J Microbiol Immunol Infect
2006;39:45-53

Original Article

Clinical and laboratory features in the early stage of severe acute respiratory syndrome

Cheng-Kuo Fan[1], Kuo-Ming Yieh[2], Ming-Yieh Peng[2], Jung-Chung Lin[2], Ning-Chi Wang[2], Feng-Yee Chang[2]

[1]Department of Internal Medicine, Tao-Yuan Armed Forces General Hospital, Tao-Yuan County; and
[2]Division of Infectious Diseases and Tropical Medicine, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

Received: July 28, 2005 Revised: August 26, 2005 Accepted: August 30, 2005

Background and Purpose: To characterize the clinical and laboratory features of severe acute respiratory syndrome (SARS) in the early stage and to compare them with those of patients initially suspected of having SARS who were later determined to have other febrile diseases.

Methods: Between March and June 2003, 122 patients with possible SARS were admitted to the isolation ward of Tri-Service General Hospital. SARS was diagnosed according to the modified World Health Organization case definition (May 1, 2003). Among them, 43 were classified as probable SARS cases and a SARS etiology was excluded in 32 patients.

Results: Presenting symptoms on admission included fever (97.7% of probable cases, 84.4% of excluded cases), chills (39.5% vs 18.8%), cough with sputum production (16.3% vs 40.6%), dry cough (23.3% vs 9.4%), dyspnea (18.6% vs 9.4%), diarrhea (14.0% vs none), rhinorrhea (2.3% vs none), and myalgia (7.0% vs 6.6%). Common laboratory features included lymphopenia and elevated aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, C-reactive protein and creatine kinase values. Intubation and mechanical ventilation were required in 12 probable cases and 6 excluded cases. Five patients with probable SARS (11.6%) died. A scoring system which was developed to differentiate SARS patients from other febrile patients in the emergency room could differentiate probable cases from excluded cases with a sensitivity of 36.4% and a specificity of 70.6%.

Conclusions: The clinical presentation and laboratory features at the early stage do not allow differentiation of patients with SARS-CoV infection from other febrile patients. Thus, it is mandatory for all healthcare workers to strictly follow standard isolation precautions during an outbreak to minimize disease transmission.

Key words: Biological markers, early diagnosis, SARS virus infection, severe acute respiratory syndrome, signs and symptoms

Introduction

The global outbreak of severe acute respiratory syndrome (SARS) seriously threatened public health and socioeconomic stability [1-4]. This disease is caused by a novel coronavirus, SARS-associated coronavirus (SARS-CoV) [5]. SARS-CoV is thought to have originated from wild animals and serologic evidence indicated that the virus was spread through interspecies transmission from wild game markets in Guangdong, China [6]. The disease is highly contagious and caused a very large epidemic that spread rapidly from China to more than 30 countries. In Taiwan, there were 3032 reported SARS cases during the epidemic period in 2003. Among them, 668 were probable cases, 1320 were suspected cases and a SARS etiology was subsequently excluded in 1044 cases [7].

The primary mode of transmission of SARS-CoV is by the airborne spread of large droplets [1,8-10]. However, a number of SARS cases occurred in health-care workers (HCWs) following exposure to high-risk aerosol- and droplet-generating procedures despite wearing protective equipment [11-14]. A small group of patients appear to be highly infectious and have been referred to as “super-spreaders”.

Corresponding author: Feng-Yee Chang, Division of Infectious Diseases and Tropical Medicine, Department of Internal Medicine, Tri-Service General Hospital, No 325, Section 2, Cheng-Kung Road, Neihu 114, Taipei 104, Taiwan.
E-mail: fychang@ndmctsgh.edu.tw

The clinical features of SARS patients have been described in many clinical studies and fever is the major symptom [11,14-27]. Atypical presentation of the disease and asymptomatic cases have also been described, but in small numbers [28-31]. During the SARS epidemic, differentiation of SARS cases from other diseases mimicking SARS at presentation was a critical task for the implementation of effective clinical management and isolation precautions. However, few studies have compared the clinical and laboratory features at presentation of SARS-probable, -suspected and -excluded patients.

A variety of SARS diagnostic tests are now available including nested reverse transcriptase-polymerase chain reaction (RT-PCR) or real-time PCR for viral RNA detection, and detection of anti-SARS-CoV antibody by immunofluorescent assay, enzyme-linked immunosorbent assay (ELISA), and Western blot [32-40]. But these tests are still insufficiently sensitive for primary screening in the first week after fever onset in SARS patients.

We retrospectively compared the clinical and laboratory characteristics of 43 SARS-probable cases and 32 SARS-excluded cases. A scoring system [3,41, 42] was also applied to patients in these 2 groups in order to assess its suitability as a screening tool.

Methods

From March to June, 2003, 122 patients suspected of having SARS were admitted to the isolation ward of Tri-Service General Hospital (TSGH), a teaching hospital in Taipei, Taiwan. The definition of suspected and probable SARS cases in this study was as issued by the Word Health Organization on May 1, 2003 [43]. Forty-three patients were classified as probable SARS cases, 47 as suspected SARS cases and 32 patients were subsequently excluded from having a SARS etiology. The characteristics of the 43 probable cases were compared with those of the excluded cases in this study.

Information collected from medical chart records included: demographic data; clinical manifestations at presentation; treatment and clinical outcomes; hematological data at presentation (complete blood count, clotting profile); serum biochemical measurements at presentation, including electrolytes, renal and liver function test, creatine kinase (CK), lactate dehydrogenase (LDH), C-reactive protein (CRP); history of contact with SARS-affected person or travel to an endemic area; medical comorbidities; date of hospital admission; and results of bacteriological examination including *Mycobacterium tuberculosis*, *Mycoplasma pneumoniae*, *Legionella pneumophila*, and *Chlamydia pneumoniae*.

Viral laboratories were established in our hospital and RT-PCR was done for SARS-CoV in 91 patients. The method used to identify SARS-CoV followed the protocols established by the Center for Disease Control (CDC) Taiwan central laboratory, which were modifications of the protocols used by the Centers for Disease Control and Prevention, United States [7]. Clinical specimens for RT-PCR test consisted of blood, sputum, urine, stool, throat swabs or gargling fluid samples. An immunofluorescence assay/ ELISA was used to detect specific antibody response to SARS-CoV infection and 19 blood samples from 16 probable SARS patients with positive results of RT-PCR test were checked in the laboratory of the CDC Taiwan [7].

A previously described SARS scoring system, consisting of 6 items for predicting SARS among febrile patients presenting at the emergency department, was applied to the probable and excluded cases [3]. The clinical scores were based on the occurrence of 6 items: myalgia, diarrhea, cough, rhinorrhea or sore throat, lymphopenia (lymphocyte <1000/μL), and thrombocytopenia (platelet $<150 \times 10^3/\mu L$).

Statistical analysis

Differences in frequencies or proportions were analyzed using chi-squared test. Data were reported as mean ± standard deviation (SD) unless otherwise specified. Statistical Package for the Social Sciences (SPSS) [version 10.0; SPSS Inc., Chicago, USA] and Excel (Microsoft Excel 2001; Microsoft Corporation, Seattle, WA, USA) software were used for all analyses.

Results

Included in the present study were 43 probable SARS patients and 32 patients initially suspected of, but later excluded from, having a SARS etiology based mostly on RT-PCR test results. The 75 patients studied included 16 previously healthy HCWs. The demographic and clinical characteristics of the 2 groups of patients are shown in Table 1. Patients initially suspected of having SARS but later excluded had final diagnoses of pneumonia, bronchopneumonia, chickenpox, gouty arthritis with acute exacerbation, acute pharyngitis,

Table 1. Summary of demographic information of the patients

	Probable group (n = 43)	Excluded group (n = 32)
Age [years; mean (SD)]	41.0 (17.1)	42.3 (17.5)
Male (%)	22 (51.2)	28 (87.5)
Contact history (%)		
Municipal Ho-Ping Hospital	19 (44.2)	2 (6.3)
TSGH	4 (9.3)	1 (3.1)
China	1 (2.3)	2 (6.3)
Other hospital	5 (11.6)	0
Unclear	14 (32.6)	27 (84.4)
Occupation (%)		
HCWs		
Physicians	1 (2.3)	1 (3.1)
Nurses	5 (11.6)	1 (3.1)
Others	8 (18.6)	None
Soldier	4 (9.3)	8 (25.0)
Businessmen	1 (2.3)	None
Comorbidities (%)		
DM	4 (9.3)	1 (3.1)
Hypertension	4 (9.3)	3 (9.4)
CAD	None	None
CVA	3 (7.0)	2 (6.3)
Uremia	1 (2.3)	None
COPD	1 (2.3)	3 (9.4)
Liver diseases	1 (2.3)	0
None	26 (60.5)	23 (71.9)

Abbreviations: SD = standard deviation; TSGH = Tri-Service General Hospital; HCWs = health care workers; DM = diabetes mellitus; CAD = coronary arterial disease; CVA = cerebro-vascular accident; COPD = chronic obstructive pulmonary disease

cerebral hemorrhagic infarction, upper respiratory tract infection, acute cholangitis, *Salmonella* septicemia or gastroenteritis.

Among the probable SARS cases, 67.4% had a clear contact history, which could include visiting hospitals with extensive or limited intrahospital outbreak of SARS [44], such as Municipal Ho-Ping Hospital (44.2%), our hospital (9.3%), and other hospitals (11.6%), as well as any recent visit to China (2.3%). Comorbid illness was present in 39.5% of probable SARS cases.

The most common symptoms at presentation of patients with probable SARS were as follows: fever (97.7%), chills (39.5%), dry cough (23.3), dyspnea (18.6) and diarrhea (14%). For those in whom a SARS etiology was later excluded, the most common symptoms at presentation were as follows: fever (84.4%), cough (40.6%) and chills (18.8%) [Table 2].

The laboratory data (including hematological values, serum biochemical data) at presentation were collected and analyzed. In the probable SARS group, the mean lymphocyte count was 796/μL, and 71% (22/31) had lymphopenia (Table 3). The mean platelet count in the probable SARS group was 175×10^3/μL, and 45% (14/31) had thrombocytopenia. Only about 10% of probable cases had a 2-fold increase in aspartate aminotransferase (AST) or alanine aminotransferase (ALT) level. Comparison of biochemical data revealed that excluded SARS patients had higher mean sodium (Na), ALT, AST, creatinine (Cr), CK, LDH, and CRP values than probable SARS cases.

C. pneumoniae immunoglobulin G antibody test was positive in 2 patients (1 probable case and 1 excluded case). A positive *M. pneumoniae* immunoglobulin M antibodies result was found in 11 patients (7 probable cases, 4 excluded cases). *Legionella* serogroup 1 urine antigen was not detected in any of these patients. One of the SARS-excluded patients was shown to have pulmonary tuberculosis by positive result of acid-fast stain and sputum culture for *M. tuberculosis*. SARS-CoV RNA was checked using blood, sputum, urine, stool, throat swabs, or gargling fluid samples by RT-PCR in 91 of the 122 patients. A total of 459 specimens from the 91 patients included in the analysis were collected from May 5 to July 7. A positive result that fulfilled the laboratory criteria of the case definition was found in 66.7% of tested probable SARS patients (Table 3) [45]. For the serology tests, 19 serum samples were collected for ELISA from 16 patients in the probable group with positive results of RT-PCR test, and 14 samples (87.5%) were positive for antibody to SARS-CoV. The first serum sample was collected a mean of 10 ± 2.8 (mean ± SD) days after onset of fever.

Twelve probable cases (27.9%) were intubated. Among them, 7 patients (58%) had a contact history at Municipal Ho-Ping Hospital, the site of a severe nosocomial SARS outbreak, and 1 of them died; 3 patients (25%) had no known contact history and 1 of them died; the remaining 2 patients (17%) had a contact history at other hospitals and both of them died. The mean intubation period of these probable cases was 20.2 ± 9.2 days. Five probable cases (11.6%) died. None of the infected HCWs died.

A comparison of the 6 items of the SARS scoring system used in this study between patients with probable or confirmed SARS in previously reported studies is shown in Table 4. The clinical scores of the probable and excluded patients in this study are shown in Table 5 and Table 6. Among the probable cases, 33 had complete records of hematological values at presentation. Among

Table 2. Analysis of clinical manifestations at presentation of the patients

Variable (n [%] or mean [SD])	Probable group (n = 43)	Excluded group (n = 32)
Temperature (°C)	37.4 (15.6)	37.5 (15.4)
Respiratory rate/min	23.4 (6.2)	22.2 (6.0)
Pulse rate/min	91 (14)	87 (14)
Blood pressure (mm Hg)	116/69 (17/9)	117/66 (15/13)
Fever	42 (97.7)	27 (84.4)
Chills	17 (39.5)	6 (18.8)
No appetite	1 (2.3)	0
Dizziness	1 (2.3)	0
Headache	3 (7.0)	3 (9.4)
Myalgia	3 (7.0)	2 (6.3)
Weakness	4 (9.3)	2 (6.3)
Diarrhea	6 (14.0)	0
Nausea/vomiting	1 (2.3)	3 (9.4)
Abdominal pain	2 (4.7)	1 (3.1)
Dry cough	10 (23.3)	3 (9.4)
Cough with sputum	7 (16.3)	13 (40.6)
Dyspnea	8 (18.6)	3 (9.4)
Chest pain	2 (4.7)	3 (9.4)
Sore throat	2 (4.7)	2 (6.3)
Rhinorrhea	1 (2.3)	0

Abbreviation: SD = standard deviation

Table 3. Analysis of initial laboratory data and microbiological data of the patients

	Probable group (n = 43)	Excluded group (n = 32)
Hematologic (mean SD)		
WBC (/μL)	6672 (5250) [n = 31]	9169 (3668) [n = 17]
Lymphocyte (/μL)	796 (444) [n = 31]	986 (597) [n = 17]
<1000/μL	22 cases	10 cases
Platelet ($\times 10^3$/μL)	175 (79) [n = 31]	231 (148) [n = 17]
<150 $\times 10^3$/μL	14 cases	4 cases
Hb (g/dL)	12.6 (1.6) [n = 31]	12.4 (2.8) [n = 17]
Biochemical (mean SD)		
Sodium (mmol/L)	136 (4.2) [n = 30]	157 (4.5) [n = 14]
Potassium (mmol/L)	3.9 (0.5) [n = 30]	3.9 (0.7) [n = 14]
ALT (U/L)	31 (24) [n = 33]	101 (169) [n = 15]
>2-fold upper limit	2 cases	4 cases
AST (U/L)	41 (28) [n = 33]	150 (268) [n = 15]
>2-fold upper limit	3 cases	4 cases
Cr (mg/dL)	1.0 (0.22) [n = 29]	1.3 (1.1) [n = 15]
CK (U/L)	231 (408) [n = 31]	188 (203) [n =1 0]
LDH (U/L)	798 (496) [n = 19]	1751 (1712) [n = 7]
CRP (mg/dL)	6.8 (8.9) [n = 29]	11.4 (11.3) [n = 10]
Microbiologic (positive case/tested case)		
Legionella Ag	0/9	0/0
Chlamydia IgG Ab	1/24	1/22
Mycoplasma IgM Ab	7/34	4/18
AFB stain	0/2	1/1
RT-PCR test	24/36	0/26
SARS Ab	14/16	0/0

Abbreviations: SD = standard deviation; WBC = white blood cell count; Hb = hemoglobin; ALT = alanine aminotransferase; AST = aspartate aminotransferase; Cr = creatinine; CK = creatine kinase; LDH = lactate dehydrogenase; CRP = C-reactive protein; Ag = antigen; IgG = immunoglobulin G; Ab = antibody; IgM = immunoglobulin M; AFB = acid-fast bacilli; RT-PCR = reverse transcriptase-polymerase chain reaction; SARS = severe acute respiratory syndrome

Table 4. Comparative characteristics of patients with probable or confirmed severe acute respiratory syndrome (SARS) in different studies

Variable (n [%] or mean [SD])	NTUH (%) SARS[a] (n = 8)	TSGH probable (n = 43)	CDC Taiwan[b] (n = 526)	Toronto[c] (n = 144)	Hong Kong[d] (n = 267)
Myalgia	6 (75)	3 (7.0)	82 (15.6)	71 (49)	134 (50)
Diarrhea	4 (50)	6 (14)	105 (20)	34 (23.6)	41 (15)
Cough	0	17 (40.0)	325 (62)	107 (74.3)	118 (44)
Rhinorrhea		1 (2.3)	27 (5.1)	3 (2.1)	30 (11)
Sore throat	1 (12.5)	2 (4.7)	77 (14.6)	18 (12.5)	36 (14)
Lymphocyte ($\times 10^3/\mu L$)[e]	0.9 ± 0.3	0.8 (n = 31)	1.0 (n = 433)	0.9	0.7
Platelet ($\times 10^3/\mu L$)	144.1 ± 36.3	175 (n = 31)	186.2 (n = 303)	183	146

Abbreviations: SD = standard deviation; NTUH = National Taiwan University Hospital; TSGH = Tri-Service General Hospital; CDC = Center for Disease Control

[a]Probable SARS patients.

[b]Probable SARS patients.

[c]Suspected or probable SARS patients.

[d]Confirmed or probable SARS patients.

[e]Lymphopenia: <1000/μL; thrombocytopenia: $<150 \times 10^3/\mu L$.

the 33 probable cases, 9 (27%) had negative scores (4 of them had a positive PCR test result), 13 had positive scores and 11 had a score of zero. In contrast, among the excluded cases, 6 (35%) patients had positive scores. The sensitivity of the scoring system was 36.4% and the specificity was 70.6%.

Discussion

SARS is a rapidly progressive disease and results in serious economic damage in affected and non-affected epidemic and non-epidemic areas. The main reason for the enormous societal disruption was the lack of an effective diagnostic method that could be used in the early stage of the disease. Hence, development of specific diagnostic method for the early stage of SARS is a public health priority.

History of travel to the epidemic areas and/or contact with SARS patients was not usually a reliable and accurate indicator of infection risk. Seroconversion against SARS-CoV does not occur and viral detection by using RT-PCR is not indicated in the early stage of SARS infection. Accordingly, clinical presentations seemed to have good potential for use as parameters to screen patients in the early stage of the disease.

The scoring system used in this study, developed by Chen et al [41], is based on clinical presentations and laboratory data and was designed for use as a screening method which can be used in the emergency room [3,42]. The scoring system is comprised of 2 scores, the symptom score and the clinical score. According to Chen et al's report, all patients with fever (≥38°C) can be evaluated by this scoring system and only those patients with positive scores for both the symptom and clinical components should be isolated. However, the absence of consistency of symptoms at presentation among study groups of SARS patients affects the sensitivity and specificity of the scoring system. For example, comparison of the clinical symptoms between patients treated at TSGH and National Taiwan University Hospital (NTUH) revealed higher percentages of myalgia and diarrhea among probable SARS patients at NTUH. In addition, the percentages of rhinorrhea/sore throat were higher among non-SARS patients treated at NTUH as compared to other series (Table 4). These results may suggest that the initial clinical and laboratory characteristics of SARS patients might be not specific enough for the early diagnosis of SARS infection. Therefore, the ability to differentiate between SARS-CoV pneumonia and other pneumonia (or infection) in the early stage of the disease has been a matter of controversy.

Application of the scoring system to the probable and excluded cases in this study revealed a sensitivity of 36.4% and specificity of 70.6%. Due to the retrospective design of this study, symptoms and laboratory data might not have been recorded comprehensively which may have affected the results. Further study is needed for the validation of the scoring system.

Some of our SARS patients had positive *Chlamydia* or *Mycoplasma* antibody reaction. It was not known whether these patients had coinfection with these organisms [46]. From the viewpoint of clinical management, use of antibiotics in SARS patients may

Table 5. Clinical scoring of severe acute respiratory syndrome (SARS)-probable cases

Case	Myalgia	Diarrhea	Cough	Rhinorrhea/ Sore throat	Symptom score[a]	Lymphocyte (/μL)[b]	Platelet ($\times 10^3$/μL)[b]	Laboratory score[c]	Clinical score[d]	RT-PCR result	SARS-Abs
1	–	–	+	–	–2	1942	412	0	–2	+	–
2	–	–	+	–	–2	848	340	+1	–1	–	N
3	–	–	–	–	0	489	78	+2	+2	N	N
4	–	+	+	–	–1	1009	133	+1	0	+	+
5	–	–	–	–	0	1020	213	0	0	+	N
6	–	–	–	–	0	1016	160	0	0	+	+
7	–	–	–	–	0	1444	223	0	0	+	+
8	–	+	+	–	–1	881	153	+1	0	+	+
9	–	–	+	–	–2	620	60	+2	0	+	+
10	–	–	+	–	–2	340	125	+2	0	+	N
11	–	–	+	–	–2	290	94	+2	0	–	N
12	–	+	+	–	–1	269	200	+1	0	–	N
13	+	–	+	–	–1	758	284	0	–1	–	N
14	–	–	–	–	0	1822	209	0	0	–	N
15	–	–	+	–	–2	460	93	+2	0	N	N
16	–	–	–	–	0	600	191	+1	+1	+	+
17	–	–	–	–	0	838	79	+2	+2	+	+
18	–	+	–	–	+1	201	100	+2	+3	+	N
19	–	–	–	–	0	649	163	+1	+1	+	N
20	–	–	–	–	0	1231	116	+1	+1	+	+
21	–	–	–	–	0	531	168	+1	+1	–	N
22	–	–	–	–	0	468	231	+1	+1	–	N
23	–	–	–	–	0	984	315	+1	+1	–	N
24	–	–	–	–	0	848	212	+1	+1	–	N
25	–	–	–	–	0	499	249	+1	+1	N	N
26	–	–	–	–	0	280	121	+2	+2	N	N
27	–	–	–	–	0	498	147	+2	+2	N	N
28	–	–	+	+	–3	1068	148	+1	–2	+	+
29	–	–	+	–	–2	1018	112	+1	–1	+	+
30	–	–	+	–	–2	277	154	+1	–1	+	+
31	–	–	+	–	–2	1072	148	+1	–1	–	N
32	–	–	+	–	–2	290	187	+1	–1	–	N
33	–	–	+	+	–3	1440	235	0	–3	N	N

Abbreviations: RT-PCR = reverse transcriptase-polymerase chain reaction; Abs = antibodies; + = with this symptom; – = without this symptom; N = not done

[a]If symptom score is <0, then SARS is less likely.

[b]Lymphopenia: <1000/μL (+1); thrombocytopenia: <150 $\times 10^3$/μL (+1).

[c]Lymphopenia + thrombocytopenia.

[d]If clinical score is >0, then SARS is likely; clinical score = symptom score + laboratory score.

be justified in the early stage of the disease because of the difficulty in accurate determination of the etiology and the possibility of coinfection.

In conclusion, criteria are needed to help clinicians to quickly differentiate SARS from other illnesses with overlapping symptoms of fever and respiratory symptoms in the early stage of illness. This study demonstrated the non-specific nature of clinical and laboratory characteristics of SARS patients at presentation. Once the pathogenesis of SARS is more fully understood, better methods for case identification at the early stage should emerge. In the meantime, it is important for all HCWs to strictly follow standard precautions in suspected cases and throughout the entire disease course of patients during any future outbreak of SARS, to minimize disease transmission.

Acknowledgment

This study was partly supported by C.Y. Foundation for Advancement of Education, Sciences and Medicine at Taipei.

Table 6. Clinical scoring of severe acute respiratory syndrome (SARS)-excluded cases

Case	Myalgia	Diarrhea	Cough	Rhinorrhea/ Sore throat	Symptom score[a]	Lymphocyte (/μL)[b]	Platelet ($\times 10^3$/μL)[b]	Laboratory score[c]	Clinical score[d]	RT-PCR result	SARS-Abs
1	–	–	+	–	–2	1527	307	0	–2	N	N
2	–	–	+	–	–2	788	204	+1	–1	N	N
3	–	–	+	–	–2	650	294	+1	–1	–	N
4	–	–	+	–	–2	755	189	+1	–1	–	N
5	–	–	+	–	–2	1176	148	+1	–1	–	N
6	–	–	+	–	–2	1064	206	0	–2	–	N
7	–	–	+	–	–2	582	170	+1	–1	–	N
8	–	–	–	–	0	130	37	+2	+2	N	N
9	–	–	–	–	0	744	690	+1	+1	–	N
10	–	–	–	–	0	683	101	+2	+2	–	N
11	–	–	–	–	0	475	313	+1	+1	–	N
12	–	–	–	–	0	701	61	+2	+2	N	N
13	–	–	–	–	0	1800	269	0	0	–	N
14	–	–	–	–	0	120	123	+2	+2	–	N
15	–	–	–	–	0	1599	235	0	0	–	N
16	–	–	–	–	0	2092	229	0	0	–	N
17	–	–	–	–	0	1863	347	0	0	–	N

Abbreviations: RT-PCR = reverse transcriptase-polymerase chain reaction; Abs = antibodies; + = with this symptom; – = without this symptom; N = not done

[a]If symptom score is <0, then SARS is less likely.

[b]Lymphopenia: <1000/μL (+1); thrombocytopenia: $<150 \times 10^3$/μL (+1).

[c]Lymphopenia + thrombocytopenia.

[d]If clinical score is >0, then SARS is likely; clinical score = symptom score + laboratory score.

References

1. Christian MD, Poutanen SM, Loutfy MR, Muller MP, Low DE. Severe acute respiratory syndrome. Clin Infect Dis 2004; 38:1420-7.
2. Hsueh PR, Yang PC. Severe acute respiratory syndrome (SARS) — an emerging infection of the 21st century. J Formos Med Assoc 2003;102:825-39.
3. Su CP, Chiang WC, Ma MH, Chen SY, Hsu CY, Ko PC, et al. Validation of a novel severe acute respiratory syndrome scoring system. Ann Emerg Med 2004;43:34-42.
4. Blendon RJ, Benson JM, DesRoches CM, Raleigh E, Taylor-Clark K. The public's response to severe acute respiratory syndrome in Toronto and the United States. Clin Infect Dis 2004;38:925-31.
5. Peiris JS, Lai ST, Poon LL, Guan Y, Yam LY, Lim W, et al. Coronavirus as a possible cause of severe acute respiratory syndrome. Lancet 2003;361:1319-25.
6. Martina BE, Haagmans BL, Kuiken T, Fouchier RA, Rimmelzwaan GF, Van Amerongen G, et al. Virology: SARS virus infection of cats and ferrets. Nature 2003; 425:915.
7. Su IJ, Hsiu KH, Jiang YL, Shih WY, Lin T, Chen TH, et al. Memoir of severe acute respiratory syndrome control in Taiwan. Center for Disease Control, Department of Health, Executive Yuan, Taiwan. 1st ed. 2003.
8. Seto WH, Tsang D, Yung RW, Ching TY, Ng TK, Ho M, et al. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). Lancet 2003;361: 1519-20.
9. Dye C, Gay N. Modeling the SARS epidemic. Science 2003; 300:1884-5.
10. Riley S, Fraser C, Donnelly CA, Ghani AC, Abu-Raddad LJ, Hedley AJ, et al. Transmission dynamics of the etiological agent of SARS in Hong Kong: impact of public health interventions. Science 2003;300:1961-6.
11. Ho AS, Sung JJ, Chan-Yeung M. An outbreak of severe acute respiratory syndrome among hospital workers in a community hospital in Hong Kong. Ann Intern Med 2003;139:564-7.
12. Chiang CH, Chen HM, Shih JF, Su WJ, Perng RP. Management of hospital-acquired severe acute respiratory syndrome with different disease spectrum. J Chin Med Assoc 2003;66: 328-38.
13. Centers for Disease Control and Prevention (CDC). Cluster of severe acute respiratory syndrome cases among protected health-care workers--Toronto, Canada, April 2003. MMWR Morb Mortal Wkly Rep 2003;52:433-6.
14. Lau JT, Yang X, Leung PC, Chan L, Wong E, Fong C, et al. SARS in three categories of hospital workers, Hong Kong. Emerg Infect Dis 2004;10:1399-404.

15. Fowler RA, Lapinsky SE, Hallett D, Detsky AS, Sibbald WJ, Slutsky AS, et al. Critically ill patients with severe acute respiratory syndrome. JAMA 2003;290:367-73.
16. Liu CL, Lu YT, Peng MJ, Chen PJ, Lin RL, Wu CL, et al. Clinical and laboratory features of severe acute respiratory syndrome vis-à-vis onset of fever. Chest 2004;126:509-17.
17. Tsang KW, Ho PL, Ooi GC, Yee WK, Wang T, Chan-Yeung M, et al. A cluster of cases of severe acute respiratory syndrome in Hong Kong. N Engl J Med 2003;348:1977-85.
18. Lew TWK, Kwek TK, Tai D, Earnest A, Loo S, Singh K, et al. Acute respiratory distress syndrome in critically ill patients with severe acute respiratory syndrome. JAMA 2003;290:374-80.
19. Jang TN, Yeh DY, Shen SH, Huang CH, Jiang JS, Kao SJ. Severe acute respiratory syndrome in Taiwan: analysis of epidemiological characteristic in 29 cases. J Infect 2004;48: 23-31.
20. Choi KW, Chau TN, Tsang O, Tso E, Chiu MC, Tong WL, et al. Outcomes and prognostic factors in 267 patients with severe acute respiratory syndrome in Hong Kong. Ann Intern Med 2003;139:715-23.
21. Lee N, Hui D, Wu A, Chan P, Cameron P, Joynt GM, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. N Engl J Med 2003;348:1986-94.
22. Hsueh PR, Yang PC. Severe acute respiratory syndrome epidemic in Taiwan, 2003. J Microbiol Immunol Infect 2005; 38:82-8.
23. Leung WK, To KF, Chan PK, Chan HL, Wu AK, Lee N, et al. Enteric involvement of severe acute respiratory syndrome-associated coronavirus infection. Gastroenterology 2003;125: 1011-7.
24. Cheng VC, Hung IF, Tang BS, Chu CM, Wong MM, Chan KH, et al. Viral replication in the nasopharynx is associated with diarrhea in patients with severe acute respiratory syndrome. Clin Infect Dis 2004;38:467-75.
25. Zou Z, Yang Y, Chen J, Xin S, Zhang W, Zhou X, et al. Prognostic factors for severe acute respiratory syndrome: a clinical analysis of 165 cases. Clin Infect Dis 2004;38:483-9.
26. Wong KT, Antonio GE, Hui DS, Lee N, Yuen EH, Wu A, et al. Severe acute respiratory syndrome: radiographic appearances and pattern of progression in 138 patients. Radiology 2003; 228:401-6.
27. Donnelly CA, Ghani AC, Leung GM, Hedley AJ, Fraser C, Riley S, et al. Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. Lancet 2003;361:1761-6.
28. Yu WC, Tsang TH, Tong WL, Ng TK, Lim W, Yeung HC, et al. Prevalence of subclinical infection by the SARS coronavirus among general practitioners in Hong Kong. Scand J Infect Dis 2004;36:287-90.
29. Singh K, Eong OE, Kumarsil B, Saw S, Sethi S. Severe acute respiratory syndrome without respiratory symptoms or abnormal chest radiograph findings. Clin Infect Dis 2004;38: 585-6.
30. Ho KY, Singh KS, Habib AG, Ong BK, Lim TK, Ooi EE, et al. Mild illness associated with severe acute respiratory syndrome coronavirus infection: lessons from a prospective seroepidemiologic study of health-care workers in a teaching hospital in Singapore. J Infect Dis 2004;189:642-7.
31. Woo PC, Lau SK, Tsoi HW, Chan KH, Wong BH, Che XY, et al. Relative rates of non-pneumonic SARS coronavirus infection and SARS coronavirus pneumonia. Lancet 2004; 363:841-5.
32. Centers for Disease Control and Prevention (CDC). Severe acute respiratory syndrome (SARS) and coronavirus testing--United States, 2003. MMWR Morb Mortal Wkly Rep 2003; 52:297-302.
33. Chim SS, Tsui SK, Chan KC, Au TC, Hung EC, Tong YK, et al. Genomic characterization of the severe acute respiratory syndrome coronavirus of Amoy Gardens outbreak in Hong Kong. Lancet 2003;362:1807-8.
34. Nitsche A, Schweiger B, Ellerbrok H, Niedrig M, Pauli G. SARS coronavirus detection. Emerg Infect Dis 2004;10: 1300-3.
35. Peiris JS, Chu CM, Cheng VC, Chan KS, Hung IF, Poon LL, et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. Lancet 2003;361:1767-72.
36. Poon LL, Chan KH, Peiris JS. Crouching tiger, hidden dragon: the laboratory diagnosis of severe acute respiratory syndrome. Clin Infect Dis 2004;38:297-9.
37. van Elden LJ, van Loon AM, van Alphen F, Hendriksen KA, Hoepelman AI, van Kraaij MG, et al. Frequent detection of human coronaviruses in clinical specimens from patients with respiratory tract infection by use of a novel real-time reverse-transcriptase polymerase chain reaction. J Infect Dis 2004;189: 652-7.
38. Wang WK, Chen SY, Liu IJ, Chen YC, Chen HL, Yang CF, et al. Detection of SARS-associated coronavirus in throat wash and saliva in early diagnosis. Emerg Infect Dis 2004;10: 1213-9.
39. Nie Y, Wang G, Shi X, Zhang H, Qiu Y, He Z, et al. Neutralizing antibodies in patients with severe acute respiratory syndrome-associated coronavirus infection. J Infect Dis 2004;190: 1119-26.
40. Chen X, Zhou B, Li M, Liang X, Wang H, Yang G, et al. Serology of severe acute respiratory syndrome: implications for surveillance and outcome. J Infect Dis 2004;189: 1158-63.
41. Chen SY, Su CP, Ma MH, Chiang WC, Hsu CY, Ko PCI, et al. Predictive model of diagnosing probable cases of severe acute

respiratory syndrome in febrile patients with exposure risk. Ann Emerg Med 2004;43:1-5.
42. Chen SY, Chiang WC, Ma MH, Su CP, Hsu CY, Ko PCI, et al. Sequential symptomatic analysis in probable severe acute respiratory syndrome cases. Ann Emerg Med 2004;43: 27-33.
43. World Health Organization. Case definitions for surveillance of severe acute respiratory syndrome (SARS). Available at: URL: http://www.who.int/csr/sars/casedefinition/en. Accessed May 16, 2003.
44. Centers for Disease Control and Prevention (CDC). Severe acute respiratory syndrome--Taiwan, 2003. MMWR Morb Mortal Wkly Rep 2003;52:461-6.
45. Centers for Disease Control and Prevention (CDC). Revised U.S. surveillance case definition for severe acute respiratory syndrome (SARS) and update on SARS cases--United States and worldwide, December 2003. MMWR Morb Mortal Wkly Rep 2003;52:1202-6.
46. Brogden KA, Guthmiller JM, Taylor CE. Human polymicrobial infections. Lancet 2005;365:253-5.

