

The investigation of the characteristics of inflammatory factors and cardiac enzymes in children with Covid-19 hospitalized with the initial manifestation of fever without other symptoms hazrat Ali-Asghar Hospital in Tehran in 2018–2019

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ABSTRACT

Introduction: The prevalence of asymptomatic fever among children is high and may be confused with fever caused by corona. The purpose of this study is to investigate the characteristics of inflammatory factors and cardiac enzymes in children with Covid-19 hospitalized with the initial manifestation of fever without other symptoms. **Methods:** In this descriptive-analytical cross-sectional study, all 200 children with positive Covid-19 were hospitalized in Hazrat Ali-Asghar Hospital in Tehran between 2018 and 2019. For gathering data, clinical records and demographic information of patients were noted in the made-researcher's checklist and the collected data were analyzed using SPSS software version 24. **Results:** It was found that the relationship between the degrees of fever of the patients with the number of platelets was also inverse and significant. In addition, there was a significant relationship between the degrees of fever of the patients and the LDH number, ALT number and segment and lymphocyte percentage of the patients. In addition, it was found that the passing time of fever has a significant relationship with ALT and ESR in such a way that with the passage of time, there is a higher probability of seeing an increase in ESR, but in the case of ALT, it increases in a shorter period of time and decreases more after the passage of time. **Conclusion:** According to the results of the present study, in case of suspected to Covid and fever in patients, along with other tests, AST, ALT, D-dimer, and CKMB can be used to diagnose Covid, in such a way that in Covid, AST is probably normal and mentioned other tests can be higher than normal.

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Introduction

Severe and acute respiratory infection syndrome coronavirus 2 (SARS-CoV-2) was recognized as the causative agent of Covid-19 disease in late December 2019 in China.^[1] In the initial reports of this disease, few cases of children's involvement were reported, and it seemed that children were immune from this disease or that their symptoms appeared milder and less than 2% of hospitalized patients included the children.^[2] Although Covid-19 was relatively mild in most children, pediatric multisystem inflammatory syndrome (MIS-C) or pediatric multisystem inflammatory syndrome which was associated with SARS-CoV-2 (PIMS-TS) has been recognized as a post-infection inflammatory condition with abnormal immune function, left ventricular dysfunction, coronary artery aneurysm, atrial block and clinical deterioration with multi-organ involvement. In fact, multisystem inflammatory syndrome in children (MIS-C) is a group of symptoms which is associated with swollen or inflamed organs or tissues.^[3] People with MIS-C require hospital care. In other words, multisystem inflammatory syndrome in children (MIS-C) is a condition that causes inflammation in different parts of the body, including the heart, lungs, kidneys, brain, skin, eyes, or digestive organs.[4]

Children with MIS-C may have fever and symptoms such as abdominal (intestinal) pain, vomiting, diarrhea, neck pain, skin rash, bloodshot eyes, or extreme fatigue. The exact cause of MIS-C has not yet known, but it is a syndrome associated with Covid-19. However, children with MIS-C had the virus that caused Covid-19 or were around a patient with Covid-19.^[5] But with the more spread of the disease and the involvement of most families and children, reports regarding severe and even fatal cases of the disease in children were published which eventually led to the recognition of multisystem inflammatory syndrome in children caused by Covid-19, which was reported by the World Health Organization and the Centers for Disease Control in the United States as a severe complication of the disease in children.^[6] Currently, in worldwide, the prevalence of this disease in children is 2.4%, although its prevalence is higher in children with the risk of multisystem inflammatory disease, multi-organ failure, under chemotherapy, and shock.[7]

Cardiac complications also occur in 60–80% of children which its prevalence is higher than Kawasaki disease^[8], and these manifestations include ventricular dysfunction, coronary artery aneurysm, conduction disorder, and arrhythmia and if this disease is suspected, a cardiac complete evaluation including troponin level and brain natriuretic peptide (BNP) and ECG should be performed immediately.^[8] Considering that the prevalence of asymptomatic fever among children is high and may be confused with fever caused by coronavirus, the investigation of the relationship between the occurrence of corona disease among this group of children has great importance and helps a lot to estimate the prediction and management of its treatment. Therefore, finding the appropriate diagnostic factors in patients who are sometimes referred with a critical condition, as well as their timely evaluation, can be helpful in the timely diagnosis and treatment of a wide range of children suffering from this disease. Therefore, in this research, we decided to investigate the characteristics of inflammatory factors and cardiac enzymes in children with Covid-19 hospitalized with the initial manifestation of fever without other symptoms in Hazrat Ali-Asghar Hospital in Tehran between 2018 and 2019.

Materials and Methods

Type of research and studied community

This study is a descriptive-analytical cross-sectional study. The studied community includes patients under 18 years of age with Covid-19 and with fever manifestations without other symptoms who were hospitalized in Hazrat Ali-Asghar Hospital between 2018 and 2019.

Sampling method and sample size

In this study, sampling method was performed using the census method and all patients hospitalized with fever manifestations and positive Covid symptoms from 2018 to 2019 in Ali-Asghar Hospital based on the inclusion and exclusion criteria were included in the study.

Inclusion and exclusion criteria of study

The presence of age over 1 month and under 18 years, the presence of fever manifestation without other symptoms and the presence of a positive PCR test (mouth-throat sample to check the virus genome) or serology (IgM antibody test for Covid-19) or lung CT involvement (radiologist's report) and the presence of a written consent form were included of the inclusion criteria into the study. Exclusion criteria of the study include the existence of a proven underlying disease and the use of medication, as well as the absence of a written consent form.

Method of sample size calculation and number of it

Since this study was conducted using census method, all patients including 200 children over 1 month and under 18 years hospitalized with positive Covid and fever manifestations were included in the study.

Data collection tool

In this study, data was collected using the made-researcher's checklist, which consisted of two parts of demographic information, age, gender and clinical information including the degree of fever, parameters including D-dimer, ferritin, CBC, diff, ESR, CRP, AST, ALT, LDH, CPK, CK MB, troponin, proBNP. Also, the validity and reliability coefficient of the mentioned questionnaire were calculated based on Cronbach's alpha equal to 0.90, which indicates the appropriate validity of this questionnaire.

Work method

In this descriptive-analytical cross-sectional study, after the approval of the project at the Iran University of Medical Sciences and Health Services and the approval of the ethics committee in medical research to the code of ethics with the number of IR.IUMS.FMD. REC.1400.074, all 200 children over 1 month having positive Covid-19 with the initial manifestation of fever without other symptoms hospitalized in Hazrat Ali-Asghar Hospital between 2018 and 2019 were included into the study based on the inclusion and exclusion criteria, which then the inclusion criteria are based on either the PCR test for Covid-19 (mouth-throat sample to check the virus genome) or serology (IgM antibody test for Covid-19) or lung CT involvement (radiologist's report) and the exclusion criteria include the existence of a proven underlying disease and the use of medication.

For gathering data, clinical records of patients hospitalized in Hazrat Ali-Asghar Hospital were studied and demographic information of patients, including age, gender, and clinical information, including degree of fever and duration of fever, were noted in the made-researcher's checklist. In addition to the above items in the checklist, parameters including D-dimer, ferritin, CBC, diff, ESR, CRP, AST, ALT, LDH, CPK, CK MB, troponin, proBNP were recorded and studied, and finally, the information were analyzed using SPSS software version 24.

Data analysis method

The obtained data were statistically analyzed using SPSS statistical software version 24. To describe the data in terms of the data type, the mean and standard deviation and for the data analysis according to the distribution of the Chi-square tests, *t*-test were used. In the analytical analysis, for the comparison mean of inflammatory factors and cardiac enzymes in the studied groups (gender and age group) using the independent sample *t*-test or, if necessary, its non-parametric equivalent was used. A significance level of 0.05 was considered.

Ethical considerations

Participation in the study was completely optional, and before the patients were included into the study, the consent form for participation in the study was filled out by the parents of the children in a fully informed manner. No name of the patients was mentioned in any part of the study during the study, and all the information of the patients will remain completely confidential by the researcher and the researcher committed to keep their information.

Results

The mean age of the studied children was equal to 3.12 ± 3.24 . The youngest participating child was 1 month old, and the oldest participating had 16 years old. Also, since the age variable in this study did not follow the normal distribution measured using the Kolmogorov–Smirnov test; the mean of this variable was also measured which was equal to 2. Among all the participants, 116 patients (58.3%) were males and 83 patients (41.7%) were females. The average degree of fever in all studied patients was equal to 38.26 ± 0.37 degrees. The average interval between the onset of fever and hospitalization in hospital for all patients was calculated in terms of 2.52 ± 1.3 days. The distribution of the two variables of fever degree and the interval between the onset of fever and hospitalization in hospital was also measured using the k-s test, and it was found that these two variables do not follow the normal distribution. The median variable of fever was equal to 38.1 degrees, and the variable of the interval between the onset of fever and hospitalization was equal to 2 days. The results of the patients' blood tests have been summarized in Table 1, and a summary of the results of cardiac factors can be seen in Table 2.

In Table 3, it has been determined that how many people have changes in their blood, inflammatory, and cardiac factors? As it is found, the changes in blood factors are very small and mostly have seen in the form of decrease in WBC and Hb, and in general, most of the changes are in the form of inflammatory and cardiac factors. In the section on inflammatory factors, we mostly see an increase in CRP and with less prevalence, we see an increase in ESR and ferritin.

In the cardiac factors section, CKMB and D-dimer had the most changes and proBNP and troponin had the least changes. The way of distribution of the laboratory variables was measured, and it was found that none of the factors does not follow a normal distribution (P value = 0.0001) and only hemoglobin follows a normal distribution (P value = 0.200) [Table 4].

As it has shown in Table 4, only the number of lymphocytes has a significant relationship with gender, and the mean percentage of lymphocytes in female's patients (42.38%) was significantly higher than that of male's patients (36.06%) (P = 0.027). In other cases, no significant relationship was observed [Table 4].

In order to determine the relationship between age and laboratory results of patients, first, people were divided into three age groups: under 1 year, 1 to 5 years, and over 5 years, and the results of the relationship between age groups and blood tests are shown in Table 5.

There was observed a significant relationship between the degree of fever of the patients with the number of platelets, the number of LDHs, the number of ALTs and segment and lymphocyte percentage (P < 0.05). The relationship between the degree of fever of the patients with the number of platelets has been inverse and significant. In other words, the increase in the degree of fever of the patients was significantly associated with a decrease in the number of platelets [Chart 1].

The relationship between the degree of fever of the patients and the number of LDHs, the number of ALTs and segment, and lymphocyte percentage of the patients was positive and significant. In other words, the increase in the degree of fever of the patients was significantly associated with an increase in the number of LDHs, the number of ALTs and segment and lymphocyte percentage [Table 6]. It was also found that the time passed of fever has a significant relationship with ALT and ESR, in such a way that with the passage of time, there is a higher

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| Table 1: Blood test results of the patients | | | | | | |
|---|--------|--------------------|--------|---------|---------|-------------------|
| | Mean | Standard deviation | Median | Maximum | Minimum | Normal |
| WBC | 9.26 | 5.80 | 7.80 | 39.30 | 1.20 | 4-10 |
| Hb | 10.78 | 1.70 | 10.70 | 18.60 | 4.50 | Under 2 years >11 |
| Plt | 267.69 | 138.97 | 235.00 | 876.00 | 37.00 | 140-440 |
| Segs | 52.24 | 20.54 | 55.00 | 93.00 | 6.00 | - |
| Lymph | 38.70 | 20.75 | 35.00 | 91.00 | 4.00 | - |
| ESR | 22.79 | 23.46 | 14.00 | 130.00 | 1.00 | Females <20 years |
| | | | | | | Males <15 years |
| AST | 81.90 | 313.12 | 14.60 | 3600.00 | 10.00 | Male: 15-40 |
| | | | | | | Female: 13-35 |
| ALT | 43.61 | 139.73 | 41.00 | 1780.00 | 5.00 | <45 years |
| CRP | 35.40 | 41.39 | 14.60 | 231.0 | 0.4 | <1 year |
| Ferritin | 184.01 | 566.36 | 75.30 | 7402.0 | 14.0 | 127 |
| LDH | 585.67 | 481.76 | 517.50 | 42.5 | 5300 | <615 |

| Table 2: Cardiac factors | | | | | | |
|--------------------------|--------|--------------------|--------|---------|---------|------------|
| | Mean | Standard deviation | Median | Maximum | Minimum | Normal |
| CKMB | 28.21 | 19.98 | 21.00 | 7 | 119 | Up to 24 |
| Troponin | 3.25 | 43.45 | 0.12 | 0.001 | 607 | Up to 0.16 |
| proBNP | 21.68 | 71.71 | 10.00 | 0.10 | 953 | Up to 125 |
| D-dimer | 364.25 | 663.86 | 180.00 | 4366 | 0.3 | <200 |
| CPK | 129.44 | 184.87 | 87.00 | 22 | 2250 | 20-200 |

probability of observing an increase in ESR, but in the case of ALT, it increases in a shorter period of time and after the passage of time decreases more [Table 6].

Discussion

MIS-C is a rare disease that sometimes occurs in children with Covid-19 infection. Symptoms of MIS-C usually develop two or more weeks after involving to Covid-19 and include inflammation of various parts of the body, such as the heart, lungs, kidneys, brain, skin, eyes, or digestive system. The cause of MIS-C in some children is unknown. MIS-C can be serious or even fatal, but most children improve with medical care. This syndrome can be resulted in an abnormal immune response to severe and acute respiratory syndrome coronavirus (SARS-CoV-2).^[9] SARS-CoV-2-associated endothelial dysfunction and cytokine storm have been implicated as mechanisms of end-organ damage in MIS-C.^[10] In a study, it was observed that the spike protein of SARS-CoV-2 was able to activate the immune system and act similarly to staphylococcal enterotoxin B. This abnormal immune response can cause multiple organ damage and failure. Myocardial damage may be associated with cardiomyopathy, coronary artery involvement that leads to ischemia, viral myocarditis, and systemic inflammation.[11] Also, in a study, autopsy findings have been shown evidence of pericarditis, myocarditis, and endocarditis associated with the infiltration on inflammatory cells, as well as the presence of the SARS-CoV-2 virus in the tissue of the heart.^[8] The present study was conducted with the aim of determining the characteristics of inflammatory factors and cardiac enzymes in children with Covid-19 hospitalized with the initial manifestation of fever without other symptoms in Ali-Asghar Hospital during 1400-1398



Chart 1: The relationship between the degree of fever and number of platelets

on 200 children over 1 month old. One of the advantages of this study was to deal with a completely new subject which according to the conducted searches, no similar study has been performed so far and most of the studies have dealt with the characteristics of MIS-C disease. In the present study, it was found that blood and inflammatory factors remained within the normal range in the majority of people. However, in the study of Shahbaz Nejad et al.,^[12] it was stated that lymphopenia and neutrophilia are seen in the tests of people. In addition, an increase in ferritin, CRP, D-dimer, troponin, and proBNP was also reported. In the study of DUFORT et al.,^[13] in all 95 children with Covid-19 who referred with fever, an increase of CRP, an increase of D-dimer in 91% of people and an increase of troponin in 71% of people was observed. But in the present study, 23.1% of people had lymphopenia and 14.1% of people had neutrophilia, and in general, changes in WBC were seen in 46% of people. Also, an increase in ferritin was seen in 25% of people, CRP in 52.3% of people, D-dimer in 34.7%, troponin in 00.5%, and proBNP in 2.5% of people. In the present study, it was found that there is a significant relationship between age and hemoglobin, platelets, percentage of neutrophils and lymphocytes, ESR, ALT, CPK, CRP, LDH, and CKMB; but gender only had a significant Khosravi, et al.: Inflammatory factors and cardiac enzymes in children with Covid-19

| Table 3: Changes in blood, inflammatory, and cardiac tests of patients | | | | | | |
|--|--------|------------|--------|------------|----------|------------|
| Blood and | Dec | rease | No | ormal | Increase | |
| inflammatory factors | Number | Percentage | Number | Percentage | Number | Percentage |
| WBC | 24 | 12.1 | 107 | 53.8 | 68 | 34.2 |
| Hb | 87 | 43.7 | 112 | 56.3 | 0 | 0 |
| Plt | 29 | 14.6 | 152 | 76.4 | 18 | 9.0 |
| Seg | 20 | 10.1 | 151 | 75.9 | 28 | 14.1 |
| Lymph | 46 | 23.1 | 147 | 73.9 | 6 | 3.0 |
| ESR | 0 | 0 | 110 | 55.3 | 89 | 44.7 |
| CRP | 0 | 0 | 95 | 47.7 | 104 | 52.3 |
| AST | 2 | 1 | 150 | 75.4 | 47 | 23.6 |
| ALT | 2 | 1 | 164 | 82.4 | 33 | 16.6 |
| СРК | 3 | 1.5 | 174 | 87.4 | 22 | 11.1 |
| LDH | 0 | 0 | 179 | 89.9 | 20 | 10.1 |
| CKMB | 0 | 0 | 110 | 55.3 | 89 | 44.7 |
| Troponin | 0 | 0 | 198 | 99.5 | 1 | 0.5 |
| D-dimer | 0 | 0 | 130 | 65.3 | 69 | 34.7 |
| Ferritin | 0 | 0 | 149 | 74.9 | 50 | 25.1 |
| proBNP | 0 | 0 | 194 | 97.5 | 5 | 2.5 |

| Table 4: Comparison of blood test results between male | | | | | | | |
|--|--------|--------|--------------------|--------|--------|--|--|
| and female patients | | | | | | | |
| | Gender | Mean | Standard deviation | Number | Р | | |
| WBC | Male | 9.44 | 6.66 | 116 | 0.496 | | |
| | Female | 9.02 | 4.35 | 83 | | | |
| Hb | Male | 10.89 | 1.75 | 83 | 0.300 | | |
| | Female | 10.63 | 1.63 | 116 | | | |
| Plt | Male | 10.63 | 1.63 | 83 | 0.270 | | |
| | Female | 259.89 | 138.36 | 116 | | | |
| Segs | Male | 278.60 | 139.91 | 83 | 0.060 | | |
| | Female | 54.50 | 21.0 | 116 | | | |
| Lymph | Male | 49.09 | 19.56 | 83 | *0.027 | | |
| | Female | 36.06 | 20.59 | 116 | | | |
| ESR | Male | 42.38 | 20.52 | 83 | 0.414 | | |
| | Female | 20.12 | 19.749 | 116 | | | |
| AST | Male | 26.57 | 27.57 | 82 | 0.979 | | |
| | Female | 74.05 | 243.64 | 116 | | | |
| ALT | Male | 92.89 | 391.52 | 83 | 0.351 | | |
| | Female | 38.52 | 81.44 | 116 | | | |
| D-dimer | Male | 50.72 | 194.30 | 83 | 0.185 | | |
| | Female | 323.35 | 589.83 | 116 | | | |
| CRP | Male | 421.6 | 755.69 | 83 | 0.373 | | |
| | Female | 33.38 | 39.82 | 116 | | | |
| Ferritin | Male | 38.22 | 43.58 | 83 | 0.106 | | |
| | Female | 145.57 | 250.30 | 116 | | | |
| CPK | Male | 237.91 | 826.41 | 83 | 0.823 | | |
| | Female | 139.52 | 228.59 | 116 | | | |
| CKMB | Male | 115.34 | 94.35 | 83 | 0.136 | | |
| | Female | 26.33 | 18.86 | 116 | | | |
| Troponin | Male | 30.85 | 21.29 | 83 | 0.969 | | |
| | Female | 0.14 | 0.119 | 113 | | | |
| LDH | Male | 7.54 | 67.01 | 82 | 0.295 | | |
| | Female | 575.88 | 499.05 | 116 | | | |
| proBNP | Male | 26.70 | 91.27 | 116 | 0.428 | | |
| | Female | 14.66 | 25.48 | 83 | | | |

relationship with pain and the amount of lymphocytes. But so far, no study has been found that investigates the relationship

between these factors with age and gender in Covid-19 and fever. However, the relationship between age and hemoglobin in people without Covid has also been observed in other studies and review studies^[10,11] and in order to determine and prove this relationship with Covid of patients, more studies and the use of a control group are needed. There was observed a significant relationship between the degree of fever of the patients with the number of platelets, the number of LDHs, the number of ALTs and segment and lymphocyte percentage (P < 0.05). The relationship between the degree of fever of the patients with the number of platelets has been inverse and significant. In other words, the increase in the degree of fever of the patients was significantly associated with a decrease in the number of platelets, and in other words, low platelets indicate a higher severity of the disease. The relationship between the degree of fever of the patients and the number of LDHs, the number of ALTs and segment and lymphocyte percentage was positive and significant. In other words, the increase in the degree of fever of the patients was significantly associated with an increase in the number of LDHs, the number of ALTs and segment and lymphocyte percentage. In addition, it was found that the time elapsed of fever has a significant relationship with ALT and ESR, in such a way that with the passage of time, there is a greater possibility of observing the increase in ESR, but in the case of ALT, it increases in a shorter period of time and decreases more after the passage of time.

29 According to the results of the present study, in case of suspicion of Covid and fever in patients, along with other tests, AST, ALT, D-dimer, and CKMB can be used to diagnose Covid, in such a way in Covid, AST is probably normal and the other mentioned cases are higher than normal.

In this regard, two ways to diagnose can be taken:

2- If the statistic number of Covid infections in the community is high, first in case of referring a child with fever without other

| Table 5: Comparison of blood test results between age groups | | | | | | |
|--|--------------|--------|--------------------|--------|---------|--------------------------|
| | Age groups | Mean | Standard deviation | Number | Р | Significant relationship |
| WBC | Under 1 year | 9.00 | 5.39 | 45 | 0.644 | Has not |
| | 1 to 5 years | 9.50 | 5.76 | 106 | | |
| | Over 5 years | 8.99 | 6.35 | 48 | | |
| Hb | Under 1 year | 9.86 | 1.31 | 45 | 0.0001* | Has |
| | 1 to 5 years | 10.91 | 1.54 | 106 | | |
| | Over 5 years | 11.37 | 2.03 | 48 | | |
| Plt | Under 1 year | 326.77 | 136.77 | 45 | 0.0001* | Has |
| | 1 to 5 years | 262.03 | 137.38 | 106 | | |
| | Over 5 years | 224.81 | 128.02 | 48 | | |
| Segs | Under 1 year | 33.68 | 17.70 | 45 | 0.0001* | Has |
| | 1 to 5 years | 56.56 | 18.35 | 106 | | |
| | Over 5 years | 60.10 | 17.23 | 48 | | |
| Lymph | Under 1 year | 570.2 | 17.45 | 45 | | |
| | 1 to 5 years | 35.23 | 18.78 | 106 | 0.0001* | Has |
| | Over 5 years | 29.18 | 17.31 | 48 | | |
| ESR | Under 1 year | 15.53 | 16.48 | 45 | 0.012* | Has |
| | 1 to 5 years | 24.21 | 26.12 | 105 | | |
| | Over 5 years | 26.50 | 21.74 | 48 | | |
| AST | Under 1 year | 61.08 | 71.41 | 45 | 0.184 | Has not |
| | 1 to 5 years | 72.95 | 252.06 | 106 | | |
| | Over 5 years | 121.20 | 513.97 | 48 | | |
| ALT | Under 1 year | 39.28 | 33.76 | 44 | 0.0001* | Has |
| | 1 to 5 years | 32.50 | 82.13 | 106 | | |
| | Over 5 years | 72.20 | 254.92 | 48 | | |
| D-dimer | Under 1 year | 375.81 | 851.68 | 44 | 0.185 | Has not |
| | 1 to 5 years | 389.37 | 676.03 | 105 | | |
| | Over 5 years | 298.69 | 396.28 | 48 | | |
| CRP | Under 1 year | 20.55 | 33.09 | 45 | 0.012* | Has |
| | 1 to 5 years | 38.45 | 38.86 | 106 | | |
| | Over 5 years | 42.56 | 50.34 | 48 | | |
| Ferritin | Under 1 year | 182.40 | 241.73 | 44 | 0.234 | Has not |
| | 1 to 5 years | 181.35 | 723.29 | 105 | | |
| | Over 5 years | 191.28 | 355.72 | 48 | | |
| CPK | Under 1 year | 172.91 | 329.64 | 45 | 0.004* | Has |
| | 1 to 5 years | 123.58 | 110.52 | 106 | | |
| | Over 5 years | 101.62 | 110.89 | 48 | | |
| CKMB | Under 1 year | 36.07 | 25.37 | 45 | 0.0001* | Has |
| | 1 to 5 years | 29.49 | 19.64 | 106 | | |
| | Over 5 years | 18.03 | 7.02 | 48 | | |
| Troponin | Under 1 year | 0.15 | 0.11 | 44 | 0.277 | Has not |
| | 1 to 5 years | 6.03 | 59.79 | 103 | | |
| | Over 5 years | 0.12 | 0.11 | 48 | | |
| LDH | Under 1 year | 692.57 | 771.13 | 45 | 0.001* | Has |
| | 1 to 5 years | 591.30 | 408.76 | 105 | | |
| | Over 5 years | 473.14 | 149.83 | 48 | | |
| proBNP | Under 1 year | 13.09 | 24.41 | 45 | 0.130 | Has not |
| | 1 to 5 years | 26.45 | 94.94 | 106 | | |
| | Over 5 years | 19.20 | 29.00 | 48 | | |

symptoms, in addition to CBC, diff, ESR, CRP, CKMB, D-dimer, and liver enzymes must be examined and using this method can be reduced the missing data.

WBC are normal and with a slight high of CRP, it is suspected for Covid and in case of high ALT, D-dimer, CKMB symptoms and or being normal AST, we are closer to the diagnosis of Covid.

In case of low prevalence of Covid, according to the national statistics of a child who referred with fever without other symptoms, CBC, diff, ESR, and CRP symptoms should be evaluated first, and in case of lack of significant points, ESR and

It should be noted that in the algorithm proposed by the Ministry of Health of Iran, high CRP is one of the cases of high severity of the disease and is mostly seen in complicated Covid cases.^[1]

| Table 6: The relationship between the | he degree | of fever | and |
|---------------------------------------|-----------|----------|-----|
| blood and inflammatory | y factors | | |

| Factor | Р | Spearman correlation |
|----------|--------|----------------------|
| WBC | 0.578 | -0.040 |
| Hb | 0.294 | -0.75 |
| Plt | 0.023* | -0.163 |
| Segs | 0.004* | 0.952 |
| Lymph | 0.036* | 0.617 |
| ESR | 0.071 | -0.128 |
| AST | 0.128 | 0.108 |
| ALT | 0.021* | 0.164 |
| D-dimer | 0.704 | -0.027 |
| CRP | 0.667 | 0.031 |
| СРК | 0.080 | 0.124 |
| LDH | 0.001* | 0.228 |
| CKMB | 0.757 | 0.22 |
| Troponin | 0.399 | 0.061 |
| proBNP | 0.667 | -0.031 |
| Ferritin | 0.429 | 0.057 |

In general, the results of this study are the basis for the next steps of WORKUP in children referred with fever without other symptoms and CBC diff are normal but ESR and CRP is high. In the current situation and despite the presence of other infections besides Covid, such as influenza, the suggestion of this study is that in case of a child referred with fever without other symptoms and normal CBC, diff, ESR, and high CRP, in the next step to discard the diagnosis of Covid, cardiac enzyme, D-dimer, and liver enzymes should be examined.

Conclusion

MIS-C is a complication of Covid-19 that causes a multi-inflammatory syndrome that can affect almost any organ system. Most patients have high inflammatory markers and may have an abnormal ECG or echocardiogram. According to the results of the present study, in case of suspicion of Covid and fever in patients, it is recommended to perform AST, ALT, D-dimer and CKMB tests in addition to other tests for diagnosis.

Execution limitations of plan

The incompleteness of the files and the lack of cooperation of the archive personnel are considered as the limitations of the present study, for the first case, if possible, information of the people was made more complete by calling the patient, and for the second case, with the necessary coordination with the management, all the permissions were taken to review all the files.

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Conflicts of interest

There are no conflicts of interest.

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