ORIGINAL ARTICLE

The rationale of fever surveillance to identify patients with severe acute respiratory syndrome in Taiwan

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Study objective: To establish a predictive scoring system and to determine its effectiveness for severe acute respiratory syndrome (SARS) cases confirmed by RT-PCR in patients with fever.

Methods: A study was conducted of 484 consecutive patients seen in the emergency department (ED) of our tertiary care center during the SARS outbreak in Taiwan. The scoring system was divided into triage and screening station stages. Data were analysed with multivariable and logistic regression analysis.

Results: Of 737 patients who presented to our ED for possible SARS from March to June 2003, we enrolled 484 patients with a temperature $>38.0^{\circ}\text{C}$ ($>100.3^{\circ}\text{F}$) (age >18 years). Dyspnoea, diarrhoea, travel, close contact, hospital exposure, and household history were identified as predictive indicators in the triage stage. The triage score was the total of six items. With a one-point cutoff value, the sensitivity and specificity were 81.8% (18/22) and 73.6% (340/462). Leukocytosis, thrombocytopenia, lymphopenia, and CXR were identified as predictive indicators in the fever screening stage. Screening station scores (the sum of 10 items) consisted of triage scores, white blood cell count, and CXR. With a three-point cutoff value, the sensitivity and specificity were 95.5% (21/22) and 87.2% (403/462).

Conclusions: Syndromic and traditional surveillance play a role in early identification of SARS in an endemic area. The SARS scoring system described is easily applicable and highly effective in screening patients during outbreaks.

Severe acute respiratory syndrome (SARS) is a brand new infectious disease. Since March 2003, SARS outbreaks have become a worldwide threat, especially in East South Asia during a short period. Taiwan had the third highest number of cumulative SARS cases and SARS death behind mainland China and Hong Kong.¹ Before 21 April 2003, there was no community or hospital outbreak and no SARS mortality in Taiwan. However, on 21 April, the Department of Health (DOH) in Taiwan announced that hospital transmission might have happened. From that point on, the number of SARS cases increased and these were associated with health systems primarily.² More than 90% of SARS cases in Taiwan have been correlated with the hospital settings.³ Hospitals were seen as the source of SARS, even in areas where there were very few or no cases of SARS.

During the SARS catastrophe, emergency departments (EDs) played an important role in controlling the SARS outbreak. Many patients with fever, either suspected or non-suspected SARS, were anxious to rule out the possibility of SARS infection and were referred to EDs with typical or atypical clinical presentation. In this situation, it was very difficult for emergency physicians to identify patients with SARS early, specifically if there was neither a reliable exposure history nor a rapid diagnostic tool. Therefore, EDs had the greatest risk of exposure to new cases of SARS. Hospital managers took additional policies, such as setting a fever screening station or outdoor emergency room to stop hospital transmission and prevent any possible SARS cases into the hospital.⁴ In addition, according to the World Health Organization (WHO) definition of suspected and probable cases of SARS, there were low sensitivity and specificity rates in detecting SARS in the Hong Kong area.⁵ To improve the possibly low sensitivity of the WHO criteria, we established a predictive scoring system using a two-stage stepwise method at fever screening stations to early detect possible SARS cases and contain SARS outbreak effectively.

MATERIALS AND METHODS

The study was conducted in a tertiary care centre in a northern Taiwan, university affiliated, teaching hospital. Seven hundred and thirty seven patients presented to our ED for possible SARS from 29 March to 30 June 2003. For final analysis, we enrolled 484 patients with a documented temperature higher than 38.0°C ($>100.3^{\circ}\text{F}$) and age greater than 18 years. The institutional review board (IRB) of the study hospital approved the study protocol.

All teaching hospitals have been appointed as SARS screening hospitals by the Taiwan DOH. During the SARS outbreak, any patients who were consulted in the EDs of these tertiary care centres—regardless of the chief complaint—would be asked the following standard questions which were then were carefully recorded in the chart:

- Was there any SARS contact history in past 10 days?
- Was there any history of traveling to an endemic area in the past 10 days?
- Was there any experience of fever, cough, respiratory distress, diarrhoea, myalgia, or headache in the past 3 days?
- Did any relatives or friends experience the above signs and symptoms?

All febrile patients underwent laboratory investigation that included complete blood count (CBC). Chest x ray (CXR) also was taken in the fever screening station. The ED physicians assimilated all of the above information, including the clinical history and results of the investigation. Patients that met the SARS reporting criteria set by the CDC were

Abbreviations: CBC, complete blood count; CDC, Centers for Disease Control and Prevention; CXR, chest x ray; DOH, Department of Health; SARS, severe acute respiratory syndrome; WHO, World Health Organization

transferred to the isolation unit. Specimens of probable cases were collected and sent for SARS-CoV PCR or antibody examinations by a special SARS team of the hospital.

Our study was divided into two stages. In the triage stage, patients had their temperature taken. Symptoms and history were obtained using a structured questionnaire. Information was documented about recent travel within the last 10 days to an area with current or recent documented cases of SARS. Additional data were recorded about close contact (within the past 10 days) with a person known or suspected to have SARS infection. The patient was also queried about recent visitation (at least once within the last 10 days) at a hospital with current documented non-social transmission. The patient was asked whether he or she lived with documented SARS patients or in an area with current documented community transmission.

The next stage was the screening station stage, which included CBC and CXR. The local health centre also was notified at the same time. Other febrile patients, who did not meet SARS criteria, then would be asked by the physicians to undergo follow up at the ED within two days following discharge. This routine follow up would continue until all clinical symptoms disappeared. The research assistant would follow up patient progress on the 10th day and record the final diagnosis.

Our study included all febrile patients who presented to ED or fever screening station with a body temperature $>38^{\circ}\text{C}$ in the past three days. All patients <18 years old were excluded from this study. According to the flow chart of the reporting criteria of SARS suspected cases set by the Centers for Disease Control and Prevention (CDC), patients with any of the following criteria would be taken as SARS suspected cases:

- febrile patients who met the WHO criteria of suspected SARS were prospectively enrolled in the study beginning March 2003,¹³ and
- history of exposure and associated symptoms, such as cough, dyspnea, myalgia, diarrhoea, joint pain, headache, and general malaise.

All patients were completely evaluated in two stages: the triage stage and the screening station stage as previously described. The other biochemical measurements depended on the symptoms of the febrile patients; throat swab, sputum, or both were collected for Gram's stain. Screening tests were performed for common viruses, notably influenza A and B and respiratory syncytial virus. Legionella and pneumococcal antigen testing were also conducted.

Final diagnosis of SARS was documented by the CDC in Taiwan after polymerase chain reaction and paired serum for coronavirus antibody were measured. With positive polymerase chain reaction, positive paired serum, or both, the patients were confirmed as having SARS. All procedures were performed under isolation conditions.

The diagnosis of a probable SARS case was based on the WHO criteria, which included contact history, occurrence of fever and respiratory symptoms, progression of response to antibiotic treatment observed on chest roentgen, any possibility of spreading the disease to others, and the results of SARS-CoV PCR or antibody examinations.⁸ If any new evidence contrary to the diagnosis appeared during the course of treatment, the CDC would correct the case immediately and notify the reporting hospital. In the early stage of the disease, some patients may not qualify as SARS suspected patients as outlined by the CDC SARS reporting criteria. Thus, the patients may leave the emergency room. However, when these patients were diagnosed by other hospitals as SARS probable cases, the CDC would then notify the hospitals to which the patient previously presented.

SPSS for Windows (version 11, SPSS Inc, Chicago, IL, USA) was used to analyse the data. Fisher's exact test was used to evaluate the categorical variables. Continuous variables were expressed as the mean (standard deviation). The χ^2 test or Fisher's exact test was used to establish statistical significance. The sensitivity, specificity, and overtriage and undertriage rates of CDC reporting criteria for identifying probable SARS cases were also determined. The receiver operator characteristic (ROC) curves analysis was used to determine the cut off points of each score and the areas under the curves were calculated to obtain the best balance between sensitivity and specificity.

RESULTS

Between March and June 2003, a total of 737 people with a history of fever consulted the fever screening centres of emergency departments of tertiary care centres in Taiwan. Among the 484 patients enrolled in the final analysis, there were 22 cases with positive of RT-PCR and 462 non-SARS febrile patients (table 1). The clinical features of these 484 patients are shown in the SARS scoring system (table 2).

Clinical features and patient history fit to the triage stage included six items as two symptomatic factors (dyspnea and diarrhoea) and four historical factors (travel, close contact, hospital contact, and household history). The screening station stage included four items as three CBC factors (leukocytosis, thrombocytopenia, and lymphopenia) and chest radiography.

The above 10 items were identified as predictive indicators to follow the algorithm of management for febrile patients (fig 1). The cut point of the triage score was set at one, dependent upon the six items (dyspnoea, diarrhoea, travel, close contact, hospital, and household history). Out of the 22 RT-PCR (+) SARS patients and 462 non-SARS patients, the triage score was found to respectively have a sensitivity of 81.8% (18/22), a specificity of 73.6% (340/462), a positive predictive value of 12.9% (18/140), and a negative predictive value of 98.8% (340/344).

The cut point of the screening station score was three, with the four items as leukocytosis, thrombocytopenia, lymphopenia, and chest x ray. This score had a sensitivity of 95.5% (21/22), a specificity of 87.2% (403/462), a positive predictive value of 26.3% (21/80), and a negative predictive value of 99.8% (403/404). The rationale of fever surveillance to identify a patient with SARS is based on the triage score, CBC, and chest x ray result. The ROC curves analysis was used to determine the cut off points of each score and the areas under the curves were calculated to obtain the best balance between sensitivity and specificity (fig 2)

Limitations

There are limitations to the present study. Firstly, the predictive ability of the scoring system needs to be validated in other endemic areas. Secondly, the same groups of researchers did not obtain the history of febrile patients. However, all followed our special chart. The questionnaires were designed only based on Yes or No answers. Thirdly, symptoms after hospitalisation were not included in our analysis, although these symptoms may be helpful in making an early diagnosis. Fourthly, other infectious diseases, such as bird flu or influenza, could also affect the predictive ability.

DISCUSSION

Rapid detection of SARS outbreak was needed for timely intervention to limit exposure and to implement prophylaxis. The WHO reporting of confirmed SARS is slow and less sensitive for these purposes, although it remained necessary. Most emergency physicians found diagnosis of SARS difficult according to the WHO criteria.⁶⁻⁷ In addition, although some

Table 1 Demographic data and presenting signs and symptoms of febrile patients with suspected SARS

	Non-SARS (n* = 462)		SARS (n = 22)		p Value
	Mean (SD) or n (%)	95% CI	Mean (SD) or n (%)	95% CI	
Age (years)	55.6 (SD 22.4)	53.5–57.6	38.5 (SD 19.8)	39.7–57.2	0.148
Sex (M/F)	294/168 (63.6)	59–68	11/11 (50)	27–73	0.258
Symptoms					
Cough	102 (21.1)	18–26	7 (31.8)	11–53	0.290
SOB*	24 (5.0)	3.2–7.2	4 (18.2)	6.8–36	0.032
Diarrhoea	32 (6.6)	4.6–9.3	5 (22.7)	3.7–42	0.020
Malaise	10 (2.1)	0.8–3.5	1 (4.5)	–4.9–14	0.400
Myalgia	17 (3.5)	2.0–5.4	2 (9.1)	–3.9–22	0.210
Joint pain	1 (0.2)	–0.2–0.6	0 (0)	0	1.000
Headache	28 (5.8)	3.9–8.2	3 (13.6)	–1.9–29	0.160
Sore throat	49 (10.1)	7.8–13	1 (4.5)	–4.9–14	0.720
Personal history					
Travel	14 (2.9)	1.5–4.6	3 (13.6)	–1.9–29	0.037
Close contact	24 (5.0)	3.2–7.2	6 (27.3)	7.0–47	0.001
Hospital	35 (7.2)	5.2–10	5 (22.7)	3.7–42	0.028
Household contact	7 (1.4)	0.4–2.6	3 (13.6)	–1.9–29	0.008
Laboratory data					
WBC count > 10 ($\times 10^9$ /l)	247 (51.0)	49–58	4 (18.2)	0.6–35	<0.001
Haemoglobin, g/dl	12.8 (SD 4.7)	12.3–13.2	11.7 (SD 2.3)	10.7–12.8	0.318
Platelet count < 150 ($\times 10^9$ /l)	75 (15.5)	13–20	12 (54.5)	32–77	<0.001
Lymphocyte count < 1.0 ($\times 10^9$ /l)	189 (39.0)	36–45	16 (72.7)	52–93	0.004
Initial abnormal CXR†	97 (20.0)	17–25	21 (95.5)	86–105	<0.001

*SOB, shortness of breath.

†CXR, chest x ray.

confirmatory tests, such as real time polymerase chain reaction and measurements of coronavirus antibody have been conducted in many laboratories,* they could not provide instant and correct information for clinicians initially. Therefore, in the absence of effective diagnostic tools during the SARS endemic, syndromic surveillance (such as fever) augments traditional surveillance (such as travel history to endemic area and SARS contact history taking) by monitoring other information to identify a possible SARS outbreak.^{9, 10} In our cohort study, there were four personal histories and two symptoms of the six predictive risk factors. Although many studies demonstrated the array of initial symptoms occurring in SARS patients, such as fever, cough, myalgia, diarrhoea, and dyspnoea,^{5–9, 12, 13} only two symptomatic risk factors—dyspnoea and diarrhoea—were identified in univariate analysis. At the cut off value of one point, the triage scores had a sensitivity of 81.8% and a specificity of 73.6% for SARS. This result revealed that if a patient with fever had any one of the epidemiological histories or symptoms, he should be referred to the fever screening station for further investigation.

By using stepwise risk categorisation, CBC and chest x ray were evaluated at the fever screening station to detect SARS cases further. After calculating the sum of the two stages of scores at the cut off value of three points, the screening station score had a sensitivity of 95.5% and a specificity of 87.2% for SARS. These effective clinical decision rules provided higher sensitivity and specificity than the WHO criteria. According to our 10 item clinical scores and a cutoff value of 3, patients presenting with a total score equal to or more than 3 would be considered as probably having SARS. This predictive scoring system helped our hospital out of SARS transmission and outbreak. In addition, overdiagnosis and stringent isolation and quarantine could be avoided, especially in the lack of adequate isolation rooms. In our study, SARS patients had a higher prevalence of lymphopenia, thrombocytopenia, and lung infiltration in chest radiography as compared to non-SARS patients with fever. The finding of leukocytosis occurred less often in SARS patients. As a result, we suggested that haematological and chest

Table 2 SARS scoring system

Items	OR (95% CI)	p Value	Score
<i>Triage stage</i>			
SOB*	4.1 (1.3–13.0)	0.032	1
Diarrhoea	4.0 (1.4–11.4)	0.020	1
Travel	5.05 (1.3–19.0)	0.037	1
Close contact	6.8 (2.5–19.0)	0.001	1
Hospital contact	3.6 (1.3–10.3)	0.028	1
Household contact	10.3 (2.5–42.8)	0.008	2
<i>Fever screening station stage</i>			
Leukocytosis ($> 10 \times 10^9$ /l)	0.2 (0.1–0.6)	<0.001	–1
Thrombocytopenia ($< 150 \times 10^9$ /l)	6.1 (2.6–14.9)	<0.001	1
Lymphopenia ($< 1.0 \times 10^9$ /l)	3.9 (1.5–10.0)	0.004	1
Initial abnormal CXR†	79.0 (10.5–594.8)	<0.001	2

*SOB, shortness of breath.

†CXR, chest x ray.

Figure 1 Algorithm of management for febrile patients with possible SARS is depicted. ED, emergency department.

Figure 2 The ROC curve of the triage score is shown as a solid line; fever screening score as a dotted line. For the triage score line, the reflection point (cut off value) is at 1, with a sensitivity of 81.8% and a specificity of 73.6%. For fever screening score line, the reflection point (cut off value) is at 3, with a sensitivity of 95.5% and a specificity of 87.2%.

roentgen examination could make the screening process more reliable and suitable in the outdoor fever screening station. By using the model of two stages of a predictive scoring system, all emergency physicians should take our study results into consideration when dealing with this new contagious disease.

A good reporting system and well developed surveillance were paramount to prevent the spread of SARS. Syndromic surveillance was reinitiated in spring 2003 for severe acute respiratory syndrome. According to the WHO case definition and triage advice, we created an ED triage screening tool. This scoring system is simple and useful in both the hospitals and community screening. If the scoring system could be applied in community hospital EDs, the consequence of unnecessary admission and isolation, stringent quarantine, or massive society anxiety could be minimised—even during an outbreak such as the Amoy Garden Outbreak in Hong Kong. Vehicles with portable x ray and complete white blood count machines could be sent to the epidemic areas to screen any possible febrile patients promptly. Early detection and proper surveillance could be achieved by performing current predictive scoring system.

In summary, no matter what kind of novel or contagious disease appears in the future, the SARS scoring system described is easily applicable and highly effective in screening patients during outbreaks. It would be able to identify infectious diseases at an early stage in the absence of other confirmatory diagnostic tools.

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