

# COVID 19 and newly diagnosed type I diabetes mellitus in paediatrics

## Abstract

**Introduction:** Covid 19 has a complex relationship with diabetes. There is anecdotal evidence that it could be causative for new onset diabetes in paediatrics. In this audit, we aim to study our cohort of new onset diabetes in children and young people (CYP) during the Covid pandemic in a DGH setting. We sought to identify any causative or associational link between Covid 19 and new onset diabetes.

**Method:** We reviewed the handwritten notes, e-notes and investigations available on the pathology server for our newly diagnosed diabetes CYP from February 2020 to January 2022. We compared the number of new diagnosis and DKA presentation, with the previous two years (February 2018 till Jan 2020), which was pre-Covid.

**Results:** A total of 65\* cases were included in this audit, of which 39 boys and 26 girls. Age ranged from 9 months to 17 years. 47 were White British. The most common presenting symptom was polyuria followed by polydipsia and weight loss. 55% of patients presented to the hospital within three weeks of the beginning of their symptoms. 40% of patients were in DKA at presentation. GAD and/or IA2 antibodies were present in 60 (90%) cases. Only four patients were positive for Covid-19, 40 cases were negative at the time of presentation and rest were not tested. In comparison to the two years pre-Covid, the newly diagnosed type I diabetes cases number increased by 25%. DKA at presentation in this time increased by 3% and was not attributed to delayed presentation.

**Conclusion:** We have demonstrated a 25% increase in new onset diabetes during the 2 years of pandemic, with a 3% increase in rate of DKA. 90% of the newly diagnosed CYP were autoantibody positive, hence had the immune predisposition. However, we have not been able to prove a direct link between Covid-19 infection and new onset diabetes in CYP. Hence whether Covid 19 is causative or associational, begs further studies.

**Keywords:** COVID19, diabetes mellitus, paediatrics

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## Introduction

Type 1 diabetes (T1D) is traditionally viewed as a disease of pancreatic  $\beta$ -cells being attacked by autoreactive T lymphocytes, leaving a person in danger of hyperglycaemia- and hypoglycaemia-related complications.<sup>1</sup>

A potential relationship between viruses and T1D has been suggested, with many viruses being incriminated, including enteroviruses, rotavirus, cytomegalovirus, Epstein-Barr virus, parechovirus, influenza, parvovirus, mumps, and rubella.<sup>2</sup> An increase in the number of children with newly diagnosed type 1 diabetes (T1D) has been reported during the COVID-19 pandemic,<sup>3</sup> and several reports from regions heavily impacted by the pandemic suggest that more children with new-onset T1D now present with severe diabetic ketoacidosis (DKA).<sup>3-8</sup>

Diabetic ketoacidosis (DKA) is a potentially life-threatening complication of T1D that occurs with severe insulin deficiency, consisting of hyperglycaemia, ketosis, and metabolic acidosis.<sup>9</sup> This acute condition is responsible for most of the diabetes-related morbidity and mortality in affected children.<sup>10,11</sup> Indeed, recent data showed that DKA remains the leading cause of death in individuals aged <15 years newly diagnosed with T1D.<sup>12</sup>

Despite the association between T1D and DKA with infection during COVID-19 epidemic, different findings have been reported. Gottesman et al.,<sup>13</sup> reported an increase in the incidence of new-onset T1D among US children during the COVID-19 pandemic. Salmi et

al.,<sup>14</sup> also reported a similar picture in Finnish children. Similarly, in a multicentre regional data from Northwest London, Unsworth et al.<sup>15</sup> describes an increase in new-onset type 1 diabetes in children during the COVID-19 pandemic, with evidence of SARS-CoV-2 infection or exposure in a proportion of those tested.<sup>15</sup>

In contrast, Ho et al.,<sup>16</sup> reported no change and Rabbone et al.,<sup>17</sup> reported a decrease in T1D frequency. Despite different outcomes in the development of new-onset T1D, these studies have shown a significant increase in DKA and severe DKA in the diagnosis of diabetes in children and adolescents during the COVID-19 pandemic.<sup>13,16-18</sup> Recently, Rahmati et al.,<sup>19</sup> in their systematic review and meta-analysis of 26 studies demonstrate a global significant increase in the incidence of childhood new-onset T1D, DKA, and severe DKA with elevated hyperglycaemia and mean HbA1c levels at T1D diagnosis in the first year of the COVID-19 pandemic compared to pre-COVID-19 period.

In our study, we compared the incidence of type one DM in children in a District General Hospital settings in the two years before and during the COVID -19 pandemic.

## Methods

This is a retrospective study that included all children and young people with new onset diagnosis of diabetes, this study compared two epochs; the two years of COVID 19 pandemic, from February 2020 to January 2022 and pre COVID 19 data, from February 2018 to January 2020. We reviewed handwritten notes, e-notes and investigation

results on the pathology server. The COVID testing was done as per the trust policy to screen all admitted patients for the COVID 19 antigen. This was considered as a service evaluation, hence, no ethical permission was required.

### Results

In the period from February 2020 to January 2022, there were 65 newly diagnosed cases of diabetes in our trust. These included 39 boys and 26 girls. The age at the time of presentation ranged from 9 months to 17 years. 72% of cases were of British White origin. The most

common presenting symptoms in our cases were polyuria, polydipsia, and weight loss. 70% of cases presented to the hospital within three weeks of their symptoms. Through the COVID 19 antigen screening tests, 4 cases were positive, 40 cases tested negative and the test was not done in 21 cases. Only one case had a direct contact with a confirmed COVID 19 case (Table 1).

The number of newly diagnosed cases in the study period was higher than the number of diagnosed cases in the preceding two years by 25%. The number of patients that presented in DKA increased by 3% (Table 2). The findings were not statistically significant cases.

**Table 1** Newly diagnosed type one Paediatric diabetes cases in the period from February 2020 to January 2022

Sex	(n=65 cases)		
	Male, n (%)	39 (60)	
Age at presentation	Female, n (%)	26 (40)	
	< 5 years, n (%)	13 (20)	
	5-10 years, n (%)	27 (42)	
Ethnicity	>10 years, n (%)	25 (38)	
	White British, n (%)	47 (72)	
	Not stated, n (%)	9 (14)	
	Other-White, n (%)	5 (8)	
Presenting symptoms	Other Ethnic groups, n (%)	3 (6)	
	Polyuria, n (%)	50 (77)	
	Polydipsia, n (%)	38 (58)	
	Weight loss, n (%)	21 (32)	
	Other symptoms, n (%)	25 (38)	
Period from symptoms to diagnosis	Asymptomatic, n (%)	3 (4)	
	Within three weeks, n (%)	46 (71)	
	>three weeks, n (%)	19 (29)	
Islet Cell antibodies	GAD antibodies	Positive, n (%)	39 (60)
		Negative, n (%)	21 (32)
		Unknown, n (%)	5 (8)
	IA2 antibodies	Positive, n (%)	42 (65)
		Negative, n (%)	18 (28)
		Unknown, n (%)	5 (7)
COVID-19 status	Positive, n (%)	4 (6)	
	Negative, n (%)	40 (62)	
	Unknown, n (%)	21 (32)	
COVID-19 contact	Contact with confirmed cases, n (%)	1 (1.5)	
	No contact with confirmed cases, n (%)	64 (98.5)	

**Table 2** Comparison in the number of the newly diagnosed type 1 diabetes cases and DKA incidence at the time of presentation between the two periods

	February 2018 to January 2020	February 2020 to January 2022	P value
Total number of cases, n	61	81	0.255315
Number of cases presented in DKA, n (%)	23 (37)	26 (40) *	0.33505

\*Of 65 studied.

### Discussion

In this retrospective two epoch analysis, we made a comparison between the number of newly diagnosed type one diabetes in paediatrics during the COVID-19 pandemic and the number of new diagnoses in the preceding two years. Based on our data, we noticed a non-statistically significant rise in the number of cases during the pandemic period. These findings support the findings of Gottesman et al.,<sup>13</sup> and Salmi et al.,<sup>14</sup> who reported an increase in the incidence of new-onset T1D during the COVID-19 pandemic among US and Finnish children respectively. Similarly, Rahmati et al.,<sup>19</sup> in their

systematic review and meta-analysis demonstrate a global significant increase in the incidence of childhood new-onset T1D. In contrast, Ho et al.,<sup>16</sup> reported no change in the incidence of T1D during the COVID-19 pandemic, while Rabbone et al.,<sup>17</sup> reported a decrease in T1D frequency.

Although Unsworth et al.,<sup>15</sup> found evidence of SARS-CoV-2 infection or exposure in a proportion of tested patients in their multicentre regional data from Northwest London, we did not find evidence of COVID-19 infection or direct contact with confirmed cases. The presence of pancreatic autoantibodies points to the autoimmune process rather than direct impact from COVID-19 infection on the

pancreatic cells. In the TEDDY study, the relationship between upper respiratory infections and T1D is attributed to an increase in autoimmunity in the beta cells of the pancreas.<sup>20</sup> A limitation of our study is that only the COVID antigen at the time of diagnosis was checked but not the antibody which may indicate previous exposure to COVID-19. Viral infections seem to trigger autoimmune insulinitis and progressive pancreatic beta cell destruction. Although, therefore we are unable to ascertain a direct causal link, we cannot exclude that past COVID infection may have triggered autoimmune T1D following a latent period. This mechanism requires further investigation.

The aforementioned studies have shown a significant increase in DKA and severe DKA in the diagnosis of diabetes in children and adolescents during the COVID-19 pandemic.<sup>13,16–18</sup> The relationship between COVID-19 and the Renin Angiotensin Aldosterone System may play a role in the pathophysiology of DKA as the Angiotensin Converting Enzyme 2 acts as a receptor for SARS-CoV-2.<sup>21</sup> Our study supports this rise in showing a non-significant trend towards increasing numbers of patients presenting with DKA. In our study, this was not related to a delayed presentation or difficult access to the healthcare system during the lockdown.

## Conclusion

In comparison with previous two years, the number of the newly diagnosed type one diabetes cases in paediatrics has increased during COVID-19 pandemic. More studies are needed to find out whether this is related to the direct effect of COVID-19 virus on the pancreatic cells or not.

## Acknowledgements

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## Conflict of interest

The authors declare no conflict of interest.

\*The total number of cases in the study period was 81 cases. We had access to 65 cases' data only.

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