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RESEARCH ARTICLE **OPEN ACCESS**

A Comparative Study of Complete Blood Count (CBC) Tests in Children with COVID-19 in the Fifth Peak Compared to Other Peaks: A Cross-sectional Study

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Abstract:

Background: Awareness and recognition of the changes resulting from laboratory results in patients with COVID-19 can lead to effective clinical judgment and evidence-based care.

Aim: This study was conducted to compare the results of complete blood count (CBC) tests in children with COVID-19 hospitalized in the fifth peak with other COVID-19 peaks.

Methods: This cross-sectional study was carried out by census method on 112 hospitalized cases of children suffering from COVID-19. The data were collected using a researcher-made checklist by referring to the medical records unit of the hospital and analyzed with SPSS-25 statistical software and descriptive and inferential statistical tests at a significance level of 0.05.

Results: In the examined peaks, iron deficiency anemia was related to the severity of COVID-19, so MCV and RBC levels were reduced in children with COVID-19. The average blood platelet in the fifth peak was significantly lower than in the third and fourth peaks.

Conclusion: Decreased values of some CBC indices, such as MCV, RBC, and platelets in the fifth peak during hospitalization, can predict poor clinical outcomes in patients with COVID-19. Moreover, according to the Mentzer index, the degree of iron deficiency anemia affects the clinical course and prognosis of patients with COVID-19, therefore, knowing the laboratory results can help the clinical judgment of doctors in treating patients.

Keywords: Blood index, Complete blood count (CBC), Mentzer index, COVID-19, Children, Patients.

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1. INTRODUCTION

COVID-19 can infect people of any age, but there are differences between the incidence of this disease in children and adults. This difference in the number of infections may be due to the lower vulnerability of children to infection or the lower occurrence of symptoms in children, which leads to the non-referral diagnosis of many patients [1-3]. In the initial reports of this disease, few cases of children's involvement were reported, so it was thought that children are immune from this disease or show mild symptoms of it, and less than 2% of them were hospitalized [4]. However, with the spread of the disease and the involvement of families and children, reports of severe and even fatal cases of the disease in children were published [5].

Moreover, children often suffer from a milder form of the disease and rarely suffer from severe pneumonia, which is probably due to the difference in the expression of ACE2 receptors [less expression in children] and the difference in the performance and development of the immune system, which is due to the body's different response to infection. It is caused by a virus caused by COVID-19 [6, 7]. Moreover, another reason in this context is the simultaneous presence of a greater number of other viruses in the airways of children, which may lead to a decrease in its growth through competition with SARS-CoV-2 [8]. In addition to the mentioned differences in the prevalence, symptoms, and severity of the disease between children and adults, some studies have also pointed to differences in imaging and laboratory findings. Some studies indicate differences in the results of hematological, inflammatory, kidney, liver, *etc*. tests between children and adults [9-12].

A complete blood cell count (CBC) is a test that analyzes cells in the bloodstream. These cells include red blood cells, white blood cells, and platelets. The CBC test can evaluate the overall health of the body and help diagnose various diseases such as infection, anemia, inflammation, and blood cancer (leukemia) [13]. The results of the studies indicate the examination of blood indices, including red blood cell count, white blood cell count, platelet count, hemoglobin, hematocrit (Hct), average red blood cell volume, average red hemoglobin, average red blood cell hemoglobin concentration and range of distribution of blood cell size. Red blood cells are of particular importance in the treatment and care of patients with COVID-19 [14-16]. The results of the studies show that one of the important causes of death due to this disease is the decrease in the amount of oxygen in the blood [14, 17]. In the severe form of the disease, red blood cells decrease [18, 19]. By retaining iron (the mechanism of causing anemia in chronic and infectious diseases), affecting the coagulation system, and causing thrombosis, the virus reduces the amount of hemoglobin and the number of red blood cells and causes anemia [20, 21].

Moreover, the results of the study show that the laboratory symptoms caused by COVID-19 in children are associated with a decrease in white blood cells. In some cases, there may be a decrease in peripheral blood neutrophils (neutropenia) or a decrease in lymphocytes (lymphopenia). Moreover, the presence of thrombocytopenia can indicate a dire prognosis. In severe cases of the disease, an increase in liver enzymes and serum lactate dehydrogenase and disturbances in coagulation parameters are observed [22, 23]

In the context of the emergence of viral infectious diseases and the limitation of information about children, the role of children in the transmission cycle is not clear [24]. Therefore, attention should be paid to the clinical manifestations in sick children, and the clinical manifestations are defined after collecting more information in children's cases [25]. Therefore, wider studies in the field of children's laboratory findings to understand this disease and its impact on children and society seem necessary. Because the incidence and severity of the disease in the fifth peak are higher than the previous peaks, the present study aims to compare the results of complete blood cell count tests in children with COVID-19 who were hospitalized in the fifth peak with other COVID-19 peaks.

2. MATERIALS AND METHODS

This is a descriptive, analytical, cross-sectional study. The research population was all children hospitalized with a definite diagnosis of COVID-19 in Imam Khomeini (RA) Jiroft Hospital, who were selected and examined by census method in 2023. After obtaining permission from Jiroft University of Medical Sciences, the medical records unit of the hospital was referred, and the desired data was collected from the medical files of the patients. Finally, 112 medical records of hospitalized children with a definite diagnosis of COVID-19 were examined according to the entry and exit criteria. The inclusion criteria were age range from 2 to 18 years, absence of chronic or specific diseases related to anemia, not receiving medication or diets for anemia, no previous history of a definitive diagnosis of anemia, completeness of medical records, and a positive PCR test. Incompleteness of patients' medical records was also considered an exclusion criterion. The data collection tool included a checklist created by the researcher. Checklist according to the items listed in the patient's medical record form, including demographic information (age and sex) and clinical information (number of hospitalization days, need for oxygen therapy, average WBC, average Hg, average Hct, average MCH, average MCHC, and average PLT), was prepared. The Mentzer Index was used to measure the severity of iron deficiency anemia in the examined children. This index shows the ratio of MCV to the number of red cells (MCV/RBC). To take ethical considerations into account, after obtaining the code of ethics and making the necessary arrangements, the researcher went to the medical records unit of Imam Khomeini Hospital in Jiroft and collected the necessary information from the patient's medical records. The data was collected without the names and characteristics of the patients, and all the information of the patients, including the name and

national information, was completed, and the results were reported in general. After completing the forms, the data were entered into the statistical software SPSS version 25 for analysis. Quantitative data were reported as “mean ± standard deviation”, and qualitative data were reported as “number (percentage)”. The chi-square statistical test or Fisher's exact test was used to investigate the relationship between qualitative variables. The level of significance in the tests was considered 0.05. To comply with ethical issues in the research, data collection was done after obtaining the code of ethics from Jiroft University. The collected information remained confidential and was used only in line with the research objectives.

3. RESULTS

One hundred and twelve medical records of hospitalized children with a definite diagnosis of COVID-19 were examined in Imam Khomeini Hospital in Jiroft. Table **1** shows the information related to the demographic variables in the investigated children. The average age of the children was 12.4 ± 4.8 years in the age range of 3 to 18 years, and the highest frequency was in the age group of 16 to 18 years (41.2 percent), and the lowest frequency was observed in the age group under 5 years (14.2%); 50.8 percent of the patients were boys, among them, 40 (35.8 percent) were hospitalized for 1 to 3 days, 56 [50 percent] for 4 to 6 days, 10 (8.9 percent) for 7 to 9 days and 6 (5.3%) for more than 10 days.

Table 1. Determination of demographic variables in hospitalized children.

Variables		Frequency	Percent
Age (Year)	< 5	16	14.2
	5-10	22	19.6
	11-15	28	25
	16-18	46	41.2
Sex	Male	57	50.8
	Female	55	49.2
Number of hospitalized days	1-3	40	35.8
	4-6	56	50
	7-9	10	8.9
	>10	6	5.3

Table **2** shows information about the frequency of need for oxygen therapy, mean WBC, Hg, HCT, MCH, MCHC, and PLT of children hospitalized in the fifth peak compared to other peaks. Out of 38 people with oxygen therapy, 3 people were in the third peak, 12 people were in the fourth peak, and 23 people were in the fifth peak. Statistically, there was no significant relationship between the studied groups in terms of the frequency of oxygen therapy (P-value>0.05). The average WBC in the third, fourth, and fifth peaks was 7.7, 8.5, and 7.2, respectively, and the highest average was observed in the fourth peak; statistically, there was no significance (P-value>0.05). The average Hg in the third, fourth, and fifth peaks was 14.5, 11.8, and 12.2, respectively, and the highest average was observed in the third peak; statistically, there was no significance (P-value>0.05). The average HCT in the third, fourth, and fifth peaks was 42.9, 35.8, and 37.2, respectively, and the highest average was observed in the third peak; statistically, there was no significance (P-value>0.05). The average MCH in the third, fourth, and fifth peaks was 27.8, 26.5, and 27.1 pg, respectively, and the highest average was observed in the third peak, and statistically, there was no significant relationship (P-value>0.05). The average MCHC in the third, fourth, and fifth peaks was 33.9, 33.7, and 32.8%, respectively, and the highest average was observed in the third peak, and statistically, there was no significant relationship (P-value>0.05). The average PLT in the third, fourth, and fifth peaks was 281.5, 266.1, and 239.2, respectively, and the highest average was observed in the third peak; statistically, there was a correlation between the studied groups in terms of the obtained averages and was significant (P-value<0.05).

Table **3** shows the information related to the frequency of the Mentzer index in children hospitalized in the fifth peak compared to other peaks; the frequency of the Mentzer index was more than 13 in the third, fourth, and fifth peaks in 5, 24 and 73 people, respectively. The results show an increase in the prevalence of iron deficiency anemia in the fifth peak.

Table **4** shows the information related to the Mentzer index according to the prevalence of anemia in children with COVID-19 peak, the Mentzer index according to the age of the children, and the Mentzer index according to the gender of the investigated children. The average of anemia in the third, fourth, and fifth peaks was 15.6, 17.8, and 18.2, respectively, and the highest average was observed in the fifth peak; statistically, a relationship was observed between the studied groups in terms of the obtained averages, which was significant (P-value<0.05). In the Mentzer index less than 13, the highest frequency was observed in the age group of 15 to 18 years, and in the index greater than 13, the highest frequency was observed in the age group of 15 to 18 years. Statistically, there was a significant relationship between the Mentzer index and the age of children (P-value<0.05). No significant relationship was observed between Mentzer's index and the gender of children (P-value>0.05).

4. DISCUSSION

After about four years since the beginning of the COVID-19 pandemic, extensive research is needed to identify as much of this disease and the behavior of this virus as possible. In the first published reports about COVID-19, leukopenia, lymphopenia, anemia, and thrombocytopenia were mentioned [26]. Blood disorders, especially anemia and thrombocytopenia, are widespread and important in patients with COVID-19, and they play a significant role in the treatment and management of patients [27]. Therefore, the present study compares the results of complete blood cell count tests in children with COVID-19 hospitalized in the fifth peak with other COVID-19 peaks.

The results of the study showed that in the examined peaks, iron deficiency anemia was related to the severity

Table 2. The frequency of need for oxygen therapy, average WBC, average Hg, average HCT, average MCH, average MCHC, and average PLT of children hospitalized in the fifth peak compared to other peaks.

Peak	Oxygen Therapy		P-value
	Yes	No	
	Frequency (Frequency Percent %)	Frequency (Frequency Percent %)	
Third	3 (50)	3 (50)	0.37
Forth	12 (41.3)	17 (58.17)	
Fifth	23 (29.8)	54 (70.2)	
Peak	WBC		P-value
	Mean	Standard deviation	
Third	7.7	3.7	0.41
Forth	8.5	4.1	
Fifth	7.2	4.3	
Peak	Hg		P-value
	Mean	Standard deviation	
Third	14.5	2.4	0.4
Forth	11.8	1.8	
Fifth	12.2	1.7	
Peak	Hct		P-value
	Mean	Standard deviation	
Third	42.9	5.5	0.56
Forth	35.8	4.7	
Fifth	37.2	4.3	
Peak	MCH		P-value
	Mean	Standard deviation	
Third	27.8	4.2	0.42
Forth	26.5	4.4	
Fifth	27.1	3.7	
Peak	MCHC		P-value
	Mean	Standard deviation	
Third	33.9	1.9	0.40
Forth	33.7	2.2	
Fifth	32.8	1.7	
Peak	PLT		P-value
	Mean	Standard deviation	
Third	281.5	72.1	0.02
Forth	266.1	101.1	
Fifth	239.2	90.7	

Table 3. Determining the prevalence of mentzer's index in children admitted in the fifth peak compared to other peaks in Imam Khomeini (RA) Jiroft Hospital.

Peak	Mentzer Index	
	13> Frequency (Frequency percent %)	>13 Frequency (Frequency percent %)
Third	1 (16.6)	5 (83.4)
Forth	5 (17.2)	24 (82.8)
Fifth	4 (5.1)	73 (94.9)
P-value	0.04	0.03

of COVID-19, so in children with COVID-19, the level of MCV and RBC decreased. The COVID-19 virus, in the fifth wave compared to the past, was stronger and more contagious, and the patients' involvement with this virus was longer and more severe. In the study by Qavami *et al.*, the serum level of iron in patients with COVID-19 is lower than in healthy individuals and is associated with a high risk of severity and adverse consequences in these patients; also, the serum level of iron has an inverse relationship with the level of proinflammatory cytokines

[28]. In the study conducted by Lv *et al*., by comparing laboratory parameters in patients with COVID-19, MCV and MCH indices and red blood cell count in patients were found to be significantly decreased, and MCHC increased compared to healthy individuals [29]. The study by Dai *et al*. indicated that in patients with COVID-19, MCV and MCHC indices were decreased in most patients [30].

Table 4. The average mentzer index of the prevalence of anemia in different COVID-19 peaks, the prevalence of mentzer index according to age, and the prevalence of mentzer index according to gender in children hospitalized in the fifth peak compared to other peaks in imam khomeini [ra] jiroft hospital.

Peak	Mentzer's average index in the prevalence of anemia in children hospitalized for different coronavirus peaks		P-value
	Mean	Standard deviation	
Third	14.6	2.2	0.03
Forth	17.8	5.1	
Fifth	18.2	3.4	
Age	Prevalence of Mentzer's index in hospitalized children according to age		P-value
	13> Frequency (Frequency percent %)	>13 Frequency (Frequency percent %)	
5>	3 (30)	13 (12.7)	0.03
5-10	2 (20)	20 (19.6)	
11-15	1 (10)	27 (26.4)	
16-20	4 (40)	42 (41.3)	
Sex	Prevalence of Mentzer's index in hospitalized children according to gender		P-value
	13> Frequency (Frequency percent %)	>13 Frequency (Frequency percent %)	
Female	3 (30)	42 (50.9)	0.08
Male	7 (70)	50 (49.1)	

In Lu *et al*.'s study, it was also found that people who were hospitalized with more severe symptoms showed a decrease in red blood cell and hemoglobin counts [31]. Lorente *et al*., in Spain, observed that the hematocrit level decreased with the reduction of red blood cells in people with COVID-19 [32]. In Jafarabadi *et al*.'s study, it was concluded that anemia was an underlying factor with chance probability (OR=22) in the severity of COVID-19 disease in two groups of outpatients and inpatients. If people with severe anemia get infected with the coronavirus and suffer from gastrointestinal complications and gastrointestinal bleeding during their treatment, they will face a drop in hemoglobin and more serious problems may arise in these people [33]. Many review studies have shown that iron plays a role in the immune system and the host's susceptibility to infection. Iron regulates the function of T lymphocytes. Iron deficiency leads to thymus atrophy and affects immune function. It also leads to the impairment of cellular immunity and the function of neutrophils [34]. An adequate amount of iron is required for both the host and the pathogen. People who suffer from severe iron deficiency should take care of their health more than others because the treatment process in these patients will be slower than others if they are infected with COVID-19 [35]. Therefore, it is recommended to get anemia treated, especially due to iron deficiency, in this era of the coronavirus crisis, because with the weakening of the immune system, the risk of infection will increase.

Another finding was the reduction of blood platelets in the fifth peak compared to the third peak. In explaining this result, it can be said that the fifth wave of COVID-19 is the most severe wave, and the results of the research have shown that the coronavirus can directly or indirectly attack blood platelets. The reduction in blood platelets has also been related to the severity of the disease [36, 37]. In another study on 7613 patients, it was found that the number of platelets decreased in patients with severe COVID-19 infection. In the studies conducted, about a quarter of patients with COVID-19, especially during the first week of hospitalization, experienced anemia caused by a decrease in blood platelets compared to the normal level or thrombocytopenia [38]. Thrombocytopenia is a common abnormality in critically ill patients, which can be associated with clinical consequences, including death. Of course, this state is not always an initial event in this disease, and a significant number of patients experience it during the progression of the disease, and some others experience thrombocytopenia after discharge from the hospital [39]. These cases have also been proven in research conducted on patients. In another study conducted on hospitalized patients suffering from coronavirus in America, out of 253 cases of patients with COVID-19, 24.9% were diagnosed with thrombocytopenia. The amount of this reduction has been reported in some cases at an acute level [40].

The most important function of blood platelets is to prevent bleeding from stopping during any damage to the blood vessels. In some cases, a number of these platelets suffer from coagulation disorders due to genetic conditions or an autoimmune reaction, but what is clear is that COVID-19 causes dynamic changes in normal blood parameters, including platelets [41]. There is also a direct relationship between thrombocytopenia and COVID-19 [41]. The results of the study show that the number of platelets decreases when infected with COVID-19. It has been proven that in the most severe cases of COVID-19, the number of platelets decreases drastically [25]. However, these abnormalities are relatively small in the early manifestations of COVID-19, and about 5-18% of all patients studied in this research had a decrease of 100,000 microliters of platelets. In the meantime, people who are affected by this disease suffered from thrombocytopenia during hospitalization [42]. Changes in normal platelet parameters in patients with COVID-19

were higher and more pronounced, and in severe and critical COVID-19 patients, platelet levels were reported to be significantly lower than in patients with moderate severity [43].

In the study by Lee *et al*. in China, in the investigation of platelet parameters (MPV, PDW, and P-LCR) in patients with mild, moderate, and severe COVID-19 compared to non-infected people, the results of the study showed increased severity of the disease, decreased platelet parameters and a significant difference between the patients and the control group [44]. Scientists have proposed several mechanisms for changes in blood platelets and the occurrence of thrombocytopenia due to COVID-19. The first mechanism of cytokine storm is caused by the infectious agent of the disease. This condition is an inflammatory reaction of the body's immune system to COVID-19, and it occurs when a high number of inflammatory molecules are released in the body at the same time and eventually cause the destruction of platelets. In the second mechanism, the coronavirus infects and destroys the bone marrow cells, which reduces the level of blood platelets. In the third mechanism, COVID-19 may be produced by the production of autoantibodies or immune complexes, which target the blood platelets, causing thrombocytopenia [44, 45].

During the infection with COVID-19, the process of hematopoiesis changes from steady state to hematopoiesis under stress. In justifying the change of CBC indicators in patients with COVID-19, it has been determined that during the infection with COVID-19, the unregulated production of type 1 interferons, the delay in the production of neutralizing antibodies or the insufficient production of these antibodies, the occurrence of cytokine storm, the direct reaction of the virus with blood progenitor cells through the speak protein has been cited as one of the reasons that affect the production and maturation process of different blood cells and cause changes in CBC indices [46].

Hospitalization of patients with COVID-19 in itself can lead to imposing a significant psychological and economic burden on patients, families, and the health system. At the same time, some of the patients with COVID-19 need hospitalization and their treatment may include long-term use of ventilators, corticosteroids, and neuromuscular blockers. Some studies observed hemoglobin level and CRP as the most important factors related to the increased hospital stay of COVID-19 patients [47]. In the study by Abdulhaipour *et al.*, higher-than-normal values of hemoglobin and WBC significantly increased the average length of stay in the ICU [48]. In the face of this new and rapidly spreading virus, which has unknown characteristics in today's modern medicine, identifying biomarkers that can predict the severity and prognosis of the disease seems essential to guide clinical care. Arriving at an accurate and comprehensive evaluation of laboratory indicators in all clinical stages of the disease can help doctors provide more care to more people at risk. The most important limitation of this study was the incompleteness of the information available in the patient's files. Although the intended study was a cross-sectional study, due to space and time limitations, it was not possible to examine all causes of intervention in it.

CONCLUSION AND RECOMMENDATIONS

In general, the results showed that the decreased values of some CBC indices, such as the amount of MCV, RBC, and platelets in the fifth peak at the time of hospitalization, may predict a poor clinical outcome in patients with COVID-19. According to the Mentzer index, the degree of iron deficiency anemia affects the course of COVID-19. Research findings highlight the potential of some CBC indices, including MCV, RBC, and platelet levels during the fifth peak hospitalization, as prognostic markers for clinical outcomes in COVID-19 patients. These blood parameters can serve as early indicators of disease severity and help in risk classification and treatment planning for people infected with the virus. Furthermore, the association between iron deficiency anemia, as indicated by the Mentzer index, and the clinical course of COVID-19 emphasizes the importance of monitoring and addressing nutritional deficiencies in patients. This suggests that screening and preventive management of anemia, especially iron deficiency, may positively influence the course of COVID-19 and patient outcomes.

Given these findings, health policymakers must include regular hematologic assessments, including MCV, RBC, platelet count, and iron status assessment, in standard diagnostic and surveillance protocols for COVID-19 patients. Inclusion of these parameters in clinical decision-making processes can facilitate early identification of individuals at higher risk of adverse outcomes and enable appropriate interventions. Additionally, there is a need for comprehensive nutritional support strategies to address iron deficiency and anemia in COVID-19 patients, potentially reducing the impact of these conditions on the disease process. By recognizing the role of hematological parameters and nutritional status in the management of COVID-19, policymakers can optimize patient care and improve prognosis through targeted and preventive healthcare interventions.

LIMITATIONS OF THE STUDY

This study was hampered by several limitations. One of the restrictions was the exclusion of some patients from the study because their files did not contain all of the necessary information. Additionally, this study only included patients hospitalized in the Imam Khomeini Hospital in Jiroft. As a result, caution should be exercised when extrapolating the findings. To improve the precision and accuracy of COVID-19 disease characterization, it is advisable to conduct comprehensive and prolonged

studies. This research was a cross-sectional study, which makes it difficult to conclude causality. Considering the mentioned limitations, it is suggested that future studies be conducted with a larger sample size and in different hospitals so that the findings are more reliable. It is also suggested to check the level of electrolytes in the serum of patients with the level of consciousness and other hemodynamic components, as well as changes in the cardiovascular and respiratory systems.

AUTHORS' CONTRIBUTIONS

It is hereby acknowledged that all authors have accepted responsibility for the manuscript's content and consented to its submission. They have meticulously reviewed all results and unanimously approved the final version of the manuscript.

ABBREVIATION

CBC = Complete Blood Count

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This article reports the results of a research project approved by Jiroft University of Medical Sciences, Jiroft, Iran with the code of ethics IR.JMU.REC.1402.055.

HUMAN AND ANIMAL RIGHTS

No Animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Informed consent was obtained.

STANDARDS OF REPORTING

STROBE guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of the article is available in the Zenodo Repository at https://openpublichealthjournal.com/availability-of-data-materials.php

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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