SUPPLEMENTARY MATERIAL

New-onset type 1 diabetes in Finnish children during the COVID-19 pandemic

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SUPPLEMENTARY METHODS

Patient selection for pediatric intensive care unit (PICU) admission

There are no absolute admission criteria to our PICU for children who do not require invasive mechanical ventilation, vasoactive therapy or extracorporeal support; admission is based on a joint evaluation by an emergency care paediatrician and a paediatric intensivist. A child with DKA is admitted if he or she is deemed to require constant monitoring of the level of consciousness, more than 2-4 hourly blood gases or immediate central venous access. Consequently, children with severe DKA (pH <7.10), severe hyperosmolarity or altered level of consciousness will, in most cases, be admitted to PICU.

Laboratory tests and data extraction

All laboratory parameters, except SARS-CoV-2 antibodies, were analysed by the Helsinki University Hospital (HUH) accredited centralized clinical laboratory HUSLAB. In 2016, the method for HbA1C measurement allowed exact measurements of values over 130 mmol/mol, whereas thereafter, they were reported as >130 mmol/mol. Thus, values exceeding 130 mmol/mol in 2016 were converted to 130 mmol/mol. Similarly, as β-Hydroxybutyric acid was occasionally measured using point of care test reporting values over 8 mmol/l as > 8 mmol/l, all values above 8 mmol/l were converted to 8 mmol/l. Duration of symptoms at the time of the diagnosis was categorized to the nearest entire week for up to 4 weeks, and to more than 4 weeks thereafter and cumulative incidence plots were created using survival survival and ggsurvminer packages[1,2].
SARS-CoV-2 antibody tests

Available serum samples were tested for the presence of IgG antibodies against SARS-CoV-2 spike protein using enzyme-linked immunosorbent assay (ELISA). SARS-CoV-2 spike protein was produced in Expi293 cells and ELISA was performed according to previously described protocols[3,4], with the exception that ELISA coating was 100 instead of 200 ng/well. The test has FDA authorization for emergency use in patient diagnostics [5]. One sample that gave a weak positive result in the ELISA test was further tested using a microneutralization assay[6].
SUPPLEMENTARY TABLES

Supplementary table 1. Admissions to paediatric intensive care unit due to new onset T1D during each study period (April 1 to October 31) 2016-2020. As the study period was 7 months each year, yearly population sizes at risk were scaled to 7-month person times and incidence was reported as rates per 100 000 person years. For pre-pandemic period 2016-2019 all events and scaled person years were pooled together.

T1D, type 1 diabetes
CI, confidence interval

<table>
<thead>
<tr>
<th>Year</th>
<th>Events</th>
<th>Population</th>
<th>Scaled person years</th>
<th>Incidence rate per 100 000 person years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>6</td>
<td>370 948</td>
<td>216 386</td>
<td>2.77 (1.25-6.17)</td>
</tr>
<tr>
<td>2017</td>
<td>6</td>
<td>371 716</td>
<td>216 834</td>
<td>2.77 (1.24-6.16)</td>
</tr>
<tr>
<td>2018</td>
<td>9</td>
<td>371 223</td>
<td>216 547</td>
<td>4.16 (2.16-7.99)</td>
</tr>
<tr>
<td>2019</td>
<td>4</td>
<td>369 807</td>
<td>215 721</td>
<td>1.85 (0.70-4.94)</td>
</tr>
<tr>
<td>2016 - 2019</td>
<td>25</td>
<td>1 483 694</td>
<td>865 488</td>
<td>2.89 (1.95-4.27)</td>
</tr>
<tr>
<td>2020</td>
<td>20</td>
<td>366 754</td>
<td>213 940</td>
<td>9.35 (6.03-14.49)</td>
</tr>
</tbody>
</table>
**Supplementary table 2. Children registered to Finnish pediatric diabetes registry due to new onset T1D during each study period (April 1 to October 31) 2016-2020.** As the study period was 7 months each year, yearly population sizes at risk were scaled to 7-month person times and incidence was reported as rates per 100 000 person years. For pre-pandemic period 2016-2019 all events and scaled person years were pooled together.

T1D, type 1 diabetes

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<thead>
<tr>
<th>Year</th>
<th>Events</th>
<th>Population</th>
<th>Scaled person years</th>
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</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>58</td>
<td>253 210</td>
<td>147 706</td>
<td>39.3 (30.4-50.8)</td>
</tr>
<tr>
<td>2017</td>
<td>53</td>
<td>255 533</td>
<td>149 061</td>
<td>35.6 (27.2-46.5)</td>
</tr>
<tr>
<td>2018</td>
<td>58</td>
<td>257 141</td>
<td>149 999</td>
<td>38.7 (29.9-50.0)</td>
</tr>
<tr>
<td>2019</td>
<td>62</td>
<td>257 958</td>
<td>150 476</td>
<td>41.2 (32.1-52.8)</td>
</tr>
<tr>
<td>2016 - 2019</td>
<td>231</td>
<td>1 023 842</td>
<td>597 241</td>
<td>38.7 (34.0-44.0)</td>
</tr>
<tr>
<td>2020</td>
<td>84</td>
<td>257 158</td>
<td>150 009</td>
<td>56.0 (45.2-69.3)</td>
</tr>
</tbody>
</table>
FIGURE LEGEND

Supplementary figure 1. Cumulative incidences of T1D diagnoses and time since symptom onset for PICU admission (left panel) and patients registered to FPDR (right panel). The differences between the pre-pandemic and pandemic periods were not statistically significant (PICU cohort $P=0.09$; and FPDR cohort $P=0.29$).

T1D, type 1 diabetes; PICU, paediatric intensive care unit; FPDR, Finnish pediatric diabetes registry
REFERENCES


