

Short Communication

Risk Factors for SARS Infection within Hospitals in Hanoi, Vietnam

Ayako Nishiyama*, Naomi Wakasugi, Teruo Kirikae, Tran Quy¹, Le Dang Ha², Vo Van Ban³,
Hoang Thuy Long⁴, Naoto Keicho, Takehiko Sasazuki and Tadatoshi Kuratsuji

*Research Institute, International Medical Center of Japan, Tokyo 162-8655, Japan; ¹Bach Mai Hospital;
²Institute of Clinical Research in Tropical Medicine; ³Hanoi-French Hospital; and
⁴National Institute of Hygiene and Epidemiology, Hanoi, Vietnam*

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SUMMARY: We investigated a nosocomial infection of severe acute respiratory syndrome (SARS) in Vietnam in 2003 and attempted to identify risk factors for SARS infection. Of the 146 subjects who came into contact with SARS patients at Hospital A, 43 (29.5%) developed SARS, and an additional 16 (11%) were asymptomatic but SARS-coronavirus (CoV) seropositive. The asymptomatic infection rate accounted for 15.5% of the total number of infected patients at Hospital A, which was higher than that of 6.5% observed at Hospital B, to where all patients from Hospital A were eventually transported ($P < 0.05$). At Hospital A, the risk for developing SARS was 12.6 times higher in individuals not using a mask than in those using a mask. The SARS epidemic in Vietnam resulted in numerous secondary infections due to its unknown etiology and delayed recognition at the beginning of the epidemic. The consistent and proper use of a mask was shown to be crucial for constant protection against infection with SARS.

The first massive outbreak of severe acute respiratory syndrome (SARS) was reported (1) in Vietnam in February 2003, and 8,098 patients with this disease and 774 resulting deaths had been reported by the World Health Organization (WHO) (2) as of August 2003. In Vietnam, a Chinese American with signs of severe pneumonia was transported to Hospital A in Hanoi from Hong Kong on 26 February 2003 (1). The disease subsequently spread, initiated by transmission within the hospital, to 63 individuals in Vietnam, including 5 who died. When the initial case was transported to Hospital A, the hospital staff members were not aware of SARS and hence no special measures were taken prevent transmission of the disease. As a result, the disease spread primarily among hospital staff members.

In the present study, we followed the course of a massive outbreak of SARS that developed at a single hospital and of which the initial case was known. The aims of this study were to analyze the infection rate and disease incidence, as well as to explore risk factors that divided subjects into infected and non-infected groups, with the ultimate goal of collecting useful information for the prevention of future SARS epidemics.

Hospital A was a private general hospital with 56 beds and was not equipped with an isolation ward for patients with infectious diseases. The subjects in this study were 320 individuals involved in the SARS epidemic which began at Hospital A. The subjects were divided into four groups: Group 1 (43 individuals who developed SARS within Hospital A between March 3 and 17), Group 2 (103 individuals who had contact with SARS patients within Hospital A, but did not develop SARS), Group 3 (124 individuals who had contact with SARS patients at Hospital B), and Group 4 (the negative control group; 50 staff members at Hospital C located in the same region as Hospital B, none of whom had contact with SARS patients). In this study, thorough follow-up infor-

mation was available for 68.3% (43/63) of all symptomatic SARS patients in Vietnam. Analyses of risk factors for SARS infection and onset were conducted on Group 1 and Group 2.

Informed consent was obtained in writing from each individual who agreed to participate in the study. A questionnaire-type survey was administered, by means of an interview, by Vietnamese physicians from October 2003, 7 months after the beginning of the SARS epidemic, to November 2003 for Groups 1 and 2, and in May 2004 for Groups 3 and 4. This study was carried out in accordance with the Ethical Guidelines for Research on the Human Genome and Gene Analysis in Japan (29 March 2001, Ministry of Education, Culture, Sports, Science and Technology, Ministry of Health, Labour and Welfare, and Ministry of Economy, Trade and Industry) and the Standards of the Vietnamese Ethics Committee for Studies in Medical Science (No. 5129/2002/QD-BYT, 19 December 2002).

The clinical diagnosis of SARS was made by Vietnamese physicians in each probable case in accord with the WHO diagnostic criteria (2). To check for SARS infection, serum antibody levels, sampled 6 months after the epidemic, were measured by ELISA (SARS ELISA; MP Biomedicals Asia Pacific Pte. Ltd. (formerly Genelabs Diagnostics Pte. Ltd.), The Cavendish Singapore Science Park, Singapore) using recombinant SARS-coronavirus (CoV) protein N, U274 as the antigen. The cut-off level was set at the mean \pm 3SD for the 50 subjects assigned to Group 4. Antibody levels higher than the cut-off level were considered as representative of positivity.

Contact with SARS patients was rated by each subject as either direct or indirect. Direct contact was defined as physical contact with a SARS patient or his/her excretions. For individuals who developed SARS, the SARS exposure period was defined as the length of time from the day when the subject most likely had either direct or indirect contact with a SARS patient to the day when he/she developed SARS. For individuals who did not develop SARS, the SARS exposure period was defined as the duration of the period during which these individuals likely had direct or indirect contact with a

*Corresponding author: Present address: Department of Pediatrics, Shiseikai Daini Hospital, 5-19-1 Kamisoshigaya, Setagaya-ku, Tokyo 157-8550, Japan. Tel: +81-3-3300-0366, Fax: +81-3-3307-6731, E-mail: crea_ayako@yahoo.co.jp

SARS patient. In both of these groups, the SARS exposure period was determined on the basis of information reported by each individual subject, but the first and last days of the period were designated as 26 February 2003, when a SARS-infected case first presented at Hospital A, and 8 April 2003, the day when the last SARS patient was discharged from the hospital, respectively.

The Kaplan-Meier method was used to analyze the SARS incidence among subjects at Hospital A reflecting the SARS exposure period; the log-rank test was employed to test the significance of intergroup differences. To identify risk factors for nosocomial infection with SARS at Hospital A, a multivariate logistic regression analysis was conducted on 85 staff members in Groups 1 and 2. SPSS version 10 was

the software used for the analysis.

Of the 146 subjects who came into contact with SARS patients at Hospital A, 43 (29.5%) developed SARS, and an additional 16 (11%) were asymptomatic but SARS-CoV seropositive. The antibody levels of the 43 symptomatic SARS patients were significantly higher (141.4) than those of the 16 asymptomatic but SARS-CoV seropositive cases (38.7) ($P < 0.01$, Student's *t* test). No subjects at Hospital B or C developed SARS (Table 1). In another study, Le et al. reported a lack of SARS seropositive cases at Hospital B (3). Our study identified seropositive cases at Hospital B, which is inconsistent with the previously reported findings. We speculate that the discrepancy could have been due to the use of different antigens for antibody detection, and/or that SARS antibody measurement in their study was conducted at a point in time too early for detection. In our study, out of 16 SARS patients whose antibodies were tested at two time points (2-3 months and 6 months), 6 (37.5%) were seronegative at 2-3 months and yet had seroconverted by 6 months. On the other hand, in the study by Le et al. (3), the antibody level was measured only at 8-10 weeks; it is possible that the seroconversions had not occurred by that point in time.

Figure 1 shows the relationship between the proportion of individuals who did not develop SARS and the exposure period by occupational category or frequency of mask use. As regards the protective effects of mask use, the dose-response effect is shown in Figure 1. As compared to individuals who always used a mask, those who never used a mask had a 12.6-fold higher risk of developing SARS.

The present study revealed some SARS-CoV-seropositive cases, despite the absence of clinical symptoms of the disease in these subjects. The percentage of seropositive but asymptomatic SARS cases was significantly higher at Hospital A (15.5%), where the epidemic began, than at Hospital

Table 1. SARS seropositive rate and mean antibody level by groups

	Total	Symptomatic cases (no.)	Seropositive cases (no.)	Seropositive rate (%)	Antibody level ¹⁾
Group 1	43	43	43	100.0	141.4
Group 2	103	0	16	15.5	38.8
Group 3	124	0	8	6.5	27.4
Group 4	50	0	1	2	22.7

Group 1: SARS symptomatic cases at Hospital A.

Group 2: Individuals who contacted with SARS patients closely and asymptomatic at Hospital A.

Group 3: Individuals who contacted with SARS patients closely and asymptomatic at Hospital B.

Group 4: Individuals who have no history of contact with SARS patients at Hospital C.

¹⁾: Mean of the antibody levels in SARS seropositive cases.

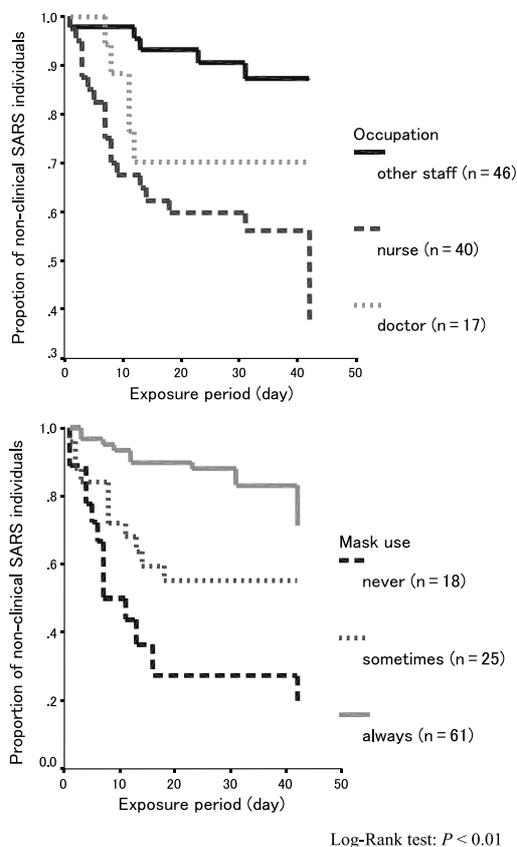


Fig. 1. Comparison of the proportion of non-clinical SARS individuals with exposure period by occupation (left) and by mask use (right). X axis represents the total number of SARS exposure days. Y axis represents the proportion of individuals who do not develop SARS.

Table 2. Risk factors for developing SARS among contacted individuals at Hospital A ($n = 85$)

Factor	no.	AOR (95% CI) ¹⁾	<i>P</i>
Age	85	0.97 (0.90-1.03)	0.28
Severity of patient			
no oxygen	36	1.00	
oxygen supply	49	2.65 (0.66-10.7)	0.17
Mask use			
always	50	1.00	
sometimes	22	2.90 (0.73-11.6)	0.13
no	13	12.6 (2.00-80.0)	<0.01
Hand washing before ²⁾			
always	56	1.00	
sometimes	17	1.25 (0.25-6.10)	0.79
no	12	3.69 (0.56-24.2)	0.17
Occupation			
other staff	30	1.00	
doctor	17	40.9 (2.65-630)	<0.01
nurse	38	57.3 (5.28-621)	<0.01
Contact episode with SARS patient			
direct contact	73	1.00	
indirect contact	12	6.06 (0.63-58.7)	0.12
Attendance at a lecture on nosocomial infection			
yes	58	1.00	
no	27	5.49 (0.90-33.4)	0.06

¹⁾: Adjusted for each variables listed above.

²⁾: Washing hands before any contact with a patient.

CI, confidence interval; AOR, adjusted odds ratio. $R^2=0.427$.

B (6.5%), the hospital to which patients were transferred from Hospital A ($P < 0.05$) (Table 1). At Hospital A, the necessity of providing a diagnosis and treatment in the absence of information regarding the features of this infection resulted in hospital workers having extensive, unprotected contact with SARS patients. In contrast, SARS patients were admitted to Hospital B with knowledge of the nosocomial transmission of this previously unknown disease. This difference is likely to account for the observed difference in the seropositive rate between these two hospitals.

The multivariate analyses conducted in the present study suggested that infection with SARS-CoV and disease onset were closely related to the use of protective measures such as wearing a mask, rather than to clinical severity (i.e., the severity of the condition of patients with whom the subjects had contact) and host factors (e.g., age) (Table 2). Thus, comprehensive protective measures such as consistently wearing a mask during patient care are expected to markedly reduce the transmission of this disease. In general, routine basic measures to prevent nosocomial infection are crucial. Such

protective measures could be supplemented by ensuring that hospital workers are made aware of cases in which they are dealing with infectious patients. In any event, in epidemic-stricken areas both inside and outside of hospitals, wearing a mask appears to be useful for preventing the spread of SARS.

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