

ASYMPTOMATIC SARS-CoV-2 INFECTION IN CHILDREN

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Abstract

The aim was to determine hematological and biochemical changes in children who are carriers of SARS-CoV-2. Unlike H1N1 influenza-like illness the predictive factors of SARS-CoV-2 in asymptomatic children (carriers of SARS-CoV-2) are distinctive ratio between lymphocytes and monocytes more than 2, with occasional eosinophila, and a decrease in erythrocyte indices (MCH and MCV), and a rapid and strong increase in serum LDH value. The predictive factors are, presumably, useful for fast and cheap triage of children “from contact” until a PCR test result for SARS-CoV-2 arrives.

INTRODUCTION

The cruelty and severity of the coronavirus disease 2019 (covid19) pandemic admonished the human race that it have done overextension with changes, carried out on the Earth globe¹. This is not the first pandemic of infectious disease, but the clinical presentation of coronavirus-19 (SARS-CoV-2) infection is significantly different from the clinical picture of all known viral infections and viral epidemics. SARS-CoV-2 is specially adapted to avoid immune detection and suppress human immune responses². During the covid19 pandemic, comparing with adults, a small number of children had symptomatic disease, and the most often were asymptomatic, or a very small number of children had a severe clinical picture (respiratory and insufficiency of other organs)^{3,4}.

The aim of this brief report is to analyze the basic hematological and biochemical parameters in children with a positive polymerase chain reaction (PCR) test for SARS-CoV-2 but without symptoms of this infection i.e. carriers of SARS-CoV-2. There is almost no similar research.

METHODS

This is a study of 8 hospitalized patients because the confirmed covid-19 in their parents in the time of beginnings of pandemic and when it has existed the fear of severe covid19 in children and when the covid19 in children was an absolutely unknown disease. The short time after that, we didn't hospitalized the asymptomatic children (carriers of SARS-CoV2) which justifies a small sample. Inclusion criteria were: 1) children up to 14 years of age, 2) laboratory confirmed SARS-CoV2 viral infection by PCR technique from nasopharyngeal swab, on admission in clinic, 3) asymptomatic patients on the day of admission in clinic and during 14 days of hospitalization, 4) performed basic hematological, biochemical and radiographic diagnostics, on admission in clinic. The diagnosis of asymptomatic COVID-19 was made on the basis of the Guidelines for the Diagnosis and Treatment of Novel Coronavirus Pneumonia (6th Trial Edition) proposed by the National Health Commission of the People's Republic of China⁵. The basic hematological values contained a complete blood count⁶. The basic biochemical values included transaminases (SGOT, SGPT) and lactate dehydrogenase (LDH), and as basic inflammatory marker was determined a C-reactive protein (CRP)⁶.

In all asymptomatic subjects, on admission to the hospital, the PCR test for SARS-CoV-2 was positive. During 14 days of follow-up of asymptomatic subjects, the PCR test for SARS-CoV-2 became negative. From all subjects, we obtained data on a positive epidemiological history of SARS-CoV-2 virus infection, i.e. all subjects had one or more family members with positive PCR test for SARS-CoV-2. Observed signs and symptoms of SARS-CoV-2 infection were fever, cough, sore throat, shortness of breath, difficulty breathing, smell and taste dysfunction, sneezing, stuffy or runny nose, fatigue and tiredness, body aches, headache, diarrhea, vomiting, abdominal pain, conjunctival injection, watery eyes, mucous membrane changes, lymphadenopathy, and rash. The research was conducted in accordance with the Ethics Committee.

RESULTS

On the day of hospitalization, all subjects were in good general condition, with normal vital parameters, without above listed symptoms and all subjects underwent a complete blood count with leukocyte formula, CRP, transaminases, LDH and X-ray of the lungs. Bearing in mind the small sample (n=8), we didn't do statistical data processing, but only the presentation of the results individually per examinee, which is shown in Table 1.

Reference values (r.v.) of hematological and biochemical analyzes are presented according to the patient's age⁶. CRP and cytological and biochemical urine findings were normal in all asymptomatic covid19 subjects. An X-ray with a pronounced reticular pattern was found in 2 of 8 patients (2/8). Platelet counts and transaminase values were within r.v. in 7/8 patients.

None of the subjects had any other comorbidities or other illness that had preceded to carrying of SARS-CoV-2.

DISCUSSION

SARS-CoV2 is a single-stranded RNA virus from the coronavirus group with an unusual property of penetration in the cell and the ability to break down the beta-1 chain of hemoglobin so that the iron separates as free and hemoglobin loses its ability to bind oxygen, which leads to resistant hypoxemia and multiorganic dysfunction named pediatric multisystem inflammatory disease, COVID-19 related^{7,8}. Compensatory, the organism increases the synthesis of hemoglobin and ferritin, which explains their increased concentration in the serum, and it should be borne in mind that this compensation continues because too much hemoglobin has lost the ability to carry oxygen. High ferritin (non-toxic iron storage) is a bad prognostic sign^{7,8}. As soon as iron is separated from hemoglobin and it found in the circulation, the level of ferritin increases and the toxic effect of free iron manifests with strong oxidative damage to the lungs, what results in inflammation by alveolar macrophages i.e. incitement of inflammatory storm, and all listed changes in the lungs are radiographically presented as multiple peripheral atelectasis^{7,8}. The high concentration of iron and increased hemoglobin synthesis affect on rise of blood viscosity, which results in disseminated micro- and macro-circulatory thrombosis and embolization of tissues and organs, followed by a fast increase in D-dimmer and a sudden clinical patient deterioration and, eventual, deathly outcome^{7,8}.

During the early compensatory reaction of the organism, a larger number of monocytes are released from the bone marrow because they want to remove the excess iron from the organism. Differentiation and proliferation of the monocyte line is favored, what for developed a lymphopenia⁵. However, in asymptomatic covid19 patients included in our serial case reports, lymphocytosis was found in 7 of 8 patients (7/8), with normal white blood cell (Le) count in 7/8 patients, monocytosis in 8/8, and eosinophilia in 3/8 patients asymptomatic covid19 examinees of child age.

We compared this findings with findings related to influenza-like illness. In those likely to have H1N1 virus infection exist relative lymphopenia with or without monocytosis⁷, while in our asymptomatic covid19 patients exist monocytosis with lymphocytosis and normal or increased leukocyte count predominate, what is important differential diagnostic characteristic between these two infections. For the suspicion on SARS-COV-2 infection and before the arrival of PCR results, it is useful to determine the relationship between lymphocytes and monocytes. This ratio of lymphocytes to monocytes less than 2 with normal or low

leukocytes is found in 90% of patients with influenza-like illness and has been suggested as a replacement instead of a rapid influenza test⁷. Unlike influenza carriers, SARS-CoV-2 carriers have a lymphocyte-monocyte ratio greater than 2 with normal or increased leukocytes. Given that the covid19 pandemic is ongoing and there are indices that a new waves will occur in the future, it is important to establish clear hematological differences between this two viral infections.

The rise of the hemoglobin (Hb), which were seen in symptomatic covid19 patients were not found in any asymptomatic patients. In most children (6/8) without symptoms and carriers of SARS-CoV-2, there were no changes in erythrocyte indices, which is an important difference in relation to symptomatic covid19 patients. A fall of certain erythrocyte indices was found in a pair of children carriers of SARS-CoV-2, and that are: a fall of the mean corpuscular Hb (MCH) in 1/8 and of mean corpuscular volume (MCV) in 2/8 asymptomatic covid19 patients (carriers of SARS-CoV-2). Mean corpuscular Hb concentration (MCHC) was within normal limits in all asymptomatic pediatric covid19 patients. Found values of erythrocyte indices and their mutual relations in a pair of patients (2/8) indicate the initial accelerated consumption of Hb and the change in the volume of erythrocytes into microcytic and hypochromic, in children who are carriers of SARS-CoV-2. These findings indicate that carriers of SARS-CoV-2 had, presumably, “silent” or “minimal” inflammation that induced microcytic anemia.

The determined relationship between the number of monocytes, lymphocytes and eosinophils with normal white blood cells (WBC) number, normal Hb concentration and showed changes in erythrocyte indices in the complete blood count may be a pattern for the suspicion on the SARS-CoV-2 infection and predictive factors of asymptomatic covid19 in children, what has important practical significance in pediatrics.

The presented hematological changes were followed with a multiple rise of lactate dehydrogenase (LDH) in serum in all asymptomatic covid19 children (carriers of SARS-CoV-2). Strong oxidative lung damage and resistant hypoxemia during covid19 were accompanied by an rise of concentration of LDH in serum^{6,9}. The initial damage on cells (erythrocyte hemolysis) and tissues caused with SARS-CoV-2 is accompanied by significant activity of this enzyme (LDH) in the blood^{6,8,9}. A multiple increase of LDH levels in serum was found in all (8/8) asymptomatic covid19 subjects (carriers of SARS-CoV-2), which means that the increase in LDH is an early biochemical sign of this infection in children. In all (8/8) asymptomatic covid19 children (carriers of SARS-CoV-2), it was found multiple rise of serum LDH values with a normal red blood cell (Er) count, without an increase in Hb, already fall of erithrocyte indices, and the distinctive ratio between lymphocytes and monocytes, with occasional eosinophila. Such a haematological and biochemical finding may be a predictive factors of SARS-CoV-2 in asymptomatic children. The carriers of SARS-CoV-2, in contrast to carriers of influenza virus, have other changes in leukocyte formula⁶, and high LDH values⁶. This finding suggests the need to analyze the values of five specific serum LDH isoenzymes in order to quickly predict and set of suspicion on SARS-CoV-2 infection in patients named the “contact from covid19 patients” or the “reservoir of SARS-CoV-2”⁶. Biochemical analysis of specific LDH isoenzymes is a rapid method in contrast to the PCR test for SARS-CoV-2, the result of which is often waiting for more than 24 hours⁶.

Low-income countries have a frequent problem with a shortage of tests for rapid diagnosis of SARSCoV2 (antigen or PCR-real-time), so our suggestion would be useful for fast and effectiv triage of asymptomatic patients and the implementation of stricter isolation for children of any age from 0 to 14 years. Asymptomatic covid19 children (carriers of SARS-CoV-2) stay at home and do not cough, haven’t a fever, shortness of breath, difficulty breathing, or other characteristic symptoms and signs but there is a characteristic relationship between their the basic hematological and biochemical changes. The suspicion on asymptomatic covid19 children (carriers of SARS-CoV-2) may be, presumably, based on the factors which implies hemato-logical changes in the complete blood count (monocytosis, lymphocytosis, eosinophilia, the fall of erithrocyte indices-MCH and MCV) and a rapid and strong increase in serum LDH value. The practical applicability of the lymphocyte-to-monocyte ratio (more than 2) with normal or increased leukocytes for fast and cheap identification (finger prick) of asymptomatic covid19 children needs to be considered in the future, as and for simple distinguishing from H1N1 influenza-like illness.

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