



## Decreased incidence of acute immune thrombocytopenia in children during the COVID-19 pandemic

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Received: 31 August 2022 / Revised: 17 December 2022 / Accepted: 19 December 2022 / Published online: 12 January 2023  
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We read the recent article by Sakamoto et al. [1] with interest. The authors noted a significantly decreased incidence of hemophagocytic lymphohistiocytosis during the coronavirus disease 2019 (COVID-19) pandemic according to the Japanese Society of Hematology's public Blood Disease Registration dataset. Interestingly, they also noted that the incidence of acute immune thrombocytopenia (aITP) decreased significantly during the pandemic [1]. In their analysis, the incidence of aITP decreased by 78.4% among all age groups and 52.6% among those aged under 20 years during the pandemic, relative to pre-pandemic figures [1]. Thus, their observations suggest a significantly reduced incidence of aITP in younger people during the pandemic. Since approximately two-thirds of children with ITP experience a preceding febrile illness, ITP in the majority of pediatric patients is attributable to generation of antiviral antibodies that are cross-reactive with platelet antigens [2].

During the pandemic, the person-to-person transmission of viral diseases was significantly reduced due to community-level preventative measures against the coronavirus. Indeed, both in Japan and here in Yamanashi Prefecture, the incidences of many acute viral infections in children, such as influenza, infectious gastroenteritis, hand-foot-and-mouth disease, and respiratory syncytial virus (RSV) infection, markedly decreased, at least during the first 9 months (March–November 2020) of the pandemic [3]. Yamanashi prefecture, one of the smaller prefectures in Japan by population (in 2020, 0.81 million or 0.64% of the Japan total), has the advantage of being able to perform a population-based epidemiologic study of childhood diseases. In fact, we recently reported that the incidence of Kawasaki disease during the first 9 months of the pandemic significantly decreased to 46.3% to that of the corresponding 9-month periods during the previous 5 years [3]. Thus, in this population-based retrospective study conducted in Yamanashi, we intended to verify whether the incidence of aITP decreased among children during the pandemic.

This comment refers to the article available online at <https://doi.org/10.1007/s12185-022-03302-2>.

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**Table 1** Comparison of the clinical features of acute and chronic ITP before and during the COVID-19 pandemic

Variable	aITP			cITP		
	Before <sup>a</sup>	During <sup>b</sup>	Total	Before <sup>a</sup>	During <sup>b</sup>	Total
Number ( <i>n</i> )	47	7	54	14	3	17
Age (y), median	1–15, 3	1–8, 4	1–15, 4	1–15, 5.5	2–7, 6	1–15, 6
Male ( <i>n</i> ), %	28, 60.0%	5, 71.4%	33, 61.1%	7, 50.0%	1, 33.3%	8, 47.1%
Incidence (mean ± SD)	4.85 ± 1.64	3.65 ± 2.17	4.62 ± 1.69	1.45 ± 0.82	1.57 ± 0.72	1.47 ± 0.77
Preceding infection ( <i>n</i> ), %	20, 42.6%	2, 28.6%	22, 40.7%	4, 28.6%	1, 33.3%	5, 29.4%

<sup>a</sup>Before COVID-19 pandemic, diagnosed from 2011 to 2019

<sup>b</sup>During COVID-19 pandemic, diagnosed from 2020 to 2021

We conducted a multicenter analysis of patients under 15 years of age diagnosed with ITP at all 11 inpatient facilities caring for pediatric patients in Yamanashi. Since Yamanashi Prefecture is geographically surrounded by mountain ranges on all sides, its medical system is almost independent from that of the neighboring prefectures. Indeed, the coverage ratio of Kawasaki disease in the same 11 facilities was almost 100% in the comparison of our recent study [3] with the nationwide epidemiologic survey of Kawasaki disease [4].

The study was approved by the Research Ethics Committee of the University of Yamanashi Hospital (Approval Number 2353). Diagnoses of aITP and chronic ITP (cITP) were retrospectively confirmed based on diagnostic criteria designed by the international working group [2].

From January 2011 to December 2021, 54 cases of aITP and 17 of cITP were diagnosed (Table 1). The median age of onset and male–female ratio were 4 years and 61% for aITP, and 6 years and 47% for cITP. Age at diagnosis was significantly lower among aITP patients than cITP patients ( $p=0.04$ , Mann–Whitney test). Sixty-one cases of ITP (47 aITP and 14 cITP) were diagnosed during the 9 years before the pandemic (January 2011–December 2019), while 10 cases (7 aITP and 3 cITP) were diagnosed during the selected 2 years of the pandemic (January 2020–December 2021). No patient was judged to have developed ITP in association with COVID-19 infection or SARS-CoV-2 vaccination. Of note, although statistically insignificant ( $p=0.48$  in Mann–Whitney  $U$  test), documentation of preceding infectious episodes in aITP cases decreased from 42.6% before the pandemic to 28.6% during the pandemic.

We evaluated the annual incidence rate per 100,000 children under 15 years old before and during the pandemic based on annual demographic data published by the Yamanashi Prefectural Government. The average incidences (mean ± SD) of aITP and cITP for 9 years before the pandemic were  $4.85 \pm 1.64$  and  $1.45 \pm 0.82$ , respectively, while those during the pandemic were  $3.65 \pm 2.17$  and  $1.57 \pm 0.72$ , respectively.

The incidence of aITP during the pandemic decreased to 75.3% of that before the pandemic, while the incidence

of cITP was almost unchanged (108.2%). Accordingly, although our results were statistically insignificant ( $p=0.43$ , Mann–Whitney  $U$  test), our population-based retrospective study of childhood aITP in Yamanashi was consistent with the findings in the recent article by Sakamoto et al. [1].

These epidemiological findings may support the proposed pathophysiological mechanism of aITP, whereby generated antiviral antibodies are thought to cross-react with platelet antigens [2]. In this context, since the incidence of COVID-19 in children is markedly increasing after the outbreak of the Omicron variant in Japan, careful monitoring is required to determine the prevalence of aITP.

## Declarations

**Conflict of interest** The authors declare that they have no conflict of interest.

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