CORRELATION BETWEEN CIRCULATING CYTOTOXIC MARKERS (CD3 & CD8) AND DISEASE SEVERITY IN PNEUMONIA COVID-19 PATIENTS

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The COVID-19 etiologic agent was first discovered in Wuhan, China towards the end of 2019 (Huang *et al*., 2020 and Wu *et al*., 2020). COVID-19 symptoms can range from moderate illness to severe ones; respiratory failure is the main factor that contributes to patient mortality (Fajnzylber *et al*., 2020). Acute respiratory distress syndrome (ARDS) and pulmonary dysfunction can result from viral pneumonia, which is the most frequent reason for hospital admission (Ketcham *et al*., 2021). According to Chen *et al*., (2021) and Yang *et al*., (2021), the severity of COVID-19 is mostly due to a hyper-inflammatory response that results in an increased release of pro-inflammatory cytokines. In mild and acute COVID-19 patients, other investigations have suggested indicators that the adaptive immune system, particularly T cells, is committed to preventing the development of severe illness (Rydyznski *et al*., 2020; Aljabr *et al*., 2022 and Garofalo *et al*., 2023).

The significance of several biomarkers in predicting prognosis in COVID-19 patients is currently being investigated. One such biomarker of relevance is lactate dehydrogenase (LDH), particularly since higher LDH levels have previously been linked to poorer outcomes in individuals with other viral infections. Early results on COVID-19 patients have indicated a substantial difference between individuals with severe illness and those without (Henry *et al*., 2020 and Huang *et al*., 2022). One of the sensitive indicators of a generalized inflammatory response in the human body is C-reactive protein (CRP). Although not as much as in bacterial infection, CRP also rises in viral infection according to

Egypt. J. Genet. Cytol., 52:27-46, January, 2023
Web Site (*www.esg.net.eg*)

the research. A new coronavirus infection may be diagnosed, differentially diagnosed, and its prognosis predicted using CRP (Tang *et al*., 2020 and Chi *et al*., 2022). Coagulation for homeostasis disorders associated with COVID-19, factors like D-dimer level are now regarded as the most crucial prognostic tool and the best predictors of a laboratory diagnosis (Zendehdel *et al*., 2022). Additionally, it has been suggested that the enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT) may be used to predict clinical outcomes in COVID-19 patients, such as death (Wang *et al*., 2021 and Padmaprakash Kodavoor Vadira *et al*., 2022). Also recently discovered as one of the indicators of COVID-19 severity and mortality is serum ferritin (Hadi *et al*., 2022 and Kaushal *et al*., 2022). The severity of COVID-19 may actually be predicted by lower lymphocyte counts, lymphopenia, and lymphocyte counts (Huang and Pranata, 2020).

The immunological response to respiratory viral infections, such as coronavirus, includes major contributions from cytotoxic T lymphocytes (CTL). Once activated by a particular antigen on the target's surface, particularly recognized by the T cell receptor, they may release perforin and granzyme to destroy infected cells (Schmidt *et al*., 2018). After infection, CD4+ T and CD8+ T cells were found to be diminished, with the decreases in the severe patients being more pronounced than those in the moderate patients (Liu *et al*., 2020). Prior to patients leaving the hospital, reduced lymphocyte subsets also improved (Wan *et al*., 2020). The elimination of invasive infections depended heavily on the immunological response that SARS-CoV-2 infection produced. Harmful tissue damage may result from uncontrolled inflammatory innate immune reactions and compromised adaptive immunological responses (Cao, 2020). Determining immune function alterations in COVID-19 patients and searching for effective therapies to restore immunological balance were of the highest significance. The CD4+ T cell and CD8+ T cell are activated by CD3, a biomarker of mature T lymphocytes (Dong *et al*., 2019).

Therefore, this study aimed to examine how several immunological markers changed in response to different levels of COVID-19 severity and clinical outcomes. We were particularly looking for indicators of immune cell exhaustion and activity.

MATERIALS AND METHODS

Patients and data collection

Between December 2021 and February 2022, six October Central Hospital performed this prospective study on 80 people. This included 40 participants who seemed to be in good health and were selected from the internal department's outpatient clinics as well as 40 unvaccinated patients who were hospitalized and had COVID-19 symptoms. Verbal constant was obtained

from all patients who agreed to participate or their duly appointed representatives.

Samples collection and processing

A ten-milliliter sample of venous blood was drawn using sterile venipuncture and put into sterilized vacutainer tubes with EDTA for the molecular subtyping of lymphocytes, including the main panel (CD3+, CD8+). All participants underwent a thorough history-taking procedure. Routine laboratory investigations: complete blood count (CBC) determined by automated hematology analyzer (Pentra 80), serum biochemical liver function tests, laboratory investigation to assess the severity and mortality of COVID-19: lactate dehydrogenase (LDH), serum inflammatory biomarkers including C-reactive protein (CRP), serum ferritin determined by BECHMAN COULTER AU 400, D dimer determined by VIDAS. Patients were followed up for the final outcome whether survived or died were recorded.

Confirmation of COVID-19 infection

Real-time reverse-transcriptase polymerase-chain reaction (RT-PCR) examination of nasal and pharyngeal swab samples produced positive findings in all patients, confirming their COVID-19 infection, in accordance with the criteria of Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment.

Flow cytometry

Fresh cells and EDTA-anticoagulant peripheral blood were stained with anti-CD3, and anti-CD8 Abs (Beckman Coulter), and the lymphocyte subsets were examined with a flow cytometer (BD ACCURI C6 plus). With 10,000 events per sample, the data were examined by FlowJo software (Tree Star).

Statistical analysis

Information was fed to the computer to perform statistical analysis by IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp.). The system secondhand for statistical comparisons was investigated by the Mann–Whitney test for non-parametric data and the Student's t-test for parametric data. Spearman's coefficient method was adopted to perform correlation analysis. The receiver functional characteristic (ROC) curve was utilized to determine the cut-off value, and the diagnostic performance. A P-value of < 0.05 was considered significant.

RESULTS AND DISCUSSION

Patient characteristics

Baseline demographic data, sex distribution, and initial clinical findings of patients are summarized in Table (1). The mean age of all study individuals was 46.13±9.79 years; the distribution of sex was similar in COVID-19 patients and healthy control with 20 (50 %) males and 20 (50%) females for each. No significant difference between the two studied groups regarding age and sex distribution. On the other hand,

biochemical analyses such as ALT and AST showed highly significant differences among the two studied groups ($P < 0.001$).

The median values of inflammatory biomarkers were significantly different between COVID-19 patients and both control groups, as shown in Table (1). In COVID-19 patients, LDH, Ferritin, CRP and D-Dimer were higher, LDH 285 IU/L [IQR 125 – 1026], Ferritin 177 ng/mL [IQR 9 – 703], CRP 34.5 mg/l [IQR 2 – 110] and D-Dimer 883 ng/mL [IQR 270 – 4400] than control group with p-values <0.001 for all comparisons. Leukocytes were lowest in COVID-19 cases compared to controls (3.45 G/l [IQR 1.2 – 6.1] vs. G/l [IQR 6.85–10.70], P <0.001) as well as lymph count in COVID-19 patients compared to controls (0.9 G/l [IQR 0.5 – 1.2] vs. 2.32 G/l [IQR 1.8 – 3.1], P <0.001). Moreover, highly significant differences in the levels of $CD8^+$ cells between the study groups ($P < 0.0001$) were observed. The $CD8^+$ cells were significantly higher in the healthy group. On the other hand, the $CD3^+$cells were insignificantly higher in the COVID-19 patients group compared to the healthy group.

The clinical characteristics of the studied COVID-19 patients revealed that they had long duration of symptoms before admission (4.6 ± 2.3) days. Regarding the presenting symptoms, dyspnea (79%), cough (100%), myalgia (64%), hemoptysis (22%), diarrhea (73%), loss of smell (52%), and anorexia (35%). The range of these people's serum virus loads was 1.345–5.283 $\log_{10}$ RNA copies/mL, with a median value of 2.678 $\log_{10}$ RNA copies/mL.

Correlation between CD3 and CD8 with different parameters in the COVID-19 patients

As demonstrated in Table (2), an analysis of the correlation between $CD3^+$, $CD8^+$ levels, and the other studied variables. Age, AST, ALT, Ferritin, CRP, Lymphocytes, and TLC did not significantly correlate with $CD3^+$, and $CD8^+$, while LDH was positively correlated significantly with $CD8^+$ (p-value = 0.042), and the D-Dimer value was negatively correlated significantly with CD3+ (p-value = 0.022) (Fig. 1).

Diagnostic Performance of CD3 and CD8 to discriminate COVID-19 patients from control group

Table (3) displays the predictive efficacy of the of $CD3^+$ and $CD8^+$ biomarkers and pneumonia severity in COVID-19 patients. Fig. (2) shows that the $CD3^+$ T cell count in peripheral blood can distinguish the two groups. $CD3^+$ T cells had the highest area under the curve (AUC = 0.541; [95% confidence interval {CI}, 0.410 – 0.672, P = 0.529]. A negative relationship was shown between $CD3^+$ for predicted cases and the control, and $CD8^+$ T cell counts in peripheral blood can distinguish the two groups. $CD8^+$ T cells had the highest AUC (0.747, 95% CI, 0.638 – 0.856, P < .001; sensitivity = 67.50 %, specificity = 62.50 %]. A

significant positive correlation was found between $CD8^+$ for predicted cases and the control. AUC is more than 0.5, which is an excellent indicator of prediction accuracy.

Survival analysis

Using the Kaplan-Meier survival curve for overall Survival (Fig. 3). The mean time of overall survival was 26.93 day and the mortality rate of our study individuals were 20%.

Point-of-care biomarkers associated with severity and mortality

Table (4) displays the association between all studied variables and disease severity. The clinical chemistry results showed that 18/40 (45%) of patients in the severe group and 22/40 (55%) of patients in the mild/moderate group. The severe group of patients showed leukopenia and lymphocytopenia with a statistically insignificant difference (P>0.05). Moreover, the $CD3^+$ and $CD8^+$ counts were not statistically significant differences. C-reactive protein greater than 40 mg/L in the severe group (P<0.0001) and younger age (P=0.003).

Table (5) displays the association between all studied variables and survivorship status. The results showed that 8/40 (20%) of patients in the non-survivor group and 32/40 (80%) of patients in the survivor group. The non-survivor and survivor patients showed insignificant differences regarding age, sex, ALT, AST, LDH, D. Dimer, ferritin, lymph, leukocyte count, $CD3^+$, and $CD8^+$ (P>0.05). The C-reactive protein was higher in non-survivor than survivor patients with a statistically significant difference (P=0.003).

According to Israelow *et al*., (2021), Zhou and Ye (2021) and Vardhana *et al*., (2022), cellular immune responses are crucial for viral clearance and illness severity. The research has documented the relationship between inflammatory biomarker readings and COVID-19 severity. The goal of this study was to examine the relationships between changes in a few immunological markers and various levels of COVID-19 clinical outcomes, severity, and mortality. In this study, the ratio between COVID-19 disease in males and females is the same, as well as the mean age of patients and controls were (44.8 ± 9.5, and 47.6 ± 8.97) respectively, with no statistically significant differences. Male patients often had higher background disease, in contrast to this study's finding. Additionally, there are differences in the baseline illness spectrum across the sexes (Statsenko *et al*., 2022). Male patients who were younger than 50 years old or had concomitant conditions were considerably more likely to develop disease and die than female patients. Patients with COVID-19 had substantially higher levels of biochemical traits like AST and ALT compared to controls (P <0.001). This result is consistent with Wang *et al*., (2021) who reported that based on the most recent data, AST and ALT levels in COVID-19 patients should

be taken into account as predictors of clinical outcomes.

Numerous studies have recently been conducted to evaluate the usefulness of different markers suggestive of severe COVID-19. LDH activity is one of these indicators, which is increased. According to several investigations, COVID-19-related lung damage, multi-organ failure, and severe respiratory failure all exhibit increased LDH activity (Fialek *et al*., 2022). In this study, LDH levels were significantly higher in COVID-19 patients than the control group (IQR) (285 vs. 171), with a P<0.001. A crucial biomarker that can assist in managing COVID-19 is the serum ferritin level (Kaushal, 2022). In this study, a highly significant change in Ferritin concentrations has been detected in relative COVID-19 patients than in control (P < 0.001), where the average concentration of ferritin attained 177µg/L vs 44.5 µg /L in control. CRP is a constant, severe-stage reactant that is elevated in inflammation or infection. It serves as a gauge of the severity of the COVID-19 sickness. CRP has benefited from this biomarker profile, which is often used for clinical medicine diagnoses (Stringer *et al*., 2021). In the current study, CRP titer was higher in COVID-19 patients than in control IQR (34.5 vs 3.5) with a highly significant difference (P < 0.001). Furthermore, peripheral microthrombi development and significantly elevated D-dimer levels are common in severely ill COVID-19 patients (Jin *et al*., 2020). The primary finding of the study was a difference in D-dimer levels between COVID-19 patients and control IQR (883 vs 218.5), with a P < 0.001.

Wagner *et al*., (2020) demonstrated the correlation between low lymphocyte count and disease severity in COVID-19 patients. According to this study's findings, there is a significantly significant (P 0.001) correlation between low lymphocyte and total leukocyte counts and COVID-19. Analysis using flow cytometry showed that the relationship between CD3+T cell count and COVID-19 was negligible. This study's findings are consistent with those of Aljabr *et al*., (2022), who claimed that COVID-19 infection did not disclose any significant differences in CD3+. On the other hand, the $CD8^+$ T cell count in COVID-19 patients was substantially higher than in the control group (IQR) (30.1 vs. 19.4) (P<0.001). In contrast to this study's findings, Marwan *et al*., (2020) found that CD8+ levels were significantly lower in COVID-19 patients.

All inflammatory biomarkers were analyzed in relation to other demographic and clinical information. While LDH was considerably positively connected with $CD8^+$ (P= 0.042) and the D-Dimer value was significantly negatively correlated with $CD3^+$ (P= 0.022), there was a negative association between $CD8^+$ and $CD3^+$ and other parameters (ALT, AST, Ferritin, Lymphocytes, CRP, TLC, and Age) (P >0.05). This outcome is consistent with the findings of Tyurin *et al*., (2022), who discovered that the iron,

LDH, and ferritin levels in various combinations adversely associated with the main lymphocyte subpopulations ($CD4^+$ and CD8+).

AUC was high for both the $CD3^+$ and $CD8^+$ in terms of their diagnostic performance. AUC is more than 0.5, which is an excellent indicator of prediction accuracy. The area under the curve for CD3+ T cells was the largest (AUC = 0.541; [95%, CI, 0.410-0.672, P = 0.529]). The $CD3^+$ for anticipated patients and the control were shown to be negatively correlated, and $CD8^+$ T cell counts in peripheral blood can discriminate between the two groups. The greatest AUC (0.747, 95% CI, 0.638-0.856, P .001; sensitivity = 67.50%, specificity = 62.50%) was found in $CD8^+$ T cells. Between $CD8^+$ for the predicted cases and the control, there was a very strong positive association. This contradicts Mei *et al*., (2020) findings, which may be due to the sample size of the current study.

The primary cause of mortality from severe viral pneumonia, according to research by Montazersaheb *et al*., (2022), Que *et al*. (2022) and Tirelli *et al*., (2023), is the excessive inflammatory response brought on by the virus infection (cytokine release syndrome). The disease advances as a result of the overactive inflammatory response, which also leads to organ failure and death. The findings from our investigation revealed a substantial correlation between age and CRP level and COVID-19 severity in terms of illness severity. Younger age was significantly associated with severe status than mild/ moderate (P= 0.003) and higher CRP value (P < 0.0001). Sever group showed leukopenia and lymphocytopenia, slightly lower (ferritin, D. dimer) and slightly higher (LDH, $CD3^+$), but this variation is statically insignificant (P>0.05). $CD8^+$ was closely similar in both severe and mild/moderate groups. Regarding the survivorship status, the data obtained from this study showed that the non-survivor and survivor patients showed insignificant differences regarding age, sex, ALT, AST, LDH, D.Dimer, ferritin, lymph, leukocyte count, $CD3^+$, and $CD8^+$ (P>0.05). With a statistically significant difference (P=0.003), the C-reactive protein was higher in non-survivor patients compared to survivors. This led to the study that we conducted, and based on the results discussed above, we deduced that there is a link between CRP and the severity and mortality of COVID-19 patients. The results of this study are consistent with those of Mousavi-Nasab *et al*., (2020) and Tan *et al*., (2020), who observed that CRP levels raised both at the start of the disease and as it progressed and were associated with mortality and severity.

The study's limitations were the relatively small number of patients included and the fact that only the levels of inflammatory markers such as ALT, AST, leukocytes, lymphocytes, ferritin, LDH, CRP, CD3+, and CD8+ were examined. There were no resources available to examine additional factors in

these individuals, such interferon-stimulated genes and cytokines (IL6 or IL8). Neither before the pandemic nor after it, these patients' inflammatory marker levels were accessible.

Conclusion

Among common studies, C-reactive protein has been thought to be the most reliable predictor of severity and death in COVID-19 patients. According to the current findings, COVID-19 patients' severity and death were substantially linked with elevated CRP levels. Additionally, prognosis, outcome, and mortality may be predicted using the dynamic assessments of $CD3^+$, $CD8^+$, LDH, ferritin, AST, ALT, and lymphocytes in COVID-19 patients. These inflammatory biomarkers and clinical traits require extensive additional study.

Conclusion: $CD8^+$ T cells can be for diagnosing COVID-19 cases. CRP levels rose both at the beginning and during the duration of COVID-19 disease and were associated with mortality and disease severity.

SUMMARY

Background and objective: Several inflammatory biomarkers associated to COVID-19 mortality and severity. A significant drop in lymphocyte counts is seen in a large number of COVID-19 patients, depending on their lymphocytopenia status, particularly their T-cell numbers, infected individuals experience varying outcomes. We aimed to assess the CD3+ and CD8+ counts as well as other inflammatory biomarkers for the diagnosis of COVID-19, including ferritin, lactate dehydrogenase (LDH), and C-reactive protein (CRP). Investigating their relationship with COVID-19 mortality and severity as well.

Methodology: This case-control prospective study included 80 individuals, 40 unvaccinated COVID-19 patients, and 40 healthy controls. Different inflammatory biomarkers such as (CRP, ferritin, LDH, $CD3^+$, and $CD8^+$), as well as other biochemical tests such as (AST, ALT, lymphocytes, and leucocyte counts) were measured in blood samples.

Results: LDH, Ferritin, CRP, and D-Dimer were among the inflammatory biomarkers, along with ALT and AST, that demonstrated highly significant differences between the two study groups ($P < 0.001$). When compared to controls, COVID-19 subjects had lower levels of leukocytes and lymphocytes ($P < 0.001$). The healthy group had a much higher level of CD8+ cells. LDH and CD8+ showed a strong positive association ($P = 0.042$), but the D-Dimer value showed a significant negative correlation ($P = 0.022$) with CD3+. CD8+ T cells demonstrated a sensitivity and specificity of 67.50% and 62.50%, respectively, for the diagnosis of COVID-19. Patients with severe COVID-19 disease and non-survivors had considerably higher CRP

levels.

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Table (1): Comparison between the two studied groups according to patients' characteristics.

	Patients (n = 40)	Control (n = 40)	p
Sex			
Male	20 (50%)	20 (50%)	1.000
Female	20 (50%)	20 (50%)	
Age (/years)			
Mean ± SD.	44.8 ± 9.5	47.6 ± 8.97	0.180
Median (Min. – Max.)	44 (32 – 60)	49 (33 – 60)	
ALT			
Mean ± SD.	46.5 ± 14.6	31.5 ± 9.7	<0.001*
Median (Min. – Max.)	47.5 (10 – 76)	30 (15 – 49)	
AST			
Mean ± SD.	42.6 ± 19.9	29.8 ± 8.5	<0.001*
Median (Min. – Max.)	41.5 (14 – 116)	29.5 (15 – 44)	
LDH			
Mean ± SD.	319.6 ± 210.3	170.5 ± 39.1	<0.001*
Median (Min. – Max.)	285 (125 – 1026)	171 (120 – 240)	
Ferritin			
Mean ± SD.	235.5 ± 208.1	47.6 ± 34.5	<0.001*
Median (Min. – Max.)	177 (9 – 703)	44.5 (5 – 128)	
CRP			
Mean ± SD.	40.7 ± 27.7	4.1 ± 2.57	<0.001*
Median (Min. – Max.)	34.5 (2 – 110)	3.5 (1 – 10)	
D-Dimer			
Mean ± SD.	1178.4 ± 963.4	242.2 ± 96.5	<0.001*
Median (Min. – Max.)	883 (270 – 4400)	218.5 (125 – 440)	
Lymph ($\times 10^3$)			
Mean ± SD.	0.84 ± 0.19	2.34 ± 0.38	<0.001*
Median (Min. – Max.)	0.9 (0.5 – 1.2)	2.32 (1.8 – 3.1)	
TLC ($\times 10^3$)			
Mean ± SD.	3.63 ± 1.16	6.51 ± 1.75	<0.001*
Median (Min. – Max.)	3.45 (1.2 – 6.1)	6.27 (4.4 – 10.4)	
CD3			
Mean ± SD.	65.9 ± 11.72	67.31 ± 14.92	0.631
Median (Min. – Max.)	66.2 (47.7 – 88.8)	70.1 (45.1 – 89.7)	
CD8			
Mean ± SD.	33.5 ± 11.1	22.6 ± 12.0	<0.001*
Median (Min. – Max.)	30.1 (18.2 – 57.9)	19.4 (1.8 – 52.3)	

SD: **Standard deviation** p: p-value for comparing the two studied groups

*: Statistically significant at $p \leq 0.05$

Table (2): Correlation between CD3 and CD8 with different parameters in COVID-19 patients.

Variables	CD3		CD8	
	r	p	r_s	p
Age (/years)	-0.135	0.407	0.208	0.198
ALT	-0.052	0.748	-0.078	0.631
AST	-0.080	0.624	0.277	0.084
LDH	-0.047	0.774	0.323	**0.042***
Ferritin	-0.182	0.261	0.089	0.584
CRP	-0.020	0.902	0.039	0.812
D-Dimer	-0.362	**0.022***	0.156	0.337
TLC ($\times 10^3$)	-0.239	0.137	0.042	0.797
Lymph ($\times 10^3$)	0.011	0.946	0.261	0.103

r: Pearson coefficient r_s: Spearman coefficient *: Statistically significant at $p \leq 0.05$

Table (3): Diagnostic performance for $CD3^+$ and $CD8^+$ to discriminate COVID-19 patients from control.

	AUC	p	95% CI	Cut off	Sensitivity	Specificity	PPV	NPV
CD3	0.541	0.529	0.410 – 0.672					
CD8	0.747	<0.001*	0.638 – 0.856	>27	67.50	62.50	64.3	65.8

AUC: Area Under a Curve p-value: Probability value CI: Confidence Intervals
NPV: Negative predictive value PPV: Positive predictive value
*: Statistically significant at $p \leq 0.05$

Table (4): Demographic data and laboratory biomarker-related variables by COVID severity classification.

	Severe (n = 18)	Mild/Moderate (n = 22)	p
Sex			
Male	8 (44.4%)	12 (54.5%)	0.525
Female	10 (55.6%)	10 (45.5%)	
Age (/years)			
Mean ± SD.	40.11± 7.77	48.54 ± 8.94	0.003*
Median (Min. – Max.)	37 (32 -54)	50.5 (34 - 60)	
ALT			
Mean ± SD.	45.55 ± 9.92	±17.47.18	0.724
Median (Min. – Max.)	49 (29 – 62)	66 (10 - 76)	
AST			
Mean ± SD.	46.11 ± 26.39	39.64 ± 10.65	0.299
Median (Min. – Max.)	36 (24 -116)	40 (14 - 55)	
LDH			
Mean ± SD.	330.11 ± 257.52	311± 154.8	0.773
Median (Min. – Max.)	280 (125- 1026)	290 (158–767)	
Ferritin			
Mean ± SD.	220.88 ± 210.44	247.36 ± 200.57	0.687
Median (Min. – Max.)	150 (12 – 626)	220 (9 – 703)	
CRP			
Mean ± SD.	63.66 ± 23.20	21.90 ± 11.43	P < 0.0001 *
Median (Min. – Max.)	50 (42 – 110)	27 (2 -33)	

Table (4):Cont'

D-Dimer			
Mean ± SD.	941 ± 728.57	1372,05 ± 1061.72	0.152
Median (Min. – Max.)	600 (294 - 2340)	920 (270 - 4400)	
Lymph ($\times 10^3$)			
Mean ± SD.	0.82 ± 0.19	0.85 ± 0.18	0.612
Median (Min. – Max.)	0.8 (0.5 – 1.2)	0.9 (0.5 -1.1)	
TLC ($\times 10^3$)			
Mean ± SD.	3.51 ± 0.98	2 ± 1.25 3,7	0.565
Median (Min. – Max.)	3.2 (2.7 - 6.1)	4.3 (1.2 -5.1)	
CD3			
Mean ± SD.	67.07 ± 10.87	64.88± 12.02	0.553
Median (Min. – Max.)	66.6 (48.3 – 84.6)	66.1 (47.7 – 88.8)	
CD8			
Mean ± SD.	33.52 ± 12.05	33.49 ± 9.91	0.993
Median (Min. – Max.)	30 (19 – 57.9)	30.15 (18.2 -55.4)	

SD: Standard deviation p: p-value for comparing the two studied groups *: Statistically significant at $p \leq 0.05$

Table (5): Demographic, clinical and laboratory profiles by survivorship status

	Non-survivor (n=8)	Survivor (n= 32)	p
Sex			
Male	4 (50%)	16 (50%)	1.00
Female	4 (50%)	16 (50%)	
Age (/years)			
Mean ± SD.	44.13 ± 9.74	44.9 ± 9.33	0.837
Median (Min. – Max.)	44 (32 – 60)	44 (32- 60)	
ALT			
Mean ± SD.	48.38 ± 7.95	45.97 ± 15.62	0.677
Median (Min. – Max.)	49.5 (34 – 62)	46 (10 -76)	
AST			
Mean ± SD.	50.75 ± 25.79	40.5 ± 17.19	0.182
Median (Min. – Max.)	44 (29 -116)	39 (14 -116)	
LDH			
Mean ± SD.	346.5 ± 265.39	312.88 ± 189.89	0.682
Median (Min. – Max.)	270 (125 – 1026)	290 (125 -1026)	
Ferritin			
Mean ± SD.	174 ± 164.28	250.81 ± 211.79	0.346
Median (Min. – Max.)	139 (12 – 564)	189.5 (9 - 703)	

Table (5): Cant'

CRP			
Mean ± SD.	65.25 ± 24.47	34.56 ± 24.37	0.003*
Median (Min. – Max.)	57.5 (35 -110)	31 (2- 110)	
D-Dimer			
Mean ± SD.	1486.25 ± 1319.23	1101.44 ± 816.35	0.302
Median (Min. – Max.)	745 (294 – 4400)	883 (270 – 4400)	
Lymph ($\times 10^3$)			
Mean ± SD.	0.84 ± 0.20	0.84 ± 0.18	1.00
Median (Min. – Max.)	0.9 (0.5 – 1.1)	0.9 (0.5 -1.2)	
TLC ($\times 10^3$)			
Mean ± SD.	3.73 ± 1.05	3.6 ± 1.16	0.775
Median (Min. – Max.)	3.25 (2.7 - 6.1)	3.6 (1.2 -6.1)	
CD3			
Mean ± SD.	67.89 ± 11.79	65.36 ± 11.46	0.582
Median (Min. – Max.)	69.25 (49.3 – 84.6)	66.2 (47.7 – 88.8)	
CD8			
Mean ± SD.	34.88 ± 10.17	33.16 ± 11.07	0.692
Median (Min. – Max.)	31.4 (23.3 – 57.1)	29.8 (18.2 – 57.9)	

SD: Standard deviation p: p-value for comparing the two studied groups *: Statistically significant at $p \leq 0.05$

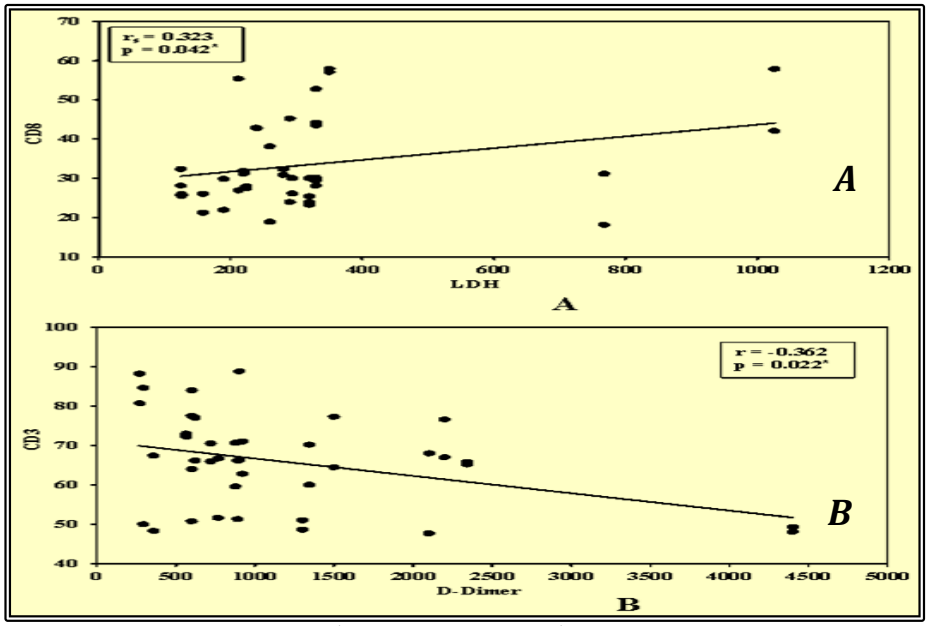

Fig. (1): Correlation of A: $CD8^+$ with LDH; B: $CD3^+$with D-Dimer in COVID-19 patients.

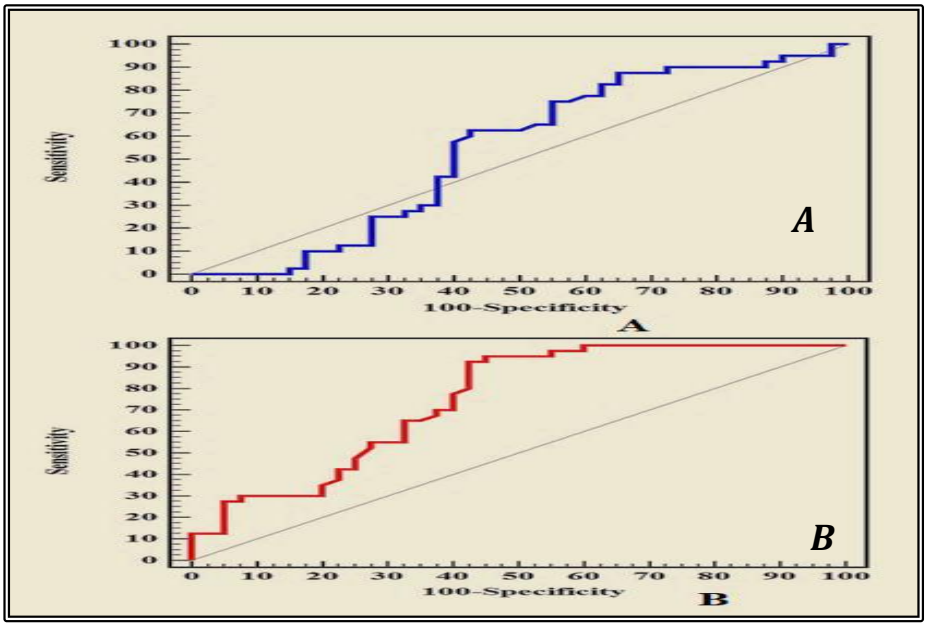

Fig.(2): ROC curve for A: CD3; B: CD8 to discriminate COVID-19 patients from control.

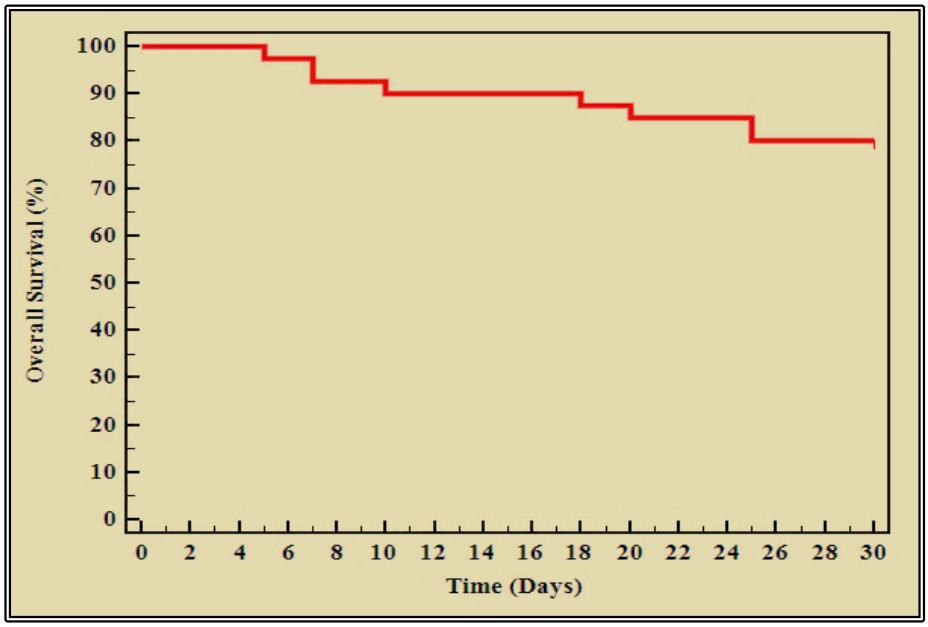

Fig. (3): Kaplan-Meier survival curve for overall survival.