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BRIEF COMMUNICATION

Impact of SARS-CoV-2 variants on the incidence of paediatric inflammatory multisystem syndrome (PIMS-TS)

In Spring 2020, following temporary success during the first wave of the world-wide pandemic of the novel 2019 coronavirus disease (COVID-19) with very few positive cases, the Czech Republic (CZ) subsequently suffered from one of the highest incidences of individuals who tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In March 2022, the cumulative number of positive cases reached almost 3.5 million (34.1% of the population).[1] Individual pandemic waves in CZ were characterised with predominant genetic variants, namely: B.1.258 in the second wave in late 2020, alpha (B.1.1.7) in the third wave in early 2021, delta (B.1.617.2) in the fourth wave in late 2021, and finally Omicron (B.1.1.529) in the last wave in early 2022.[1]

At the same time, paediatricians faced paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS).[2] The incidence of PIMS-TS among SARS-CoV-2 positive children varies at around 0.3:1000.[3] However, no data have been published on the impact of variants or lineages of SARS-CoV-2 on the occurrence of PIMS-TS. The aim of this study was to analyse the association between SARS-CoV-2 lineage and the incidence of PIMS-TS cases.

Patients and Methods

We performed a prospective nationwide observational study based on patients hospitalised with PIMS-TS in CZ. Medical training procedures, data sheet collection, and results evaluation

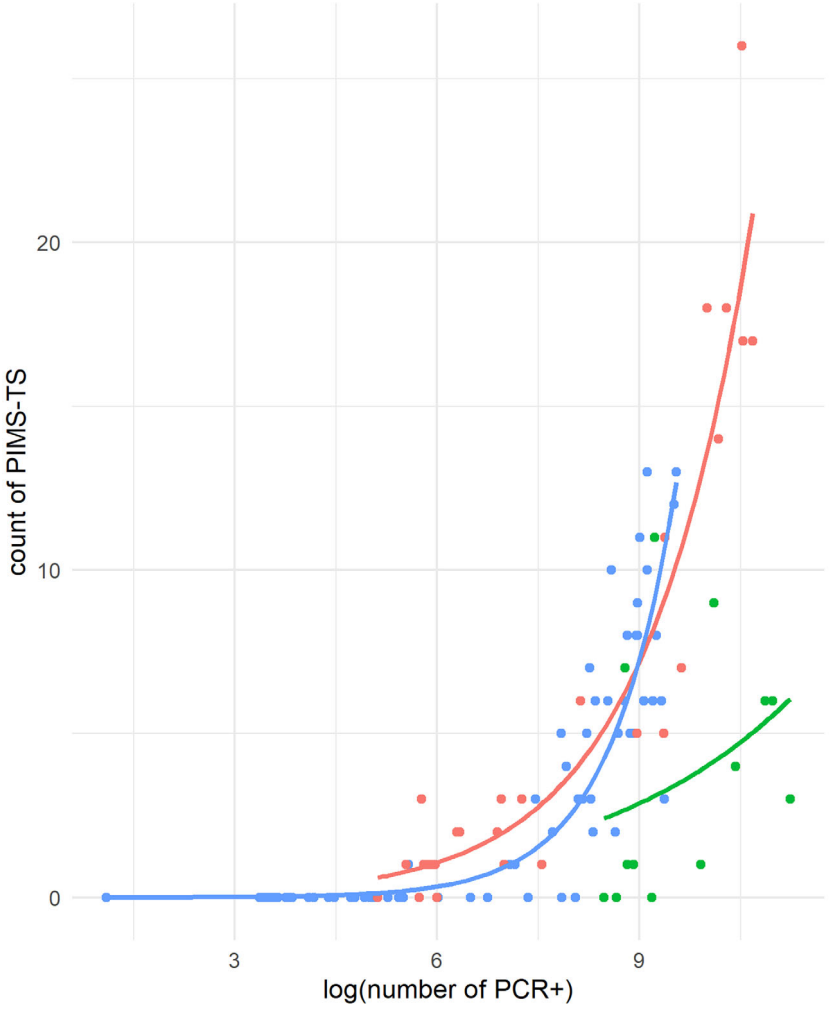

Fig. 1 Association of predominated variant of SARS-CoV-2 and PIMS-TS occurrence. Due to the time between SARS-CoV-2 infection and PIMS-TS, we moved the date of PIMS-TS diagnosis 28 days back. PCR+: PCR positivity of SARS-CoV-2. Lines Poisson regression according to predominated variant of SARS-CoV-2: (—●—) Delta, (—●—) Omicron and (—●—) Other.

within this study were conducted under the authorisation of the Czech Paediatric Society. Soon after the occurrence of the first cases of PIMS-TS in October 2020, diagnostic and therapeutic guidelines using the already available recommendations were updated. Medical staff from all Czech paediatric departments participated in an online training programme on the recognition and treatment of PIMS-TS. The recommendations were published using multiple information channels and were also available for all primary care paediatricians. All representative physicians were instructed to collect and report a standard set of data on all children diagnosed with PIMS-TS.

Patients with PIMS-TS according to World Health Organization definition,[2] who were admitted to the hospital in CZ between 1 November 2020 and 31 March 2022, were included in the study. Anonymised data were provided by collaborators. To ascertain the completeness of the nationwide data set of patients hospitalised with PIMS-TS, chairs of all inpatient paediatric departments were re-contacted, which led to the confirmation that all cases were reported.

Data on reverse transcription-polymerase chain reaction (RT-PCR) SARS-CoV-2 positive individuals and vaccination data were retrieved from reviews according to the IHIS of CZ.[1] The lineage of SARS-CoV-2 was obtained from the Czech Academy of Sciences (https://virus.img.cas.cz/samples). We categorised lineage into three groups: Omicron ('B.1.1.529', 'BA.1', 'BA.1.1', 'BA.2', 'BA.3', 'BA.4' and 'BA.5'), delta ('B.1.617.2' and 'AY.*') and other variants. Data of SARS-CoV-2 sequences were available from 108 weeks (total of 117). The Omicron variant was the most frequent over 13 weeks, delta over 28 weeks (see Appendix S1). Due to the time between SARS-CoV-2 infection and PIMS-TS, we moved the date of PIMS-TS diagnosis 28 days back.

Results

Using inclusion criteria, 429 patients with PIMS-TS were enrolled in this study. In the monitored period, the overall incidence of PIMS-TS was 0.2:1000 of general paediatric population aged 0–19 years. The incidence based on 429 patients with PIMS-TS out of 815 241 SARS-CoV-2 RT-PCR positive children was 0.53:1000. The SARS-CoV-2 infection waves and occurrence of PIMS-TS are displayed on the density plot (Figs. S1, S2). The relationship between the number of PIMS-TS cases per week and number of SARS-CoV-2 PCR positive cases according to prevalent variant of SARS-CoV-2 are displayed in Figure 1. During predominance of Omicron lineage, we found an incidence rate ratio of 0.25 (95% confidence interval, 0.18–0.34) compared to other SARS-CoV-2 variants using Poisson regression adjusted for cumulative number of vaccinated children (Table S1). Table S2 shows the number of PIMS-TS cases by variant, number of SARS-CoV-2 notifications by variant and calculation of incidence.

Discussion

We revealed that when Omicron was the predominant variant, the incidence of PIMS-TS was reduced fourfold. Thanks to a system of nationwide data collection, we could summarise data of all patients hospitalised with clinical symptoms of PIMS-TS within a defined time period of 17 months in the entire (clearly defined) population. During the same period, the data on cases of PCR positivity and numbers of vaccinated persons were continuously published and sequencing results of a representative part of all positive samples were also available. Thus, we were able to assess the association between variants of SARS-CoV-2 and incidence of PIMS-TS. To our knowledge, this is the first report showing association of the SARS-CoV-2 lineage or variant and the occurrence of PIMS-TS.

Different clinical features linked with SARS-CoV-2 variants have been published. The possible association between B.1.617.2 infection (delta variant) and increased severity of COVID-19 (pneumonia, respiratory failure) was described.[4] The explanation is increased transmissibility, viral load and prolonged viral shedding. On the contrary, B.1.1.529 infection (Omicron variant) is associated with significantly less severe outcomes for children under the age of 5 years.[5] Similarly, when Omicron is the predominant variant, the incidence of PIMS-TS is significantly reduced and cannot be simply predicted based on the data from different waves of epidemic. Our data confirmed preliminary and previously published studies.[6,7] This could be explained by a reduced ability of Omicron to trigger hyperinflammation.

This study had several limitations. The data were collected from several paediatric departments from all over the country and no specific standardisation of laboratory testing methodology could be done. Despite the online training of all medical staff, mild differences in establishing diagnosis, evaluating clinical findings and thus individualising treatment procedures cannot be excluded. However, all potential participating hospital staff were trained according to national diagnostic and treatment guidelines. Also, the exact distribution of SARS-CoV-2 variants in the Czech population was not known, so we could only estimate by dominant variant in individual pandemic waves.

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Ethics Statement

The observational study was approved by the Ethics Committee of the University Hospital Motol (number 705/21). Data were

collected from clinical reviews only and further analysed in the anonymous form, consent from patients (parents) was not required.

Data Availability Statement

Any reasonable requests to share deidentified data (including study protocol) will be considered by the senior authors and corresponding author subject to institutional agreements and ethics approvals. Data requests should be sent to the corresponding author (jan.david@centrum.cz). Authors whose names appear on the submission have contributed sufficiently to the scientific work and therefore share collective responsibility and accountability for the results.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix S1 Supporting Information