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Risk-stratified seroprevalence of SARS coronavirus in children residing in a district with point-source outbreak compared to a low-risk area

Key Messages

1. SARS coronavirus has low transmissibility at the community level.
2. Subclinical SARS coronavirus infection is rare in children.

Introduction

SARS was a newly emerged infectious disease, and its aetiology was attributed to a novel coronavirus, SARS coronavirus (SARS-CoV). Hong Kong was one of the most severely affected areas, with a total of 1755 local residents infected and 302 fatalities.[1] Children, in contrast to adults, had less severe disease and paediatric SARS constituted only 6.9% of the total number of SARS cases in Hong Kong. The territory-wide age-specific attack rate was 8.9 cases per 100 000 persons aged younger than 18 years compared to 30.0 cases per 100 000 adults.[2] Similar findings were also noted in Taiwan, where only 7.2% of SARS patients were 20 years or younger.[3] Reviews on clinical features, investigations, and prognostic indicators on paediatric SARS in Hong Kong have been published, however there is a lack of data on possible asymptomatic infection in children at the community level. Since clinical SARS in children was mild, whether there were more subclinical infections in this age-group was unanswered.

Our objective was to determine the seroprevalence of SARS-CoV among asymptomatic children aged 6 to 15 years from three large housing estates around the Amoy Gardens, where a superspreading event giving rise to 330 cases occurred. We also set out to obtain comparative data from a paediatric sample, living in a low-risk housing estate with no SARS case in that different district.

Methods

This study was conducted from September to October 2003.

Study design

Risk-stratified seroprevalence study of children under 15 years old, living in a high-risk area where large community outbreaks had occurred (Amoy Gardens, Ngau Tau Kok Estates, and Telford Gardens), was compared with those living in a low-risk area (Wah Fu Estate). Subjects were approached and recruited via primary and secondary schools in the two areas.

Sample size

A total of 353 children living in the high-risk area and 361 living in the low-risk area were recruited.

Study instruments

Using a standardised questionnaire, the information collected included: socio-demographic data, history of SARS infection in the subjects and members of the household. Questions were also directed at any history of contact with known cases of SARS, presence of SARS-like symptoms since March 2003, travel history of the child and his/her relatives within 15 days prior to any such symptom onset, use of health services as a result of such symptoms, and whether there were deaths of relatives as a result of SARS. Parents of all the subjects who joined the study were contacted by telephone, and the above questionnaire was administered by a trained research nurse.

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Table. Subject characteristics

Characteristic	High-risk area (n=353)	Low-risk area (n=361)	P value
Sex			
Male	187 (53.0%)	173 (47.9%)	0.18
Female	166 (47.0%)	188 (52.1%)	
Mean (SD) age (years)	10.5 (2.3)	10.5 (2.4)	0.97
Housing type			
Private housing	132 (37.4%)	128 (35.5%)	0.65
Public housing	221 (62.6%)	233 (64.5%)	
SARS-CoV immunoglobulin G			
Positive	2 (0.6%)	0	0.24
Any household member diagnosed to have SARS	11 (3.1%)	0	0.002
Any SARS contact outside household	3 (0.8%)	0	0.24
Any relative(s) died of SARS	1 (0.3%)	0	0.99
Presence of clinical symptoms			
Yes	43 (12.2%)	74 (20.5%)	0.004
Fever	28 (7.9%)	28 (7.8%)	1.00
Chills	17 (4.8%)	34 (9.4%)	0.03
Cough	4 (1.1%)	17 (4.7%)	0.01
Shortness of breath	1 (0.3%)	2 (0.6%)	1.00
Headache	4 (1.1%)	8 (2.2%)	0.40
Generalised malaise	5 (1.4%)	5 (1.4%)	1.00
Diarrhoea	3 (0.8%)	5 (1.4%)	0.75
Medical consultation because of clinical symptoms	40/43 (93.0%)	60/74 (81.1%)	0.14
Still went to school despite having above symptoms	10/43 (23.3%)	36/74 (48.6%)	0.01

SARS-CoV immunoglobulin G (IgG) antibody testing was performed on all subjects. Immunofluorescence assay was performed and any positive results were confirmed by a virus neutralisation test.

Results

Subject characteristics stratified by risk categories are shown in the Table. The SARS-CoV infection rate in the high-risk area was >70 per 1000 persons, whereas that in the low-risk area was 0.1-0.4 per 1000 persons. The high- and low-risk areas had similar population densities; the number of residents below the age of 15 years was 10 340 per km^2 and 9498 per km^2, respectively. The sex ratios of children in the two groups were similar. None of the subjects in either group reported a previous history of SARS. Two (0.6%) of 353 children from the high-risk area were found to be seropositive for SARS-CoV antibody (95% confidence interval [CI], 0.07-2.0%). Both had been completely asymptomatic of any SARS-like illness since March 2003 until the current test. All 361 children in the low-risk area were seronegative (seroprevalence=0%; 95% CI, 0-1.0%). The difference in seropositivity rates between high-risk and low-risk areas were not statistically different (P=0.24).

In the high-risk group, 11 (3.1%) children had close family members diagnosed with SARS that included one who died, while none of the family members of children in the control group had SARS (P=0.002). Three other children (0.8%) had a history of contact with persons who were diagnosed to have SARS outside the household. All 14 of these children who had known SARS contacts were seronegative for SARS-CoV. None of the children in the control group had a positive contact history.

More children (20.5%) in the low-risk area reported having symptoms during the SARS epidemic compared to the high-risk group (12.2%) [P=0.004]. Chills (9.4%) and cough (4.7%) occurred significantly more commonly in children from the low-risk group compared to the high-risk group (4.8% had chills [P=0.03] and 1.1% had cough [P=0.01]). Overall reported rates of respiratory symptoms were lower in the high-risk group.

Discussion

Much progress has been made in characterising the clinicopathological features and epidemiology of SARS in the 2 years since its emergence. A review of its clinical features in adults and children showed that there were two major differences between adult and paediatric SARS patients: (1) the incidence in children was substantially lower than in adults, and (2) SARS was much milder in children and none aged less than 18 years died anywhere in the world.[4] The present study was the first community-based seroepidemiological survey in children. The key question concerns whether asymptomatic infection with SARS-CoV represented another end of disease spectrum in children, and if so, whether the potential caseload was significant enough to constitute a source for spread in the community.

The fact that paediatric patients affected by SARS had a relatively mild clinical course led some to postulate that children might have only mild symptoms or remain asymptomatic after being infected by SARS-CoV. Such patients might never present to the health care system and could thus explain the apparently lower incidence of SARS in the paediatric population. Our study showed that within a

geographic area where superspreading events had occurred, positive serology for SARS-CoV in healthy asymptomatic children was also very uncommon (0.57%); the difference in rates between the respective areas was not statistically significant. Only two cases of asymptomatic infection with SARS-CoV were documented in our study. 'Subclinical' SARS, as revealed by positive anti-SARS CoV IgG in asymptomatic individuals, has been consistently found to be an uncommon entity across different seroepidemiological surveys in both hospital and community settings. A systematic review[5] of SARS-CoV seroprevalence studies showed that the overall seroprevalence in asymptomatic population groups was 0.1% (95% CI, 0.02-0.018%). The seroprevalence in high-risk groups such as health care workers and close contacts of SARS patients was only slightly higher (0.23%; 95% CI, 0-0.37%) than the overall seroprevalence. The study concluded that seroconversion was an extremely rare event in individuals who did not develop SARS, and SARS-CoV infection almost certainly led to clinically apparent disease which in the majority of patients was of great severity warranting hospitalisation during the 2003 epidemic. In a study on SARS-CoV seroprevalence in close contacts of all SARS patients in Hong Kong, only two (0.19%) were seropositive, and one of them was a 4-year-old boy who lived with his parents and grandfather who all had SARS.[6] In fact, when restricted to close contacts of SARS cases from Amoy Gardens, the seroprevalence in that study was 0.62% (1/161), which was virtually identical to our present estimate (P=0.99).

Although symptoms of SARS in children were more non-specific, the majority of patients could be reliably identified by vigilant frontline health care professionals according to stringent diagnostic case definition criteria. The reported incidence of paediatric SARS from hospital cases very likely represents the true incidence of SARS in Hong Kong children. It was unlikely that subclinical SARS, with such a low prevalence, could have assumed a role in the spread of SARS within the community.

There are several explanations for the low incidence of SARS in children from an epidemiological point of view. The SARS outbreak in Hong Kong first started in hospital settings and mostly involved health care workers and adult patients. There was no reported SARS outbreak in paediatric wards, and it has been routine practice in Hong Kong that children are not allowed to visit hospital wards, thereby limiting their risk of exposure during that critical period. The inherent transmissibility of SARS in the community setting was low, and this was further reduced by stringent public health measures including early admission of all suspected SARS cases to hospital, quarantine of Amoy Gardens Block E residents, school suspension, and reinforcement of strict environmental hygiene. In fact, the majority of SARS patients in Hong Kong were victims of point-source outbreaks at the Prince of Wales Hospital or Amoy Garden residential complex, and infection without a direct epidemiological link was uncommon. There was no spread of SARS in the school setting, despite many infected children having attended school until they developed symptoms of infection. Retrospectively, the risk of contracting the disease through casual contacts within the community was minimal.

There are several limitations of this study. Young children aged less than 6 years were not included, as we only recruited our subjects by approaching primary and secondary schools in the two areas. A relatively low subject recruitment rate was another drawback. Difficulties were encountered when seeking consent from parents, probably due to reluctance with respect to blood-taking in young children, as well as less concerns about SARS after the epidemic. Recall and reporting bias about SARS-associated symptoms was also possible, as the questionnaire was administered several months after the peak of the SARS epidemic.

Conclusion

By determining the prevalence rate of SARS-CoV IgG antibody in children in both high-risk and low-risk residential areas, our study confirmed previous observations that SARS-CoV had low transmissibility at that community level, and subclinical SARS-CoV infection was rare in children. This community-based serological survey also indicated that SARS-CoV was transmitted in very specific settings, and that its spread could be effectively controlled by early detection and isolation of symptomatic patients. However, the low seroprevalence rate in the community means that the public will have little protection from herd immunity, should SARS re-emerge.

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