet count (cells/cumm)	1.62±0.58	1.6	0.5225	0.3384
6.	N.L.R.	10.35±7.18	8.65	7.56	51.12
7.	D-dimer (ng/ml)	3861.08±7326.00	1490.5	2222.7	53133714
8.	CRP (mg/L)	43.66±29.89	45.4	34.7	885
9.	LDH (U/L)	639.63±291.937	653	449.9	84375
10.	SGPT (IU/L)	73.03±82.26	51.5	35.75	6767.2
11.	SGOT (IU/L)	89.66±78.48	71.75	51.75	6160
12.	Ferritin (ng/ml)	865.36±468.29	849.95	520.5	219303

CRP: C-reactive protein, IQR: Interquartile range, LDH: Lactate dehydrogenase, NLR: Neutrophil-to-lymphocyte ratio, SD: Standard deviation, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT:Serum glutamic-pyruvic transaminase TLC: Total Leucocyte count

Table 6: Showing Comparison of laboratory parameters between Non Deceased and Deceased cases at the time of hospital admission

S.No.	Characteristics	Non-deceased		Deceased		p-value
		Mean ± SD	Median(IQR)	Mean ± SD	Median (IQR)	
1.	Age (Years)	50.83 ±14.92	51.5(22)	55.30±14.24	55.5(20.75)	0.00316*
2.	TLC (cells/cumm)	8785±4521.19	7700(5000)	13987±7489.24	11350(9900)	< .00001*
3.	Neutrophil count (%)	75.73±13.38	78.5(16.75)	85.43±7.80	87(8.75)	< .00001*
4.	Lymphocyte count (%)	19.80±12.3478	16.5(16)	11.39±6.63	10(6.75)	< .00001*
5.	Platelet count (cells/cumm)	2.08±0.91	1.8(0.91)	1.62±0.58	1.6(0.52)	< .00001*
6.	N.L.R.	6.58±6.34	4.51(5.95)	10.35±7.18	8.65(7.56)	< .00001*
7.	D-dimer (ng/ml)	2322.84±7319.55	685.2(1144.9)	3861.08±7326.00	1490.5(2222.7)	0.00771*
8.	CRP (mg/L)	32.42±23.62	30.7(41.95)	43.66±29.89	45.4(34.7)	0.00017*
9.	LDH (U/L)	419.39±237.89	357.5(236.75)	639.63±291.937	653(449.9)	< .00001*
10.	SGPT (IU/L)	49.69±73.44	55(64.5)	73.03±82.26	51.5(35.75)	0.240791
11.	SGOT (IU/L)	58.75±40.65	47(42.5)	89.66±78.48	71.75(51.75)	< .00001*
12.	Ferritin (ng/ml)	591.03±644.44	461(518.2)	865.36±468.29	849.95(520.5)	0.00008*

CRP: C-reactive protein, IQR: Interquartile range, LDH: Lactate dehydrogenase, NLR: Neutrophil-to-lymphocyte ratio, SD: Standard deviation, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT:Serum glutamic-pyruvic transaminase TLC: Total Leucocyte count.
*significant p-value

more in them as compared to survived patients. Higher degree of inflammation in deceased group as compared to non-deceased group was proven by increased levels of inflammatory markers like CRP and Ferritin.

As per the clinical, hematological and biochemical findings of this study, we can predict the severity in early course of the COVID19 disease. Thorough follow-up of clinical findings as well as for hematological and biochemical inflammatory markers is required. Increase in total Leukocyte count, Neutrophil count, NLR, D-dimer, SGOT, LDH and inflammatory markers (CRP and Ferritin) while decreased platelet count and lymphocyte count may significantly predict the critical illness. However these parameters need further evaluation with larger sample size.

5. Conclusion

At the end, from our study we can conclude that elderly males were more vulnerable to COVID-19 disease severity/mortality than younger age group and females. The Laboratory parameters-TLC, Neutrophil count, Platelet count, D-dimer, LDH, SGOT, Ferritin and systemic inflammatory markers like NLR and CRP were significantly higher in deceased group suggesting that it can be used as a clinical guide for predicting the outcome in earlier course of the disease. Furthermore, biomarkers combined with clinical presentation and timely interventions can help us to save more lives from this dreaded disease in this pandemic.

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7. Conflicts of Interest

None.

8. Source of Funding

None.

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