

Paediatric Type 2 Diabetes Presentation and Trends Four Years Pre- and Post-COVID-19 Pandemic in Klang Valley, Malaysia

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Abstract

Background. The recent COVID-19 pandemic has led to a rise in the incidence of obesity both in children and adults. Studies on the effect of the pandemic on Type 2 diabetes mellitus (T2DM) trends in children are limited. In this study, we aim to evaluate the frequency, clinical characteristics and demographics of newly-diagnosed paediatric T2DM cases 4 years before and after the pandemic.

Methodology. The frequency and clinical data of patients aged ≤ 18 years with newly-diagnosed T2DM in 4 tertiary centers in urban Malaysia from 18 March 2016 until 17 March 2020 (pre-pandemic) and 18 March 2020 until 17 March 2024 (post-pandemic) was collected.

Results. Seventy-five (75) patients were recorded with newly-diagnosed T2DM pre-pandemic and fifty-four (54) patients were recorded with newly-diagnosed T2DM post-pandemic. There was no significant increase in T2DM cases and diabetic ketoacidosis (DKA) during pandemic and T2DM cases fell to below pre-pandemic levels in the 3rd and 4th year post-pandemic. HbA1c and serum glucose were lower post-pandemic than pre-pandemic: 10.1% vs 11.9%, $p = 0.008$ and 12.0 mmol/L vs 16.1 mmol/L, $p = 0.038$ respectively.

Conclusion. The incidence of T2DM and DKA did not increase during the pandemic and further declined in year 3 and 4 post-pandemic. Lower HbA1c and serum glucose in the post-pandemic group may suggest improved screening services and greater access to medical care.

Key words: COVID-19 pandemic, diabetic ketoacidosis, type 2 diabetes mellitus, obesity

INTRODUCTION

The COVID-19 pandemic was a global health crisis that significantly impacted the healthcare system worldwide in the year 2020 and 2021. One of the major health burdens observed was the unprecedented rise in the incidence of new onset type 1 diabetes mellitus (T1DM) and the surge in diabetic ketoacidosis (DKA) cases, especially severe DKA.¹⁻⁵ The rise in T1DM cases was hypothesised to be due to selective beta cell destruction led by the expression of SARS-CoV-2 main entry host receptor on pancreatic beta cells, though this could not be confirmed due to lack of COVID-19 screening in asymptomatic individuals and paucity of positive COVID-19 status among DM patients.⁵⁻⁷ The delay in seeking medical consultation during the pandemic may have also led to a surge in DKA cases with more severe presentations.⁶⁻⁹

Another concerning impact of the pandemic is the rise in the occurrence of obesity amongst children and adolescents during the pandemic lockdown. Recent data from the CDC had shown that the monthly rate of body mass index (BMI) increase in the paediatric population aged 2-19 years old in the United States had doubled in 2020 as compared to in 2018 and 2019 (pre-pandemic).¹⁰ In Malaysia, the incidence of obesity in adolescents aged 13-17 years old had risen from 10.6% in 2012 to 14.3% in 2022.¹¹ The trend of T2DM during the pandemic in 2020 and 2021 as well as after the pandemic has not yet been studied in Malaysia.

Studies on the effect of the COVID-19 pandemic on paediatric T2DM trends in other regions of the world have showed mixed findings, with the majority of studies showing an increase in T2DM cases during the pandemic.¹²⁻¹⁹ The increase in cases of T2DM and DKA were primarily

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reported in the United States.⁵ Studies in Asia are limited with mixed results.^{12,18} As most of the studies on T2DM only report the incident cases during the pandemic, the long-term trend of T2DM after the pandemic is still not known.⁵

Malaysia was under a movement control order (MCO) between 18 March 2020 and 3 May 2020 as well as between 1 June 2021 and 28 June 2021. During the MCO, most of the population were confined at home as education was provided virtually, resulting in unhealthy diets, lack of physical activities, and increased screen time. Social isolation had also caused higher stress levels promoting a state of insulin resistance in this population group. It is unknown if the social isolation experienced during the pandemic period had resulted in long-term increase in paediatric T2DM or DKA cases in Malaysia. The objective of this study is to evaluate the trends of T2DM and DKA cases during the 4-year period after the pandemic onset (18th March 2020 to 17th March 2024) as compared to the 4-year period before pandemic onset (18 March 2016 to 17 March 2020). 18th March 2020 was taken as the date of pandemic onset following the date when the MCO was first implemented. We also aim to determine the demographic and clinical characteristics of T2DM cases in children who presented during the 4-year period post-pandemic in comparison to the pre-pandemic period. Knowledge on the T2DM and DKA trends would be invaluable to strategise efforts to combat obesity and prevent metabolic syndrome. Evaluation of the demographics and clinical characteristics of T2DM patients during these two time periods will also enable identification of patients at risk of T2DM and DKA.

METHODOLOGY

Subjects

A retrospective study was conducted at 4 paediatric endocrine tertiary centres in Klang Valley, Malaysia during the 4-year period before the pandemic onset (18 March 2016 to 17 March 2020) and the 4-year period after the pandemic onset (18th March 2020 to 17th March 2024). These 4 tertiary centres are paediatric endocrine referral centers for Selangor and Wilayah Persekutuan in Malaysia. The sampling method used was universal sampling of all T2DM patients aged ≤ 18 years who had presented during these two time periods. The sample size for this study was estimated to be 96 using the formula for hypothesis testing for two proportions and was based on a study by Marks BE et al. wherein the DKA proportion during the pandemic was 0.234 and 1-year pre-pandemic was 0.04 among T2DM youths ≤ 21 years of age.^{15,20}

The diagnosis of T2DM included symptoms of hyperglycemia with the absence of diabetic autoantibodies and any one of the following: 1) fasting blood glucose ≥ 7 mmol/L, 2) 2-hour plasma glucose on OGTT ≥ 11.1 mmol/L, 3) random plasma glucose ≥ 11.1 mmol/L or 4) HbA1c $\geq 6.5\%$.²¹ Patients with maturity onset diabetes of the young (MODY), syndromic patients and patients with preexisting

conditions (e.g., Cushing's syndrome) or medications that could affect blood glucose (e.g., steroids or immunosuppressives), were excluded from the study. This study had obtained approval from the Malaysian Medical Research and Ethics Committee (NMRR ID 22-02002-OLV [IIR]).

MATERIAL AND METHODS

The demographic characteristics of T2DM patients at the initial presentation (gender, ethnicity, BMI z-score, BMI status and age of diagnosis) during the two time periods before and after the pandemic were retrieved. Information on the clinical characteristics (HbA1c, initial serum glucose, duration of symptoms, DKA proportion, DKA severity, pH, HCO₃, hospitalisation duration, PICU admission) was also reviewed. BMI status was categorised to obese (BMI $>95^{\text{th}}$ centile), overweight (85th to 95th centile) and normal (BMI $<85^{\text{th}}$ centile) by CDC growth charts. DKA was characterized by venous pH <7.3 or serum bicarbonate (HCO₃) <18 mmol/L; blood glucose >11 mmol/L and ketonemia or ketonuria.²¹ DKA severity was categorised as 1) mild: venous pH <7.3 or HCO₃ <18 mmol/L; 2) moderate: venous pH <7.2 or HCO₃ <10 mmol/L; and 3) severe: venous pH <7.1 or HCO₃ <5 mmol/L.²¹

Statistical analysis

Data analysis was performed with Statistical Package of Social Science (SPSS) Windows Version 29. Descriptive analysis was performed whereby continuous variables were presented as medians and interquartile ranges (IQR = Q25, Q75) or mean \pm SD and categorical variables were presented as proportions (%). Continuous variables pre- and post-pandemic period were analysed by Mann-Whitney test if they were not normally distributed or student t-test if normally distributed. Chi Square test or Fisher's exact test were used for comparison of categorical variables in the two time periods. Missing data was checked and identified. Subjects with missing data were excluded from statistical analysis. A p value of <0.05 was considered statistically significant.

RESULT

T2DM and DKA frequency

There was a total of 129 children and adolescents with newly-diagnosed T2DM. Seventy-five (75) patients presented between 18 March 2016 and 17 March 2020 and 54 patients presented between 18 March 2020 and 17 March 2024. Compared to the 1-year pre-pandemic period wherein 17 T2DM cases were reported, there was only a slight increase of T2DM cases in the first 2 years of the pandemic (20 cases in the 1st year and 19 cases in the 2nd year). Subsequently, T2DM cases fell to below pre-pandemic levels in the 3rd and 4th year post-pandemic (Figure 1). We also did not observe any rise in DKA cases amongst our T2DM patients during the pandemic. There was only a total of 12 DKA cases throughout the two time periods; 7 presented before

the pandemic onset and 5 presented after the pandemic onset (Figure 1).

Clinical characteristics and demographics of T2DM patients

The demographic characteristics of the T2DM patients before and after the pandemic was shown in Table 1. There was no significant difference in the gender, ethnicity, age, BMI z-score and BMI status of the T2DM patients before and after the pandemic onset. A rise in BMI z-score was initially observed in the 1st 2 years post-pandemic, but this had reduced to pre-pandemic levels in the 3rd and 4th year post-pandemic (Figure 2).

The clinical characteristics of our T2DM patients are shown in Table 2. No difference was observed in the proportion of patients with DKA and in DKA severity before and after the pandemic onset. There was also no difference in the requirement for hospital or PICU admission and duration of hospitalisation between these two time periods. Patients who presented post-pandemic had a significantly lower HbA1c 10.1% (7.3%, 12.5%) compared to pre-pandemic 11.9% (9.4%, 14.0%), $p = 0.008$. The initial serum glucose at presentation was also significantly lower post-pandemic compared to pre-pandemic 12.0 mmol/L (8.1 mmol/L, 20.3 mmol/L) vs 16.1 mmol/L (12.2 mmol/L, 22.1 mmol/L), $p = 0.038$. The duration of symptoms was shorter

post-pandemic compared to pre-pandemic, 14 days (1, 30) vs 17.5 days (3, 60) even though this was not significant ($p = 0.064$).

In this study, COVID-19 screening was not uniformly performed during the post-pandemic period. Only one patient had been detected to be positive for the SARS-CoV-2, wherein he had presented with moderate DKA requiring PICU admission.

DISCUSSION

Diabetes and COVID-19 infection share a bidirectional relationship. Patients with diabetes are more prone to severe COVID-19 infections. Conversely, COVID-19 infection is linked to a deterioration of beta cell function and an inflammatory cytokine storm that can lead to the presentation of diabetes and DKA. In a previous study involving 180 patients in the same 4 tertiary centres in Malaysia, a marked increase in frequency of T1DM cases was observed after the pandemic onset as compared to pre-pandemic, i.e., 38 cases in 2020 and 58 cases in 2021 compared to 30 cases in 2018 and 27 cases in 2019. In the same study, a significantly higher proportion of T1DM patients presenting with DKA post-pandemic was reported compared to pre-pandemic (79.8 % vs 64.8%, $p = 0.025$).⁷ The proportion of severe DKA among these T1DM patients had also increased (46.8 % vs 28.2 %, $p = 0.012$).⁷

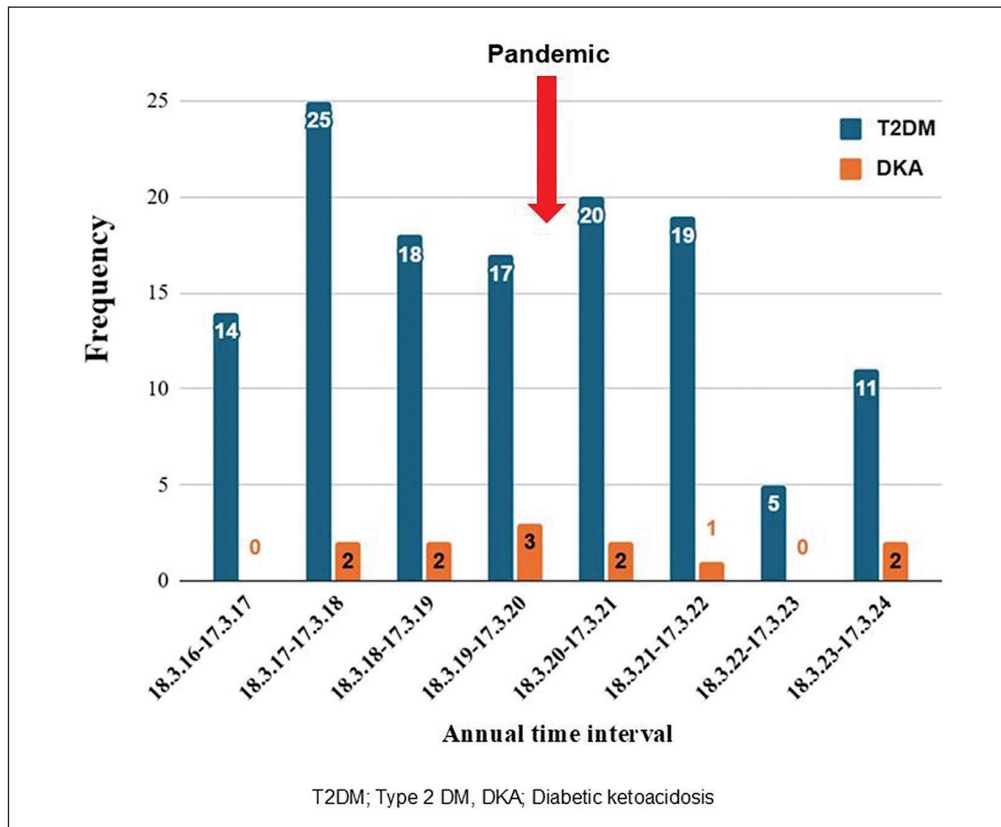


Figure 1. Frequency of T2DM and DKA at annual intervals pre- and post-pandemic. The blue bar indicates the annual frequency of T2DM. The orange bar indicates the annual frequency of DKA. The red arrow denotes the onset of the pandemic on 18.3.20, demarcating the 4-year pre-pandemic period and 4-year post-pandemic period.

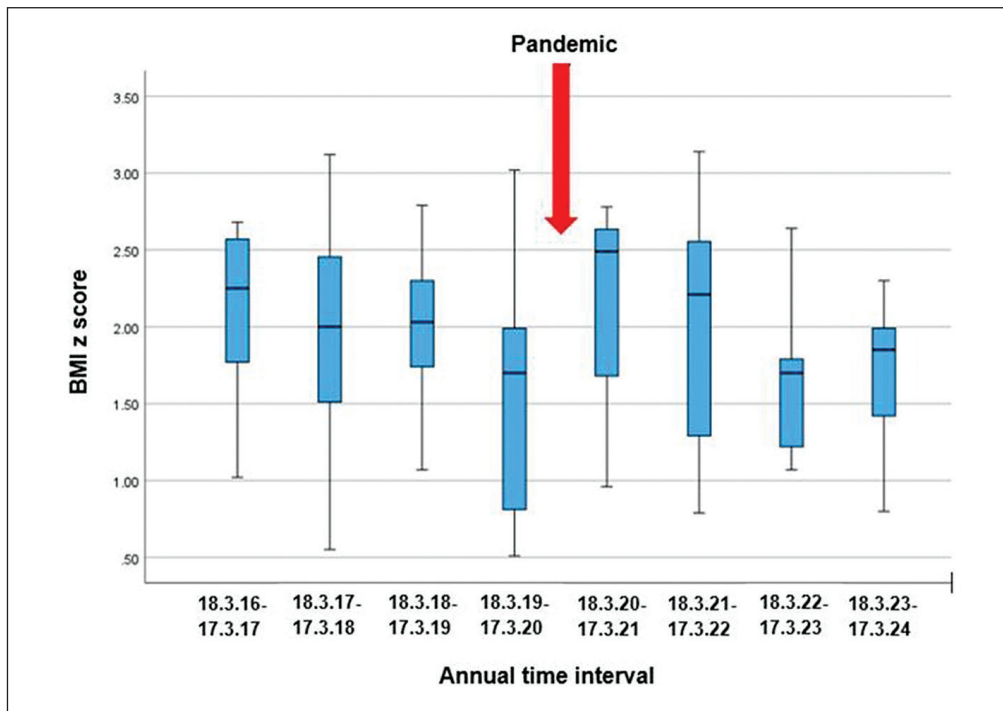


Figure 2. Median BMI z-score and range trends at annual intervals pre- and post-pandemic. The red arrow denotes the onset of the pandemic on the 18.3.20 and demarcates the 4-year pre-pandemic period and 4-year post-pandemic period.

In this present study, the increase in T2DM cases was only very marginal in the 1st and 2nd years of the pandemic and the T2DM frequency reduced to below pre-pandemic levels in the 3rd and 4th year post-pandemic. There was also no increase in DKA presentation amongst the study population during the pandemic. The rise of T1DM and DKA during the pandemic could be due to the underlying pathophysiological mechanism of SARS-CoV-2 which may precipitate beta cell failure. Type 2 DM occurs in the setting of insulin resistance in individuals who are overweight or obese and have a slower insidious course. In our population of T2DM patients, we observed an increase in BMI z-score in the first two years of the pandemic, likely due to the sedentary lifestyle and unhealthy eating habits due to the lockdown during the pandemic. The BMI z-scores, however, declined to pre-pandemic levels in the subsequent 3rd and

4th year post-pandemic. The decline in the BMI z-scores also coincided with the lower frequencies of T2DM cases in the 3rd and 4th year post pandemic:

The trend of T2DM post-pandemic in other regions of the world has been heterogenous. In contrast to our study findings, an increase in T2DM cases during the pandemic had been observed in the United States, especially among the non-Hispanic Black ethnic group.¹⁴⁻¹⁷ A higher BMI, higher serum glucose, lower pH and bicarbonate as well as higher proportion of DKA and hyperosmolar DKA were reported amongst T2DM in the American studies.¹⁴⁻¹⁷ Similarly, an increase in T2DM cases from 13 in 2017-2019 (pre-pandemic period) to 33 in 2020-2022 (pandemic period) was also observed in a multicenter regional study in Thailand.¹² The random blood glucose during the pandemic was higher

Table 1. Demographic characteristics of newly diagnosed T2DM patients (N = 129)

Variables	4-year period pre-pandemic (N = 75)	4-year period post-pandemic (N = 54)	P value
Age at diagnosis (years)	11.2 (10, 13.7)	11.5 (10, 13.2)	0.930 [†]
Gender n (%)			0.274 [†]
Male	31 (41.3%)	17 (31.5%)	
Female	44 (58.7%)	37 (68.5%)	
Ethnicity n (%)			0.361 [†]
Malay	40 (53.3%)	31 (57.4%)	
Chinese	9 (12%)	4 (7.4%)	
Indian	26 (34.7%)	17 (31.5%)	
Others	0 (0%)	2 (3.7%)	
BMI z score	1.9 (1.4, 2.4)	2.0 (1.5, 2.6)	0.323 [†]
BMI status			0.134 [†]
Normal weight	9 (12.2%)	2 (3.7%)	
Overweight	11 (14.9%)	13 (24.1%)	
Obese	54 (73%)	39 (72.2%)	

[†]Mann Whitney; [†]Chi Square test

Table 2. Clinical characteristics of newly diagnosed T2DM patients (N = 129)

Variables	4-year period pre-pandemic (N = 75)	4-year period post-pandemic (N = 54)	P value
Symptoms duration (days)	17.5 (3, 60)	14 (1,30)	0.064 [‡]
HbA1c %	11.9 (9.4, 14)	10.1 (7.3, 12.5)	0.008 [*]
DKA n(%)			1.000 [¶]
Yes	7 (9.5%)	5 (9.3%)	
No	67 (90.5%)	49 (90.7%)	
DKA severity n (%)			0.867 [¶]
No DKA	68 (90.7%)	49 (90.7%)	
Mild DKA	1 (1.3%)	0 (0%)	
Moderate DKA	1 (1.3%)	2 (3.7%)	
Severe DKA	5 (6.7%)	3 (5.6%)	
Initial serum glucose (mmol/L)	16.1 (12.2, 22.1)	12.0 (8.1, 20.3)	0.038 [*]
pH	7.4 (7.3, 7.4)	7.4 (7.3, 7.4)	0.519 [¶]
HCO₃ (mmol/L)	23 (19.8, 24.1)	22.4 (21.1, 25)	0.429 [¶]
Hospital admission n (%)			0.350 [¶]
Yes	51 (68%)	31 (58.5%)	
No	24 (32%)	22 (41.5%)	
Hospitalisation duration (days)	7 (5, 8)	7 (5, 10)	0.357 [¶]
PICU admission n (%)			1.000 [¶]
Yes	5 (6.7%)	4 (7.4%)	
No	70 (93.3%)	50 (92.6%)	
PICU duration (days)	3 (1.5, 11.5)	3 (1.3, 4.8)	1.000 [¶]

[‡]Mann Whitney; [¶]Chi Square test; ^{*}P <0.05

but no difference was observed in DKA frequency, DKA severity, age, anthropometric data and symptom duration during the two periods.¹² A study from South Korea involving 4 academic centres shared similar findings to our study wherein there was no increase in T2DM cases during the pandemic (58 T2DM cases in 2018-2019 vs 33 cases in 2020), but a higher frequency of T1DM and DKA cases was reported during the pandemic.¹⁸ Reports on the incidence of insulin-treated T2DM in Australia also did not find a rise in cases in 2020 after the pandemic onset.¹⁹

Similar to our study, reduction in the T2DM trend in the 3rd year post-pandemic was also observed in other studies. A recent study in Germany demonstrated a 48.5% annual increase in T2DM from 2018 to 2021, followed by a 43% decrease in 2022.¹³ A single retrospective study conducted in the United States also showed that T2DM cases and DKA rates declined to pre-pandemic levels in the 3rd year of pandemic after an initial rise in the 1st two years.²² The downward trend of T2DM cases in the 3rd year post-pandemic may be due to the reduced infection rate and disease severity of SARS-CoV-2 attributable to prior infection and vaccination. In addition, the return to normalcy has allowed for adoption of more healthy lifestyle habits among children, such as increased physical activity, healthier eating habits, and reduced stress.

The recent introduction of the Malaysian Clinical Practice Guideline on management of obesity in 2023 was part of the Ministry of Health's initiatives to increase awareness and provide guidance in managing children and adolescents with obesity.²³ Greater emphasis on obesity multidisciplinary care and early screening for metabolic complications after the pandemic lockdown have led to patients with prediabetes and T2DM being diagnosed

earlier than before. This explained the shorter duration of symptoms, lower HbA1c and lower serum glucose levels in the post-pandemic period observed in our study. The recent availability of GLP1-agonist has also revolutionised the management of obesity and helped to prevent metabolic complications.

The lower frequency of T2DM cases and reduction in BMI z-score back to pre-pandemic levels in our study population in the 3rd and 4th year post-pandemic may reflect more effective obesity multidisciplinary care. In Australia, a return of BMI to pre-pandemic levels was also observed in two hospitals in New South Wales 21 months post-pandemic, after an initial spike at the pandemic onset, possibly attributed to state-wide policies aiming to curb childhood obesity. However, it is also likely that the reduction in the T2DM cases post-pandemic may also be due to the lack of presentation of these cases to the tertiary care hospitals as much of the public health services are still overwhelmed due to the aftereffects of the pandemic. As the course of T2DM in children is insidious, there is still a need for greater vigilance to detect this group of patients.

Limitations

Our study has several limitations. The retrospective design precludes the causative link between SARS-CoV-2 infection and T2DM. Furthermore, our study duration includes the 3rd and 4th year post-pandemic where routine screening of the SARS-CoV-2 infection is no longer compulsory. Thirdly, even though our study sites are referral centres for T2DM in Klang Valley, there may still be referral biases whereby patients may have presented to other healthcare facilities in Malaysia as this study was only based on the experiences in 4 centers in Klang Valley. There is also a

possibility that there are T2DM patients that have not yet been diagnosed due to being asymptomatic. The strength of our study is that it was conducted in 4 different hospitals in urban Klang Valley that caters for 40-44% of T2DM patients diagnosed in Malaysia and provided data on the T2DM trend and patient profile following the pandemic. The slow and insidious course of T2DM may however have a delayed presentation post-pandemic and warrants continuous surveillance amongst overweight and obese individuals.

CONCLUSION

The frequency of T2DM and DKA did not increase in our study population, and we observed a decline in T2DM in year 3 and 4 post-pandemic. The lower HbA1c and shorter duration of symptoms post-pandemic may reflect greater access to medical care and the effectiveness of screening among target population groups. However, it is uncertain whether these study findings can be generalised to other population cohorts. As T2DM has an insidious course, larger longer longitudinal studies are required to evaluate the long-term effect of the pandemic on T2DM trends.

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Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

CRedit Author Statement

YLL: Conceptualisation, Methodology, Validation, Formal Analysis, Investigation, Resources, Data curation, Writing – original draft preparation, Writing – review and editing, Visualization, Project administration; **NMS:** Validation, Resources, Writing – review and editing; **FFWAN:** Conceptualisation, Investigation, Validation, Writing – review and editing; **AAZ:** Validation, Resources, Writing – review and editing; **NS:** Investigation, Validation, Writing – review and editing; **PGL:** Validation, Resources, Writing – review and editing; **MYJ:** Validation, Resources, Writing – review and editing.

Data Availability Statement

Datasets generated and analyzed are included in the published article.

Authors Disclosure

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