Outcomes and Prognostic Factors in 267 Patients with Severe Acute Respiratory Syndrome in Hong Kong

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Background: Severe acute respiratory syndrome (SARS) has become a global public health emergency.

Objective: To evaluate the characteristics and outcomes of patients with SARS in Hong Kong and to identify predictors of mortality.

Design: Retrospective cohort study.

Setting: Quarantine hospital for patients with SARS in Hong Kong.

Patients: 267 consecutive patients hospitalized from 26 February to 31 March 2003 for probable or confirmed SARS.

Measurements: Clinical, laboratory, and radiographic measures; 3-month mortality rate.

Results: According to our case definition, there were 227 cases of confirmed SARS and 40 cases of probable SARS. Common presenting symptoms were fever (99% of patients), chills (74%), malaise (63%), and myalgia (50%). Laboratory findings included lymphopenia (73%), thrombocytopenia (50%), hyponatremia (60%), and elevated levels of lactate dehydrogenase (47%) and C-reactive protein (75%). During hospitalization, incidence of diarrhea (53%), anemia (53%), and acute renal failure (6%) increased. Sixty-nine patients (26%) required intensive care because of respiratory failure. The 3-month mortality rate was 12% (95% CI, 8% to 16%). Factors contributing to mortality were respiratory failure, acute renal failure, and nosocomial sepsis. On multivariate Cox regression, age older than 60 years (relative risk, 5.10 [CI, 2.30 to 11.31]; P < 0.001) and lactate dehydrogenase level greater than 3.8 µkat/L at presentation (relative risk, 2.20 [CI, 1.03 to 4.71]; P = 0.04) were independent predictors of mortality.

Conclusion: Because of the longer follow-up period in our cohort, the mortality rate in these patients is higher than rates reported in previous studies. Advanced age and high lactate dehydrogenase level at presentation predict mortality.

METHODS

Case Definition

We defined a case as probable SARS if the patient presented with a body temperature of 38 °C or higher, radiographic evidence of lung infiltrate (on chest radiography or computed tomography of the thorax) with or without respiratory symptoms, and relevant history of contact with a patient with SARS or travel history within 10 days of symptom onset. Diagnosis of SARS was confirmed by positive results on reverse transcriptase polymerase chain reaction (RT-PCR) or serologic testing for SARS coronavirus (2).

Recruitment of Patients

We recruited 267 consecutive patients admitted to Princess Margaret Hospital between 26 February and 31 March 2003 for probable or confirmed SARS. We managed this cohort of patients with a standard protocol that consisted of using structured forms for recording the history and physical findings on admission, ordering laboratory and radiographic studies and treatment, and charting the patients’ progress and results of serial laboratory and radiographic studies. Patients’ hospital records were reviewed retrospectively. We followed all survivors for at least 3 months after their first day of hospitalization.
Laboratory and Radiographic Studies

Routine serial hematologic, biochemical, and microbiological tests were performed. Sputum samples were screened for bacterial and mycobacterial infection. Nasopharyngeal aspirates were examined for common respiratory viruses by using a direct immunofluorescence test and culture. Single or paired serum samples were tested for Mycoplasma pneumoniae, Chlamydia pneumoniae, and C. psittaci. Urinary antigen detection tests were performed for Legionella pneumophila and Streptococcus pneumoniae. Reverse transcriptase polymerase chain reaction for SARS coronavirus was performed on nasopharyngeal aspirates on days 1 and 7 of hospitalization. An assay for SARS coronavirus antibody was done on days 1, 7, and 14 of hospitalization (2). Chest radiographs were obtained for all patients and were monitored serially. Computed tomography of the thorax was performed in select cases. Postmortem examination was done in 2 patients who died of SARS.

Treatment

All patients received either amoxicillin–clavulanate and clarithromycin or levofloxacin monotherapy for treatment of community-acquired pneumonia after admission (4). In accordance with the local treatment recommendation (1, 5), therapy with intravenous ribavirin, 24 mg/kg of body weight per day, and hydrocortisone, 10 mg/kg per day in divided doses, was initiated if patients did not respond to antibiotic therapy within 48 hours and other symptoms were compatible with SARS. Only 1 patient in our cohort did not receive this combination of antiviral and corticosteroid therapy. Intravenous methylprednisolone, given in 2 to 3 pulses each time (500 to 1000 mg/d), was offered to patients who had progressive disease despite initial antiviral treatment.

Statistical Analysis

We compared the differences in epidemiologic, clinical, and laboratory measures between patients who had documented infection by SARS coronavirus and those who did not. We also evaluated the differences in these mea-

Table 1. Demographic and Epidemiologic Characteristics of 267 Patients with Severe Acute Respiratory Syndrome*

| Characteristic                                                   | All Patients (n = 267) | Patients with Probable SARS (n = 40) | Patients with Confirmed SARS (n = 227) |
|------------------------------------------------------------------|------------------------|--------------------------------------|----------------------------------------|
| **Demographic**                                                  |                        |                                      |                                        |
| Median age (range), y                                            | 39 (18–96)             | 42 (19–75)                           | 39 (18–96)                             |
| Men/women, n/n                                                   | 104/163                | 13/27                                | 75/152                                 |
| Ethnicity, n                                                     |                        |                                      |                                        |
| Ethnic Chinese                                                  | 261                    | 39                                   | 222                                    |
| Indonesian                                                      | 2                      | 1                                    | 1                                      |
| Filipino                                                         | 4                      | 0                                    | 4                                      |
| **Epidemiologic**                                                |                        |                                      |                                        |
| Health care worker managing patients with SARS, n                | 24                     | 1                                    | 23                                     |
| Physician                                                       | 6                      | 0                                    | 6                                      |
| Nurse                                                           | 11                     | 1                                    | 10                                     |
| Ward assistant                                                  | 5                      | 0                                    | 5                                      |
| Allied health worker                                            | 2                      | 0                                    | 2                                      |
| Recent travel to areas with SARS outbreak, n                    | 49                     | 6                                    | 43                                     |
| Southern China                                                  | 46                     | 6                                    | 40                                     |
| Beijing, China                                                  | 1                      | 0                                    | 1                                      |
| Vietnam                                                         | 2                      | 0                                    | 2                                      |
| Case clustering, n                                               | 170                    | 19                                   | 121                                    |
| Amoy Garden (a local apartment complex)                         | 140                    | 19                                   | 121                                    |
| Household contact outside the above cluster                     | 24                     | 3                                    | 21                                     |
| Contact with a family physician with SARS                       | 2                      | 0                                    | 2                                      |
| Staying in the same hotel as a patient with SARS                | 1                      | 0                                    | 1                                      |
| Casual contact with a patient with SARS in the workplace        | 2                      | 0                                    | 2                                      |
| Taxi driver in contact with a patient with SARS while working   | 1                      | 0                                    | 1                                      |

* SARS = severe acute respiratory syndrome.
Symptoms and Vital Signs at Presentation in 267 Patients with Severe Acute Respiratory Syndrome*  

| Variable | All Patients (n = 267) | Patients with Probable SARS (n = 40) | Patients with Confirmed SARS (n = 227) |
|----------|------------------------|--------------------------------------|---------------------------------------|
| Fever    | 263 (99)               | 38 (95)                              | 225 (99)                              |
| Chills   | 197 (74)               | 29 (73)                              | 168 (74)                              |
| Myalgia  | 134 (50)               | 16 (40)                              | 118 (52)                              |
| Cough    | 118 (44)               | 20 (50)                              | 98 (43)                               |
| Rigor    | 106 (40)               | 14 (35)                              | 92 (41)                               |
| Headache | 89 (33)                | 13 (33)                              | 76 (33)                               |
| Anorexia | 62 (23)                | 9 (23)                               | 53 (23)                               |
| Sputum   | 53 (20)                | 8 (20)                               | 45 (20)                               |
| Shortness of breath | 51 (19)              | 5 (13)                              | 46 (20)                               |
| Dizziness | 48 (18)               | 9 (23)                               | 39 (17)                               |
| Diarrhea | 41 (15)                | 6 (15)                               | 35 (15)                               |
| Sore throat | 36 (14)              | 4 (10)                               | 32 (14)                               |
| Running nose | 30 (11)             | 5 (13)                               | 25 (11)                               |
| Chest pain | 21 (9)                | 6 (15)                               | 15 (7)                                |
| Vomiting | 19 (7)                 | 3 (8)                                | 16 (7)                                |
| Palpitation | 5 (2)               | 1 (3)                                | 4 (2)                                 |
| Hemoptysis | 4 (2)                | 2 (5)                                | 2 (1)                                 |
| Confusion | 2 (1)                 | 1 (3)                                | 1 (0.4)                               |

| Vital signs† | All Patients (n = 267) | Patients with Probable SARS (n = 40) | Patients with Confirmed SARS (n = 227) |
|--------------|------------------------|--------------------------------------|---------------------------------------|
| Temperature, °C | 38.6 (36.0–41.0)      | 38.3 (36.6–40.3)                     | 38.7 (36–41)                          |
| Heart rate, beats/min | 100 (60–130)         | 100 (65–115)                         | 100 (60–170)                         |
| Respiratory rate, breaths/min | 18 (14–35)          | 19 (18–20)                           | 18 (14–35)                           |
| Systolic blood pressure, mm Hg | 125 (90–196)      | 126 (90–196)                         | 124 (90–190)                         |
| Diastolic blood pressure, mm Hg | 70 (45–105)        | 70 (60–105)                          | 70 (45–95)                           |

* SARS = severe acute respiratory syndrome.  
† Data are expressed as the median (range).

Table 2. Symptoms and Vital Signs at Presentation in 267 Patients with Severe Acute Respiratory Syndrome*

Results

Epidemiology and Clinical Features

We categorized patients into 2 groups: 1) those who fit the case definition of probable SARS and had negative results on confirmatory tests for SARS coronavirus (n = 40) and 2) those with confirmed SARS (n = 247). Tables 1 and 2 show demographic, epidemiologic, and clinical features at presentation. Most patients were ethnic Chinese, and the cohort contained more women than men. The median patient age was 39 years. Overall, 52% of patients developed SARS through the Amoy Garden outbreak, the cause of which was believed to be a faulty sewage system (12). Fifteen patients had 1 or more coexisting active conditions: diabetes mellitus in 7, ischemic heart disease in 3, chronic rheumatic heart disease in 1, hypertrophic obstructive cardiomyopathy in 1, sick sinus syndrome in 1, cerebrovascular disease in 4, cirrhosis secondary to chronic hepatitis B in 1, bronchiectasis in 1, end-stage renal failure in 1, the Sjögren syndrome in 1, and nasopharyngeal carcinoma in 1.

As shown in Table 2, the most common presenting symptoms were fever (99% of patients), chills (74%), malaise (63%), and myalgia (50%). Except for crackles detected by chest auscultation in 20% of patients and mental confusion in 2 patients, physical examination was unrevealing. Epidemiologic and clinical characteristics did not significantly differ between the probable and confirmed SARS groups.

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Table 3 summarizes the laboratory findings. Many patients had hematologic abnormalities at presentation: anemia (hemoglobin level < 120 g/L) in 16% of patients, leukopenia (leukocyte count < 4 × 10^9 cells/L) in 27%, lymphopenia (lymphocyte count < 1 × 10^9 cells/L) in 73%, and thrombocytopenia (platelet count < 150 × 10^9 cells/L) in 50%. The activated partial thromboplastin time was prolonged (>38 seconds) in 18% of patients. Electrolyte abnormalities included hyponatremia (plasma sodium level < 135 mmol/L) in 60% of patients and hypokalemia (plasma potassium level < 3.5 mmol/L) in 41%. Levels of the following enzymes were elevated: alanine aminotransferase (>40 U/L) in 31% of patients, creatine phosphokinase (>4.1 μkat/L) (but normal troponin I levels) in 19%, and lactate dehydrogenase (>3.8 μkat/L) in 47%. Seventy-five percent of patients had elevated C-reactive protein levels (>6 mg/L).

At presentation, patients with confirmed SARS had a lower total leukocyte count than patients in the probable SARS group (4.9 × 10^9 cells/L vs. 6.2 × 10^9 cells/L; P = 0.02), a lower lymphocyte count (0.7 × 10^9 cells/L vs. 0.9 × 10^9 cells/L; P = 0.02), and higher lactate dehydrogenase levels (3.9 μkat/L vs. 3.3 μkat/L; P = 0.05). The confirmed SARS group also had a lower nadir lymphocyte count (0.4 × 10^9 cells/L vs. 0.5 × 10^9 cells/L; P = 0.02) during hospitalization. Other laboratory measures did not significantly differ between the 2 groups.

Microbiological Findings

Sixty-five percent of patients had at least 1 positive result on RT-PCR in nasopharyngeal secretions, and 78% had a 4-fold increase in SARS coronavirus antibody titer or a single titer of 100 or greater. Fifty-seven percent of patients had positive results on both RT-PCR and serologic testing, and 40 patients had negative results on both tests. We found no evidence of other infection in the latter group. Eight percent of patients tested positive on RT-PCR but negative on serologic testing, and 21% of patients had positive serologic results but negative RT-PCR results.

Radiographic Findings

On admission, 96% of patients had abnormalities on chest radiography. All these abnormalities were pneumonic changes indistinguishable from other causes of community-acquired pneumonia. In 34% of patients, initial chest radiography showed lung infiltrates at more than 1 site. For 12 patients with apparently normal chest radiographs on admission, high-resolution computed tomography of the thorax showed patchy ground-glass opacification of the lung parenchyma. In patients with evidence of respiratory distress, serial monitoring with chest radiography showed progression of lung infiltrates with multiple, patchy consolidation of both lungs, which coincided with or sometimes preceded clinical deterioration. Subcutaneous edema, pneumothorax, and pneumomediastinum were...
detected in 6 patients (2.2%) who had not received positive-pressure ventilation.

**Postmortem Findings**

Postmortem examination of the lungs was performed on 2 patients. The first patient, a 49-year-old man, had an early case of SARS and did not receive steroids or ribavirin. He died of respiratory failure on day 16 of hospitalization. The salient findings were features of diffuse alveolar damage in both acute and reparative phases, present in about 80% of the lung tissue assessed. The alveolar septa were largely intact, but necrotizing alveolar septa and loss of septa were noted in focal areas. Areas in acute phase of damage showed fibrinoid alveolar exudate with mixed acute and chronic inflammatory cells. Examination also showed hyaline membrane formation. Focal alveolar hemorrhage was present, but alveolar edema was not prominent. In the reparative areas, alveolar spaces were filled with foamy histiocytic cells, occasional multinucleated histiocytes, hyperplastic type 2 pneumocytes, and fibroblasts. Many of these histiocytes and pneumocytes showed vacuolated cytoplasm. Examination identified focal areas with dilated terminal air space and collapsing alveoli suggestive of early honeycomb changes.

The second patient was a 34-year-old woman. She received ribavirin and corticosteroids immediately after admission, and pulse methylprednisolone was administered during the second week after she developed respiratory distress. She had sudden cardiac arrest and died on day 15 of hospitalization. Gross examination revealed a few occluded pulmonary vessels consistent with minor thromboembolism. Microscopic examination showed patchy involvement of the lungs by diffuse acute-phase alveolar damage, representing about 10% of the lung tissue assessed; other areas of lung tissue were well aerated and relatively normal. Reparative changes in the areas of diffuse alveolar damage were minimal. Examination confirmed minor pulmonary thromboembolism, which had contributed to her death.

In both patients, results of RT-PCR performed on lung tissue were positive for SARS coronavirus.

**Hospital Courses and Outcomes**

Only 1 patient in our cohort did not receive ribavirin and corticosteroid therapy. During hospitalization, diarrhea became increasingly prevalent, affecting up to 53% of patients. None of the patients with diarrhea had positive bacteriologic culture or detection of *Clostridium difficile* toxin in a stool sample. Serial monitoring of laboratory measures revealed increases in the incidence of anemia, from 16% to 53%. Incidence of lymphopenia also increased from 73% to 97%. Ninety percent of patients had hypokalemia, and 56% of patients developed elevated alanine aminotransferase levels during hospitalization.

Sixty-nine patients (26%) required mechanical ventilation. Other complications were subcutaneous emphysema, pneumothorax, and pneumomediastinum in 6 patients (2%); acute renal failure (defined as an abrupt decline in parenchymal renal function in a matter of hours or days) in 15 patients (6%); and acute liver failure (defined as rapid development of severe acute liver injury with impaired synthetic function and encephalopathy in a person who had a normal liver or previous well-compensated liver disease) in 2 patients (1%).

As of this writing, 234 patients have been discharged home. Only 1 patient was still hospitalized for convalescent care. Thirty-two patients died, and the following complications contributed to mortality: respiratory failure (100% of the patients who died), acute renal failure (44%), nosocomial sepsis in the form of focal infections (19%) or septicemia (25%), bilateral pneumothoraces in 1 patient (3%) undergoing mechanical ventilation, and acute liver failure in 2 patients (6%) (1 of the patients with liver failure had cirrhosis due to chronic hepatitis B; the other had septic shock leading to ischemic hepatitis). We followed all survivors for at least 3 months after their first day of hospitalization. The 3-month mortality rate, calculated by the Kaplan–Meier method, was 12% (95% CI, 8% to 16%).

**Figure 1** shows the survival curve.

**Predictors of Mortality**

Table 4 summarizes results of univariate analysis. We evaluated the effect of the following measures on mortality by using univariate and multivariate Cox regression: age older than 60 years, neutrophil count greater than \(10 \times 10^9\) cells/L at presentation, and lactate dehydrogenase level greater than 3.8 \(\mu\)kat/L at presentation. In the univariate Cox regression model, risk for death was increased 4-fold in patients older than age 60 years (relative risk, 4.00 [CI, 1.85 to 8.64]; \(P < 0.001\)). Lactate dehydrogenase levels greater than 3.8 \(\mu\)kat/L were also associated with...
with increased risk for death (relative risk, 2.40 [CI, 1.12 to 5.13]; P = 0.02). Mortality rates were not significantly increased in patients with a neutrophil count greater than 10 x 10^9 cells/L on presentation (relative risk, 1.59 [CI, 0.38 to 6.63]; P > 0.2).

We then performed multivariate Cox regression, assuming that age older than 60 years and high lactate dehydrogenase level were independent predictors of mortality. Table 5 and Figure 2 show the results. Age older than 60 years (relative risk, 5.10 [CI, 2.30 to 11.31]; P < 0.001) and lactate dehydrogenase level greater than 3.8 μkat/L (relative risk, 2.20 [CI, 1.03 to 4.71]; P = 0.04) were independently associated with mortality. The Cox analyses showed no evidence of nonproportional hazards.

### DISCUSSION

The clinical, laboratory, and radiographic features in this cohort of patients with SARS in Hong Kong were nonspecific and similar to those in other series (6–11). We sought to examine the effect of documented SARS coronavirus infection on patient characteristics at presentation. Compared with patients who had suspected SARS, patients with confirmed SARS had lower total leukocyte counts, neutrophil counts, and lymphocyte counts and higher lactate dehydrogenase levels at presentation. They also showed a greater decrease in lymphocyte count during hospitalization. These patients may have had a higher viral load at presentation, which may have led to the apparent worsening of laboratory values. Another possibility is that patients with probable SARS might have had another cause of their illness. Overall, the 2 groups of patients had similar clinical profiles; the entire cohort can be considered homogenous.

The latest versions of SARS case definition from the World Health Organization (WHO) (13) and the Centers for Disease Control and Prevention (CDC) (14) differ from ours: Those organizations require the presence of respiratory symptoms for diagnosis. Under the WHO definition, probable SARS is differentiated from a suspected case by the radiographic presence of lung infiltrates. The CDC defines suspected and probable cases of SARS according to the severity of respiratory symptoms. In our cohort, however, up to 13% of patients did not present with respiratory symptoms, although they did have fever, lung infiltrates, and a history of contact with a patient with SARS. Another concern is that 6% of our patients had no evidence of lung infiltrate on chest radiographs at presentation; instead, lung infiltrates were confirmed by computed tomography of the thorax after hospitalization. A prospective study that examined the accuracy of the WHO case definition reported a sensitivity of 26% and a specificity of 96% (15). Thus, given the lack of a reliable test for rapid diagnosis (16) and the contagiousness of the disease, the case definition should be revised to improve its sensitivity.

In our cohort, the incidence of diarrhea increased dramatically, from 15% on admission to 53% after hospitalization. The diarrhea was watery, and it occurred a median of 3 days after hospitalization. The frequency ranged from 3 to 20 bowel movements per day. None of the patients with diarrhea had microbiological proof of other enteric infection or C. difficile-associated diarrhea. Because RT-PCR on stool samples was not included in our initial management protocol, this test was not performed routinely. Patients with diarrhea had a higher rate of positive findings for SARS coronavirus on serologic testing (85% vs. 82% of patients without diarrhea) and on RT-PCR in nasopharyn-
geal secretions (71% vs. 67%); however, these differences were not statistically significant.

Peiris and colleagues (17) have also reported that diarrhea is a common manifestation of SARS. They used RT-PCR to show the shedding of SARS coronavirus into stool, which could persist through the third week of illness. More than 70% of their patients reported diarrhea during hospitalization. Enteric infection by SARS coronavirus thus seems to be a possible explanation of diarrhea in our patients; this issue requires further study. Antibiotic treatment may also have caused diarrhea in our patients.

Acute renal failure was documented in 15 patients and contributed to mortality in 13 patients. No previous series have described acute renal failure as a complication of SARS; the likely contributing factors include dehydration due to diarrhea and poor oral feeding, septic shock as a result of nosocomial sepsis, and the side effects of drugs. Whether coronavirus has a pathogenic effect on kidneys warrants further study.

Hematologic abnormalities were common in our cohort. Sixteen percent of patients had anemia at presentation; the incidence increased to 53% during hospitalization. Because all patients received ribavirin during hospitalization, drug-induced hemolytic anemia is probably a major cause for the increased incidence. The incidence of lymphopenia was 73% at presentation and 97% during hospitalization. In Wong and colleagues’ report (18), CD4+ and CD8+ T lymphocytes were selectively depleted early in the course of SARS, and low CD4+ and CD8+ lymphocyte counts at presentation were associated with adverse outcomes. The authors found no evidence of bone marrow suppression or hemophagocytosis in their patients, and they postulated that lymphopenia was due to the virus’s direct effects on the lymphocytes or to various effects of cytokines. In our patients, ribavirin therapy may also have contributed to lymphopenia.

Thrombocytopenia was also common in our patients. The association of thrombocytopenia and other viral infections has been described elsewhere (19); this phenomenon could be immune in origin or due to the direct effects of virus on megakaryocytes and platelets. Ribavirin may have contributed to the thrombocytopenia noted in our patients. Ribavirin’s precise mechanism of action on lymphocyte and platelet count is uncertain, but bone marrow suppression may play a role. During follow-up of the discharged patients, the hematologic abnormalities resolved. The relative importance of ribavirin and the virus on these hematologic manifestations requires further study.

During hospitalization, 56% of our patients had elevated alanine aminotransferase levels. Twenty-one patients (8%) tested positive for hepatitis B surface antigen, and lamivudine prophylaxis was offered to all of them since they were receiving high-dose corticosteroids. Unlike Peiris and colleagues (17), we found no statistically significant association between chronic hepatitis B and mortality, and the prevalence of hepatitis B in our cohort could not explain the liver dysfunction observed. Whether SARS coronavirus can lead to hepatitis is unknown. Use of ribavirin and antibiotics such as clarithromycin and amoxicillin–clavulanate may have contributed to the liver function derangement. Other frequent laboratory abnormalities were elevated levels of C-reactive protein and lactate dehydrogenase.

We defined confirmed SARS according to a positive result on RT-PCR in nasopharyngeal secretions or on serologic testing for SARS coronavirus. The concordance rate of these tests was 57% in our cohort. The time of sampling plays a crucial role in the results of these two tests. Serologic methods based on enzyme-linked immunosorbent assay reliably detect antibody response beginning 20 days...
after the onset of illness, and immunofluorescence assay can detect antibodies after 10 days (16). Unfortunately, our patients were not uniformly tested by either method, which made the interpretation of results difficult. The sensitivity of RT-PCR in nasopharyngeal secretions varies from 30% or less within the first 3 days of illness to about 65% at day 7 of the illness. A better method of rapid diagnosis is urgently needed.

The autopsy findings in our cohort are in line with those described in other case series (20). The second patient who underwent autopsy had much less severe and extensive diffuse alveolar damage than did the first. Both patients died in the third week of the disease. The pathologic changes in the first patient could be interpreted as the natural course of the disease. Use of ribavirin and steroids in the second patient may have altered the natural course of pulmonary damage. Because our study was retrospective, we could not evaluate the effect and toxicity of antiviral therapy. One study showed that despite the multiple mechanisms of antiviral action (21), ribavirin did not inhibit the growth of coronavirus in vitro (22). Researchers have argued that ribavirin may act through its immunomodulatory effect, and immunopathologic damage due to overexuberant host response may be the cause of lung damage (17). At present, the optimal antiviral regimen remains undefined (5).

We identified 2 independent predictors of mortality in multivariate analysis: age older than 60 years and lactate dehydrogenase level greater than 3.8 µkat/L at presentation. We did not choose presence of comorbid diseases for analysis because of the problem of collinearity with age. Other reports have implicated advanced age and high lactate dehydrogenase level as predictors of mortality (6, 7, 10). The latter probably reflects tissue damage. We examined the accuracy of these factors in predicting mortality. When presence of either factor was considered predictive, the sensitivity was 69% and the specificity was 53%; when presence of both factors was considered predictive, the sensitivity was 22% and the specificity was 97%.

The mortality rate in our cohort is higher than in other case series (6, 7) because of our longer follow-up period. In fact, on the basis of a statistical model based on 1400 patients, Donnelly and colleagues reported an estimated case-fatality rate of 13% for patients younger than 60 years of age and 43% for those age 60 years or older. They also found that patient age was strongly associated with outcome (10).

Our study has several limitations. First, it was retrospective and relied on data collected from case records. Therefore, we may have missed important information in some patients. Because all but 1 of our patients received steroids and ribavirin during hospitalization, we could not delineate the efficacy or adverse effect of these therapies. The validity of the predictive factors for mortality derived from our cohort remains tentative; further validation with another data set is necessary. Strengths of our study include the large sample size and longer follow-up period, which make results of the statistical analysis more reliable.

In conclusion, SARS poses a major threat to the Hong Kong community, and its associated mortality is substantial. We need to refine the current case definition, search for a reliable rapid diagnostic test, and explore effective and safe antiviral therapy.

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