



Letter to the Editor

Covid-19 and Children with Immune Thrombocytopenia: Emerging Issues

Keywords: Covid-19; Immune thrombocytopenia; Children.

Published: May 1, 2020

Received: March 21, 2020

Accepted: April 5, 2020

Citation: Lassandro G., Palladino V., Palmieri V.V., Amoruso A., Del Vecchio G.C., Giordano P. Covid-19 and children with Immune Thrombocytopenia: emerging issues. *Mediterr J Hematol Infect Dis* 2020, 12(1): e2020028, DOI: <http://dx.doi.org/10.4084/MJHID.2020.028>

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

To the editor.

Immune thrombocytopenia (ITP) is the most common acquired bleeding disorder during childhood. The pathogenesis of ITP is complex and currently not completely clear. Autoantibodies and cytotoxic CD8+ T cells mediate the anti-platelet response leading to thrombocytopenia. Abnormal immune response against circulating platelet and megakaryocytes results in decreased platelet survival as well as impaired platelet production.¹ Frequently, the autoimmune response in children is triggered by previous silent or overt viral infections, vaccinations, or antiviral drugs. Some specific viruses such as cytomegalovirus, Epstein Barr virus, parvovirus, rubella, and measles are commonly associated with ITP.^{2,3} Moreover, how new-onset pathogens could affect the immune response and platelet count in pediatric patients with ITP is still unknown.

The current pandemic of Covid-19 infection (coronavirus disease 2019; previously 2019-nCoV) began in Wuhan, Hubei, China in December 2019, which then spread to the rest of the country and globally.⁴ As of March 25, 2020, 183 other countries and regions, with more than 1.252.265 confirmed cases at April 5, 2020, are declared. Among the confirmed cases, 256.059 are recovered cases, and 67.999 died.⁵ Although human coronaviruses have been considered harmless for decades, their clinical importance and epidemic possibility were recognized after the outbreak of severe acute respiratory syndrome (SARS) in 2002 and the Middle East respiratory syndrome (MERS) in 2012. Particularly, Covid-19 spreads from person to person through respiratory droplets. The median time between exposure and symptoms onset is three days (ranges from 0 to 24 days). Initial symptoms are often fever, cough, and nasal congestion that can progress to pneumonia and acute respiratory distress syndrome.⁶ On the contrary, most infected children have an asymptomatic course or mild clinical manifestations with a good prognosis. Few may evolve into lower respiratory infections. Moreover, gastrointestinal

involvement and persistent positive rectal swabs in pediatric patients are recently described.⁷

Currently, whether a state of immunosuppression can contribute to worsening outcome in children during Covid-19 infection is unknown. In 2018, Ogimi et al. in a retrospective study demonstrated that children immunocompromised affected by human coronaviruses infections presented a worse clinical course and respiratory involvement compared to immunocompetent children.⁸

To date, the existence of an association between ITP and Covid-19 infection has not yet been described as well as whether the impact on platelet count differs from other well-known viruses.

However, children affected by ITP could be more susceptible to infectious diseases than others in general. It is widely acknowledged that ITP is a possible secondary manifestation of other hematological and immune disorders characterized by the deficiency of the cellular and/or humoral immune response, such as common variable immunodeficiency (CVID), selective IgA deficiency, and DiGeorge's syndrome. Additionally, the use of some medications could expose ITP patients to additional risks compared to the general population.¹ Intravenous immunoglobulin (IVIG), a therapeutic preparation comprising pooled immunoglobulin G (IgG) from large numbers of healthy people, could represent a risk of underlying infections. Generally, the risk of getting a viral infection from IVIG is considered exceedingly low. While there is no literature regarding Covid-19 infection and patients undergoing immunosuppressive therapy, the risk of immunosuppression with high dose corticosteroids, rituximab, or other immunosuppressive agents is comparable to other viruses.

Although children are less susceptible than adults to Covid-19 infection, it is indispensable to remain watchful and cautious. To prevent the spread of the infection, children with ITP should follow good hygiene practices: regular handwashing, try not to touch mouth, nose, or eyes before cleaning hands

thoroughly after returning from public places, cover the mouth with napkin or towel when coughing or sneezing, avoid crowded places and contact with sick persons, in particular those with respiratory symptoms and fever. In this context, for children affected by ITP, yet limited in recreational and motor activities, alternative strategies must be found to reduce fatigue risk and impact on health-related quality of life (HRQoL). To preserve their psychological well-being and reduce their fears, interactive methods based on positive communication should be adopted. Explaining to children preventive strategies could give them a sense of control over the risk of infection, reducing their anxiety. Regularizing daily rhythms and habits can play a crucial role in making children fearless and healthy.

Online learning, educational activities, and teaching games are significant resources supporting children's education at home. Games in which players undertake a virtual sporting activity, including bowling, hula hoop, running, a dance step, or musical instrument simulation, could represent necessary strategies to promote physical activities and reduce fatigue in children with ITP.

Although Covid-19 infection in most pediatric patients develops asymptotically or with a mild clinical course,⁷ the proportion of children who can develop a more severe disease is still unknown. A strategy to contain the spread of the infection, considering that children can be asymptomatic vehicles of disease, could be researching Covid-19 infection in all children in endemic areas. This restraining of pandemic could also result useful in protecting more

sensitive categories such as ITP pediatric patients.

In conclusion, in newly diagnosed ITP (before called "acute") we indicate to test common viral infections associated with ITP and above reported (cytomegalovirus, Epstein Barr virus, parvovirus, rubella, and measles). Moreover, in this pandemic situation, for epidemiological studies addressed to clarify a possible correlation but also for a prompt diagnosis of Covid-19 (in particular for mildly symptomatic subjects) we suggest to test new coronavirus in children with ITP and fever and/or respiratory symptoms (in progress or recent medical history).

We cannot, currently, define whether in the future an association between ITP and Covid-19 will be highlighted as well as whether the outcome of the ITP will be influenced in terms of chronicity and response to ITP therapies. These days when every daily activity has been slowed down to preserve global health, continuing to protect the psychophysical well-being of children affected by ITP allows building their future in the best way.

List of abbreviations.

ITP = immune thrombocytopenia
Covid-19 = coronavirus disease 2019
SARS = severe acute respiratory syndrome
MERS = middle East respiratory syndrome
CVID = common variable immunodeficiency
IVIG = Intravenous immunoglobulin
IgG = immunoglobulin G
HRQoL = health-related quality of life

Giuseppe Lassandro¹, Valentina Palladino¹, Viviana Valeria Palmieri¹, Anna Amoroso¹, Giovanni Carlo Del Vecchio¹ and Paola Giordano¹.

¹ Department of Biomedical Science and Human Oncology-Pediatric Unit, University of Bari "Aldo Moro," Bari, Italy.

Competing interests: The authors declare no conflict of Interest.

Correspondence to: Paola Giordano. Department of Biomedical Science and Human Oncology, Pediatric Unit, University of Bari "Aldo Moro," Bari, Italy. Tel: +390805592950. E-mail: paola.giordano@uniba.it

References:

1. Del Vecchio GC, Giordano P, Tesse R, Piacente L, Altomare M, De Mattia D. Clinical Significance of Serum Cytokine Levels and Thrombopoietic Markers in Childhood Idiopathic Thrombocytopenic Purpura. *Blood Transfus.* 2012;10:194-199. <https://doi.org/10.2450/2011.0055-11>
2. Cecinati V, Principi N, Brescia L, Giordano P, Esposito S. Vaccine administration and the development of immune thrombocytopenic purpura in children. *Hum Vaccin Immunother.* 2013;9: 1158-1162. <https://doi.org/10.4161/hv.23601> PMID:23324619 PMCID:PMC3899154
3. Elalfy MS, Nugent D. Viruses, anti-viral therapy, and viral vaccines in children with immune thrombocytopenia. *Semin Hematol.* 2016; 53 Suppl 1:S70-S72. <https://doi.org/10.1053/j.seminhematol.2016.04.021> PMID:27312173
4. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W, China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med.* 2020; 382: 727-733. <https://doi.org/10.1056/NEJMoa2001017> PMID:31978945 PMCID:PMC7092803
5. Coronavirus COVID-19 Global Cases by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). Available online: <https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6>
6. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang

- J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020; 395: 497-506. [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5)
7. Xu Y, Li X, Zhu B, Liang H, Fang C, Gong Y, Guo Q, Sun X, Zhao D, Shen J, Zhang H, Liu H, Xia H, Tang J, Zhang K & Gong S. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nat Med*. 2020. <https://doi.org/10.1038/s41591-020-0817-4>
8. Ogimi C, Englund JA, Bradford MC, Qin X, Boeckh M, Waghmare A. Characteristics and Outcomes of Coronavirus Infection in Children: The Role of Viral Factors and an Immunocompromised State. *J Pediatric Infect Dis Soc*. 2019;8(1):21-28. <https://doi.org/10.1093/jpids/pix093>
PMid:29447395 PMCid:PMC6437838