Clinical outcomes of children with COVID-19 infection in a low-risk centre in Malaysia

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ABSTRACT

Introduction: According to WHO, long-COVID or post-COVID-19 condition is defined as the continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2 months with no other explanation. A systematic review and meta-analyses published in 2022, which mainly focus on the Western population, revealed that the prevalence of long COVID was 25.24%. Literature regarding long-COVID in children in Asia was scarce. The objectives of our study were to assess the long-term effect of COVID-19 infection in children and its correlation to their acute COVID-19 infection.

Materials and Methods: This study was conducted in Hospital Kepala Batas (HKB), a district hospital in Penang State, Malaysia, which was the designated regional COVID hospital during the pandemic. It was a retrospective observational study, where children who were admitted from November 2020 to March 2021, and attended follow-up clinics from Jan 2021 to May 2021, were recruited.

Results: This study comprised 90 subjects, from 3 months old to 12 years old, mean of 6.5 years old. When comparing asymptomatic and symptomatic children, children with co-morbidities were more likely to be symptomatic with a p-value of 0.045 using the Pearson Chi-square test. All our patients' symptoms resolved upon discharge. During follow-up at 2–4 months after COVID-19 infection, all children were reported as back to their usual selves. Fifteen patients had recurrent symptoms. Most of their symptoms pointed towards an acute infection. One patient had two episodes of illness, while the rest had one. The most common symptoms were cough, fever and runny nose. The average duration of illness of these 16 episodes was 4.5 days with a standard deviation of 2.48. None of these symptoms lasted more than seven days. None of them required hospital admission. None of them had recurrent COVID-19 infections. Tweleve out of 72 children who had been going to school stopped physical school after COVID-19 infection. Our findings differed from other studies. These could be due to the limitations that we faced.

Conclusion: Most children who contracted COVID-19 infection recovered fully after acute infection, and most of them recovered fully without long-term sequelae.

KEYWORDS:
Long COVID; post-Covid follow-up; children with COVID; paediatric COVID

INTRODUCTION

According to World Health Organisation (WHO), long COVID or post-COVID-19 condition is defined as the continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2 months with no other explanation.[1] This includes ongoing symptomatic COVID-19 (from 4 to 12 weeks) and post-COVID-19 syndrome (12 weeks or more).[2] The United Kingdom (UK) Office for National Statistics estimated that 12.9% of UK children aged 2 to 11, still have symptoms 5 weeks after their first infection.[3] A systematic review and meta-analyses published in 2022, which mainly focus on the western population, revealed that the prevalence of long COVID was 25.24%, and the most prevalent clinical manifestations were mood symptoms (16.50%), fatigue (9.66%) and sleep disorders (8.42%). There were more than 40 long COVID symptoms in children and adolescents with a higher risk of persistent dyspnoea, anosmia/ageusia and/or fever compared to controls.[4] In a large cohort study which consisted of 659 286 children, the common symptoms post-infection were loss of taste or smell, myocarditis and cough. The incidence of at least one feature was 41.9% (95% Confidence Interval (CI), 41.4–42.4) among COVID-19 positive children versus 38.2% (95% CI, 38.1–38.4) among COVID-19 negative children, with an incidence proportion difference of 3.7% (95% CI, 3.2–4.2).[5] Literature regarding long COVID in children in Asia was scarce. We carried out this study during the country's Recovery Movement Control Order (RMCO) phase, where interstate travel was allowed.[6] During that time, Malaysia was undergoing the attack of Delta Wave. The objectives of our study were to assess the long-term effect of COVID-19 infection in children and its correlation to their acute COVID-19 infection at 4 months of follow-up.

MATERIALS AND METHODS

This study was conducted in Hospital Kepala Batas (HKB), a district hospital in Penang State, Malaysia, with 108 beds. Twenty-eight beds were dedicated to paediatrics. This hospital was a designated full COVID hospital during the pandemic. It received patients from the whole Seberang Prai

This article was accepted: 22 November 2023
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area. The study population included all children from age 1-month-old to 12 years old with positive COVID RT-PCR (Reverse transcription-polymerase chain reaction), who were admitted from November 2020 to March 2021 and attended follow-up clinic, either virtually or physically, from Jan 2021 to May 2021. Patients who did not come and were not contacted during follow-up were excluded. Although Malaysia already went into the country's RMCO, where there was still mandatory RTK testing and quarantine for those that were diagnosed with COVID-19 infection, interstate travel would be allowed, but only a few patients attended physical clinics. Most patients were followed up virtually by medical officers who worked in the paediatric department using hospital phone lines and documented in patients' case notes. Phone numbers of interviewees were recorded in patients' case notes during admission. Interviewees were the main caretakers. Most of them were parents to the children. For virtual clinic follow-up, children's well-being and the presence of any symptoms were determined during the virtual interview. For physical clinic follow-up, history taking and physical examination were done.

Data collection was by convenience sampling. Samples were identified via a monthly census of paediatric admissions to the Paediatric ward. Case notes were traced from the Electronic Hospital Information System (eHIS) and hospital record office. Demographic details of the patients, clinical presentation and follow-up outcomes were collected. The demographic variables included age, gender and ethnicity. Clinical presentation included the COVID-19 category, symptoms at presentation, chest X-ray findings, CT (cycle threshold)-value of RT-PCR result, co-morbidity, developmental milestone, transmission method and length of stay. Developmental milestone assessment was based on Denver II Scale. COVID-19 category was based on the Clinical Staging of COVID-19 for children.[7] Follow-up outcomes of recurrence symptoms, history of hospitalisation or clinic visit and attendance to school or childcare centre after discharge from the hospital and reason for absenteeism if any, were collected.

Data were entered into Microsoft Excel Sheet. No original records were photocopied. The data were analysed using the Statistical Package for the Social Sciences (SPSS) version 25. Continuous variables were presented as mean and standard deviation, and categorical variables were presented as frequency and percentage. Continuous variables were analysed using simple logistic regression based on one independent variable regardless of the type of variable, whilst categorical data were analysed using chi-square or Fischer's exact test. A value of $p < 0.05$ was considered statistically significant.

RESULTS

Ninety-seven children were admitted for COVID-19 during the study period. Seven children were excluded because they did not attend follow-up clinics either physically or virtually. 90 children were recruited, where 42 were in category 1, 39 in category 2, nine were in category 3 and none was in category 4 or 5. Their ages ranged from 3 months to 12 years old, mean 6.5 years, standard deviation 3.56 years. Among the symptomatic children, 64.6% had only one symptom at presentation. 16.7% had two symptoms, and the rest had three or more symptoms. The common symptoms were coryza (41.7%), fever (33.3%), cough (22.9%), anosmia (12.5%), sore throat (8.3%), diarrhoea (6.3%), chest discomfort (2.1%) and others (6.3%). Other symptoms were vomiting, poor oral intake and gum swelling. 90% of them had normal chest X-rays. Two children's RT-PCR was positive without CT value because the test was not done in our local health care system and there were no printout results attached in the case notes. The average CT value for our samples was 27.49. There were four obese children, three had bronchial asthma, two had allergic rhinitis and others had single kidney, epilepsy, congenital rubella and failure to thrive, respectively. Three children had isolated speech delay. When comparing asymptomatic and symptomatic children, as shown in Table I, children with co-morbidities were more likely to have symptomatic COVID-19 infection with a p value of 0.045. All our patients' symptoms resolved upon discharge.

During follow-up at 2–4 months after COVID-19 infection, all children were reported as well, active and back to their usual activities of daily living. Only 15 patients had recurrent symptoms. Most of their symptoms pointed towards acute infections. One patient had two episodes of acute infections, while 13 of them had one episode. One child complained of lethargy and dizziness for 2 days without evidence of infection. Eleven out of these 16 episodes of illness were presented by more than one symptom. The most common symptoms were cough (n = 12), fever (n = 9) and runny nose (n = 8). Other symptoms were vomiting, diarrhoea, sore throat, chest discomfort, lethargy and dizziness. Among these 16 episodes of illness, 12 visited the clinic, two visited the hospital casualty department, and two episodes did not need a clinic or hospital visit. Three of these episodes required salbutamol nebulisation, six were prescribed antibiotics. The average duration of illness is 4.5 days with a standard deviation of 2.48. None of these children developed new chronic symptoms after acute COVID-19 infection. None of them required hospital admission. None of them have recurrent COVID-19 infections. Among these 15 children, two had underlying bronchial asthma and allergic rhinitis and one had bronchial asthma prior to COVID-19 infections. When compared to the rest of the sample, the association between co-morbid and recurrent infection was not statistically significant, with a p-value of 0.121. The relation between co-morbidity and long COVID was not demonstrated in this study.

Before the pandemic, 80% of the children in our study were attending school or childcare centres, while the other 20% of them did not. Out of these 72 children, 12 of them stopped going to school and childcare after being infected with COVID-19, ranging from two days to two months. Six of them did not go to school for one week. Two did not state the duration. One did not go to school after the diagnosis of COVID-19 until the time of follow-up. Among the 12 of them who did not go to school, eight of them were due to recurrent symptoms, two were worried about getting reinfection, one said that would like to rest at home and one did not state the reason.

Table I: Comparison in demographic and clinical presentation between children with asymptomatic and symptomatic COVID-19 infection in Hospital Kepala Batas

Variables	Asymptomatic n = 42 n (%)	Symptomatic n = 48 n (%)	Crude OR (95% CI)	p value
Patients' demographics				
Age, yearsa	6.3 (3.41)	6.7 (3.72)	1.03 (0.92,1.16)	0.599[b]
< 1	4 (66.70)	2 (33.30)		0.555[c]
1–5	13 (43.30)	17 (56.70)		
6–13	25 (46.30)	29 (53.70)		
Gender				
Male	21 (48.80)	22 (51.20)		0.693[d]
Female	21 (44.70)	26 (55.30)		
Ethnicity				
Malays	39 (48.10)	42 (51.90)		0.504[c]
Chinese	2 (50.00)	2 (50.00)		
Indian	1 (20.00)	4 (80.00)		
Clinical presentation:				
CT-value of RT-PCR resulta	27.4 (6.93)	27.6 (5.77)	1.01 (0.94,1.08)	0.853[b]
Low CT value (<30)	25 (45.50)	30 (54.50)		0.783[d]
High CT value (30–40)	16 (48.50)	17 (51.50)		
Missing data	1	1		
Comorbid				
Have Comorbid	3 (20.00)	12 (80.00)		0.045[d]
No Comorbid	39 (52.00)	36 (48.00)		
Obesity	0 (0.00)	4 (100.00)		0.120[c]
No obesity	42 (48.80)	44 (51.20)		
Asthma	1 (33.30)	2 (66.70)		1.000[c]
No asthma	41 (47.10)	46 (52.90)		
Normal development	41 (47.10)	46 (52.90)		1.000[c]
Speech Delay	1 (33.30)	2 (66.70)		
Transmission method				
Close contact with family member	41 (46.60)	47 (53.40)		0.718[c]
Contact with family friends	1 (100.00)	0 (0.00)		
Contact with teacher	0 (0.00)	1 (100.00)		

CT - cycle threshold
Note: [a]Data presented are mean (standard deviation), [b]Simple Logistic Regression; cFisher's exact test; [d]Pearson Chi-square test; OR=Odds Ratio; 95% CI = 95% confidence interval

Table II: Comparison in follow-up outcome between children with asymptomatic and symptomatic COVID-19 infection in Hospital Kepala Batas

Follow-up outcome	Asymptomatic n = 42	Symptomatic n = 48	p value
Recurrent symptoms	8 (19.00)	7 (14.60)	0.571[a]
No recurrent symptoms	34 (81.00)	41 (85.40)	
Recurrent healthcare services visit	8 (19.00)	6 (12.50)	0.393[a]
No recurrent healthcare services visit	34 (81.00)	42 (87.50)	
Absence from school after COVID-19 infection	5 (11.90)	7 (14.60)	0.684[a]
Continue schooling after COVID-19 infection	27 (64.30)	33 (68.80)	

Note: [a]Pearson Chi-square test

As shown in Table II, there was no significant association between the COVID-19 severity in terms of risk of recurrent infection, health care facilities visits and school absentees.

DISCUSSION

During the time of the study, all children infected with COVID-19 needed to be admitted for isolation and observation. All our subjects were in category three or less because our centre was a low-risk centre. Nevertheless, none of these children deteriorated or needed step-up care. Furthermore, severe COVID-19 (category four and five) was less common in children.

To date, there are at least two long-term consequences that can occur following COVID-19 infection in children, namely multisystem inflammatory syndrome (MIS-C) and long COVID. Using the case definition released by the Centers for Disease Control and Prevention (CDC) in May 2020, the incidence of MIS-C the United State was estimated to be 5.1 cases per million person-months or 316 cases per million SARS-CoV-2 infections among persons aged <21 years.[8] None of our children developed MIS-C during the follow-up period. Contrary to the systematic review and meta-analysis published[4], as well as a recent paper published in Annals Academy of Medicine Singapore showing one in six children and younger persons in Singapore developed long COVID

with persistence of one or more symptoms after three months post-infection where persistent cough (7.4%), nasal congestion (7.6%) and fatigue (3.0%) were common symptoms[9], our study did not show any long COVID in our children. Despite having recurrent infections, none of them reported having chronic dry cough (7%), shortness of breath (6%), fatigue (4%) or headache (3%), as coded by another cohort study.[10]

During the study period, children attended school virtually and back to physical school in stages as instructed by the Malaysian Ministry of Education. The results of our study did show that the impact of COVID-19 on school attendance should not be underestimated.

Our findings differed from other studies. These could be due to the limitations that we faced. Firstly, our study was conducted among the local community who were admitted to our hospital, which was a low risk hospital, and the data was collected in a short duration. This might not represent the whole Malaysian population. Secondly, this study was conducted in the middle of the pandemic, which might not represent the whole clinical outcome of the changing variant of coronavirus. Thirdly, as per our general knowledge, recurrent infections were common in children. This study did not compare recurrent infection with children with other viral infections because during the study period, only children with COVID-19 infection were admitted to this hospital. And finally, the patient's symptoms were reported by parents, which carried the risk of recall biases and underreporting. Not all children attended the follow-up clinic physically.

CONCLUSION

In summary, most children who contracted COVID-19 infection recovered fully after acute infection, and most of them did not have long-term sequelae.

ACKNOWLEDGEMENT

We would like to thank Honorary Professor Dr ELC Ong, Consultant Infectious Diseases, Newcastle University Medicine for reviewing and editing the manuscript. We would like to thank the Director General of Health Malaysia for his permission to publish this article.

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