Mortality Factor Survey of Severe Acute Respiratory Syndrome in Taiwan

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SUMMARY

Background: Severe acute respiratory syndrome (SARS) is a new respiratory tract infectious disease caused by the highly contagious coronavirus (SARS-CoV). Its propagation and symptom progress are very rapid. This study evaluated the clinical characteristics, laboratory results and mortality factors of probable SARS cases.

Methods: This study was adopted with a retrospective research design to study probable SARS cases from the Chang Gung Memorial Hospital in Linkou and Kaoshiung from August 2003 to February 2004, with a total of 78 cases (average age, 44 years; standard deviation, 18 years; age range, 13–84 years) including 24 males (30.8%) and 54 females (69.2%).

Results: Most of the 78 cases involved nosocomial infection (56.4%). A total of 24 patients died, and the mortality rate was as high as 30.8%. Logistic regression analysis found that intubation (odds ratio, 115; $p < 0.001$) was the mortality forecast factor.

Conclusion: The mortality rate of intubation patients was 115 times higher than that of those who did not require intubation. Therefore, special care must be taken with SARS disease with severe infiltration chest X-ray images and respiratory distress. Positive medical treatment should be performed to lower the mortality rate. [International Journal of Gerontology 2009; 3(1): 31–38]

Key Words: clinical characteristic, mortality factor, severe acute respiratory syndrome

Introduction

Severe acute respiratory syndrome (SARS) is a new contagious disease and the first global epidemic of the 21st century. It is a respiratory infection disease caused by a novel, highly infectious coronavirus (SARS-CoV)[1–3]. According to the World Health Organization (WHO), statistics from November 1, 2002 to August 7, 2003, 32 countries reported 8,422 probable SARS cases[4]. Ninety-six percent of probable SARS cases were in Asia[4], and Taiwan was one of the important epidemic regions. SARS mortality rates worldwide have varied from 5.6% to 20.8% [5–10], and the Taiwanese mortality rate ranked at the top[5,8]. However, only seven literature references related to SARS progress have been published to date[5,6,8,9,11–13]. In light of such a high mortality rate in Taiwan, it is necessary to build a larger database to further understand mortality factors.

As shown in the literature, when SARS has been coupled with other chronic diseases[5], high initial C-reactive protein (CRP) levels[5,6] and high initial lactate dehydrogenase (LDH) values[6,7] were predictable factors of death. In addition, age[5,7], CRP[5,6] and severe chest X-ray signs[5] were also reported to be related factors to predict the possibility of respiratory failure[5]. Liu et al.[8] mentioned that 11 of 12 SARS patients receiving respiratory

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treatment died, indicating that acute respiratory failure is an important factor in determining death.

According to the literature, age has been associated with poor prognoses in patients with other chronic diseases such as chronic heart failure[14–17] and chronic renal failure[18–20]. However, the association between mortality rates and age has been limited in SARS patients[5]. Therefore, the aims of this study were to: (1) examine the associations among age, education, past history of disease (e.g., cancer, pulmonary disease), severity of the illness (e.g., chest X-ray findings and laboratory data), and mortality rate in patients with SARS; and (2) determine the significant predictors of death in patients with SARS.

Materials and Methods

Probable SARS cases were collected from Chang Gung Memorial Hospital in Linkou and Kaoshiung from August 2003 to February 2004. The inclusion criterion was any case diagnosed to be a probable SARS case according to the WHO definition modified on May 1, 2003[21]. There were 79 cases in total, including 78 effective cases (98.7%). One case could not be retrieved because of incomplete medical records.

From retrospective medical records retrieval, objective data about probable SARS cases from emergency departments, hospitalizations, discharges or deaths were gathered. This covered patient basic information, vital signs, disease progression, laboratory and physical examinations, medical treatment, and revisit tracking.

To assess the severity of chest X-rays, we quantified chest X-ray graphs into division numbers in terms of "feature" and "invasion extent". One point was given if infiltration was present, 2 points if the feature was consolidation, and 3 points if the feature was fibrosis. Invasion extent was rated by dividing bilateral lungs into four sections: (1) invasion of one-quarter of bilateral lungs rated 1 point, (2) invasion of two-quarters of bilateral lungs 2 points, (3) invasion of three-quarters of bilateral lungs 3 points, and (4) invasion of both lungs 4 points. The scores ranged from 0–7, with a higher score indicating a more severe chest X-ray graph.

Statistical analysis

For continuous variables (e.g., age, blood test report data), a dependent *t* test was used to check the relationship with mortality. For categorical variables (e.g., marital status, education, medical care staff), Chi-squared and Fisher's exact tests were used to verify the impact on mortality, the significance level was set at 0.05, and a two-tailed test was adopted for all probabilities. Significant variables (probable SARS case risk factors related with mortality) of univariate analyses were put into logistic regression analyses to calculate odds ratios so as to interpret the impact of independent variables on dependent variables.

Results

Demographic characteristics

The mean age of the 78 patients was 44 ± 18 years (range, 13–84 years). There were 24 males (30.8%) and 54 females (69.2%). Most were married (59.0%) with a college education (23.1%) and were infected by nosocomial infection (56.4%), followed by cross infection in family and unknown infections (15.4% each). About 36% of the patients were medical care staff. In terms of past disease history, a total of 20 patients (25.6%) had contracted chronic diseases (see Table 1).

Clinical characteristics

In terms of early emerged physiologic symptoms (during hospitalization and before hospitalization), except for one case, 77 cases (98.7%) had a fever. Average temperature was an axial temperature of 38°C (standard deviation, SD, 1.0). Cough rate was 48.7%, split evenly between dry and wet coughs (50.0%). The rate of sore all over was 24.4%, shortness of breath rate was 21.8%, and chill and rigor, and asthenia universalis rates were 20.5% each (Table 2).

In terms of hematologic and biochemical laboratory examinations, abnormal rate on admission to hospital (blood test data of the first visit to emergency department) and peak abnormal rate during hospitalization are shown in Table 3. When the patient entered the emergency department or lived in a HEPA isolation ward, medical staff took specimens from the patients' throat, urine, feces and blood. SARS-CoV was isolated from the throat, nasopharynx, urine, blood test specimens of 47 patients, and sensitivity was 67.1% (eight missing values). Using reverse transcription–polymerase chain reaction (RT-PCR), among the probable SARS patients subjected to RT-PCR, 41 were found to be positive (58.6%) (eight missing values).

Table 1. *Demographic characteristics of probable severe acute respiratory syndrome cases (n = 78)**	
Age, mean ± SD (yr)	44 ± 18 (range, 13–84)
Sex	
Male	24 (30.8)
Female	54 (69.2)
Marital status	
Single	26 (33.3)
Married	46 (59.0)
Widowed	5 (6.4)
Missing value	1 (1.3)
Education	
Illiterate	4 (5.2)
Elementary school	9 (11.5)
Junior high school	3 (3.8)
Senior high school (occupational)	6 (7.7)
College	18 (23.1)
University	11 (14.1)
Higher research institute	1 (1.3)
Missing value	26 (33.3)
Living status	
Alone	8 (10.3)
Cohabit	62 (79.4)
Hospice	1 (1.3)
Missing value	7 (9.0)
Probable infection cause	
Nosocomial infection	44 (56.4)
Travel contact	3 (3.8)
Cross infection in family	12 (15.4)
Other factor	7 (9.0)
Unknown cause	12 (15.4)
Medical care staff	
No	47 (60.3)
Yes	28 (35.9)
Missing value	3 (3.8)
Chronic disease history	20 (25.6)
Diabetes	5 (6.4)
Cancer	7 (9.0)
Heart disease	2 (2.6)
Pulmonary disease	13 (16.7)
Renal disease	1 (1.3)

**Data are presented as n (%). SD = standard deviation.*

Chest X-ray feature

On admission to the emergency department, chest X-rays showed pathology in 71.8% of cases, and the ratio increased to 97.4% during hospitalization. Lobes of both sides were invaded (75.6%). In cases of single lobe invasion, the lower right lung lobe was more often attacked (58.8%). Chest X-rays showed worsening after hospitalization for 7.1 days (SD, 6.6 days).

During hospitalization, among the 22 cases whose initial chest X-ray graphs were normal, 20 (90.9%) developed into abnormal patterns after hospitalization for 3.5 days (SD, 2.6 days) (Table 4). Among the 56 cases whose initial chest X-ray graphs were abnormal, 30 (38.4%) had a topical focus, in which 24 (80%) turned to multiple topical foci or diffusive pneumonia along with disease progress. Among 19 cases with multiple topical foci upon admission to hospital, nine cases (47.4%) developed into diffusive pneumonia. As seen in Table 5, death cases often manifested multiple topical foci or diffusive pneumonia in chest X-ray graphs during hospitalization, and cases with a diffusive pattern (75.0%) were more susceptible. The mean chest X-ray score of 32 cases requiring intubation was 4.5 points. Average intubation time of these 32 cases was 8.4 days after hospitalization (SD, 7.5 days), of which the mean endotracheal retention time of nine surviving cases was 15 days (SD, 12.9 days) and the mean endotracheal retention time of 23 death cases was 8 days (SD, 10.6 days).

Among the 78 probable cases, 24 patients died. The mortality rate was as high as 30.8%. The mean number of hospitalization days was 18.7 days (SD, 12.0 days). During hospitalization, 53 patients (67.9%) received oxygen treatment, and 32 of those cases (41.0%) were subjected to intubation–respiratory treatments owing to acute respiratory failure (31 patients, 96.9%)

Table 2. *Initial clinical symptoms of probable severe acute respiratory syndrome cases (n = 78)*	
Initial clinical symptom	*n* (%)
Fever	77 (98.7)
Cough	38 (48.7)
Dry cough	19 (50.0)
Wet cough	19 (50.0)
Sore all over	19 (24.4)
Shortness of breath	17 (21.8)
Chill and rigor	16 (20.5)
Asthenia universalis	16 (20.5)
Diarrhea and stomachache	10 (12.8)
Anorexia	10 (12.8)
Sore throat	10 (12.8)
Headache	9 (11.5)

Table 3.	*Laboratory data in probable severe acute respiratory syndrome patients on hospital admission and during hospitalization**

Variable	On admission	During hospitalization
Hematologic examinations		
Leukopenia (<4,000/μL)	18/77 (23.4)	13/26 (50.0)
Leukocytosis (>10,000/μL)	13/77 (16.9)	17/32 (53.1)
Thrombocytopenia (<150,000/μL)	27/77 (35.1)	28/50 (56.0)
Segmented neutrophils (>74%)	45/77 (58.4)	27/32 (84.4)
Lymphopenia (<1,000/μL)	53/77 (68.8)	27/32 (84.4)
Biochemistry examinations		
Creatine kinase (>130 U/L)	17/63 (27.0)	4/11 (36.4)
Lactate dehydrogenase (>140 U/L)	19/67 (28.4)	22/38 (57.9)
Aspartate transaminase (>34 U/L)	24/68 (35.3)	4/4 (100)
Alanine transaminase (>36 U/L)	14/66 (21.2)	15/21 (71.4)
C-reactive protein (>5 mg/L)	49/63 (77.8)	31/34 (91.2)
SARS-CoV assays		
RT-PCR-positive	41/70 (58.6)	40/70 (67.1)

**Data are presented as n (%). SARS-CoV = severe acute respiratory syndrome-coronavirus; RT-PCR = reverse transcription–polymerase chain reaction.*

Table 4.	*Chest X-ray patterns of probable severe acute respiratory syndrome patients during hospitalization (n = 78)**

Chest X-ray pattern	Initial patients	Patients with worsening chest X-ray condition during hospitalization	Worst chest X-ray condition in hospitalization		
			Topical	Multiple topical	Diffusive
Normal	22 (28.2)	20 (90.9)	4 (18.2)	11 (50.0)	5 (22.7)
Abnormal	56 (71.8)				
Topical	30 (38.4)	24 (80.0)		15 (50.0)	9 (30.0)
Multiple topical	19 (24.4)	9 (47.4)			9 (47.4)
Diffusive	7 (9.0)	7 (100)			7 (100)

**Data are presented as n (%).*

Table 5.	*Chest X-ray pattern of probable severe acute respiratory syndrome cases during hospitalization and after recovery (n = 78)**

Chest X-ray pattern during hospitalization	Patients ($n = 78$)	Casualty ($n = 24$)
Normal	2 (2.6)	0 (0.0)
Abnormal	76 (97.4)	24 (30.8)
Topical	10 (13.2)	0 (0.0)
Multiple topical	36 (47.4)	6 (25.0)
Diffusive	30 (39.4)	18 (75.0)

**Data are presented as n (%).*

and poor chest X-rays (one patient, 3.1%). The remaining eight cases (25.0%) underwent a successful endotracheal tube-removing operation, and tracheotomy was performed in one case (3.1%).

Mortality factors

Significant influential factors related with death were found in a univariate analysis (Table 6), which included age ($t = -4.9$, $p < 0.001$), marital status ($\chi^2 = 10.819$, $p = 0.004$), education ($\chi^2 = 13.200$, $p = 0.040$), medical care staff ($p = 0.004$), history of cancer ($p = 0.003$) or pulmonary disease history ($p = 0.002$), first white blood cell (WBC) value ($t = -3.134$, $p = 0.004$), and segment value ($t = -3.709$, $p < 0.001$) in week 1 after admission. In week 2 after admission, those variables were changed significantly, including first WBC value ($t = -3.827$, $p < 0.001$), segmented neutrophil value ($t = -3.857$, $p < 0.001$), lymphocyte value ($t = 2.998$, $p = 0.004$), and chest X-ray value ($t = -4.393$, $p < 0.001$). Only the variable of chest X-ray score was found to be significantly different in the third week after admission. As a result, we found in the logistic regression

Table 6. Univariate analysis of probable severe acute respiratory syndrome case casualty ($n=78$)				
Variable	Surviving ($n=54$)	Casualty ($n=24$)	χ^2 or t	p
Age (yr)	38.1±15.3	57.3±17.5	–4.9	<0.001†‡
Marital status			10.819	0.004†§
Single	24 (45.3)	2 (8.3)		
Married	27 (50.9)	19 (79.2)		
Widowed	2 (3.8)	3 (12.5)		
Missing value	1			
Education			13.200	0.040†§
Illiterate	1 (2.8)	3 (18.8)		
Elementary school	4 (11.1)	5 (31.3)		
Junior high school	2 (5.6)	1 (6.3)		
Senior high school (occupational)	3 (8.3)	3 (18.8)		
College	17 (47.2)	1 (6.3)		
University	8 (22.2)	3 (18.8)		
Above research institute	1 (2.8)	0 (0.0)		
Missing value	18	8		
Medical care staff				0.004†‖
No	27 (51.9)	20 (87.0)		
Yes	25 (48.1)	3 (13.0)		
Missing value	2	1		
Past cancer				0.003†‖
No	53 (98.1)	18 (75.0)		
Yes	1 (1.9)	6 (25.0)		
Past pulmonary disease				0.002†‖
No	50 (92.6)	15 (62.5)		
Yes	4 (7.4)	9 (37.5)		
White blood cells (first test in the 1st week) (/μL)	5,520.4±2,737.7	10,650.4±7,645.5	–3.134	0.004†‡
Segmented neutrophils (first test in the 1st week) (%)	73.8±10.5	83.1±8.7	–3.709	<0.001†‡
White blood cells (first test in the 2nd week) (/μL)	7,772.9±4,624.2	13,066.7±4,847.2	–3.827	<0.001†‡
Segmented neutrophils (first test in the 2nd week) (%)	77.3±17.1	90.0±8.4	–3.857	<0.001†‡
Lymphocytes (first test in the 2nd week) (/μL)	861.8±650.3	470.0±352.3	2.998	0.004†‡
Chest X-ray in the 2nd week	2.8±1.3	4.5±1.3	–4.393	<0.001†‡
Chest X-ray in the 3rd week	2.5±1.4	4.1±1.5	–2.796	0.008†‡

**Data are presented as mean±standard deviation or n (%); †$p<0.05$; ‡t test of independent samples; §Chi-squared test; ‖Fisher's exact test.*

analysis that the mortality odds ratio of intubation patients was 115 times higher than non-intubation patients ($p<0.001$) (Table 7).

Discussion

SARS cases were primarily females (60.2%), consistent with most literature[5–10,12]. Among them, 28 cases (35.9%) were medical care staff, with nurses making up 57.1%, which might explain why most patients of probable SARS cases are females. The medical care staff ratio (35.9%) in our study was similar to the literature[6–9,12]; therefore, a latent occupational risk of medical care staff could be seen.

In this study, the earliest symptom to emerge was fever, accounting for 98.7% of cases, which is consistent with the literature[8]. Although the rate decreased gradually after admission, there were still 34 patients (43.6%) who required fever medicine a week after admission. Thus, a decreased fever rate does not mean improvement of the disease. In the early stage of disease

Table 7. *Logistic regression analysis of probable severe acute respiratory syndrome case casualty (n = 78)*

	n	Casualty ratio	Odds ratio	95% confidence interval	*p*
Intubation during hospitalization					< 0.001*
Without intubation	46	4.2	Reference	–	
With intubation	32	95.8	115	13.72–962.57	

(in hospitalization and before hospitalization), 48.7% of cases had cough symptoms. Dry cough and wet cough each accounted for half of the cases, differing from the mostly dry cough symptoms found in the literature[6,8]. In this study, 16.7% of patients had contracted pulmonary disease in the past, which may have played a role. After disregarding cases with pulmonary disease history, the cough type of the remaining probable SARS cases was primarily dry cough (58.6%).

In laboratory examination, blood test values for the first visit to emergency department on admission, including lymphopenia, thrombocytopenia, creatine kinase, aspartate transaminase, alanine transaminase and CRP, increased abnormally, somewhat similar to the literature[5,6,8,9]. The leukopenia rate in this study was 23.4% and the other values reported in the literature were between 10.3% and 19.7%[5,6,9]. CRP abnormally rising rates reached 91.2%, whereas previous literature showed the rates of 93.4–97.2%[5,6].

SARS-CoV viruses were identified in samples from 47 (60.3%) of all probable SARS cases. Among the 70 probable SARS patients with RT-PCR results, 41 patients (58.6%) were positive, and the sensitivity fell to within the range in the literature (range, 34.5–85%)[5–9]. Although no SARS-CoV viruses were isolated from samples of the other 29 cases (41.4%), it does not exclude the possibility of false-negative results[7,8], because samples of most cases were collected in the emergency department or during hospitalization, and perhaps virus titers at that time did not reach its peak[22], leading to lower examination sensitivity.

In this study, cases of chest X-ray pathology on admission accounted for 71.8% of cases, somewhat similar to the literature (range, 59–99.6%)[5,6,8,9,23]. Abnormal rates during hospitalization even rose to 97.4%, again similar to the literature (range, 98–100%)[5,8,23]. Chest X-ray results worsened after hospitalization for 1 week (mean, 7.1 days), slightly different to those in the literature (range, 7.4–9.8 days)[5,6,9]. All casualty cases occurred when chest X-rays depicted multiple topical foci or diffusive pneumonia in a particular diffusive pattern (Table 5). Therefore, chest X-ray severity is closely related with death ($t = -4.393$, $p < 0.001$). The wider the chest X-ray invasion extent, the higher the intubation probability and the greater the mortality rate.

Intubation was performed on 32 cases in this study. The average score of intubation chest X-ray was 4.5 points and average intubation time was 8.4 days from hospitalization (SD, 7.5 days). Among them, the average endotracheal retention time of nine surviving cases was 15 days (SD, 12.9 days) and the mean endotracheal retention time of 23 casualty cases was 8 days (SD, 10.6 days). Therefore, it may take at least 2 weeks from intubation to recovery period. Among the cases included in this study, there were only two cases in which chest X-ray graphs manifested as normal, indicating that although chest X-ray examination is important for early diagnosis of SARS, epidemiologic history and other clinical symptoms must not be ignored for the identification diagnosis.

There were a total of 24 casualty cases in this study. The mortality rate was as high as 30.8%, higher than that in the literature (range, 5.6–20.8%)[5–10]. Further analysis of the mortality rates from Chang Gung Hospital in Linkou and Kaohsiung revealed that three patients died among the 30 probable SARS cases in Chang Gung Hospital of Linkou, with a mortality rate reaching 10%. Twenty-one patients died among the 48 probable SARS cases in Chang Gung Hospital of Kaohsiung, with a mortality rate as high as 43.8%, probably related to a nosocomial infection outbreak in Chang Gung Hospital of Kaohsiung. As a result, the total mortality rate of this study was higher than in the literature.

In SARS, demography, age, marital status, education, medical care staff, past cancer and pulmonary disease history are significantly correlated with mortality. Older patients and patients with a history of cancer or pulmonary disease might be more vulnerable to SARS infections. There were several factors affecting elderly mortality, which reportedly consisted of age[14–20], preexisting comorbidity and a decreased host resistance by reduced physical reserves and less ability to compensate, thus leading to death in older victims[24]. The significant relationship between marriage and death might be because most married people live with families, making them vulnerable to cross infection, which is one of the SARS epidemiologic features. Most SARS infection cases were caused by nosocomial infection. In this study, over 35% were confirmed by medical records to be medical care staff, which may explain why most medical care staff who had to care for infected cases closely were of a higher education. Therefore, it makes sense that education and medical care staff significantly correlated with death. Previous studies reported that correlations of age[5,7], chest X-rays[5] and past disease history (cancer and pulmonary disease)[5] with casualty were regarded to be associated with death from SARS. Logistic regression statistic results indicated that intubation was a significant predictor for death. However, Liu et al.[8] suggested that acute respiratory failure was also a crucial recovery factor from SARS as well.

Conclusion

Knowing the most common symptoms in SARS progression (i.e., fever, cough, chill and rigor, asthenia universalis and all-over soreness, and shortness of breath) can aid clinical medical personnel in understanding the physiologic symptoms of SARS and provide on-time physiologic care. Results of this study showed that all casualty cases occurred when chest X-ray graphs manifested multiple topical foci or diffusive pneumonia, especially in a diffusive pattern. Endotracheal intubation was also shown to be an important predicting factor for death, so these patients must be more carefully and actively treated. Death occurred in SARS patients with an average age of 57 years, while the survivors had an average age of 38 years. This study may help medical staff understand the illness course and how it progresses so that they can explain this to patients' families properly. It is expected that the cross integration of all probable SARS case data between organizations and even countries can provide even more significantly statistically accurate results.

As the populations of probable SARS cases are few and hard to sample, it is indeed beneficial for this study to collect 78 probable SARS cases, i.e., 25% of all probable SARS cases in Taiwan. Because 25 cases (32.1%) of this study were transferred from other hospitals, blood test data, clinical symptoms or chest X-rays on admission may not represent changes of the initial period of disease. It is recommended to consider this point in related future research and to try and track medical records in other hospitals by interhospital cooperation to make study results more convincing.

Data collection through medical records might still involve the missing of data concerning the variables in basic demography, cough type, chest X-ray and PCR results and blood test items. Medical records for each patient were not completed at the same time and the tracking date differed. When retrospectively assessing clinical symptoms, we have to consider whether medical staff observed all physical and mental features of the patient or whether the patient might not have taken the initiative to complain about discomfort symptoms. These are the inevitable constraints in a study of this design. Future research shall adopt a prospective design to observe directly in order to enhance study validity.

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