

A Retrospective Study of Inflammatory Biomarkers in COVID-19 Patients

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Abstract

Objective: Covid-19 has impacted the health of the people and 20% of the patients were critical and hospitalized with the need for ventilation and intensive care unit (ICU) support. This study aimed to study the association of inflammatory biomarkers with severity of COVID-19 infection.

Material & Method: For this study, 545 Covid-19 infected patients admitted in New Civil hospital, Bharuch were selected. The infection related to Covid-19 was confirmed using the Real-Time Reverse Transcription Polymerase Chain Reaction (RT-PCR) test. Pearson correlation was used to assess the correlation between inflammatory markers and laboratory indicators. A p-value of <0.05 was used as a cut-off value for significance.

Results: The inflammatory markers and WBC count was significantly elevated in the critical COVID-19 patients. Moreover, patients with lower absolute lymphocyte count (ALC) were significantly associated with severe to critical COVID-19 infection compared to the mild to moderate form that showed higher lymphocyte count ($P < 0.0001$). Moreover, patients with evidence of acute cardiac injury showed a significantly lower ALC ($1.08 \pm 0.628 \times 10^3$ cells/ μ L) compared to ($1.38 \pm 0.72 \times 10^3$ cells/ μ L) ($P < 0.0001$).

Conclusion: From the study, it can be concluded that there is a significant association between different inflammatory markers, clinical as well as the laboratory profile of the Covid-19 patients affecting the recovery.

Keywords: Inflammatory biomarkers, Covid-19, Acute respiratory distress syndrome, Absolute lymphocyte count.

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Introduction

Covid-19 has impacted on the health of the people and 80% of patients were having

mild or moderate symptoms that require the minimal medical intervention[1].

However, 20% of the patients were not having serious issues and hospitalized with the need for ventilation and intensive care unit (ICU) support. To provide the better support and care to these patients, the different studies and efforts were made by the care experts to improve the understanding of the Covid-19 pathogenesis[2]. This has helped to identify the risk factors that have adverse impact on the health of the people. The study has provided the information related to different predictive markers that requires the aggressive medical interferences and support for the patients[3].

The proper understanding and knowledge related to risk factors and biomarkers of the patients that influencing the health of the individual can be helpful for offering the care and additional support[4]. The optimal use of the available resources and infrastructure is helpful for the medical staff to offer the extensive care to the patients[5]. According to various reports and analysis, it has been carried out that inflammation is having direct damage to the essential mechanisms that contribute to the severity of Covid-19[6]. The inflammation is causing issues in the patient that increasing the proinflammatory cytokines in the serum of Covid-19 patients that increase the level of severity[7]. Moreover, the higher level of inflammatory markers that include the C-reactive protein, neutrophil – to – lymphocyte ratio and various inflammatory cytokines and chemokines[8].

The analysis of patients in previous studies have involved clinical characteristics of the patients and investigated the role of the biomarkers[9]. The current study will focus on the association between inflammatory markers and progression and outcome of the Covid-19 patients[10]. It will highlight the severity level, duration of ICU admission, mortality and laboratory indicators. Moreover, the study will also focus on the markers and

biomarkers considering the evidence of organ injuries[11].

Aim

To study retrospectively association between inflammatory biomarkers in COVID-19 patients.

Method and material

This study was conducted at Dr. Kiran C. Patel Medical College & Research Institute and New Civil Hospital, Bharuch. For conducting the Epidemiological, were 545 number of patients selected for the analysis of the risks factors related to Covid-19, those who were admitted in New Civil Hospital, Bharuch between the time period of March to June 2021. The infection related to Covid-19 was confirmed using the polymerase chain reaction (PCR) test collecting the nasal swab sample. Moreover, the Real-Time Reverse Transcription Polymerase Chain Reaction (RT-PCR) test was also done in laboratory. Moreover, the study has focused on the presence of organ failure or injury was considered as per the criteria that previously used in the analysis of the inflammatory biomarkers. Moreover, the acute cardiac injury was also considered to analyze the health of the patient. Acute kidney injury was defined as patient having a raise in the serum creatinine of 26.5 $\mu\text{mol/liter}$ within 48 hours or increase in serum creatinine 1.5 times than the baseline that occurred within the preceding 7 days; or if there were reduction in the urine volume $<0.5 \text{ ml/kg/hr.}$ for 6 consecutive hours. Acute liver injury was defined as patient having high ALT and/or high AST by more than 5 times the upper limit of normal range. In addition to the definition of ARDS which was made using Berlin definition. Ethical approval was obtained from the ethics committee at Dr. Kiran C. Patel Medical college hospital for conducting the study.

Patient characteristics and laboratory profile were summarized and tabulated using the standard descriptive statistics. All our variables were continuous

variables. For that reason, data were tabulated and presented as mean SD. SPSS 21.0 (BM Corporation, Armonk, NY) software was used for the statistical analysis. Pearson correlation was used to assess the correlation between

Results

inflammatory markers and different laboratory indicators. A p - value of <0.05 was used as a cut-off value to differentiate between significant or non-significant differences.

Table 1: Demographic, Clinical & Laboratory indicators of COVID-19 patients

Variables	%
Age (mean± SD)	49.64±14.98
Gender (No., %)	
Male	418 (76.69%)
Female	127 (23.30%)
BMI	29.57 ±5.90
Time from symptom onset to admission, Mean ± SD, days	5.9±3.0
Disease severity	
Mild-moderate	190(34.86%)
Sever	205(37.61%)
Critical	150(27.52%)
ICU admission	155(28.44%)
No ICU admission	390(71.55%)
Laboratory indicators	
Hemoglobin (gm/dL)	13.32±2.05
WCC (x10 ³ /mcL)	9.65±7.90
Neutrophil count (x10 ³ /mcL)	7.67±35.83
Lymphocyte count (x10 ³ /mcL)	1.46±0.78
Platelet count (x10 ³ /mcL)	249.4±99.89
INR	1.06±1.19
D-dimer (mg/l)	2.45±5.74
Ferritin (mcg/L)	930.6±1378
CRP (mg/l)	82.45±96.49
Urea (mmol/L)	7.80±27.40
Creatinine (µmol/L)	117.9±314.5
Sodium (Na) (mmol/L)	139.2±4.699
Potassium (K)(mmol/L)	5.13±1.98
LDH (IU/L)	415.4±319.3
Serum bilirubin (µmol/L)	17.77±39.70
ALT (IU/L)	68.49±120.7
AST (IU/L)	59.73±116.7
ALP (IU/L)	89.02±53.80
Albumin(gm/L)	31.83±7.201
Procalcitonin (µg/L)	0.98±4.20

According to the outcome of the Table 2, the inflammatory markers and WBC count was significantly elevated in the critical COVID-19 patients. Also, significant association was seen in patients requiring long ICU admission, mortality and patients requiring ventilation.

Table 2: Association between inflammatory markers with clinical outcome in Covid-19 patients:

	WBC count	Neutrophils count	Lymphocytes count	CRP	D-Dimer	Ferritin	Procalcitonin	LDH
Disease severity								
Mild-moderate	7.50± 3.61	4.90±3.20	1.85±0.84	20.69±34.87	0.99± 2.29	332.8± 445	0.33±1.79	270.7± 290.60
Severe	8.98± 11.60	6.34 ± 3.32	1.32 ± 0.86	89.17±101.3	1.44± 2.7	1180± 1069	0.76±4.70	497.1± 196.90
Critical	10.0± 4.87	13.97 ± 67.38	0.999±0.50	157.5±98.56	5.9± 9.30	1590± 2021	1.89±5.10	589.5± 412.70
P- value	0.005	0.048	<0.0001	<0.0001	<0.0001	<0.0001	0.0209	<0.0001
ICU admission	9.89± 4.17	13.78 ± 66.69	0.99±0.68	140.9±99.00	5.09± 8.89	1520± 1980	1.89±5.61	560.4± 420.7
No ICU admission	8.20± 8.98	5.71±3.36	1.80±0.90	58.90±91.66	1.70± 3.39	799± 990	0.48±3.49	360.9± 263.5
P-value	0.0259	0.0190	<0.0001	<0.0001	<0.0001	<0.0001	0.0017	<0.0001
Died	10.78±4.60	8.90± 3.69	0.79±0.49	140.9±99	5.09± 8.99	1490±1960	2.50±6.33	620.4±489.70
Alive	8.60± 8.47	5.90 ± 4.48	1.49 ± 0.84	58.80±85.66	1.44± 3.28	802 ± 987	0.52 ± 3.39	369.5±246.8
P-value	0.0133	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0002	<0.0001
No Ventilation	8.30± 9.29	6.69±4.32	1.66 ± 0.84	65.05±88.67	1.69± 3.98	828.6± 1093	0.60 ± 3.72	341.70± 232.8
Ventilation	10.69±4.92	9.22±4.75	0.82±0.66	169± 101	6.32± 9.65	1596± 2224	1.96 ± 4.86	589.40± 313
P-value	0.0055	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0051	<0.0001
ARDS	9.91± 4.67	8.28 ± 4.370	0.96 ± 0.50	146.5±96.80	5.59± 9.15	1571± 1962	1.66 ± 4.96	581.4±413.0
NO ARDS	7.93± 3.52	5.64 ± 3.92	1.63 ± 0.95	59.85±89.9	1.20± 2.24	782 ± 991	0.60 ± 3.80	361.7±282.8
P-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0050	<0.0001

Also patients with lower absolute lymphocyte count were significantly associated with severe to critical COVID-19 infection compared to the mild to moderate form that showed higher

lymphocyte count ($P<0.0001$). Moreover, patients who presented with features of ARDS showed a significantly lower level of absolute lymphocyte count.

Table 3: Association between Inflammatory markers & organ involvement in Covid-19 patients

	WBC count	Neutrophils count	Lymphocytes count	CRP	D-Dimer	Ferritin	Procalcitonin	LDH
Acute cardiac injury	12.27±5.55	8.91± 4.60	1.09±0.728	142.6± 115.6	5.86± 10.4	1328± 2891	2.20 ± 5.81	569.7± 549.7
No Acute cardiac injury	9.38± 8.87	5.89±3.51	1.48±0.92	78.22± 90.91	2.43± 3.28	982± 1171	0.499±3.39	399.1± 248.5
P-value	0.0241	<0.0001	<0.0001	<0.0001	<0.0001	0.0077	0.0005	<0.0001
Acute renal injury	10.88±4.98	8.99±4.69	0.89±0.62	138± 99.74	6.19± 9.01	1604± 2089	2.14±6.10	592.4± 481.1
No Acute renal injury	8.23± 8.21	5.98±3.28	1.486±0.85	69.51± 92.35	1.91± 4.80	875±1069	0.494±3.32	371.1± 244.2
P-value	0.0020	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0002
Acute liver injury	9.21± 3.97	7.49±3.83	1.107±0.56	126± 131	3.03± 5.88	1781± 2171	1.20±5.34	567.7± 485.8
No Acute liver injury	8.52± 8.45	6.06±3.80	1.42±0.75	70.98± 83.27	2.32± 5.55	813± 1015	0.82±3.86	377.3± 248.2
P-value	0.4192	0.0007	<0.0001	<0.0001	0.2602	<0.0001	0.4287	<0.0001

Our results also highlighted a significant association between lymphopenia and multiple organ injury. Indeed, patients with evidence of acute cardiac injury showed a significantly lower Acute lymphocyte

count ($1.09±0.728 \times 10^3$ cells/ μ L) compared to patients with no cardiac involvement ($1.48±0.92 \times 10^3$ cells/ μ L) ($P<0.0001$). Significant association was also seen between organ injury and

markers of inflammation like CRP, D-Dimer, Ferritin, Procalcitonin and LDH.

Discussion

To provide the better support and care to these patients, the different studies and efforts were made by the care experts to improve the understanding of the Covid-19 pathogenesis. This has helped to identify the risk factors that have adverse impact on the health of the people. The study has provided the information related to different predictive markers that requires the aggressive medical interferences and support for the patients. The optimal use of the available resources and infrastructure is helpful for the medical staff to offer the extensive care to the patients. According to various reports and analysis, it has been carried out that inflammation is having direct damage to the essential mechanisms that contribute to the severity of Covid-19. The inflammation is causing issues in the patient that increasing the proinflammatory cytokines in the serum of Covid-19 patients that increase the level of severity.

According to the outcome of the table the inflammatory markers and the clinical outcome of WBC count was significantly elevated in the critical COVID-19 patients. Moreover, the patients with lower absolute lymphocyte count were significantly associated with severe to critical COVID-19 diseases compared to the mild to moderate form that showed higher lymphocyte count ($P < 0.0001$). Moreover, patients who presented with features of ARDS showed a significantly lower level of ALC. The study has also highlighted a significant association between lymphopenia and multiple organ injury. Indeed, patients with evidence of acute cardiac injury showed a significantly lower ALC ($1.08 \pm 0.628 \times 10^3$ cells/ μ L) compared to ($1.38 \pm 0.72 \times 10^3$ cells/ μ L) ($P < 0.0001$). According to the study of Hachim et al., (2021)[12]. There is strong association between ALC and more severe disease and worse outcome including the need for ventilation, ICU admission and higher

mortality rate. Lymphopenia was previously reported in a group of viral infections including SARS and Middle East Respiratory Syndrome[13].

Moreover, our finding that lower ALC to be associated with multiple organ injury including acute liver and renal injuries go with other reports that showed patients who developed acute kidney injury were more likely to have lymphocytopenia compared with patients without acute kidney injury. Moreover, the study of Merad and Martin (2020)[14] suggested that inflammatory markers are significantly associated with organs dysfunctions including liver, renal cardiac injuries. Also, the findings by Vabret et al. (2020)[15] showed that, these organ dysfunctions are a result of COVID-19 tissue destruction and it is related with the comorbidity usually associated with the severe disease.

Conclusion

From the study, it has been concluded that there is a significant association between different inflammatory markers and clinical profile of the Covid-19 patients affecting the recovery. Moreover, the consideration of these markers will be helpful for the healthcare professionals to have more detailed information of clinical course in covid-19 patients who require aggressive medical support considering the ventilators and ICU.

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