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Severe acute respiratory syndrome in Taiwan: analysis of epidemiological characteristics in 29 cases

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Summary Objectives. To describe the clinical characteristics and outcomes of patients with severe acute respiratory syndrome (SARS).

\textbf{Methods.} Between March 28 and June 30 \textsuperscript{2003}, 29 patients with probable SARS seen at Shin Kong Wu Ho-Su Memorial Hospital, Taipei, were analysed.

\textbf{Results.} Presenting symptoms included fever (100\%), cough (69.0\%), chills or rigor (62.1\%), and shortness of breath (41.4\%). Mean days to defervescence were 6.8 \pm 2.9 days, but fever recurred in 15 patients (51.7\%) at 10.9 \pm 3.4 days. Common laboratory features included lymphopenia (72.4\%), thrombocytopenia (34.5\%) and elevated C-reactive protein (CRP), lactate dehydrogenase (LDH), and aspartate aminotransferase (AST) (93.1, 62.1, 44.8\%, respectively). All patients except one had initial abnormal chest radiographs and 20 (69.0\%) had radiological worsening at 7.5 \pm 2.6 days. Nine patients (31.0\%) subsequently required mechanical ventilation with four deaths (13.8\%). Most patients with clinical deterioration responded to pulse corticosteroid therapy (14 out of 17) but six complicated with nosocomial infections. The risk factors associated with severe disease were presence of diarrhoea, high peak LDH and CRP, high AST and creatine kinase on admission and high peak values.

\textbf{Conclusions.} Prudent corticosteroid use, vigilant microbiological surveillance and appropriate antibiotics coverage are the key to successful treatment.

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Introduction

An outbreak of atypical pneumonia in Guangdong Province, People’s Republic of China, that has continued since November 2002, was reported to have infected 792 people and caused 31 deaths.\textsuperscript{3} This outbreak received no international attention until February 2003, when a nephrologist from Guangdong Province became ill during a one-day stay on the ninth floor of a Hong Kong hotel. Twelve
other guests became infected including 10 staying on the same floor. These hotel guests subsequently became the index patients who transported the disease to Vietnam, Singapore, Canada, Ireland, and the United States. The primary mode of transmission of SARS appears to be by the airborne spread of large droplets. As the illness has spread, the condition has been particularly prevalent among healthcare workers and their household members. Many cases progressed rapidly and often resulted in acute respiratory distress syndrome (ARDS). The syndrome was designated as ‘severe acute respiratory syndrome’ (SARS) in March 2003. As of July 4, 2003, a total of 8439 cases resulting in 812 deaths (a case-fatality proportion of 9.4%) have been reported from more than 30 countries globally.

Taiwan has a population of over 23 million. The development of SARS became a real concern in Taiwan because of the extensive business ties and inter-country travel that exist between Taiwan, Hong Kong, and especially Mainland China, which appears to be the origin of SARS. The first probable SARS patient in Taiwan returned from China via Hong Kong early in the global outbreak in February 2003. For more than a month, the daily incidence remained in the single digits until a nosocomial outbreak occurred in a municipal hospital (Hospital A) in Taipei on April 22, 2003. As of July 4, 674 probable cases and 84 deaths have been reported in Taiwan. We analyse the clinical, laboratory, and radiological features of patients with probable SARS who were seen at the Shin Kong Wu Ho-Su Memorial Hospital (SKMH) in Taipei, Taiwan. In addition, we also report the probable index case for the SARS outbreak in Taiwan.

Materials and methods
SKMH is an 817-bed teaching hospital in the city of Taipei, Taiwan. Between March 28 and June 30, 2003, 82 patients who were suspected of having SARS were admitted to the isolation rooms. Fifty-three of these patients were subsequently excluded after other explanations for their fever and abnormal chest X-rays were found. The remaining 29 patients fulfilled the World Health Organization (WHO) criteria of ‘probable SARS’ infection.

Routine microbiological tests were performed to exclude other causative pathogens, and reverse-transcriptase-polymerase-chain-reaction (RT-PCR) of oropharyngeal swabs were done for SARS-associated coronavirus in each case as described elsewhere. Initial treatment included amoxicillin/clavulanic acid or ceftriaxone and clarithromycin to target common pathogens causing community-acquired pneumonia, according to current recommendations. Oral ribavirin (2.0 g followed by 1000-1200 mg daily) or intravenous ribavirin (400 mg q8h) for severe cases was also administered.

Corticosteroid therapy included intravenous hydrocortisone (100 mg four times daily) in mild cases, and methylprednisolone (2-3 mg/kg/day) in moderate cases. Daily pulsed administration of 0.5-1.0 g of methylprednisolone for two to three days was carried out for those patients with persistent high fever, radiological worsening, increasing shortness of breath, or oxygen desaturation. In severe cases, and depending on the attending physician’s judgment, human immunoglobulin could be administered intravenously (1 gm/kg/day for 2 days).

We compared risk factors associated with complicated and uncomplicated diseases. The Wilcoxon test was used to compare distributions of continuous variables. Categorical variables were compared using the chi-square or Fisher’s exact test, as appropriate. Data are reported as means ± standard deviation (SD) unless otherwise specified. All P values were 2-tailed; P < 0.05 was considered statistically significant. For the analysis, the SPSS software package, version 10.0 (SPSS Inc., Chicago, USA) was used for the analysis.

Result

Demographics

The demographic profiles and comorbidities of the 29 cases are shown in Table 1. Their median and mean ages were 39 and 42.9 years, respectively, with a range of 22-82 years. The female-to-male ratio was 2.2:1. Six of the 29 patients (20.7%) had comorbidities that included cardiovascular diseases (n = 4), diabetes mellitus (n = 1), and chronic pulmonary disease (n = 1). Among the patients, 10 (34.5%) had been to hospitals with known SARS outbreak, 6 (20.7%) were healthcare workers, 4 (13.8%) were household contacts, 4 (13.8%) were unknown, 3 (10.3%) had recently traveled to mainland China or Hong Kong, and 2 (6.9%) had social contact with SARS patients. One of these patients is the first native SARS case without a contact history in Taiwan. She was referred from Hospital A on April 9 and may have been the index case of the Hospital A outbreak. Here we briefly describe her history.
Table 1  Summary of demographic profiles and comorbidities in 29 cases of SARS.

| Case no. | Age/sex | Onset date (year/month/day) | Contact history | Coronavirus RT-PCR | Comorbidities          | Outcome/intubation |
|----------|---------|-----------------------------|-----------------|---------------------|------------------------|-------------------|
| 1        | 57/Male | 2003/3/29                   | Imported        | +                   |                        | Discharge/no      |
| 2        | 47/Female | 2003/4/3                  | Unknown         | +                   |                        | Discharge/yes     |
| 3        | 67/Female | 2003/4/10                 | Imported        | –                   | Cardiovascular disease | Discharge/no      |
| 4        | 37/Female | 2003/4/17                  | Imported        | +                   |                        | Discharge/no      |
| 5        | 32/Female | 2003/4/18                  | Unknown         | +                   |                        | Discharge/no      |
| 6        | 23/Female | 2003/4/19                  | Healthcare worker | +               |                        | Discharge/no      |
| 7        | 57/Male | 2003/4/20                   | Hospital visit  | +                   |                        | Discharge/yes     |
| 8        | 50/Female | 2003/4/21                  | Hospital visit  | –                   | Cardiovascular disease | Discharge/no      |
| 9        | 82/Male | 2003/4/22                   | Hospital visit  | +                   | Diabetes mellitus      | Died/yes          |
| 10       | 39/Female | 2003/4/23                  | Healthcare worker | +               |                        | Discharge/yes     |
| 11       | 82/Male | 2003/4/26                   | Hospital visit  | –                   | Chronic pulmonary disease | Discharge/no      |
| 12       | 34/Female | 2003/4/28                  | Healthcare worker | –               |                        | Discharge/no      |
| 13       | 40/Female | 2003/4/30                  | Hospital visit  | +                   |                        | Discharge/yes     |
| 14       | 43/Female | 2003/5/1                   | Household contact | +                |                        | Discharge/no      |
| 15       | 29/Male | 2003/5/1                    | Household contact | +                |                        | Died/yes          |
| 16       | 22/Male | 2003/5/2                    | Social contact  | –                   |                        | Discharge/no      |
| 17       | 33/Female | 2003/5/4                   | Hospital visit  | +                   |                        | Died/yes          |
| 18       | 23/Female | 2003/5/5                   | Healthcare worker | –               |                        | Discharge/no      |
| 19       | 53/Female | 2003/5/5                   | Social contact  | –                   |                        | Discharge/no      |
| 20       | 26/Female | 2003/5/5                   | Healthcare worker | +               |                        | Discharge/yes     |
| 21       | 75/Male | 2003/5/8                    | Unknown         | –                   | Cardiovascular disease | Discharge/no      |
| 22       | 30/Male | 2003/5/9                    | Healthcare worker | +               |                        | Discharge/yes     |
| 23       | 33/Female | 2003/5/10                  | Household contact | –               |                        | Discharge/no      |
| 24       | 30/Female | 2003/5/11                  | Hospital visit  | +                   |                        | Died/yes          |
| 25       | 39/Female | 2003/5/14                  | Household contact | +                |                        | Discharge/no      |
| 26       | 29/Female | 2003/5/15                  | Hospital visit  | –                   |                        | Discharge/no      |
| 27       | 53/Female | 2003/5/20                  | Hospital visit  | –                   |                        | Discharge/no      |
| 28       | 53/Male | 2003/5/21                   | Hospital visit  | –                   | Cardiovascular disease | Discharge/no      |
| 29       | 25/Female | 2003/5/24                  | Unknown         | –                   |                        | Discharge/no      |

+, Positive; –, negative.
Probable index case of the Taiwanese outbreak

A previously healthy 47-year-old housewife was transferred to SKMH from Hospital A on April 9, 2003 on suspicion of SARS. She displayed a persistent fever accompanied by chills and a dry cough for 6 days, and had become dyspnoeic 3 days prior to transfer. She denied any previous hospital visits or recent travel outside of Taiwan. The patient recollected a 3-hour train journey to Taipei 12 days prior, when she was in close proximity to a female who had a persistent cough. The patient went to the emergency room of Hospital A in the morning of April 9, 2003. A chest X-ray showed extensive bilateral lower lung infiltrates (Fig. 1, Panel A). Soon after arrival in our hospital, she required 100% oxygen through a non-rebreathing mask to maintain her oxygen saturation. A second chest X-ray taken in the afternoon showed progressive changes (Fig. 1, Panel B). By that evening, the patient developed progressive tachypnea and had to be intubated. The sputum Gram-stain obtained after intubation showed many inflammatory cells without visible bacteria (Fig. 2). She was treated with empiric antibiotics, ribavirin and corticosteroids. On the eighth hospital day, her fever subsided, and her oropharyngeal swab came back positive for SARS-associated coronavirus by RT-PCR. On the same day, her husband and son were admitted to other hospitals in Taipei due to fever and pulmonary infiltrates. Both subsequently proved positive for coronavirus by RT-PCR. On April 23, the patient was extubated.

**Figure 1** Chest X-ray (Panel A) taken at Hospital A upon patient admittance showed extensive bilateral lower lung infiltrate. Six hours later, a follow-up chest X-ray (Panel B) taken at our hospital showed a progressive deterioration.

**Figure 2** Light microscopic examination ($1000 \times$) of a sputum Gram-stain showing prominent inflammatory cells without identifiable bacteria.

| Clinical symptoms         | Number | % (n = 29) |
|---------------------------|--------|------------|
| Fever                     | 29     | 100.0%     |
| Cough                     | 20     | 69.0%      |
| Chills or rigors           | 18     | 62.1%      |
| Shortness of breath       | 12     | 41.4%      |
| Myalgia                   | 11     | 37.9%      |
| Headache                  | 9      | 31.0%      |
| Malaise                   | 8      | 27.6%      |
| Dizziness                 | 7      | 24.1%      |
| Sore throat               | 6      | 20.7%      |
| Nausea/vomiting           | 5      | 17.2%      |
| Rhinorrhea                | 5      | 17.2%      |
| Diarrhoea                 | 4      | 13.8%      |

**Table 2** Clinical features of 29 patients with SARS at presentation.
Clinical features

The relative frequencies of all reported symptoms at the time of admission are shown in Table 2. The most common symptoms at presentation were fever (100%), cough (69.0%), chills or rigor (62.1%), shortness of breath (41.4%), myalgia (37.9%), and headache (31.0%). The mean duration of symptoms before admission was 4.8 ± 2.3 days. The mean body temperature on admission was 39.0 ± 0.7°C. The mean respiratory and pulse rates were 22.9 ± 9.0 and 90.8 ± 13.3/min, respectively. The mean days to defervescence were 6.8 ± 2.9 days. Fever recurred in 15 patients (51.7%) at a mean of 10.9 ± 3.4 days. While diarrhoea was manifest in only four patients upon admission, another 15 patients experienced diarrhoea during the first week of hospitalisation. The mean days to onset of diarrhoea were 6.5 ± 2.9 days. Twenty-five patients (86.2%) reported dyspnoea within one week of hospitalisation; and the mean days to onset were 5.8 ± 2.8 days.

Laboratory and chest radiographic findings

Laboratory investigations on presentation are shown in Table 3. The initial white blood cell count was quite variable; lymphopenia was present in 21 (72.4%), thrombocytopenia in 10 (34.5%), anemia in 6 (20.7%), and leukopenia in only three patients (10.3%). CRP was initially elevated in 27 patients (93.1%). The lactate dehydrogenase (LDH) level was elevated in 62.1% of patients. Serum aspartate aminotransferase levels were slightly elevated in 44.8% of patients, and alanine aminotransferase levels in 24.1% of patients. Creatine kinase (CK) levels were elevated in a single patient.

All patients except one had abnormal chest radiographs on presentation; 12 (41.4%) had unilateral focal involvement, and 16 (55.2%) had either unilateral multifocal or bilateral involvement. The initial radiographic changes were indistinguishable from those associated with other causes of bronchopneumonia. Radiological worsening was noted in 20 patients (69.0%) at a mean of 7.5 ± 2.6 days. Overall, 12 patients (41.4%) progressed to diffuse ground-glass appearance.

SARS-associated coronavirus RNA was detected in oropharyngeal swabs by RT-PCR in 16 (55.2%) of 29 patients at initial presentation. Routine microbiological investigation for known viruses and bacteria was negative in most cases except three patients who had evidence of coinfection with Mycoplasma, Legionella, and Streptococcus pneumoniae, respectively.

Management

All patients received empirical antibiotic therapy during the course of their hospitalization. Ribavirin was begun at a mean of 5.0 ± 2.4 (range 1-10) days after onset of illness to all patients. The mean duration of treatment with ribavirin was 9.2 ± 4.0 days (median: 11 days). All patients received oral
ribavirin except two who were switched to intravenous ribavirin due to clinical deterioration. The side effects of ribavirin treatment included anemia (decrease in haemoglobin level of at least 2 g/dL) in 14 of 29 patients (48.3%) and bradycardia in two patients. Twenty-one patients (72.4%) received intravenous corticosteroid treatment. The mean duration of intravenous steroid use was 13.1 ± 10.3 days. Pulse corticosteroid therapy was given to 17 patients (58.6%) for clinical deterioration. Of these, 12 received one course of therapy and 10 survived. Five received two or more courses due to repeated clinical deterioration and four survived. Intravenous human immunoglobulin was given to 10 of the 29 patients (34.5%).

Outcomes

There were four deaths (13.8%) in our 29 hospitalised SARS patients. Among 25 patients who survived, median hospital stay was 17 days (mean: 22.6 ± 22.0 days). Clinical deterioration generally occurred in the second week of the illness. Nine of the 29 patients (31.0%) subsequently required mechanical ventilation for worsening respiratory failure. The mean days to intubation were 9.7 ± 2.2 days. Before intubation, the mean PaO$_2$/FiO$_2$ ratio was 106.3 mmHg, and the mean respiratory rate was 41.1/min. Of those nine patients who required mechanical ventilation, four died and five improved sufficiently to be extubated (mean duration of intubation 18.8 days, range 11-40 days). Among the four patients who expired, two died of clinical sepsis (one had a positive blood culture isolate) associated with malignant hyperthermia, one had sudden onset of desaturation while on positive pressure ventilator, and one suffered from a secondary pulmonary bacterial infection due to aspiration before intubation.

Complication

Five of the 29 patients (17.2%) developed pneumothorax or pneumomediastinum. Three developed while on mechanical ventilation, and two developed spontaneously. Seven patients had several episodes of nosocomial infections including five episodes of nosocomial lower respiratory tract infections due to Pseudomonas aeruginosa, Enterobacter cloacae, Serratia marcescens, Acinetobacter baumannii, or Stenotrophomonas maltophilia in five intubated patients; four episodes of nosocomial blood stream infections due to Klebsiella pneumoniae, Burkholderia cepacia, methicillin-resistant Staphylococcus aureus, or Candida glabrata in two patients, one episode of pulmonary aspergillosis and one episode of pulmonary tuberculosis (probable reactivation). Six of the seven patients had received pulse steroid therapy before the development of infections.

The risk factors associated with severe complicated disease requiring intensive care and ventilatory support were presence of diarrhoea, a high peak LDH and CRP values, a high aspartate aminotransferase and CK on admission and a high peak value (Table 4). The age and presence of comorbid diseases did not appear to be associated with a worse clinical outcome. Twenty uncomplicated cases recovered or improved, whereas four patients (44.4%) with complicated diseases died ($P = 0.005$).

Discussion

The SARS epidemic started in Asia, with the majority of cases occurring in China and the Asian-Pacific region. Prior to the nosocomial outbreak at 'Hospital A', most cases of SARS in Taiwan had been restricted to imported cases from SARS-affected regions. Only 23 probable cases were detected in the first month. However, when seven cases of SARS were reported among healthcare workers at Hospital A on April 22, 2003, the incidence of SARS cases in Taiwan increased dramatically. The index patient was a laundry worker who lived in the basement of Hospital A and was often in the emergency room chatting with the staff. He noted the onset of fever and diarrhoea on April 12. The source of infection for the index patient remained unclear because Hospital A admitted no known SARS patients prior to the incident except for our reported case, who was treated in the emergency department of Hospital A for a few hours prior to transferring. The possibility of transmission via incidental contact at the emergency room or indirect contact through laundry items cannot be excluded.

Success in controlling SARS relies on early identification of suspect cases, proper isolation, and meticulous infection control measures. Recognition of a native case without a prior contact history plays an important role in controlling an outbreak, especially when no local transmission is reported. The important clues in our reported case included rapid progressive chest X-ray changes and lack of identifiable bacterial pathogen from the initial sputum Gram-stain. Even though the health authority initially excluded the case patient, she was kept in a negative-pressure isolation room, and her family was quarantined. These precautions
proved to be prudent, since a positive coronavirus RT-PCR result was obtained one week later. Because of our aggressive infection control policy, there was no SARS outbreak at our hospital.

We found the initial clinical features of our SARS patients to be similar to those recently reported by Lee et al. in a cohort of 138 SARS patients in Hong Kong, with the exceptions of a higher occurrence of cough in our patient population (69.0% vs. 57.3%), less frequent occurrence of myalgia (37.9% vs. 60.9%), and of headache (31% vs. 55.8%). With the exception of CRP, these findings have been noted elsewhere. Since the CRP elevation resulting from most common viral infections is not as pronounced as in SARS, CRP is a reasonable candidate marker to distinguish SARS from other viral infections early in the infectious process. In the present study, the vast majority of cases (96.6%) displayed abnormal chest radiographs on presentation, and a majority of cases (69.0%) had radiological worsening during the first week of hospitalisation (mean onset 7.5 days). A similar trend has been described by Peiris et al. with 80% of cases exhibiting radiological worsening at a mean of 7.4 days. Since the initial presentation of SARS is quite non-specific, early diagnosis largely relies on known history of potential exposure to the infection. However, once the disease develops into an epidemic, contact history becomes unreliable. Clinicians must maintain a high index of suspicion since several features of the clinical presentation may be the important clues to differentiate SARS from other infectious diseases.

| Table 4 | Risk factors associated with severe disease requiring intensive care and ventilatory support. |
|---------|-----------------------------------------------------------------------------------------------|
|         | Complicated cases (n = 9) | Uncomplicated cases (n = 20) | P  |
| Mean (SD) age (years) | 43.0 (17.29) | 42.8 (17.87) | 0.832 |
| Male/female ratio | (4/5) | (5/15) | 0.396 |
| Underlying diseases | 1 | 5 | 0.632 |
| Contact history | Imported | 0 | 3 | 0.532 |
|                  | Hospital | 7 | 9 | 0.129 |
|                  | Household contact | 1 | 3 | 1.000 |
|                  | Others | 1 | 5 | 0.632 |
| Mean (SD) duration of symptoms prior to admission (days) | 5.11 (1.69) | 4.65 (2.60) | 0.303 |
| Mean (SD) admission temperature | 39.2 (0.83) | 38.9 (0.67) | 0.813 |
| Diarrhoea | 9 | 10 | 0.011 |
| Mean (SD) initial platelet count ($ \times 10^5/\mu L$) | 150.7 (65.94) | 177.2 (53.5) | 0.238 |
| Mean (SD) initial neutrophil count (/L) | 7530 (3572) | 5411 (3898) | 0.109 |
| Mean (SD) initial lymphocyte count (/L) | 672 (342) | 1097 (798) | 0.099 |
| LDH (U/L) | On admission (SD) | 333 (196) | 389 (416) | 0.741 |
|                  | Peak (SD) | 998 (576) | 479 (430) | 0.002 |
| Aspartate aminotransferase (U/L) | On admission (SD) | 57 (27) | 56 (106) | 0.045 |
|                  | Peak (SD) | 331 (418) | 87 (118) | 0.008 |
| CK (U/L) | On admission (SD) | 187 (162) | 74 (35) | 0.005 |
|                  | Peak (SD) | 736 (447) | 110 (68) | <0.00001 |
| CRP (mg/dL) | On admission (SD) | 8.4 (9.6) | 6.7 (5.8) | 0.902 |
|                  | Peak (SD) | 20.6 (17.9) | 7.9 (5.4) | 0.002 |
| Mean (SD) days to start of ribavirin and steroids from onset of symptoms | 5.6 (2.4) | 5.0 (2.8) | 0.440 |
| Outcome | Improved or recovered | 5 | 20 | 0.005 |
| Died | 4 | 0 | 0.099 |
The discovery that a novel coronavirus is the probable cause of SARS\textsuperscript{11,19,20} provides a dramatic example of an emerging coronavirus disease in humans. SARS-associated coronavirus fulfills Koch's postulates for an infectious microbiological disease.\textsuperscript{21} RT-PCR assay is the most rapid method for the laboratory diagnosis of SARS-associated coronavirus infection. According to a recent cohort study in Hong Kong, viral RNA detection in the nasopharyngeal aspirate has a sensitivity of only 32% at presentation, but testing of multiple nasopharyngeal and faecal samples increased the sensitivity of the RT-PCR assay.\textsuperscript{16} In our study, SARS-associated coronavirus RNA was detected in oropharyngeal swabs by RT-PCR in 16 (55.1%) of 29 patients at initial presentation.

The percentage of patients in our cohort who required mechanical ventilation (31%) is much higher than the 13.8% reported by Lee et al. in a cohort of 138 SARS patients in Hong Kong.\textsuperscript{4} The different clinical courses may be related to different strains of coronavirus infection.\textsuperscript{22} Recent reports of intubation rates of 25% (19 of 75 patients in Hong Kong),\textsuperscript{16} and 30% (six of 20 patients in Singapore)\textsuperscript{23} are more similar to our cases.

Our mortality rate was 13.8% (4/29) overall and 44.4% in complicated cases. These figures are much higher than those reported from Canada (5.6%),

but comparable to a recent report from Singapore with an overall mortality rate of 13.6% (27 of 199 patients) and 52.5% (24 of 46 patients) in complicated cases.\textsuperscript{25} The low Canadian mortality rate may be partly due to short-term outcomes, which did not reflect the real mortality after long-term follow-up.

At this time, no effective treatment is known for this infection. Empirical treatment with a combination of high-dose corticosteroid and ribavirin has been advocated in certain areas.\textsuperscript{18,26,27} The rationale behind this approach is to reduce both the viral load and the inflammatory response generated by the infection. All of our patients received ribavirin without obvious therapeutic response, and 48.3% of the patients became anaemic. This finding is consistent with Booth et al. who described that 49% of their patients experienced a decrease in the haemoglobin level of 2 g/dl or greater after ribavirin use.\textsuperscript{24} Large-dose corticosteroid became the de facto mainstay of our treatment protocol. Most of our patients with clinical deterioration responded to pulse corticosteroid therapy (14 out of 17), including four out of five patients with repeated episodes of deterioration who were successfully rescued by two or more courses of pulse steroid. Recently, a report from Guangzhou by Zhao et al. also supported this approach.\textsuperscript{28} However, the use of large-dose corticosteroid is associated with the high attendant risk of infection. Six patients developed several episodes of nosocomial infections in our cohort. We emphasize that proper antibiotics coverage and careful microbiological surveillance with judicious corticosteroid use are the key to successful treatment of these patients.

Univariate analyses showed that the presence of diarrhoea, high peak LDH and CRP values, high aspartate aminotransferase and CK on admission and high peak values were associated with adverse outcomes. Rigorous multivariate analysis could not be meaningfully performed, however, given the small sample size in our series. Age and comorbidities were also not associated with an adverse outcome in our series as observed elsewhere.\textsuperscript{4,20,24,29} This may also reflect our sample size. Further reports involving larger patient populations will be necessary to clarify our understanding of the risk factors and optimal treatment of SARS.

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