



Do Men Have a Higher Case Fatality Rate of Severe Acute Respiratory Syndrome than Women Do?

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Severe acute respiratory syndrome (SARS) has been reported in 30 countries and regions, with a cumulative total of 8,099 probable cases and 774 deaths as of July 31, 2003, according to the World Health Organization. In Hong Kong, People's Republic of China, 1,755 SARS cases and 299 deaths had occurred as of September 22, 2003. The authors analyzed data from the Department of Health, Hong Kong SAR. The data series includes details regarding sex, age, and chronic disease history. Using data from early March to September 22, 2003, the authors found that males had a significantly ($p < 0.0001$) higher case fatality rate than females did, 21.9% versus 13.2%; the relative risk was 1.66 (95% confidence interval (CI): 1.35, 2.05), and it was 1.62 (95% CI: 1.21, 2.16) after adjustment for age. Subgroup analysis was conducted by excluding health care workers ($n = 386$) from the analysis. The overall crude relative risk of mortality was 1.41 (95% CI: 1.15, 1.74), and the adjusted relative risk was 1.48 (95% CI: 1.10, 2.00). Thus, among SARS patients, males may be more severely affected by the disease than females are. This finding could be related to a nonuniform case definition of SARS disease, a different treatment regimen, a past smoking history, work-environment factors, or gender-specific immune-defense factors, for instance.

case mortality; Hong Kong; SARS virus

Abbreviations: CI, confidence interval; SARS, severe acute respiratory syndrome.

Severe acute respiratory syndrome (SARS) has been reported in 30 countries and regions, with a cumulative total of 8,099 probable cases and 774 deaths as of July 31, 2003, according to the World Health Organization (1). We used SARS data from Hong Kong, People's Republic of China, to assess the role of gender in survival/mortality outcome.

During the early phase of the SARS outbreak in Hong Kong, Lee et al. reported that "univariate analysis showed advanced age, male sex, a high peak creatine kinase value, a high lactate dehydrogenase level on presentation and a high peak value, a high initial absolute neutrophil count, and a low serum sodium level were significant predictive factors for ICU [intensive care unit] admission and death" (2, pp. 1990–1991). The researchers based this conclusion on the first 138 cases of SARS in Hong Kong (66 males, 72 females); 32 patients were admitted to the intensive care unit and five died. However, only advanced age, high neutrophil count, and high peak lactate dehydrogenase were indepen-

dent predictors. Later, in a large epidemiologic study of SARS that included 1,425 cases, Donnelly et al. (3) concluded that only the age of patients strongly affected outcome, while the role of gender was not considered in their study.

To our knowledge, there has so far not been any other report on gender as a risk factor for SARS outcomes. This paper provides evidence of a gender-specific SARS mortality rate based on 1,755 Hong Kong SARS patients with a case fatality rate of 17.0 percent (170 males, 129 females) as of September 22, 2003.

MATERIALS AND METHODS

The SARS data were the same as those in the official daily reports of the Hong Kong Government in the form of press releases prepared in collaboration with each infectious disease team at the 42 Hong Kong Government hospitals (4).

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TABLE 1. Age distribution of cases and age- and-sex-specific case fatality rate for SARS* as of September 22, 2003, Hong Kong, People's Republic of China

Age (years)	Males					Females					Males vs. females		
	Total		Deaths			Total		Deaths			RR‡	95% CI	p value
	No.†	%	No.	CFR* (%)	95% CI*	No.†	%	No.	CFR (%)	95% CI			
All SARS cases included													
0–44	425	54.8	27	6.4	4.0, 8.7	607	62.0	17	2.8	1.5, 4.1	2.27	1.25, 4.11	0.007
45–74	249	32.1	77	30.9	25.2, 36.7	295	30.1	63	21.4	16.7, 26.0	1.45	1.09, 1.93	0.014
≥75	102	13.1	66	64.7	55.4, 74.0	77	7.9	49	63.6	52.9, 74.4	1.02	0.81, 1.27	1.000
All	776	100.0	170	21.9	19.0, 24.8	979	100.0	129	13.2	11.1, 15.3	1.66	1.35, 2.05	<0.0001
Health care workers excluded													
0–44	336	50.3	26	7.7	5.2, 10.3	375	53.5	14	3.7	2.2, 5.2	2.07	1.10, 3.90	0.023
45–74	230	34.4	75	32.6	26.8, 38.4	249	35.5	61	24.5	19.6, 29.4	1.33	1.00, 1.77	0.054
≥75	102	15.3	66	64.7	55.4, 74.0	77	11.0	49	63.6	52.9, 74.4	1.02	0.81, 1.27	1.000
All	668	100.0	167	25.0	22.0, 28.0	701	100.0	124	17.7	15.3, 20.1	1.41	1.15, 1.73	0.001

* SARS, severe acute respiratory syndrome; CFR, case fatality rate; CI, confidence interval.

† Chi-square testing showed that the age distributions of male and female cases were significantly different with a *p* value of <0.0001.

‡ Unadjusted relative risk (RR) of mortality for males compared with females.

The same data in the daily reports provide the basis for daily updates to the World Health Organization. The daily reports included details of the treating hospital, sex, age, and chronic disease history for each individual SARS case who died. Furthermore, the sex and age distribution of all SARS cases was obtained after personal communication with the Hong Kong Department of Health in September 2003. The current analysis is based on all SARS mortality data from early March to September 22, 2003. Subgroup analysis was conducted by excluding all health care workers (*n* = 386) from the analysis. Age and sex distribution was available for the first 374 infected health care workers (5), and the number of infected health care workers in each age- and sex-specific stratum as of September 22, 2003, was estimated from this information.

The definition of SARS cases was made by the treating physicians and was based on clinical signs, a chest radiograph, and diagnostic tests for some patients and by autopsy reports. The case definition is not uniformly applied globally, and this issue has recently been debated (6); however, the SARS cases reported here should be regarded as probable SARS patients.

RESULTS

The SARS case fatality rate in Hong Kong increased from 2.2 percent (17/761 × 100) on April 4, 2003, to 17.0 percent (299/1,755 × 100) by September 22, 2003. During the same period, among the cases whose outcome was known, the mortality rate—for which the cumulative number of deaths and patients discharged was used as the denominator—was close to constant, at about 15–17 percent (7). Of note, five

SARS patients remained hospitalized on September 22, 2003. Two were recovering patients in convalescence, while the other three were undergoing treatment for other diseases.

Based on gender, the SARS case fatality rate was 13.2 percent for females (95 percent confidence interval (CI): 11.1, 15.3) and 21.9 percent for males (95 percent CI: 19.0, 24.8), a relative mortality risk estimate of 1.66 (95 percent CI: 1.35, 2.05; *p* < 0.001) for males compared with females. We noted that of the females who died, 71.3 percent had a chronic disease history, while the corresponding figure for males who died was 64.7 percent. A chi-square test showed no statistically significant association between gender and chronic disease history among the deaths (*p* = 0.23).

Table 1 shows the number of SARS cases in each age- and sex-specific stratum and that females were significantly (chi-square-test *p* = 0.0003) younger than males: 62.0 percent of females versus 54.8 percent of males were aged 0–44 years, 30.1 percent of females versus 32.1 percent of males were aged 45–74 years, and 7.9 percent of females versus 13.1 percent of males were aged 75 years or older. The respective age- and sex-adjusted case fatality rates for the three age groups were 2.8 percent, 21.4 percent, and 63.6 percent for females compared with 6.4 percent, 30.9 percent, and 64.7 percent for males. On the basis of a logistic regression model with mortality as the dependent measure and sex and age as the independent measures, both sex and age were found to be significant (*p* = 0.004 and *p* < 0.0001, respectively), while the interaction term between sex and age was not statistically significant (*p* = 0.19). The adjusted relative risk for males compared with females was 1.62 (95 percent CI: 1.21, 2.16). Subgroup analysis was conducted by excluding health care workers (*n* = 386) from the analysis (table 1). We found that

the overall crude relative risk of mortality was 1.41 (95 percent CI: 1.15, 1.73), while the adjusted relative risk was 1.48 (95 percent CI: 1.10, 2.00).

DISCUSSION

So far, there have been no known reports, based on larger samples, of a gender difference in SARS case fatality rates. In this short study, we found that the overall case fatality rate was 17.0 percent among the cumulated 1,755 probable SARS cases in Hong Kong. Males had a significantly ($p < 0.0001$) higher case fatality rate than females did, 21.9 percent versus 13.2 percent; the relative risk was 1.66 (95 percent CI: 1.35, 2.05), and it was 1.62 (95 percent CI: 1.21, 2.16) after adjustment for age. A logistic regression model revealed that sex and age were both significantly related to the case fatality rate. However, the analysis also showed that the gender difference could not be explained by a significantly higher age distribution among the males compared with the females. Regarding the age of SARS cases, all females were significantly younger than males, which is explained by the relatively high number of infected hospital staff (22 percent) among all SARS patients, especially nurses (5); 60 percent of all infected health care workers ($n = 384$) were females less than age 45 years (5). However, this "selected" health care patient population is unlikely to have biased the gender difference observed in the mortality rate, since the vast majority, or 85.3 percent, of the deaths occurred among patients over 44 years of age, and subgroup analysis excluding all health care workers showed a significant sex difference in the mortality rate.

This observation may indicate that males are more severely affected than females by the SARS coronavirus (8). Our results show that the SARS mortality gender difference was highest for younger patients (0–44 years of age), with a relative risk of about 2 (also after excluding health care workers from the analysis). This gender difference was also observed for patients aged 45–74 years (relative risk = 1.45) but not for elderly patients, those aged 75 years or older. The diminishing gender-specific SARS mortality rate with increasing age may be due to the generally age-dependent trend of the health of a population, that is, that age becomes much more important than any possible gender difference. This possibility is suggested by the fact that the overall SARS mortality rates were 4.3 percent, 25.7 percent, and 64.2 percent for the

three age groups, respectively. However, the exact mechanism regarding how the SARS coronavirus infects and manifests itself in humans has yet to be elucidated. Before making any wider interpretation, we would be interested to see whether our findings are confirmed from data collected in other regions with a high SARS prevalence. In this short study, we did not analyze other factors that might influence the case fatality rate, such as time since the onset of the SARS outbreak in Hong Kong, the hospital involved in treating the SARS patients, or treatment regimens.

In conclusion, the reason(s) for a true gender difference in the SARS fatality rate is unknown. We speculate that it could be related to a nonuniform case definition of the SARS disease, a different treatment regimen, a past smoking history, work-environment factors, or gender-specific immune-defense factors, for instance.

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