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Long Term Effect of Post-Covid-19 Syndrome on Hematological Parameters in Iraqi People

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ABSTRACT

Background: The COVID-19 epidemic, which is still ongoing, has a significant effect on health care both in Iraq and worldwide. Further strain on health systems was caused by successive waves of altered viruses, further enhancing virus dissemination. Persistent symptoms may last for several months following the initial COVID-19 infection. The illness is called post-acute sequelae of SARS-CoV-2 infection, or Long COVID (PASC). Long-term COVID-19 infection can affect various organs and systems, including the hematological system, and cause many symptoms. Hematological problems have been observed in individuals previously infected with COVID-19, in several investigations. Poor outcomes and an increased risk of severe disease are linked to the majority of these changes. **Aim of the study:** This aims to find the post-COVID-19 effects on the hematological parameters. **Patients and methods:** This study was a case-control investigation at the As-Sadr Teaching Hospital in Maysan City- Iraq between October 13, 2023, and November 13, 2023. There were two groups: fifty-eight-patient case or experimental group along with a fifty-eight- individual control group. In this study, the randomly selected healthy individuals in the control group were matched to patients with COVID-19 according to symptoms. Except for not having COVID-19 disease, the controls had to fulfill the same requirements as the cases. Clinical profiles and hematological markers were examined and contrasted between the two groups. **Results:** The data show no significant differences ($P > 0.05$) in age, BMI, and sex between case and control groups. The results confirm alterations in hematological parameters. Blood sample analysis in the case group show a significantly higher mean of RBC and a decline in MCHC, and MCV compared to the control group. However, no significant differences in hemoglobin and hematocrit parameters exist between them. The mean HCT% and HGB are significantly lower for the age group 18-29 years than for 30-39 and 40-49 years and the alterations were more noticeable in male COVID-19 patients.

Conclusions: The results have shown altered hematological parameters after 3 years of COVID-19 infection. The changes include reduced Hg, MCH, and MCHC and higher RBC values that might affect oxygen transport through the body. The alterations were more noticeable in male COVID-19 patients, indicating that males are more affected by the disease than females. In light of the increasing number of individuals with Long-COVID, more research is required to determine the precise underlying causes of the extended altered RBC and hemoglobin value among different age groups.

Keywords: Hematological parameters, Hemoglobin, Hypoxia, Long Covid-19, SARS-CoV-2.

Article Information

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INTRUDUCTION

In December 2019, Wuhan, China, announced the first case of the extremely contagious new coronavirus, known as COVID-19 and SARS-COV-2 (1). This has led to widespread illness and death across the globe (2). On February 24, 2020, in Najaf City, the first COVID-19 case in Iraq was reported. As of April 9, 2020, confirmed cases have significantly increased to 1232 (3). The respiratory system is the main organ affected by the condition. Nevertheless, COVID-19 can also affect the hematological system, among other organs and systems. Hematological abnormalities in COVID-19 patients have been identified in several investigations. Some changes include an increase in the number of white blood cells, a decrease in red blood cell and hemoglobin levels, and an increase in total bilirubin and ferritin levels, which may occur in severe COVID-19 infection (4, 5). Additionally, there have been reports of large changes in spleen size in deceased COVID-19 patients, which is a normal reaction to anemia (6).

The symptoms of COVID-19 can vary in severity and include fever, coughing, sore throat, exhaustion, shortness of breath, body aches, and loss of taste or smell. It is crucial to emphasize that hematological abnormalities are not a common symptom of COVID-19 and that patients might differ greatly in the severity of these abnormalities(5). Certain symptoms may last for several months following the initial COVID-19 infection. In this instance, the illness is called post-acute sequelae of SARS-CoV-2 infection, or Long COVID (PASC). Even those with moderate or asymptomatic illnesses may experience these symptoms.

The consequences of Long COVID are still being studied, however, there is a wide range of symptoms. Fatigue, breathlessness, joint or chest pain, headaches, foggy thinking, trouble focusing, loss of taste or smell (7). On the other hand, people may sustain organ damage, including heart, lung, or kidney problems (8). There is evidence that the development and severity of Long COVID can be influenced by age, sex, and race (9, 10). Both men and women can contract long COVID, while some research suggests that women are more susceptible (9, 10). Furthermore, lengthy healing times and chronic symptoms are often more common among the elderly. Different racial and ethnic groups exhibit different cognitive symptomology related to long-term COVID-19 infection (11).

A recent meta-analysis revealed that smoking, high body mass index, age, and female sex were linked to a higher risk of Long COVID-19 (12). Additionally, a study showed that COVID-19 altered the size and shape of red blood cells, which may have an impact on oxygen transport (13). Blood biomarkers may be able to predict Long's COVID status and help with medical intervention and treatment. Hematological parameter changes continue in Long Covid (14).

PATIENTS AND METHODS

A case-control study was conducted from October 13, 2023, to November 13, 2023, at the As-Sadr Teaching Hospital in Maysan City-Iraq. Fifty-eight patients and fifty-eight controls are included in the total. The study paired patients exhibiting COVID-19 symptoms with randomly chosen controls. The controls had the same requirements as the cases, except not having COVID-19 disease. The two groups were compared and their clinical profiles and hematological indicators were analyzed. The ages of the studied groups are randomly selected, all ages. An informed consent was achieved from every patient and control included in this study. Every participant underwent a clinical evaluation and a thorough medical history was obtained from both patients and controls, covering details such as age, name, gender, phone number, place of employment, history of COVID-19 infection, and symptoms like fever, cough, headache, loss of taste and smell, vomiting, diarrhea, runny nose, shortness of breath, chest pain, and others, in addition to the length of the sickness and the kind of medication or vaccine that is applied.

Hematological parameters

Blood collection

Five milliliters of venous blood were taken from each person. The blood samples were taken and placed in two separate tubes. One ml was deposited in Ethylenediaminetetraacetate (EDTA) anticoagulated blood tubes for hematological parameter measurements by Auto Hematology Analyzer, including: The number of circulating blood cells, Hemoglobin (Hb), Hematocrit (the proportion of whole blood volume occupied by red cells), Red blood corpuscles Count-RBCs count (cells/mm3). Level of hemoglobin in blood (g/dl), Packed cell volume (PCV%), Mean corpuscle volume-(MCV) (femtoliter, fl), Mean corpuscular hemoglobin (MCH, Picogram) and Mean corpuscle hemoglobin concentration (MCHC)(g/dl).

STATISTICAL ANALYSIS

Statistical analyses were done by using the SPSS program (version 26). Categorical variables were presented as percentages and frequencies while continuous variables were presented as means ± standard deviations. The chi-square test was used to assess the qualitative data between categorical variables (age groups, gender). An independent t-test was used to compare the means between cases and controls. Error bars of means and standard deviations were used to compare the hematological parameters according to age groups and gender. The P values less than 0.05 will be considered statistically significant results.

RESULTS

Characteristics of the Study Patients

Table (1) displays the baseline demographic information between healthy controls and cases who became infected with COVID-19. The groups that had recovered from COVID-19 infection and the healthy controls had mean ages of 34.1±9.8 and 35.9±11.7 years, respectively, and BMIs of 29.4±8.01 and 28.6±6.1 (Kg/m2). It indicates that there is no significant difference (P > 0.05) in age, BMI, or sex between the groups.

Table (1): Demographic data of study population

Variable	Subgroup	Group		Total	P
		Cases (n=66) No.(%)	Controls (n=67) No.(%)		
Age group (years)	18-29	29 (43.9%)	24(35.8%)	53(39.8%)	0.2
	30-39	17(25.8%)	25(37.3%)	42(31.6%)	
	40-49	13(19.7%)	7(10.4%)	20(15.0%)	
	50-65	7(10.6%)	11(16.4%)	13(13.5%)	
Mean age(years) ±SD		34.1±9.8	35.9±11.7		0.3
Sex	Male	38(57.6%)	42(62.7%)	80(60.2%)	0.5
	Female	28(42.4%)	25(37.3%)	53(39.8%)	
BMI	Normal	15(22.7%)	17(25.4%)	32(24.1%)	0.8
	Overweight	26(39.4%)	28(41.8%)	54(40.6%)	
	Obese	25(37.9%)	22(32.8%)	47(35.3%)	
Mean BMI (Kg/m^2)±SD		29.4±8.01	28.6±6.1		0.6

P value< 0.05: significant. P value< 0.01: highly significant.

Hematological parameters differences between cases and control

Table (2) indicates a statistically significant (P <0.05) variation in the blood parameter values (RBC, MCHC, MCV, and MCH) between the case and control groups. The cases have a higher RBC mean of 5.2±0.7 compared to the control mean of 4.7±0.6. Comparing the mean of MCHC in cases (30.4±1.1) to the mean in controls (32.4±1.5), there is a reduction in cases mean. In addition, the cases' MCV (82.8±7.5) and MCH (24.04±2.6) mean values are lower than those of the control group (85.7±3.8 and 27.1±1.7, respectively). Nonetheless, the table shows that the parameters of hemoglobin and hematocrit are not significantly different between the patients and control groups (P > 0.05).

Table (2): Hematological parameters differences in cases and control.

Hematological assessment	Cases (n=66) mean±SD	Controls(n=67) mean±SD	P value
RBC(10^12/L)	5.2±0.7	4.7±0.6	0.0001
MCHC(g/dL)	30.4±1.1	32.4±1.5	0.0001
MCV(fL)	82.8±7.5	85.7±3.8	0.006
MCH(pg)	24.04±2.6	27.1±1.7	0.0001
HCT%	39.8±3.9	40.02±3.9	0.8
HGB(g/dl)	12.2±1.4	12.6±1.3	0.05

Hemoglobin (Hb), Hematocrit HCT%, Red blood corpuscles Count (RBCs), Packed cell volume (PCV%), Mean corpuscle volume (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscle hemoglobin concentration (MCHC). Statistically significant (P <0.05).

Comparison of the hematological parameters between cases and control across different age groups

Table (3) revealed that the age group (18-29, 30-39, and 40-49 years) had a significant increase in RBC and a decrease in MCHC, MCH MCV, and HCT% in cases than in control, while the 50-65 years old have a nonsignificant increase in RBC value. However, the hemoglobin, MCV, and HCT% decrease insignificantly in all age groups except (18-29) year which decrease significantly between cases and control. The results show no significant difference in RBC, MCHC, MCH, and MCV in cases among age groups. The mean values of the hemoglobin and hematocrit 38.5±3.9, 11.6±1.3 significantly lower in cases of the age group (18-29 years) compared to the 30-39 and 40-49 age group 41.02±3.3, 12.7±1.1and 41.1±4.1, 12.6±1.4 respectively.

Table (3): Comparison of the hematological parameters between cases and control across different age groups (years).

Age group(years)	Hematological assessment	Cases (n=66) mean±SD	Controls(n=67) mean±SD	P value
18-29	RBC(10^12/L)	5.2±0.7	4.8±0.6	0.01
	MCHC(g/dL)	30.2±0.9	32.9±1.4	0.0001
	MCV(fL)	82.2±7.5	85.6±3.8	0.01
	MCH(pg)	23.8±2.6	27.5±1.8	0.0001
	HCT%	38.5±3.9	41.7±3.4	0.002
	HGB(g/dl)	11.6±1.3	13.1±1.3	0.0001
30-39	RBC(10^12/L)	5.1±0.6	4.6±0.6	0.007
	MCHC(g/dL)	30.6±1.5	32.3±1.7	0.001
	MCV(fL)	81.9±8.4	84.3±3.6	0.2
	MCH(pg)	24.1±2.9	26.9±1.8	0.0001
	HCT%	41.02±3.3	39.5±3.6	0.2
	HGB(g/dl)	12.7±1.1	12.4±1.2	0.4
40-49	RBC(10^12/L)	5.2±0.7	4.4±0.5	0.03
	MCHC(g/dL)	30.4±0.8	31.6±1.6	0.03
	MCV(fL)	85.4±7.3	87.2±4.3	0.6
	MCH(pg)	24.6±2.3	26.6±2.1	0.08
	HCT%	41.1±4.1	38.8±3.7	0.2
	HGB(g/dl)	12.6±1.4	12.6±1.6	0.9
50-65	RBC(10^12/L)	5.2±0.7	4.6±0.4	0.07
	MCHC(g/dL)	30.6±0.8	32.1±1.5	0.02
	MCV(fL)	82.5±6.2	85.9±3.7	0.2
	MCH(pg)	23.8±2.1	26.9±1.2	0.001
	HCT%	40.3±4.1	38.3±5.2	0.4
	HGB(g/dl)	12.5±1.4	12.2±1.3	0.6

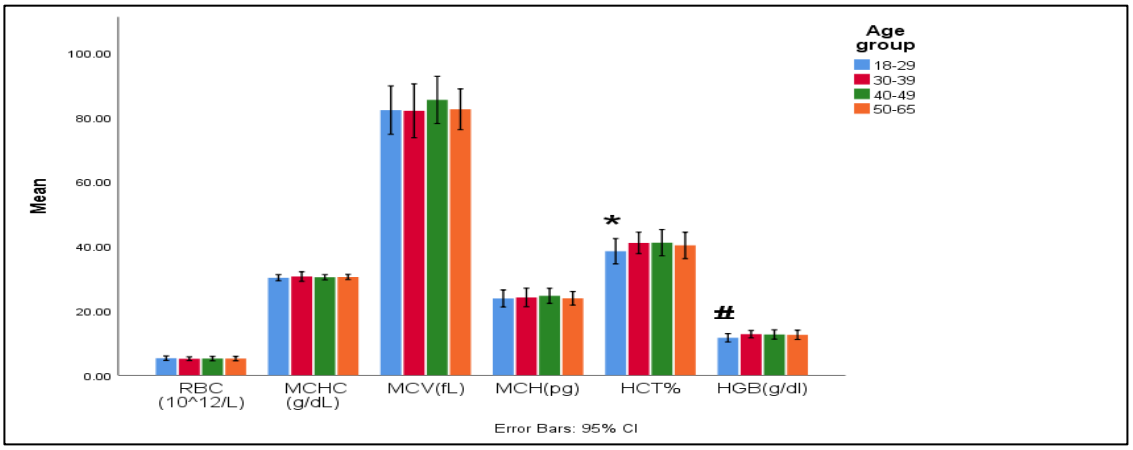

Figure (1): Comparison of the hematological parameters between cases and control across different age groups (years).

* Mean HCT% is significantly lower for the age group 18-29 years than for 30-39 and 40-49 years
#Mean HGB is significantly lower for the age group 18-29 years than 40-49 years

Hematological parameters change between males and females in cases and control

Table (4) demonstrates that males and females have a significant difference in RBC, MCHC, and MCH values in both groups (P =0.0001). The level of hemoglobin, hematocrit, and RBC increased significantly in males 12.9±1.1, 41.6±3.2, 5.3±0.6 than in females 11.2±1.1, 37.4±3.6, 5±0.7, respectively. Male hemoglobin and HCT% indicated no significant difference P= 0.9 between patients and controls, however, female cases' hemoglobin significantly decreased P= 0.007.

Table (4): Hematological parameters for male and female in cases and control

Sex	Hematological assessment	Cases (n=66) mean±SD	Controls(n=67) mean±SD	P value
Males	RBC(10^12/L)	5.3±0.6	4.8±0.5	0.0001
	MCHC(g/dL)	30.6±1.2	32.6±1.4	0.0001
	MCV(fL)	82.6±7.8	86.6±4.1	0.006
	MCH(pg)	24.1±2.6	27.2±1.6	0.0001
	HCT%	41.6±3.2	40.8±4	0.3
	HGB(g/dl)	12.9±1.1	12.9±1.2	0.9
Female	RBC(10^12/L)	5±0.7	4.3±0.5	0.0001
	MCHC(g/dL)	30.1±0.9	32.4±1.8	0.0001
	MCV(fL)	83.04±7.2	84.1±2.7	0.5
	MCH(pg)	23.9±2.5	26.9±1.9	0.0001
	HCT%	37.4±3.6	38.6±3.6	0.2
	HGB(g/dl)	11.2±1.1	12.2±1.4	0.007

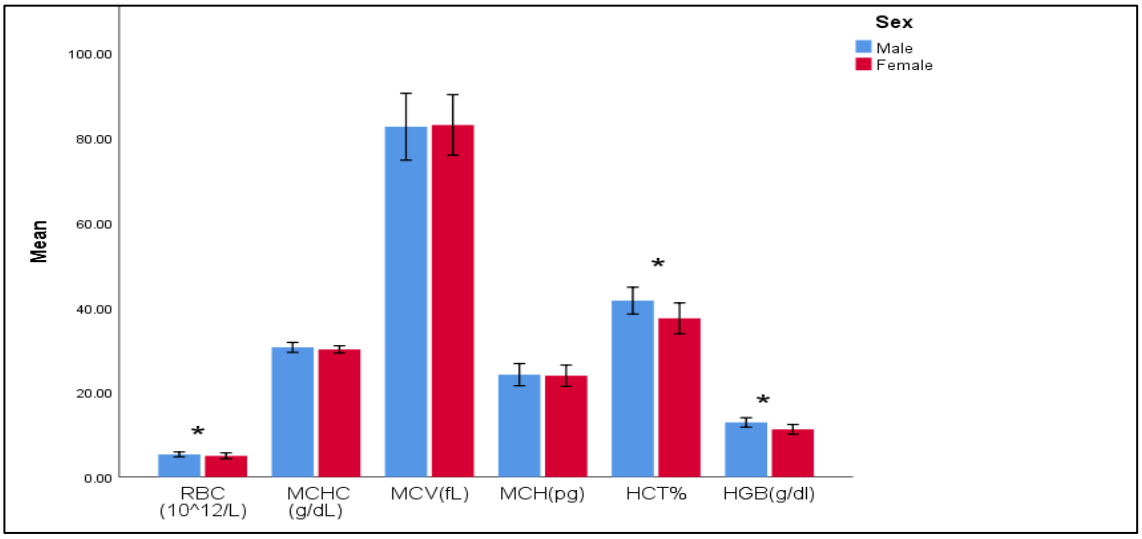

Figure (2): Hematological parameters alteration between male and female cases.

*Mean RBC, HCT%, and HGB increase significantly in male cases than in female.

DISCUSSION

The frequency of COVID-19 cases has increased worldwide. SARS-CoV-2 infection is associated with a change in RBC shape and compromised cell function (13). Looking at the COVID-19 outbreak, it is critical to evaluate clinical, demographic, and hematological characteristics. In Iraq, there is a limited number of research have examined hematological markers linked to COVID-19. However, further research is needed to fully comprehend this phenomenon, as it is becoming increasingly clear that COVID-19-related infections can last for a long time and result in long-term COVID-19. Therefore, hematological parameters such as RBCs, MCHC, MCH, MCV, HCT%, and HGB and their relation to long-term COVID-19 were examined in the current study.

This research offers a good deal of information on hematological parameters and demographic data, which indicated no significant difference in gender between cases and control; this could be explained by the impact of behavioral decisions or gender immunological variations (15). The data were gender-separated since the outcomes support previous research that found clear variations in the overall hematological parameters of males and females (13). This was linked to either periodic menstrual blood losses in women or increased testosterone levels in men (16). The present results demonstrate that the mean of RBC, HCT%, and HGB increase significantly in male cases than in females. This data is consistent with previous research (17); thus the other study also detected higher hemoglobin levels in males compared to females (18).

According to the comparison of the outcome of RBC count and its indices, MCHC, MCV, and MCH, there was a highly significant decrease observed in all mean values of indices and an increase in RBC count as compared with the control. For instance, the mean value of hemoglobin concentration of the control group was 12.6±1.3 whereas its concentration has decreased non-significantly in cases (mean 12.2±1.4) (P value=0.05). These findings were crucial in confirming that the effects of the COVID-19 virus on MCH (pg/cell), MCV (µm3), and MCHC (g/dl) concentrations were greater than those on other RBC indices like hemoglobin and HCT% because the differences were negligible and not statistically significant. The explanation of the current results which found an

increase in RBC count and normal or decreased hemoglobin level in cases compared with controls, is that the majority of COVID-19 patients experienced dyspnea and decreased physical fitness, which may be associated with lung injury and changed red blood cell (RBC) consumption of oxygen, resulting in hypoxemia. Even so, no changes were seen in hematocrit, mean corpuscular hemoglobin concentration, or RBC count (19). Based on these studies, the usual red blood cell count is acceptable; however, the red blood cells' role in oxygen transfer may have changed. According to the aforementioned research, COVID-19 has short-term impacts on red blood cells (RBCS); however, it may also have long-term effects on RBCs (20). There is sufficient data to suggest that the numbers of red blood cells (RBC) and hematocrit (HCT) rise dramatically in hypoxic environments, which is comparable to the alterations that occur by living in high altitudes (21). In response to hypoxic conditions, the kidneys produce more erythropoietin, which in turn stimulates the bone marrow to produce more red blood cells to improve oxygen transport to the body's tissues. This process leads to an increase in the number of reticulocytes, which are newly formed red blood cells that differ from mature ones (22). In that, they are typically less flexible and more spherical, and their cell membrane contains endoplasmic reticulum remnants (23). However, the research group's levels of hemoglobin were noticeably lower than those of the controls, which matched the current study results (24). COVID-19 infections cause a drop in hemoglobin levels through a variety of intricate mechanisms, by retaining iron in macrophages and decreasing its absorption from the intestinal tract leading to alterations in iron homeostasis (25). As a result, hemoglobin synthesis and circulation iron levels both decline. Additionally, compared to cases aged 30-39, 40-49, and 50-59 years, the COVID-19 patients in the age group 20-29 years old had a noticeably lower mean of hemoglobin and hematocrit. The mean age per years ±SD of COVID-19 patients in this study was 34.1±9.8, which was found younger than in other studies. This is also supported by a previous study in Saudi Arabia which suggested that this condition affects a younger age group (26). Studies have shown that patients with COVID-19 and older populations have worse results (27). This may be due to a combination of factors, including the physiological aging process and, more significantly, the higher incidence of frailty and comorbidities in older adult patients, which lower functional reserve and impair intrinsic capacity and resilience as well as the body's ability to fight infections (28).

This study had various limitations. It is possible to determine the course of the hematological consequences of prolonged COVID by evaluating the patient's hematological profile during the COVID-19 acute phase, which was not done in this study. Further, the results might be restricted by the small number of participants of older age in this study. To the best of the researcher’s knowledge, however, this is the first study to link abnormalities in hematological parameters with clinical outcomes and offer insights into these parameters for patients with long COVID up to two years. To eliminate variations that occur naturally, nonetheless, earlier research has demonstrated that hematological values remain consistent over an extended length of time.

CONCLUSIONS

The results of this study indicate a statistically significant (P <0.05) variation in the blood parameter values (RBC, MCHC, MCV, and MCH) between the case and control groups. The cases have a higher RBC mean, lower hemoglobin, MCHC, MCH, and MCV. This current study shows that the patient's age and gender have a substantial impact on individual hematological parameters in post-COVID-19 syndrome and the results demonstrate that the mean of RBC, HCT%, and HGB increase significantly in young male cases than in young

females. The current study's findings supported earlier research's observations and other findings on variations in hematological parameters and a few other variables in long-term COVID-19-infected patients. Thus, more hematological research is required to validate these findings.

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