

Role of asymptomatic children in community SARS-CoV-2 transmission

Liangjian Lu^a, Chee Teck Koh^a, Yi Heng Lim^a, Andrew Sng^{a,b}, Kok Siong Poon^c, Shaun SY Tan^c, Pao Tang Kao^{a,b}, Nancy Tee^c, Hui Kim Yap^{a,b}, Bee Wah Lee^b, Paul A Tambyah^d

^a Department of Paediatrics, Khoo Teck Puat- National University Children's Medical Institute, National University Health System, ^b Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, ^c Department of Laboratory Medicine, National University Health System, ^d Division of Infectious Diseases, National University Health System and Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore

TO THE EDITOR- Goldstein and colleagues[1] recently reviewed the limited evidence suggesting that children are less susceptible to SARS-CoV-2, and have reduced infectivity upon being infected. As they point out, given that many infected children are asymptomatic or pauci-symptomatic, these data are sensitive to errors in index case ascertainment. This adds to the concern about the potential role of children in mediating undetected SARS-CoV-2 transmission[2]. We have utilized the comprehensive contact tracing system and low rates of community transmission outside worker dormitories in Singapore to investigate this further.

We hypothesized that there would be an excess of children with COVID-19 in households with no epidemiological links to other cases after comprehensive contact tracing, i.e., “unlinked households”, compared to households with definite epidemiological links to other cases, i.e., “linked households”. The prevalence of children with COVID-19 in linked households will reflect the household secondary attack rate [3], while the prevalence of SARS-CoV-2 positive children in unlinked households will reflect the secondary attack rate plus cases in which children are an undetected index case, i.e., acting as a community reservoir of infection.

SARS-CoV-2 positive households with asymptomatic children aged between 28 days and 18 years were included, with asymptomatic children defined as those who had no symptoms within 2 weeks of index case diagnosis or had symptoms but were SARS-CoV-2 pharyngeal swab negative. They were recruited from the National University Hospital Infectious Diseases clinic, or from the Emergency Department which was a designated centre for the mandatory screening of household contacts of diagnosed COVID-19 cases. In Singapore, household contacts of diagnosed COVID-19 cases are screened by the public health authorities with a SARS-CoV-2 pharyngeal real-time reverse transcription polymerase chain reaction (RT-PCR) test

regardless of symptoms (typically two swabs- one immediately after and the other 11-14 days after index case diagnosis). All asymptomatic children in consenting households were subject to a convalescent serology at least 3 weeks after diagnosis of the index case. This was performed using the MP Diagnostics ASSURE SARS-CoV-2 IgG/IgM Rapid test (Santa Ana, CA, USA) with a point-of-care finger-prick capillary sample. In seropositive children, a fecal sample was collected and tested by SARS-CoV-2 RT-PCR using standard methods[4]. The classification of linked compared to unlinked households was obtained from the Ministry of Health, Singapore, based on their extensive contact tracing. Ethics approval for this study was obtained from the National Healthcare Group Domain Specific Review Board (Ref: 2020/00614), and appropriate informed consent was obtained.

We recruited 16 children, all under 12 years of age, from 12 households comprising 9 linked and 3 unlinked households (Table 1). Eight out of 9 (89%) linked households had children who tested positive for SARS-CoV-2, either by serology (n=6) or by contemporaneous pharyngeal RT-PCR (n=4), whereas there were no SARS-CoV-2 positive children in unlinked households (p=0.02). There were no differences in other characteristics between linked and unlinked households apart from a shorter interval between index case diagnosis and serological testing in unlinked compared to linked households (Median: 28 vs 53 days, p=0.026), arguing against waning antibody levels resulting in false negative serological tests in unlinked households[5]. Overall, 6 of 16 asymptomatic children (38%) were positive on convalescent serology, all 6 of whom had negative contemporaneous pharyngeal RT-PCR. All fecal samples were negative for SARS-CoV-2 RNA.

The absence of SARS-CoV-2 infection amongst children in unlinked compared to linked households suggested a limited role for children as a community reservoir of

infection although they are clearly susceptible to SARS-CoV-2 infection. This may be due to infected children having lower infectivity. It is not entirely clear why unlinked households may display a lower secondary attack rate. It is possible that those household index cases are unlinked because they had a longer incubation period, making contact tracing difficult, and also possibly milder disease[6], or reduced viral load and infectivity[7]. Alternatively, linked households may have had multiple exposures within the extended family household to the sources of infection whereas exposure may only have been transient in unlinked cases. In addition, the relatively high prevalence of seropositivity amongst asymptomatic and swab-negative pediatric household contacts extends existing data showing a significant seropositive rate amongst RT-PCR negative patients with probable or suspected COVID-19[8,9].

The main limitation of the current work is the small sample size, largely due to low incidence of SARS-CoV-2 transmission. Another limitation of the work is the use of point-of-care lateral flow assays.

Taken together, this work reassures us against a role of children as a major community reservoir of SARS-CoV-2 infection, and also underscores the importance of quarantining children with strong epidemiological risk factors regardless of symptoms or RT-PCR results. Careful contact tracing to identify these children may be more effective than blanket school closures[10].

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Conflict of Interest/Disclosures (includes financial disclosures)

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Corresponding author

Address correspondence to: Dr Liangjian Lu, Department of Paediatrics, Khoo Teck Puat- National University Children's Medical Institute, National University Health System, 1E Kent Ridge Road, NUHS Tower Block Level 12, Singapore 119228, david_lu@nuhs.edu.sg

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S/N^a	Classification	Age (years)	Sex	Symptoms	No. of negative swabs	Total household size	Household contacts with COVID-19	Paediatric household contact with COVID-19 (by RT-PCR)	Days between index case diagnosis and serology	Convalescent serology^b	Stool RT-PCR
1A	Linked	12	M	No	0	6	Mother, brother (24yo)	N	33	Negative	N/A
2A	Linked	7	M	No	1	6	Mother, brother (1yo)	Y	53	Negative	N/A
2B	Linked	4	F	No	1	6	Mother, brother	Y	53	Positive	Declined

							(1yo)				
2C	Linked	3	M	No	1	6	Mother, brother (1yo)	Y	53	Negative	N/A
3A	Linked	1	M	No	4	3	Father, Mother	N	65	Positive	Negative
4A	Linked	3	F	No	5	5	Grandmother, brother (6yo)	Y	101	Negative	N/A
5A	Linked	3	M	Yes ^c	1	5	Father, mother	N	99	Positive	Negative
6A	Linked	4	M	Yes ^d	1	5	Father, mother, brother (7yo)	Y	102	Positive	Negative
7A	Linked	9	M	No	2	5	Tenant	N	42	Positive	Negative
7B	Linked	4	M	No	2	5	Tenant	N	42	Negative	N/A
8A	Linked	5	M	No	3	5	Father, brother (9yo)	Y	30	Negative	N/A
8B	Linked	7	M	No	3	5	Father, brother (9yo)	Y	30	Negative	N/A
9A	Linked	1	M	No	3	4	Grandmother, Mother	N	148	Positive	Negative

10A	Unlinked	3	F	No	2	10	Grandfather	N	36	Negative	N/A
11A	Unlinked	11	M	No	2	4	Tenant	N	28	Negative	N/A
12A	Unlinked	8	F	No	2	8	Father	N	26	Negative	N/A
Linked vs unlinked (p-value) ^e		0.341	0.136	1	0.835	0.257			0.026		

Table 1: Characteristics of participants.

^a Same numeral but different suffixes refer to children in same household

^b All positive children had SARS-CoV-2 IgG but not IgM.

^c Fever, cough, rhinorrhea, fatigue

^d Fever, myalgia

^e Mann-Whitney U and Fisher's Exact Test for continuous and categorical variables respectively