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Research Article

Effect of Covid-19 Infection on Haematological and Immune Antibodies Titer among Infected Patients in the Maitega Isolation Centers, Tripoli, Libya

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Abstract

Background: Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV- 2) has become a global pandemic causing significant mortality and morbidity.

Objectives: This study aimed to examine the alterations in hematological parameters and immunoglobulin levels in COVID-19 patients and determine any potential correlation between the changes in specific hematological variables and the severity of COVID-19 infection among infected patients in the Maitega Isolation Centers, Tripoli, Libya.

Subjects and Methods: This cross-sectional study was conducted between September 2021 and March 2022. Among 50 infected patients (26 males & 24 females) and 50 healthy individuals (23 males& 27 females) without any chronic disease or respiratory symptoms were recruited for the control group. Structured questionnaires were used to obtain data. 5 ml of venous blood was collected from each participant for estimation of complete blood count (CBC), serum COVID-19 IgM and COVID-19 IgG, Ferritin, C Reactive Protein, and D-dimer using CBC PKL analyzer and The Fluorecare instrument.

Results: The results showed that patients with COVID-19 had a significant ($P<0.05$) decrease in lymphocytes count and RBCs count at first day of the infection to 7 days, and after 14 days of infection, respectively compared with the healthy individuals, non-statistically significant ($P>0.05$) changes were observed in hemoglobin concentration, WBCs, granulocytes, and platelets counts compared with the healthy individuals. The patients with COVID-19 had a significant ($P<0.0001$) increase in IgM levels during 1-7 days of infection compared with healthy individuals, respectively compared with the healthy individuals. Also, IgG levels were showed a gradual significantly ($P<0.0001$) increase during COVID-19 Virus Infection among COVID-19 patients after 14 days compared with the controls. additionally, coronavirus infection caused a significant ($P<0.0001$) increase in D-dimer, CRP, and Ferritin levels compared with the healthy control individuals,

Conclusion: It can be concluded that coronavirus infection caused a significant decrease in Lymphocytes count and an increase in IgM, IgG, D-dimer, CRP, and Ferritin levels at different periods compared to the controls. Further studies are needed to confirm these results. COVID-19 specific immunoglobulins and some inflammatory factors in COVID-19 patients. These changes in IgM, IgG, D-dimer, CRP, and Ferritin levels during COVID-19 Virus Infection among COVID-19 patients may help clinicians to better understand COVID-19 and provide more clinical treatment options.

Key Words: coronavirus disease 2019, hematological parameters, immune antibodies titer, d-dimer, crp

1.Introduction

The emergence of the coronavirus disease 2019 (COVID-19) in Wuhan, China marked the beginning of a highly transmissible virus that rapidly spread across the world, leading to a global pandemic (1). This virus, officially known as severe acute respiratory syndrome coronavirus 2 (SARS-

CoV-2), has posed a significant health challenge due to its high mortality rate and rapid spread (2). As of November 2022, the World Health Organization (WHO) has reported over (637.737.550) confirmed cases of COVID-19 globally, with 6.611.874 recorded deaths (3). Coronaviruses are a family of large viruses within the Corona viridae family (4). These viruses have a single-stranded RNA genome (5) and are surrounded by a helical capsid and a lipoprotein envelope that contains several spicules of glycoprotein, giving the virus a crown-like appearance (6). The SARS-CoV-2 virus can cause severe clinical complications, particularly in elderly patients and those with underlying comorbidities such as diabetes (7), cardio and cerebrovascular diseases (8), obesity, cancer, and pathologies of the digestive, endocrine, nervous, and respiratory systems (9).

SARS-CoV-2, a member of the Coronaviridae family, is a type of coronavirus that has been identified in avian hosts as well as several other species (10). Effective management of COVID-19 infection requires early diagnosis, appropriate treatment, and future control measures to limit the spread of the virus. Result of Laboratory parameters play a crucial role in confirming COVID-19 diagnosis and can help discriminate between severe and non-severe cases, as well as those at high or low risk of mortality (11).

The role of white blood cells, hemoglobin, and platelets in the manifestation of signs and symptoms of coronavirus disease 2019 (COVID-19) has been documented (12). Serological testing, which detects antibodies, is another common laboratory diagnostic tool that can aid in the diagnosis of the disease (13). The detection of IgM and IgG antibodies is particularly useful for serological diagnosis and for understanding the prevalence of the infection in the population, as well as for implementing control measures (14, 15). Antibody testing for SARS-CoV-2 is rapid and sensitive, making it a valuable adjunct for the diagnosis of COVID-19 (15).

During the early stages of (COVID-19) 2019, inflammatory biomarkers such as C-reactive protein (CRP) and Ferritin are notably elevated. Therefore, it is important to screen for inflammation-associated biomarkers and coagulation tests including Ferritin, C-reactive protein, and D-dimer to help in the diagnosis of the disease (16). Recent clinical studies have suggested that CRP and other factors like Ferritin, Coagulation Factors and Inflammatory indexes may be associated with the severity of COVID-19 (17). Many studies found that C-reactive protein is a reliable diagnostic tool for predicting the severity of coronavirus disease 2019 in its early stages. In summary, the available literature suggests that CRP levels could be an indicator of disease severity during the early stage of COVID-19 (18).

2. Objectives:

This study aimed to examine the alterations in hematological parameters and immunoglobulin levels in COVID-19 patients and determine any potential correlation between the changes in specific hematological variables and the severity of COVID-19 infection among infected patients in the Maitega Isolation Centers, Tripoli, Libya

3. Subjects and Methods

3.1 Study Type and Design

This study utilized a descriptive cross-sectional observational design.

3.2. Study Population:

The study population included both male and female COVID-19 infected patients from different age groups. Healthy individuals were also included as a control group for comparison purposes.

3.3. Sample Size:

In this study, a total of 150 blood samples were collected from individuals infected with COVID-19, with 100 samples representing cases in the study group. Among the study group, 50 samples were collected within the first 7 days of infection, while another 50 were collected after 14 days. Furthermore, a control group consisting of 50 healthy individuals matched for age and gender was included for comparison purposes. Out of the 50 COVID-19 patients, 26 (52%) were male and 24 (48%) were female, while the control group consisted of 23 (46%) males and 27 (54%) females (Table. 1).

Groups Gender	Control group		Covid-19 patients	
	Frequency	Percent (%)	Frequency	Percent (%)
Males	23	46%	26	52%
Females	27	54%	24	48%

Table. 1: Distribution of gender among control group and Covid -19 patients

3.4. Ethical Considerations

This study was conducted with ethical approval from the ethical committee of the Libyan Academy of Science and the Maitega Isolation Centers, which was used as a point for sample collection. Informed consent was obtained from all participants and their families before they were included in the study, ensuring compliance with ethical standards.

3.5. Sample Collection:

Each participant provided a 5 ml venous blood sample in an EDTA tube for complete blood count (CBC) analysis. An additional 3 ml of blood was collected in a plain tube for measurement of ferritin, D-dimer, C-reactive protein (CRP), and Covid-19 IgM, and IgG.

3.6. Hematological Study:

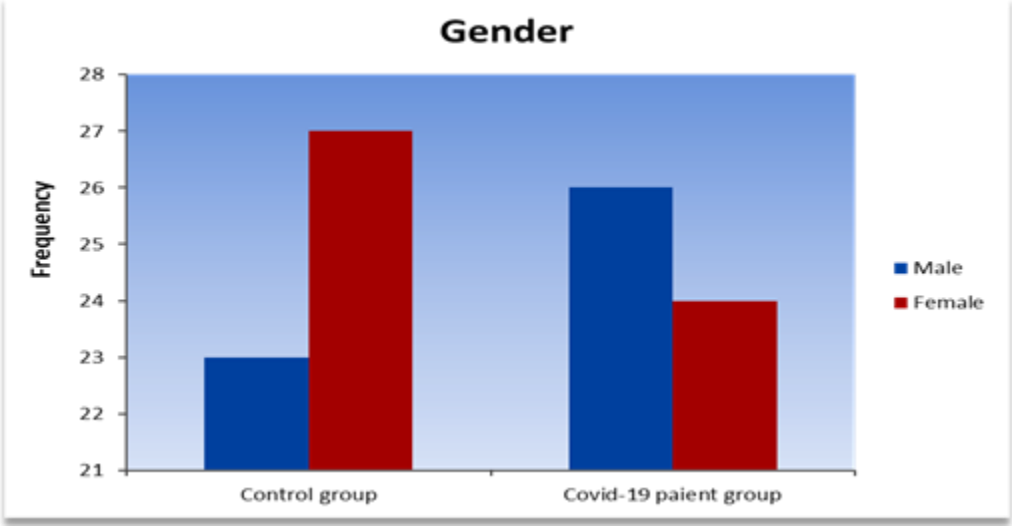
The blood samples for CBC were analyzed using an automated blood analyzer (PKL), following the manufacturer's instructions. Further investigations were conducted for ferritin, D-dimer, CRP, and Covid-19, IgM & Covid-19IgG using manual kit and automatic measurement methods by Flurocare.

3.7. Statistical Analysis:

The normal continuous variables were presented by means and standard errors (SE), the non-normal continuous variables were presented by medians and interquartile range (IQR), categorical variables were presented as counts and percentages. The statistical tools used for analyzing the data is SPSS 27 and Graph Pad Prism 8. The Shapiro-Wilk test is used to assess the normality of the distribution of the continuous variables. The statistical significance of the difference between groups were evaluated by t-test and ANOVA for normal variables, whereas for non-normal continuous variables; Kruskall-Wallis H test is used for comparing more than two independent samples, Mann-Whitney U test is used for comparing two independent samples, and Willcoxon signed rank test is used for comparing two related samples. Chi-square statistical analysis was performed to determine significant values. Pearson correlation coefficient is used to evaluate the relations between continuous variables and spearman rank correlation is used to evaluate the relations between categorical variables. A P-value of less than 0.05 is considered statistically significant.

4. Results

This study included 150 blood sample from patients infected with COVID-19, 100 of them represented cases (study group): 50 during the first 7 day of infection ,50 repeated test after 14 day, and (50) represented healthy age and gender matched subjects were included as compare group (control group). Out 50 patients with COVID-19, 26 (52%) males and 24(48%) females, were the (control group), 23 (46%) males and 27(54%) females (Figure.1).



The mean ages of the patients was 30% years (40-50) years; while the control group mean age was 24%(60-70) years (Table.2 & Figure.2).

Groups Age Groups	Control group (n=50		COVID-19 patients' group (n=50)	
	Frequency	Percent (%)	Frequency	Percent (%)
30 - 40	10	20	1	2
40 - 50	9	18	15	30
50 - 60	9	18	7	14
60 - 70	12	24	14	28
70 - 80	5	10	6	12
80 - 90	5	10	6	12
> 90	0	0	1	2

Table.2: Distribution of age among control group and Covid-19 patients.

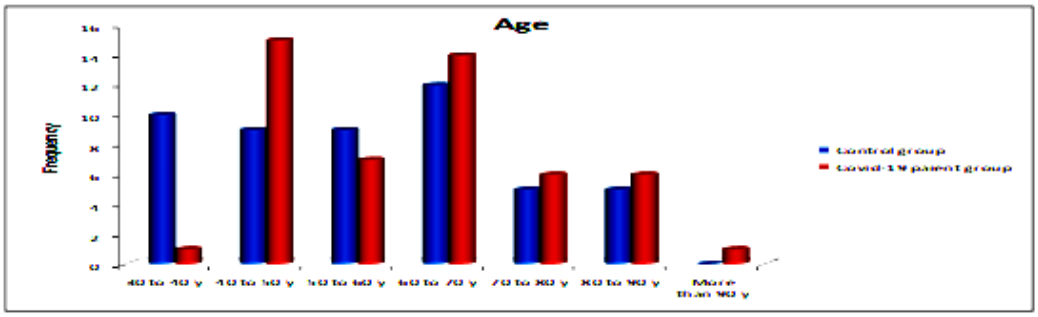


Figure.2: Descriptive of control group and patients according to ages

Table.3 and Figure.3 Shows that (60%) of control group were vaccinated with two doses while (48%) of the patients were, (20%) of control group were vaccinated with one dose while (18%) of the patients were, and (20%) of control group were not vaccinated while (34%) of the patients were non vaccinated.

Groups	Control group		COVID-19 patients	
Vaccinations	Frequency	(%)	Frequency	(%)
unvaccinated	10	20%	17	34%
single dose	10	20%	8	16%
2 doses	30	60%	25	50%
Total	50	100%	50	100%

Table 3: Disripution of vaccinated items of control group and patients

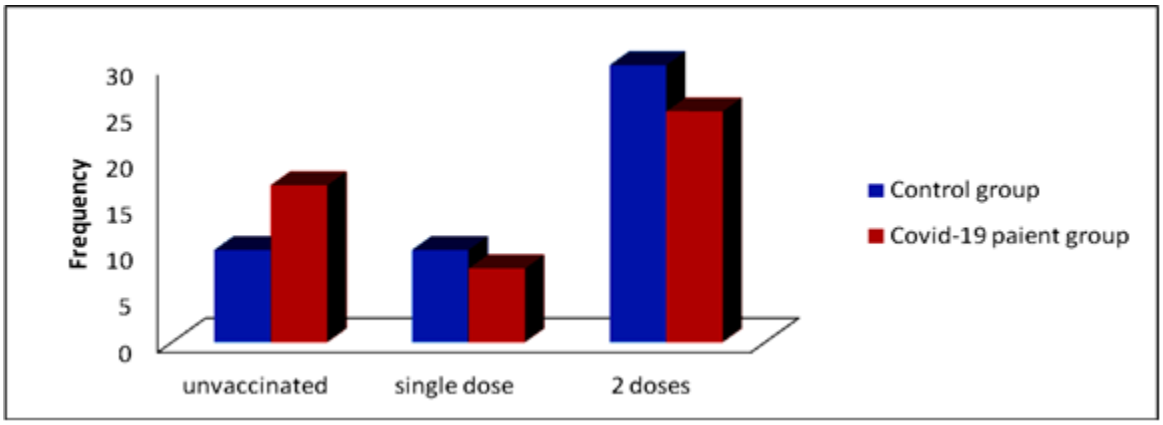


Figure 3: Distribution of control group and patients according to vaccination

Table.4 shows that the IgG means for control group and the patients after 7 days and then after 14 days 0.4004±0.08 and the IgG means for control group and the patients after 7 days and then after 14 days are 0.862±0.32 and 21.49±4.05, respectively (Figures. 4-6).

Groups Parameters	Control	7days	14 days	F	P Value
	Mean±SE	Mean±SE	Mean±SE		
Serum IgM (AU/mL)	0.00±0.00	12.50±2.68	0.032±0.01	22.07	<0.0001
Serum IgG (AU/mL)	0.4004±0.08	0.862±0.32	21.49±4.05	26.10	<0.0001

Table.4: Serum IgM and IgG levels in control and at 7 and 14 days of COVID-19 Virus Infection

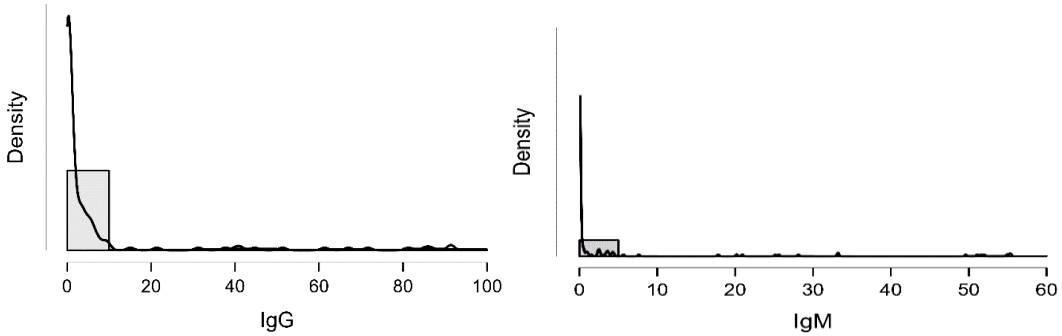


Figure 4: shows the densities of IgG and IgM which is clearly not normally distributed

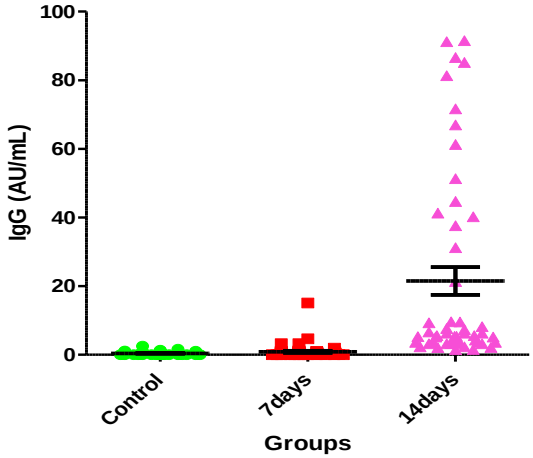


Figure 5: Medians (IQR) of IgG count in control group and the patients group during covid-19 virus infection

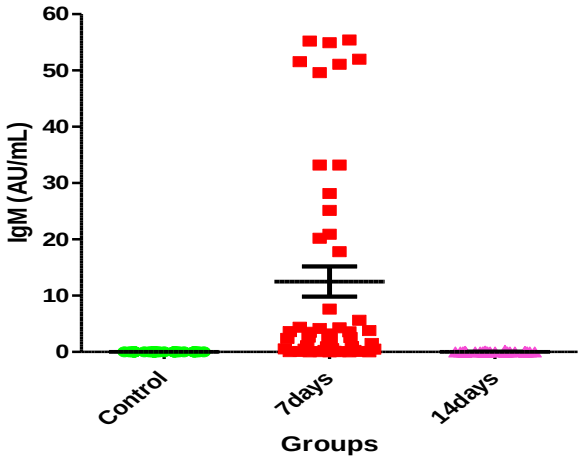


Figure 6: Medians (IQR) of IgM count in control group and the patients group during COVID-19 virus infection

In Table.5, Kolmogorov-Smirnov Z test shows that the IgG of the two independent groups (control group, patients through the first 7 days group) are similar in the shape (have the same distribution) since p-value > α, consequently; Mann-Whitney U test shows that the distributions of the two groups are equal and then there is no significant difference between the medians of the IgG of the two groups. Again, Kolmogorov-Smirnov Z test shows that the IgG of the two independent groups (control group, patients after 14 days group) differs in shape since p-value < α, and then according to Mann-Whitney U test the mean ranks of the two groups differ significantly. Similarly, for the IgM; Kolmogorov-Smirnov Z test shows that the IgM of the two independent groups (control group, patients through the first 7 days group) and again of the two independent groups (control and patients after 14 days) differs in shapes since p-values < α, and then according to Mann-Whitney U test the there is a significant difference between mean ranks of each pair of groups.

		Control			
	Group	Kolmogorov-Smirnov Z		Mann-Whitney U	
parameters		Statistic	p-value	Statistic	p-value
IgG	0-7 days	1.000	0.270	1125.500	0.391
	14 days	4.800	<0.0001	8.000	<0.0001
IgM	0-7 days	4.700	<0.0001	75.000	<0.0001
	14 days	2.900	<0.0001	525.000	<0.0001

Table 5: Mann-Whitney test for the significance of the differences in ranks of IgG and IgM between controls and patients

From Wilcoxon signed rank test for the paired samples (patients through the first 7 days and patients after 14 days), it is clear that there are statistically significant differences between the ranks of the two groups for IgG and IgM (Table.6)

		N	Mean Rank	Wilcoxon Z	p-value
IgG14 – IgG7	Negative Ranks	3	15.00	-5.720	<0.0001
	Positive Ranks	47	26.17		
	Ties	0			
IgM14 - IgM7	Negative Ranks	46	24.35	-5.884	<0.0001
	Positive Ranks	1	8.00		
	Ties	3			

Table.6: Wilcoxon signed rank test for the significancy of differences in ranks of IgG and IgM of the patients group during covid-19 virus infection

The IgG mean for non-vaccinated is (9.888±3.477) with median (0.568) and IQR (5.4515), and the IgG mean for one-dose vaccinated is (7.975±3.499) with median (0.861) and IQR (5.2525), whereas the IgG mean for two-dose vaccinated is (6.143±1.933) with median (0.886) and IQR (3.1548). And the IgM mean for non-vaccinated is (5.376±2.154) with median (0.0135) and IQR (0.522), and for one-dose vaccination is (4.059±2.133) with median (0.0095) and IQR (2.082) (Table.7).

		Mean	Std. Error	Std. Deviation	Min	Max	Median	IQR
IgG	Not	9.888	3.477	23.063	0.000	91.524	0.568	5.4515
	1-dosage	7.975	3.499	18.516	0.020	41.325	0.861	5.2525
	2-dosages	6.143	1.933	17.072	0.000	86.654	0.886	3.1548

IgM	Not	5.376	2.154	14.287	0.000	54.910	0.0135	0.5220
	1-dosage	4.059	2.133	11.285	0.000	55.210	0.0095	2.0823
	2-dosages	3.710	1.306	11.530	0.000	55.400	0.000	0.1398

Table.7: Descriptives of IgG and IgM according to number. of dosages vaccination

Table.8 shows that there are no significant differences In IgG and IgM according to the levels of vaccination and vaccination has a weak effect upon IgG and IgM. For the non-vaccinated individuals, as like as 1-dose vaccinated and 2-dose vaccinated individuals; Kolmogorov-Smirnov Z test shows that the IgG of the two independent groups (control group, patients through the first 7 days group) .there is no significant difference between the distributions of the two groups) since p-value > α, consequently; Mann-Whitney U test shows that the distributions of the two groups are equal and then there is no significant difference between the medians of the IgG of the two groups. But for the two independent groups (control group and the patients after 14 days group) are differ in shape (there is significant difference between the distributions of the two groups) for non-vaccinated, 1-dose vaccinated and 2-dose vaccinated individuals since p-values < α, consequently; Mann-Whitney U test shows that the distributions of the two groups are not equal; i.e., there is a significant difference between the two groups in mean ranks since p-values < α.

	Vaccinated	N	Mean Rank	Kruskal-Wallis H	p-value
IgG	NonVaccinated	44	75.92	0.302	0.860
	1_Dos	28	79.16		
	2_Dos	78	73.95		
IgM	Non	44	78.17	0.644	0.725
	1_Dos	28	78.45		
	2_Dos	78	72.94		

Table 8: Kruskal-Wallis signed rank test for the significancy of differences in ranks of IgG and IgM of the patients group during covid-19 virus infection

For the non-vaccinated individuals, as like as 1-dose vaccinated and 2-dose vaccinated individuals; Kolmogorov-Smirnov Z test shows that the IgG of the two independent groups (control group, patients through the first 7 days group) .there is no significant difference between the distributions of the two groups) since p-value > α, consequently; Mann-Whitney U test shows that the distributions of the two groups are equal and then there is no significant difference between the medians of the IgG of the two groups. But for the two independent groups (control group and the patients after 14 days group) are differ in shape (there is significant difference between the distributions of the two groups) for non-vaccinated, 1-dose vaccinated and 2-dose vaccinated individuals since p-values < α, consequently; Mann-Whitney U test shows that the distributions of the two groups are not equal; i.e., there is a significant difference between the two groups in mean ranks since p-values < α (Table.9).

		Group	N	Mean Rank	Kolmogorov-Smirnov Z	p-value	Mann-Whitney U	p-value
IgG	Non vaccinated	Control	10	13.40	0.768	0.598	79.000	0.763
		0-7 days	17	14.35				
		Control	10	5.50	2.509	<0.0001	0.000	<0.0001
		14 days	17	19.00				
	1-dose vaccinated	Control	10	9.20	0.846	0.471	37.000	0.513
		0-7 days	17	10.89				
		Control	10	5.50	2.176	<0.001	0.000	<0.001
		14 days	17	15.00				
	2-dose vaccinated	Control	30	26.38	0.700	0.711	326.500	0.560
		0-7 days	24	28.90				
		Control	30	15.67	3.408	<0.0001	5.000	<0.0001

Table 9: The significancy of differences between control group and patients group in IgG according to vaccination levels

From Wilcoxon Z test for related samples there is a significant difference between the level of IgG of the patients through the first 7 days and the level of IgG of the patients after 14 days in favor of the last for each of the levels of vaccination, since p-values < α as it shown in Table .10

IgG14 – IgG7		N	Mean Rank	Wilcoxon Z	p-value
Not vaccinated	Negative Ranks	1	12.00	-3.053	0.002
	Positive Ranks	16	8.81		
	Ties	0			
1-dose vaccinated	Negative Ranks	0	0.00	-2.666	0.008
	Positive Ranks	9	5.00		
	Ties	0			
2-dose vaccinated	Negative Ranks	2	3.50	-4.086	<0.0001
	Positive Ranks	22	13.32		
	Ties	0			

Table 10: The significancy of differences between patients group through the first 7 days and after 14 days in IgG according to vaccination levels

At table .11 Kolmogorov-Smirnov Z test shows that there is a difference between the distributions of the two independent groups (control and patients through the first 7 days) for the three levels of vaccination since p-values < α, and then by Mann-Whitney U test there is a significant difference between the mean ranks of the two groups since p-values < α. Whereas for the two independent groups (control and patients after 14 days) Kolmogorov-Smirnov Z test shows that there is no difference between the distributions of the two groups for the non-vaccinated and 1-dose vaccinated individuals and then by Mann-Whitney U test there is a significant difference between the medians since p-value < α, but for the 2-dose vaccinated individuals there is a significant difference between the distributions of the two groups by Kolmogorov-Smirnov Z test since p-value < α, and by Mann-Whitney U test there is a significant difference between mean ranks of the two groups.

Similarly, there is a significant difference between the level of IgM of the patients through the first 7 days and the level of IgM of the patients after 14 days in favor of the first for each of the levels of vaccination, since p-values < α as it shown in table.11.

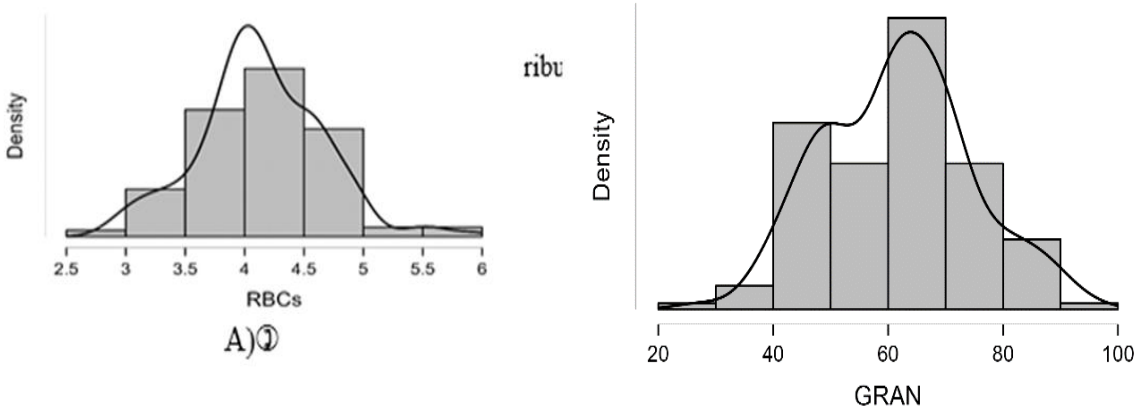
		Group	N	Mean Rank	Kolmogorov Smirnov Z	p-value	Mann-Whitney U	p-value
IgM	Non vaccinated	control	10	6.50	2.214	<0.001	10.000	<0.0001
		0-7 days	9	18.41				
		control	10	9.50	1.328	0.059	40.000	0.007
		14 days	9	16.65				
	1-dose vaccinated	control	10	5.50	2.176	<0.001	0.000	<0.0001
		0-7 days	9	15.00				
		control	10	7.00	1.451	0.030	15.000	0.003
		14 days	9	13.33				
	2-dose vaccinated	control	30	16.00	3.499	<0.0001	15.000	<0.0001
		0-7 days	24	41.88				
		control	30	20.50	2.130	<0.001	150.000	<0.0001
		14 days	24	36.25				

Table 11: The significance of differences between controls and patients in IgM according to vaccination levels

Shapiro-Wilk test table.12 shows that RBC and Granulocytes are normally distributed such that p-value > 0.05, and the others are not distributed normally since p-value < α. It can be seen clearly in figure.7 that the probability densities of RBC and GRAN are near to norma while the others are much differ of the normal distribution.

Parameters / Test	WBC	RBC	HGB	PLT	Lymphocytes	Granulocytes	D-dimer	CRP	FerrItin
Shapiro-Wilk	0.676	0.984	0.929	0.955	0.375	0.990	0.589	0.498	0.424
P-value	< 0.001	0.075	< 0.001	< 0.001	< 0.001	0.338	< 0.001	< 0.001	< 0.001

Table12: Shapiro-Wilk test for normality of the distributions of the parameter



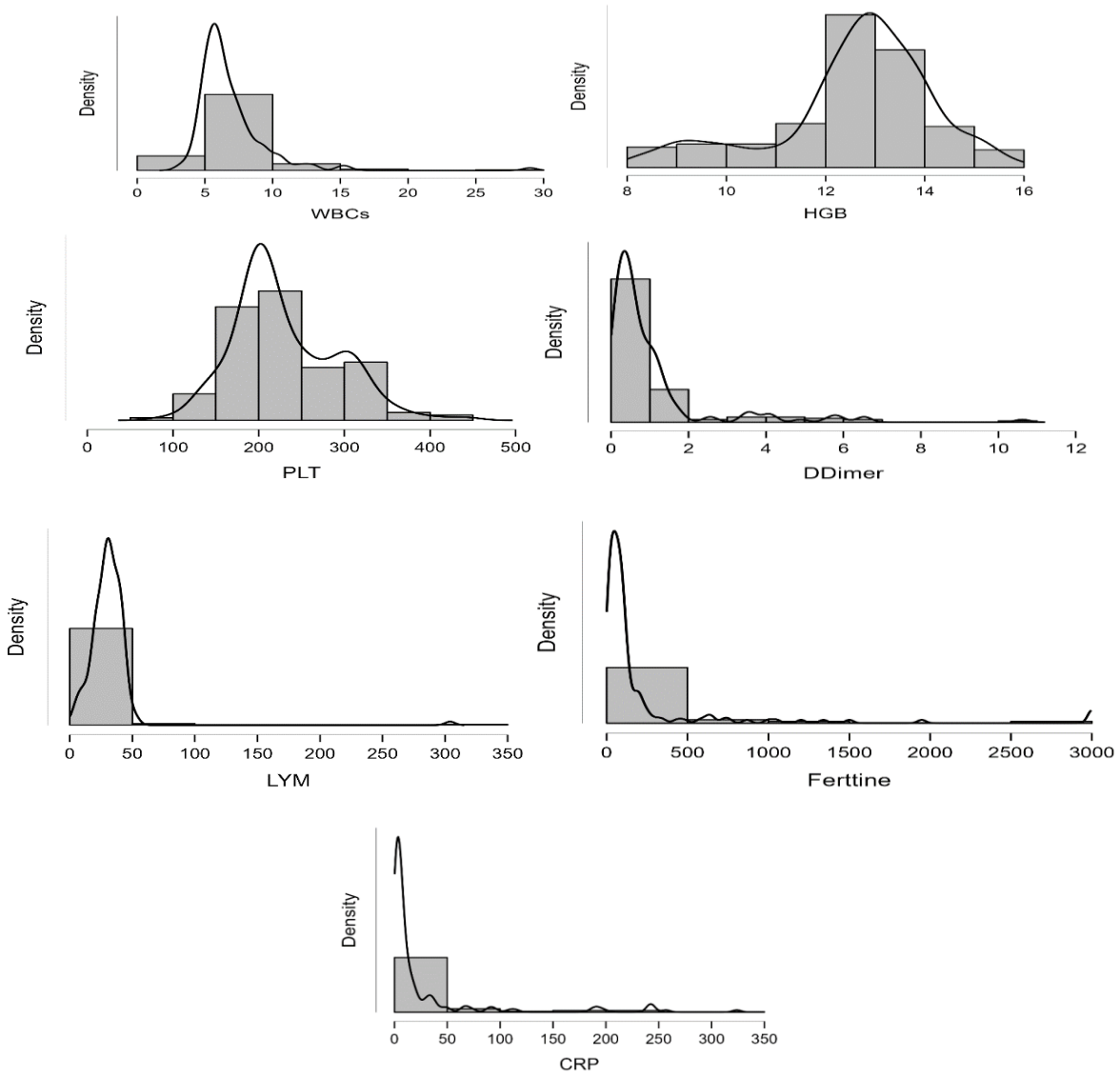


Figure7: Desities of parameters distributions

t-test for independent samples table.13 and figure 8-13 show that there are significant differences between the means of RBC for control and patients through first 7 days, as such as for controls and patients after 14 days such that p-values < α. While from t-test for paired samples there is no significant difference between means of RBC for the patients through the first 7 days and after 14 days as p-value > α. The last figures showed that t test for the paired samples (patients through the first 7 days and patients after 14 days), it is clear that there are no statistically significant differences between the ranks of the two groups for WBC, HGB, PLT and Lymphocytes since p-values > α.

Groups Parameters	Control Mean±SE	7days of infection Mean±SE	14 days of infection Mean±SE	F	P Value
RBCs count (x 10^6/µL)	3.92±0.08	4.27±0.07	4.21±0.07	6.899	0.0014
Hemoglobin (g/dl)	12.95±0.14	12.38±0.27	12.44±0.24	1.987	0.1408
WBCs count (x 10^3/µL)	6.52±0.20	7.15±0.42	6.47±0.21	1.708	0.1848
Lymphocytes %	33.46±1.13	26.34±1.83	29.19±1.08	6.671	0.0017
Granulocytes %	58.52±1.63	62.29±2.29	63.98±1.36	2.403	0.094
Platelets Count (x10^3/µL)	224.90±7.00	232.00±11.24	232.00±11.24	0.1633	0.8495

Table 13: Variations in hematological parameters

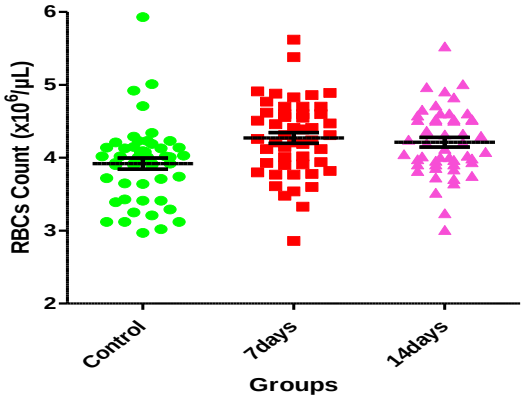


Figure8: Means (std.dev.) of RBC count in control group and the patients group during covid-19 virus infection

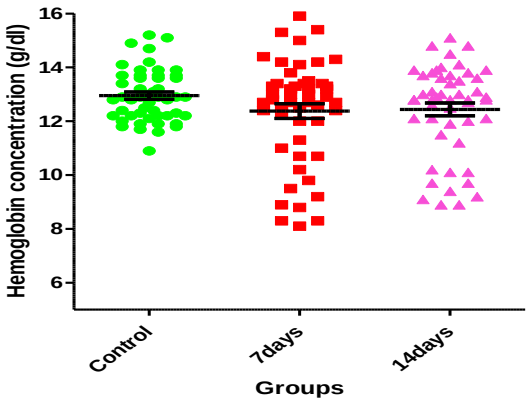


Figure 9: Medians (IQR) of HGB count in control group and the patients group during COVID-19 virus infection

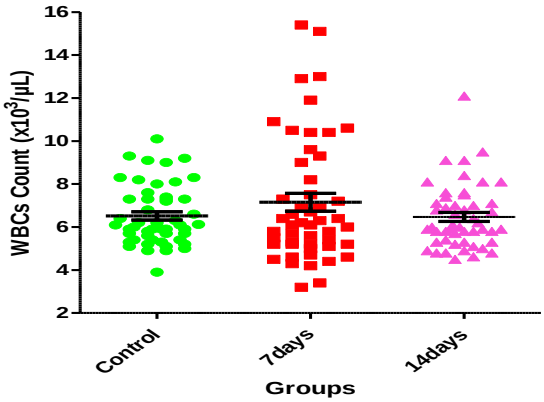


Figure10: Medians (IQR) of WBC count in control group and the patients group during covid-19 virus infection

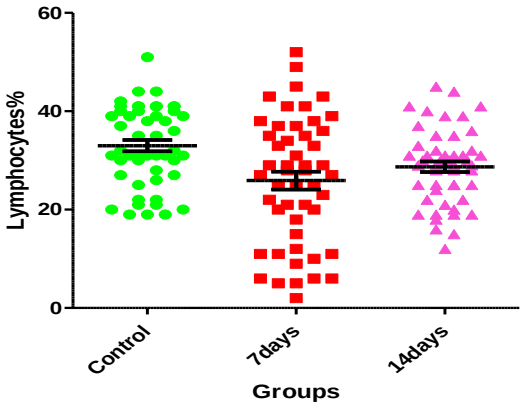


Figure11: Medians (IQR) of Lymphocgtes count in control group and the patients group during COVID-19 virus infection

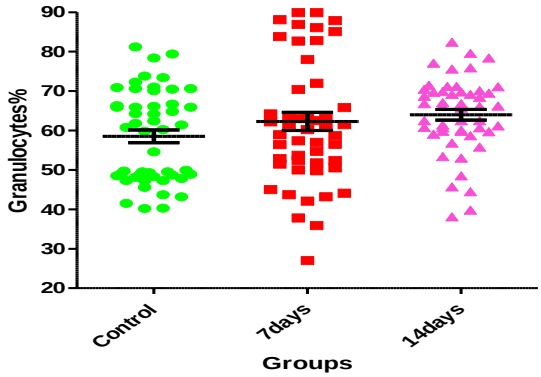


Figure12: Means (std.dev.) of Granulocytes count in control group and the patients group during covid-19 virus infection

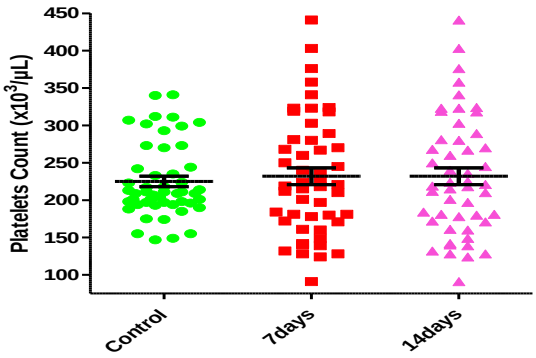


Figure 13: Medians (IQR) of PLT count in control group and the patients group during covid-19 virus infection

Table.14 shows that the mean of RBC for the non-vaccinated individuals is 4.255 with std. deviation OF 0.610, while the mean value of RBC after the 1-dose vaccinated individuals is 4.229 with std. deviation 0.515, whereas the mean value of RBC after the 2-dose vaccinated individuals is 4.033 with std. deviation 0.470.

RBC	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum
Non	44	4.255	0.610	0.0919	2.860	5.930
1_Dos	28	4.229	0.515	0.0973	3.210	5.380
2_Dos	78	4.033	0.470	0.0532	2.970	5.010
Total	150	4.135	0.530	0.0433	2.860	5.930

Table 14: Descriptive of RBC according to vaccination levels

ANOVA test.15 shows that there is no any significant difference between the means of RBC according to vaccination levels as p-value < α, and the vaccination has a weak effect upon RBC since $\eta 2=0.04 < 0.06$ (Table.15).

	Sum of Squares	df	Mean Square	F	p-value
Between Groups	**1.690**	**2**	**0.845**	**3.095**	**0.048**
Within Groups	**40.139**	**147**	**0.273**		
Total	**41.829**	**149**			

Table 15: ANOVA test for the significance of differences between the means of RBC according to the vaccination levels

Table .16 shows that the mean of Granulocyte for the non-vaccinated individuals is 60.90 with std. deviation 13.98, while the mean of Granulocytes for the 1-dose vaccinated individuals is 58.63 with std. deviation 12.50, whereas the mean of GRAN for the 2-dose vaccinated individuals is 63.05 with std. deviation 12.30.

	N	Mean	Std. Deviation	Std. Error	Min	Max
Non-Vaccinated	**44**	**60.8955**	**13.97762**	**2.10721**	**27.00**	**89.90**
1_Dos	**28**	**58.6250**	**12.50471**	**2.36317**	**39.80**	**89.90**
2_Dos	**78**	**63.0535**	**12.29573**	**1.39222**	**40.20**	**94.70**
Total	**150**	**61.5938**	**12.87490**	**1.05123**	**27.00**	**94.70**

Table 16: Descriptives of Granulocytes according to vaccination levels

From table.17 we can easily observe that for the non-vaccinated individuals the mean of WBC is 6.759 with std. deviation 2.332 and the median is 6.1, for HGB the mean is 12.322 with std. deviation 2.198 and median is 12.95, the PLT mean is 219.55 with std. deviation 57.368 and median is 207.5 and the LYM mean is 20.269 with std. deviation 10.478 and median is 31.5. For the 1-dose vaccinated individuals the WBC mean is 6.096 with std. deviation 1.55 and median is 5.8, the HGB mean is 12.841 with std. deviation 1.117 and median is 12.8, the PLT mean is 243.07 with std. deviation 63.822 and median is 223 and the LYM mean is 32.504 with std. deviation 10.004 and median is 31.6. finally for the 2-dose vaccinated individuals the WBC mean is 7.154 with std. deviation 3.224 and median is 6.2, the HGB mean is 12.65 with std. deviation 1.301 and median is 12.8, the PLT mean is 231.78 with std. deviation 61.072 and median is 211 and the LYM mean is 31.827 with std. deviation 32.572 and median is 28.6.

	Vaccinated	Mean	Std. Deviation	Min	Max	median50%	IQR
WBC	**Non**	**6.759**	**2.332**	**3.40**	**15.40**	**6.10**	**1.88**
	1_Dose	**6.096**	**1.550**	**3.20**	**9.60**	**5.80**	**1.70**
	2_Dose	**7.154**	**3.224**	**4.40**	**29.00**	**6.20**	**2.70**
HGB	**Non**	**12.322**	**2.198**	**8.10**	**15.90**	**12.95**	**3.57**
	1_Dose	**12.841**	**1.117**	**10.20**	**15.10**	**12.80**	**1.60**
	2_Dose	**12.650**	**1.301**	**8.90**	**15.40**	**12.80**	**1.30**
PLT	**Non**	**219.55**	**57.368**	**91**	**358**	**207.50**	**78**
	1_Dose	**243.07**	**63.822**	**132**	**376**	**223.00**	**103**
	2_Dose	**231.78**	**61.072**	**128**	**441**	**211.00**	**74**
LYM	**Non**	**30.269**	**10.478**	**5.40**	**49.90**	**31.50**	**12.90**
	1_Dose	**32.504**	**10.004**	**5.00**	**52.90**	**31.60**	**10.80**
	2_Dose	**31.827**	**32.572**	**2.90**	**304.00**	**28.60**	**15.41**

Table 17: Descriptives of WBC, HGB, PLT and Lymphocytes according to vaccination levels

Table .18 shows that there are no significant differences in WBC, HGB, PLT and Lymphocytes according to the levels of vaccination and vaccination has a weak effect upon WBC, HGB, PLT and Lymphocytes since $\varepsilon 2 < 0.04$.

	Vaccinated	N	Mean Rank	Kruskal-Wallis H	p-value
WBC	**Non-Vaccinated**	**44**	**75.22**	**3.494**	**0.174**
	1_Dos	**28**	**62.46**		
	2_Dos	**78**	**80.34**		
HGB	**Non**	**44**	**75.31**	**0.057**	**0.972**
	1_Dos	**28**	**77.25**		
	2_Dos	**78**	**74.98**		
PLT	**Non**	**44**	**69.09**	**2.270**	**0.322**
	1_Dos	**28**	**84.89**		
	2_Dos	**78**	**75.74**		
LYM	**Non**	**44**	**78.61**	**4.459**	**0.108**
	1_Dos	**28**	**88.54**		
	2_Dos	**78**	**69.06**		

Table 18: The significance of differences in WBC, HGB, PLT and Lymphocytes according to the levels of vaccination

Table.19 ad figures 14-16 show that the distributions of D-dimer for the two groups are differ in shape by t test Z test since p-values < controls and the patients through the first 7 days (controls and the patients after 14 days) as p-values < α. Again, the distributions of Ferritin for the two groups controls and the patients through the first 7 days are differ in shape by t test since p-values < α, there is a significant difference between the mean ranks of the groups controls and the patients through the first 7 days as p-values < α, but the two groups controls and the patients after 14 days are similar in shape by t test since p-values > α, there is no significant difference between the distributions of the groups controls and the patients after 14 days as p-values < α, i.e. there is no significant difference between the controls and the patients after 14 days Ferritin level.

Groups Parameters	Control	7days of inf.	14 days of inf.	F	P value
	Mean±SE	Mean±SE	Mean±SE		
Serum D-dimer (µg/ml)	0.333±0.04	1.584±0.28	1.221±0.21	10.10	<0.0001
Serum C-Reactive Protein (mg/L)	3.31±0.30	57.03±12.05	24.89±6.33	11.82	<0.0001
Serum Ferritin (µg/L)	61.02±7.18	457.8±117.4	203.8±49.28	7.451	0.0008

Table 19: Serum D-dimer, C- reactive protein (CRP), and Ferritin levels in control and at 7 and 14 days of COVID-19 Virus Infection.

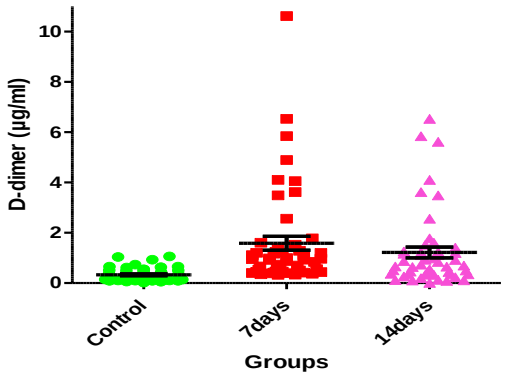


Figure 14: Medians (IQR) of D-dimer count in control group and the patients group during COVID-19 virus infection

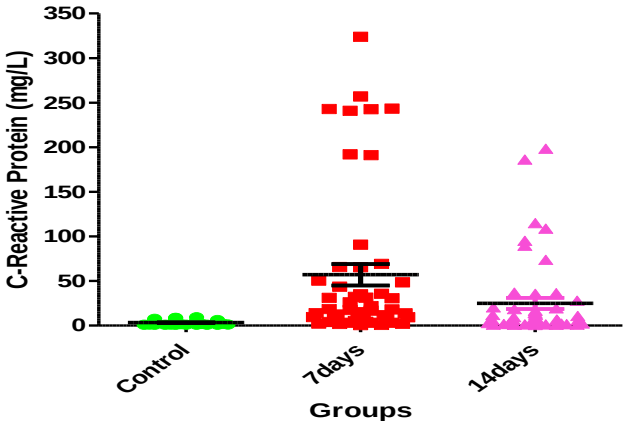


Figure 15: Medians (IQR) of CRP count in control group and the patients group during COVID-19 virus infection

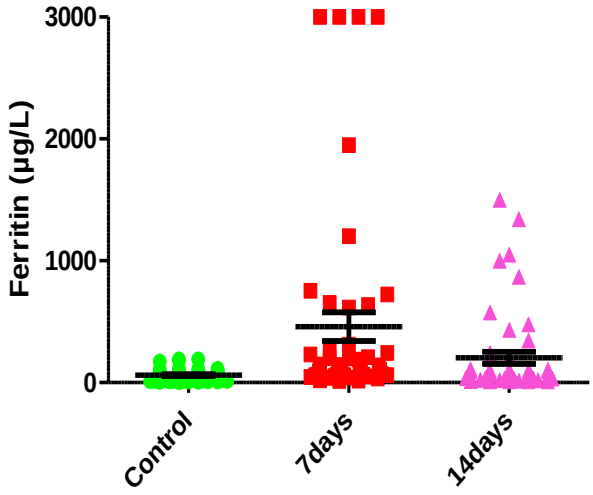


Figure 16: Medians (IQR) of Ferritin count in control group and the patients group during COVID-19 virus infection

Table.20 shows that, for the non-vaccinated individuals the mean of D-dimer is 1.456 with std. deviation 1.698 and the median is 0.638, for CRP the mean is 36.001 with std. deviation 67.75 and median is 5.255, the Ferritin mean is 351.141 with std. deviation 702.675 and median is 93.595. For the 1-dose vaccinated individuals the D-dimer mean is 0.530 with std. deviation 0.333 and median is 0.450, the CRP mean is 13.556 with std. deviation 20.869 and median is 5.020, the Ferritin mean is 102.837 with std. deviation 151.601 and median is 67.335. Finally for the 2-dose vaccinated individuals the D-dimer mean is 1.000 with std. deviation 1.616 and median is 0.591, the CRP mean is 29.460 with std. deviation 63.401 and median is 5.985, the Ferritin mean is 226.616 with std. deviation 518.658 and median is 78.450.

Parameters	Vaccinated	Mean	Std. Deviation	Min	Max	50%	IQR
D-dimer	Non-Vaccinated	1.456	1.698	0.012	6.531	0.638	1.951
	1_Dos	0.530	0.333	0.021	1.212	0.450	0.379
	2_Dos	1.000	1.616	0.053	10.620	0.591	0.889
CRP	Non-Vaccinated	36.001	67.750	0.600	243.40	5.255	26.333
	1_Dos	13.556	20.869	0.840	90.700	5.020	11.942
	2_Dos	29.460	63.401	0.931	323.91	5.985	16.292
Ferritin	Non-Vaccinated	351.141	702.675	11.00	3000.0	93.595	167.85
	1_Dos	102.837	151.601	6.99	724.00	67.335	56.54
	2_Dos	226.616	518.658	3.22	3000.0	78.450	112.11

Table 20: Descriptive of D-dimer, CRP and Ferritin according to vaccination levels

Table.21 shows that there are no significant differences in D-dimer, CRP and Ferritin according to the levels of vaccination, and vaccination has a weak effect upon D-dimer, CRP and Ferritin since $\varepsilon 2 < 0.04$.

Parameters	Vaccinated	N	Mean Rank	Kruskal-Wallis H	p-value
D- Dimer	Non	44	85.28	4.017	.134
	1_Dos	28	64.91		
	2_Dos	78	73.78		
CRP	Non	44	76.95	.450	.799
	1_Dos	28	70.55		
	2_Dos	78	76.46		
Ferritin	Non	44	81.63	1.826	.401
	1_Dos	28	67.55		
	2_Dos	78	74.90		

Table 21: The significancy of differences in D-dimer, CRP and Ferritin according to the levels of vaccination

Table.22 shows that there are statistically significant strong positive relations between; CRP and D-dimer with correlation coefficient r = 0.796, Ferritin and D-dimer with r = 0.712, CRP and Ferritin with r = 0.703. Furthermore, it shows that there are a statistically significant moderate relations between; RBC and HGB with r = 0.530, WBC and Ferritin with r = 0.515, WBC and CRP with r = 0.503, WBC and D-dimer with r = 0.451, Granulocytes and CRP with r = 0.521, Granulocytes and D-dimer with r = 0.499, Granulocytes and Ferritin with r = 0.419. Again, there are statistically significant weak positive relations between; Granulocytes and WBC with r = 0.363, IgM and PLT with r = 0.306, IgM and CRP with r = 0.265, PLT and WBC with r =

0.187, Lymphocytes and HGB with r = 0.165. Moreover, there are statistically significant weak negative relations between; HGB and D-dimer with r = -0.435, HGB and Ferritin with r = -0.381, HGB and Granulocytes with r = -0.349, HGB and CRP with r = -0.339, HGB and WBC with r = -0.279, Again between Lymphocytes and Granulocytes with r = -0.411, Lymphocytes and CRP with r = -0.268, Lymphocytes and D-dimer with r = -0.263, Lymphocytes and ferritin with r = -0.233, finally, between RBC and Granulocytes with r = -0.244.

		IgG	IgM	WBC	RBC	HGB	PLT	LYM	GRAN	D'Dimer	CRP	Ferttine
IgG	Pearson's r	—										
	p-value	—										
IgM	Pearson's r	-0.124	—									
	p-value	0.131	—									
WBC	Pearson's r	-0.033	0.130	—								
	p-value	0.690	0.113	—								
RBC	Pearson's r	0.040	-0.011	-0.114	—							
	p-value	0.629	0.897	0.164	—							
HGB	Pearson's r	-0.109	-0.155	-0.279 **	0.530 **	—						
	p-value	0.182	0.060	< .001	< .001	—						
PLT	Pearson's r	0.098	0.306 **	0.187 *	-0.065	-0.040	—					
	p-value	0.235	< .001	0.022	0.433	0.626	—					
LYM	Pearson's r	-0.064	-0.116	-0.166 *	-0.048	0.165 *	-0.004	—				
	p-value	0.440	0.160	0.042	0.564	0.043	0.960	—				
GRAN	Pearson's r	0.129	0.127	0.363 **	-0.244 **	-0.349 **	-0.007	-0.411 **	—			
	p-value	0.116	0.123	< .001	0.003	< .001	0.931	< .001	—			
D'Dimer	Pearson's r	0.086	0.130	0.451 **	-0.097	-0.435 **	0.001	-0.263 **	0.499 **	—		
	p-value	0.295	0.115	< .001	0.240	< .001	0.990	0.001	< .001	—		
CRP	Pearson's r	0.016	0.265 **	0.503 **	-0.055	-0.339 **	0.030	-0.268 **	0.521 **	0.796 **	—	
	p-value	0.842	0.001	< .001	0.501	< .001	0.719	< .001	< .001	< .001	—	
Ferttine	Pearson's r	-0.033	0.097	0.515 **	-0.149	-0.381 **	-0.094	-0.233 **	0.419 **	0.712 **	0.703 **	—
	p-value	0.685	0.237	< .001	0.068	< .001	0.252	0.004	< .001	< .001	< .001	—

Table.22: Correlation Matrix

5. Discussion

The current study showed that there was a statistically significant variation in the hematological parameters of COVID-19 patients between the 1st weeks (infection week) and 2nd week (a peak week). The current study demonstrated that there was decrease in lymphocytes and RBCs count that might be due to inflammatory responses, and these changes expanded as the disease progresses. Lymphocytopenia is frequent in patients with COVID-19, which indicates a decadence of immunity during COVID-19 infection. It is observed that the decrease of lymphocytes was below the normal range in most infected patients; this concurs with the Gao et al. (19), and Zhou et al. (20) results.

On the other hand, there were no statistically significant (P>0.05) changes observed in the, hemoglobin concentration, WBCs, granulocytes, and platelets counts. Furthermore, Guan et al. (21), study showed low thrombocyte and leukocyte. Another study by Assiri et al., (22) and Xu et al. (23), noted thrombocytopenia in the patients and leukopenia in a different study. In addition, a study reported that thrombocytes decrease significantly in pneumonia patients and this reduction is proportionate with the clinical case of the patient. Several potential reasons have been suggested for thrombocytopenia in coronavirus patients as failure in thrombocyte production from classic cytokine storm in infection or attacking directly on hematopoietic stem cells, high destruction of platelet in circulating blood and decreased peripheral PLT secondary to lung damage (24). In the Chinese population, Duarte et al. (25), and Tan et al. (26), studies have reported the presence of leucopenia on hospital admission, basically at the expense of moderate to severe lymphopenia and mild thrombocytopenia, as well as a decrease in hemoglobin, absolute monocyte counts and even tend to develop neutrophilia during hospitalization, with a peak in this period of ICU stay. Analysis of the baseline CBC parameters of the study population showed that 4 cases (12.9%) showed neutrophilia, 3(9.6%) cases showed lymphopenia, and 5 cases (16.1%) showed monocytosis. However, the baseline total leucocyte count was not increased (27). In contrast to the other studies conducted in China, whereby 63% of cases showed lymphopenia and 42% cases outside the Chinese population (28). Fan et al., (29) reported that on admission of the COVID-19 patients to the national centre for infectious diseases (NCID), leukopenia (WBC ≤4 x 109/L) was observed in 19 patients (29.2%) with only one patient presenting with severe leukopenia (WBC < 2 x 109 /L). Lymphopenia featured in 24 patients (36.9%) with 19 having moderate lymphopenia (Absolute Lymphocyte Count (ALC) 0.5 – 1 x 109/L) and 5 with severe lymphopenia (ALC <0.5 x 109/L). 28% of all patients presented with lymphopenia (ALC<1 x 109/L). Lymphopenia featured prominently in COVID-19 ICU group with a median nadir ALC of 0.4 x 109/L compared to 1.2 x 109/L in the non-IC.

The CBC parameters in a COVID case show neutrophilia, leucocytosis, lymphopenia, and thrombocytopenia (30). Huang et al. (31), and Yang et al. (32), mentioned in their articles whereby 85% of the critically ill patients of their study group with COVID- 19 showed lymphopenia. The presence of lymphopenia as a signature of severe COVID-19 was confirmed by Bai et al. (33), who reported that ICU patients suffering this infection had a median lymphocyte count of 800 cells/mm with -non-survivors exhibiting persistent lymphopenia. Also, Lippi and Plebani, (34) carried out a systematic literature review and highlighted that the most important hematological parameter abnormalities observed in COVID-19 patients, which may predict the

progression toward severe or critical forms of COVID-19, include leukocytosis, neutrophilia, and lymphopenia. Each of these prognostic parameters retains a specific clinical and biological significance, which, altogether, can contribute to reflecting the evolution toward more unfavorable clinical pictures.

Serological tests can be important tools to estimate the prevalence of virus infection, virus lethality, and provide information about risk factors and immunity such as the patient's location, and age. The current study showed that corona virus infection caused a significant (P<0.0001) increase in serum IgM and IgG levels at 1 day and 14 days, compared with the healthy individuals. Similar results were recorded by previous study by. Zhou et al. (35), The IgM level showed heterogeneity within the group of deceased cases, and some patients had very high IgM levels which might be in the active status of the disease or very low IgM levels due to the long disease course. The increased IgM level in the deceased case group might be related to the higher disease severity in these patients and indicate a poor prognosis (36).

Hsueh et al. (37), reported that seroconversion for IgG (mean 10 days) occurred simultaneously, or 1 day earlier, then that for IgM and IgA (mean 11 days for both). IgG could be detected as early as 4 days after the onset of illness. The earliest time at which these three antibodies reached peak levels were similar (mean 15 days). A high IgG level (1:800) could persist for > 3 months. Long et al. (38), reported that Seroconversion for IgG and IgM occurred simultaneously or sequentially. After seroconversion, IgM and IgG titers were plateaued within 6 days. After 17-19 days of the onset of COVID-19 symptoms, a positive virus-specific IgG was reached 100%, while after 20-22 days of the onset of COVID-19 symptoms, a positive virus- specific IgM reached a peak of 94.1%. Three weeks after the onset of the symptoms of COVID-19, the virus-specific IgM and IgG antibody titers were increased in patients (38).

The current study showed that coronavirus infection caused a significant (P<0.0001) increase in the serum Ferritin levels compared with the healthy control individuals. This result is similar to the result of the study of Dahan et al. (39), who reported that a significant increase in ferritin levels was demonstrated in patients with moderate and severe disease, compared to patients with mild disease (P = 0.006 and 0.005, respectively). Severe patients had significantly higher levels of ferritin (2817.6 ng/ml) than non-severe patients (708.6 ng/ml) P = 0.02. Cao et al. (40) reported that patients with elevated ferritin levels (>200 ng/mL) had a higher incidence of severe illness when compared with those with normal ferritin levels (≤ 200 ng/mL) (50.0% vs 2.9%). In addition, the severity of illness manifested a significantly higher level of ferritin as compared with non-severe ones (median 921.3 vs 130.7 ng/mL, p < 0.001). Furthermore, elevated ferritin group showed longer viral clearance time (median 16 vs 6 days, p < 0.001) and in-hospital length (median 18 vs 10 days, p < 0.001). These results suggest that ferritin could act as a simple and efficacious complementary tool to identify severe COVID-19 patients at an early stage and predict their outcome. This indicator would provide guidance for subsequent clinical practice, alleviate medical stress and reduce mortality. The authors concluded that serum ferritin might be an independent risk factor for severity of illness and predictor for prognosis of COVID-19 patients (40).

The present study showed that coronavirus infection caused a significant (P<0.0001) increase in the serum D-dimer levels compared with the healthy control individuals. This result is similar to the study of Guan et al. (21), who reported that the d-dimer level was significantly elevated among non-survivors compared to survivors. The d-dimer level can be a basic and helpful biomarker to identify the patients with poor prognosis in the early stages and help to the management of COVID- 19 patients (41). Also, Huang et al. (31), reported that COVID-19 patients with 0.5 µg/mL or higher levels of d- dimer on admission need critical care support. Previous studies showed that d-dimer levels were higher in non-survive COVID-19 patients compared to survive ones (42). D-dimer on admission upper than 2.0 µg/mL can predict mortality in hospitals among COVID-19 patients. The d-dimer level can be a basic and helpful biomarker to identify the patients with poor prognosis in the early stages and help to the management of COVID- 19 patients (42).

The results of current study showed that patients with COVID-19 had a significant increase in serum CRP during COVID-19 Virus Infection among COVID-19 patients at the first of infection to 7 day and 14 days compared with the controls. These results run parallel to the results of the previous study by Wang et al. (36), The CRP was elevated in 65% of COVID-19 patients on admission and elevated in 93.9% of severe COVID-19 patients CRP levels are strong biological indicators to represent the severity of the COVID-19 infection. CRP seems to be one of the first biomarkers to show physiological complications in COVID- 19 patients. Laboratory findings in patients with severe COVID-19 showed data consistent with cytokine storm involving elevated inflammatory markers, including ferritin, which has been associated with critical and life-threatening illness (43).

6. Conclusion:

It can be concluded that coronavirus infection caused a significant decrease in lymphocytes, and RBCs count However, there were no statistically significant (P>0.05) changes observed in the, hemoglobin concentration, WBCs, granulocytes, and platelets counts in comparison to the healthy individuals. Also, COVID-19 caused a significant increase in IgM, IgG, D-dimer, CRP, and Ferritin levels at different periods compared to the controls. Further studies are needed to confirm these results. COVID-19 Specific Immunoglobulin's and Some hematological variables and Inflammatory factors in COVID-19 Patients These changes in IgM, IgG, D-dimer, CRP, and Ferritin levels during COVID-19 Virus Infection among COVID-19 patients may help the clinicians to better understand the COVID-19 and provide more clinical treatment options.

7. Recommendation:

1 -Ministry of Health should develop an infectious disease preparedness and response plan that can help guide protective actions against COVID-19.

2 - Vaccination programs should be implemented including targeted to all people especially individuals with chronic diseases and pregnancy women, through all media and channels for spreading the needed Information.

3 – More studies should be conducted in order to have knowledge about the behavior of the new virus (COVID-19).

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