COVID-19 and children with diabetes: emerging knowledge

The global epidemiological and clinical patterns of COVID-19 among children with diabetes are still very limited. In this report Associate Professor May Ng investigates the current outcome data for young people with diabetes and COVID-19 and discusses the need for continued vigilance to ensure emergency paediatric conditions are dealt with urgently, as well as the essential health messages for young people with diabetes.

In March 2020, the World Health Organization declared the coronavirus disease 2019 (COVID-19) outbreak a pandemic and a public health emergency of international concern. A study of 1099 patients from China with laboratory-confirmed symptomatic COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reported that the most common symptoms of COVID-19 were fever and cough, with a median incubation period of four days.[1] Emerging research has now reported that the clinical spectrum of COVID-19 can be very variable from mild flu-like symptoms, to rash, blood disorders, pneumonia, acute respiratory distress syndrome (ARDS), respiratory failure, cardiac conditions, multiple organ failure and death.[2,3]

COVID-19 and children

A systematic review of 45 relevant scientific papers reported that children accounted for between 1–5% of confirmed COVID-19 cases, and children presented with a milder disease course and better prognosis compared to adults. Deaths were also extremely rare in children.[4] Most of the studies reported originated from China, with a few from Italy, Iran and South Korea. The review included case reports of children with COVID-19 who had other comorbidities but was unable to identify any study that quantified the prevalence of comorbidities in children. The largest cohort of paediatric COVID-19 cases were reported by Dong *et al.* based on the Chinese Center for Disease Control and Prevention epidemiological study of 2143 children under 18 years of age. In this study, one death was reported and 5.9% of the cases were categorised as severe and critical cases in children.[5]

Early evidence reports that children and young people have lower susceptibility and transmission rates of COVID-19.[6] Somekh *et al.* reported that children age 5–17 years were 61% and children of 0–4 years of age were 47% less likely to have a COVID-19 positive test compared with adults residing in the same household.[7] This was similarly reported in population-based screening studies in Iceland where children under 10 years of age had a lower incidence of COVID-19 infection,[8] and in Geneva where significantly lower sero-prevalence rates of infection were observed for children aged five to nine years.[9]

Recent reports in the United Kingdom, United States of America, France and Italy citing a link between COVID-19 and a type of Kawasaki-like multisystem hyperinflammatory syndrome, also referred to as Paediatric Inflammatory Multisystem Syndrome temporally associated with SARS-Cov-2 (PIMS-TS), has been especially worrying to parents.[10] Kawasaki disease is one of the most common known primary vasculitis disorders in childhood, typically occurring in children under the age of five. While the majority of children recover completely after a few weeks, early treatment is necessary to prevent possible severe complications such as coronary artery aneurysms.[11] SARS-CoV-2 is thought to affect multisystem organs through a combination of direct vascular and pro-inflammatory activation which occurs during an acute COVID-19 infection or post infection.[12] The relationship of Kawasaki disease to COVID-19 remains unclear and causality has not been confirmed.

COVID-19 and diabetes

People with diabetes are at risk of infections including influenza and are recommended to have the annual influenza vaccinations.[13] Diabetes remains a significant risk of morbidity and mortality in patients with COVID-19.[14–16] Of 72,314 cases of COVID-19 published by the Chinese Center for Disease Control and Prevention, an increase in mortality in people with diabetes was found (2.3% overall compared with 7.3% in patients with diabetes).[14]

National diabetes and mortality data in England reported a total of 17,882 and 372,242 deaths between 1 January 2017 and 24 April 2020 in people with type 1 and type 2 diabetes respectively.[17] This was the first and largest study to investigate the risk of mortality in hospital with COVID-19 by type of diabetes. Barron *et al.* reported that one-third of all deaths in-hospital with COVID-19 occur in people with diabetes. After adjusting for key confounders such as age, sex, deprivation, ethnicity and geographical region, people with type 1 and type 2 diabetes had 3.50 and 2.03 times the odds respectively of dying in hospital with COVID-19 compared to those without diabetes. The degree of hyperglycaemia measured by HbA1c and obesity in both type 1 and type 2 diabetes is also independently associated with increased COVID-19 mortality.[17,18] In people with type 2 diabetes, an HbA1c of ≥86mmol/mol had a hazard ratio of 1.62 (95% CI 1.48–1.79) compared with people with an HbA1c of 48–53mmol/mol. In people with type 1 diabetes, the raised risk was only statistically significant in those with an HbA1c ≥86mmol/mol (hazard ratio of 2.19, 95% CI 1.46–3.29) when compared to those with an HbA1c of 48–53mmol/mol. With regard to obesity risk, people with type 1 diabetes and a BMI of ≥40kg/m^2 had a mortality hazard ratio of 2.15 (95% CI 1.37–3.36) and in people with type 2 diabetes the hazard ratio was 1.46 (95% CI 1.50–1.79) compared to people with a BMI of 25–29.9kg/m^2. An international

panel of experts in the field of diabetes and endocrinology have published guidance and practical recommendations for the management of diabetes during COVID-19, and have advised people with diabetes who have not yet been infected with COVID-19 to intensify their glycaemic management as a means of primary prevention of COVID-19 disease.[16]

COVID-19 and children with diabetes

At the time of writing, current global reports suggest that children, adolescents, and young adults under the age of 25 years affected by type 1 diabetes have a disease pattern similar to that of children who do not have diabetes and are at no greater risk of being affected by COVID-19 than those without diabetes.[19,20] The International Society of Pediatric and Adolescent Diabetes (ISPAD) further reported that, as of 24 March 2020, paediatric endocrinologists from China and Italy reported no cases of COVID-19 in youths with diabetes less than 25 years old requiring hospitalisation.[20] This was in concordance with the national diabetes and mortality data in England which reported no deaths of people with COVID-19 and diabetes in the age group under 20 years old.[17] This was similarly reported in the United States where, out of 2572 COVID-19 confirmed cases in people age 18 years and younger, documented comorbidities information did not include either type 1 or type 2 diabetes.[21]

Continued vigilance and do not delay presentation

The global lockdown has reported on substantial reductions in paediatric emergency attendances as well as visits to the general practitioners in many countries, including the United Kingdom. Children continue to become unwell with illnesses such as sepsis, chest infections, newly-diagnosed diabetes, severe asthma and surgical emergencies such as appendicitis that are not COVID-19 related. However, delayed access to seeing hospital care has been reported due to the fear of COVID-19.[22,23] Cases of delayed presentation leading to delayed diagnosis of new-onset type 1 diabetes have been reported that led to presentation of severe diabetic ketoacidosis, a life-threatening condition. Reasons for delayed presentation have ranged from fear of contracting COVID-19 to an inability to contact/access a medical provider for timely evaluation.[23] It is critically important to stress that paediatric conditions will continue to occur and that fear and concerns of COVID-19 should not be a reason to delay a referral or access to a health care provider.

Adapting diabetes management using technology

Due to fear of COVID-19, there has been reduced access to primary care, diagnostics and hospital services for many services including diabetes care. Many resources have been implemented to maintain a level of routine diabetes care through the use of social media, telemedicine and telephone clinics.[24,25] In paediatric diabetes, health care delivery has been at the forefront of transitioning towards remote care where clinical management and structured education are now being delivered through technology-enabled approaches.[25] As the rules for access to telemedicine have become more relaxed, families and patients with diabetes are now collaborating with diabetes teams to upload data relating to their diet, physical activity data, blood glucose data and insulin pump data so that they can be reviewed together through telemedicine clinics, shared platforms and feedback given at the same time. Structured education and mental health support are being delivered remotely with good feedback.[25] In a future where the COVID-19 pandemic is over, it is likely with the success of these measures that telemedicine and remote diabetes clinic management will become part of a routine form of delivering diabetes care.

KEY POINTS

- The research and data on COVID-19 and children with diabetes are extremely limited
- Limited evidence suggests that children and young people have lower susceptibility and transmission rates of COVID-19
- At present, there is no evidence to suggest that children with diabetes are more prone to being infected with COVID-19 compared to other children without diabetes
- There is also no evidence that children with diabetes are more likely to be infected with COVID-19 paediatric multisystem inflammatory syndrome compared to children without diabetes
- It is important that children with diabetes continue to be vigilant, especially around handwashing and social distancing
- Children and families should follow the principles of management of diabetes sick days rules if they are unwell and be advised not to delay access or attendance of health care provisions
- Children and families are encouraged to continue maintaining a healthy lifestyle and to optimise their diabetes management

Conclusions

The global epidemiological and clinical patterns of COVID-19 among children with diabetes are still very limited. While no definite conclusions can be made based on the current evidence, there is emerging knowledge from research that would hopefully provide us with a better understanding of the associations between COVID-19 and diabetes in children. More studies in children with diabetes and COVID-19 are likely to have an impact on future recommendations.

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References are available online at www.practicaldiabetes.com.

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