Commentary

SARS: How to Manage Future Outbreaks?

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Abstract

Severe acute respiratory syndrome (SARS) was an unknown disease barely 3 years ago. After the World Health Organization declared the world SARS-free on 5 July 2003, there were episodic recurrences of SARS between September 2003 and May 2004, including 4 cases of laboratory-acquired SARS. SARS posed a mammoth challenge because of the impact of nosocomial transmission on healthcare manpower and facilities, and the resources needed for controlling and preventing further spread. Through worldwide scientific collaboration, the medical community has made much progress in unraveling its enigma, though much more needs to be discovered. This paper highlights how we can apply our knowledge of its epidemiology, mode of transmission, clinical course, ICU admission, complications, predictors of poor outcome, treatment and infection control to help us avert a catastrophic outbreak, and to manage our resources and patients. SARS preparedness and response planning must be flexible and dynamic so that appropriate measures can be implemented as an outbreak progresses. Even if SARS does not re-emerge, the experience gained from such planning is valuable in preparing for threats of bioterrorism or a global avian influenza A (H5N1) virus pandemic.

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Introduction

Severe acute respiratory syndrome (SARS) is caused by a novel coronavirus (SARS-CoV), which crossed from wild animals at live markets to man in mid-November 2002 in Guangdong, southern China.[1] SARS was the first pandemic of the 21st century.[2]

SARS posed an enormous challenge because of nosocomial transmission, resulting in staff attrition and the closure of "infected" facilities,[3-5] and intense resource requirements for controlling and preventing further spread.[5,6] A co-ordinated and dynamic response by inter-disciplinary groups was essential. Besides clinical services (emergency department, in-patient wards, intensive care units, radiology, laboratory services, outpatient clinics, infection control), the engineering department (air handling systems), the material management department (personal protective equipment) and the public relations department (communication with public and press) had to be involved to effectively bring the outbreak under control.

Epidemiology

The SARS pandemic affected 8096 patients in 29 countries over a short period, from 16 November 2002 to 5 July 2003.[7] Case fatality rates from the 5 worst-hit countries were: China 6.6% (349/5327), Hong Kong 17.0% (299/1755), Taiwan 10.7% (37/346), Canada 17.1% (43/251), and Singapore 13.9% (33/238).

After the SARS pandemic was declared contained on 5 July 2003, there were 17 cases of SARS between September 2003 and May 2004.[8-13] Four cases resulted from laboratory exposure, 2 of whom infected 9 other cases and resulted in 1 death.[8,9,12,13] The source of infection in another 4 cases was uncertain.[10,11]

Rapid access via modern air travel has made our world a truly global village.[1] Every country has an important role to play in keeping our world SARS-free through early, prompt and transparent reporting of SARS-like illness so that immediate appropriate public health actions, such as timely global alerts, travel advisories, border screening at

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immigration check points and heightened vigilance in healthcare facilities, can be taken.[1,8,14] Continued surveillance and strict compliance with guidelines for infection control in SARS laboratories must be enforced to prevent the recurrence of laboratory-acquired SARS.[15]

Transmission

The majority of transmission occurred in hospitals and other healthcare institutions, especially before the diagnosis of the disease and the institution of protective measures.[16] In Singapore, 76% of infection occurred in hospitals or nursing homes, where healthcare workers (HCWs), non-SARS patients and visitors were infected. Hospital transmission accounted for 72% of all cases in Toronto and 55% in Taiwan.[6]

Globally, HCWs accounted for about 21% of patients. Among the 6 worst-afflicted countries in terms of the absolute number of probable SARS patients, the largest percentage of HCW patients were in Vietnam (57%, 36/63), Canada (43%, 109/251), Singapore (41%, 97/238), Hong Kong (22%, 386/1755), Taiwan (20%, 68/346) and China (19%, 1002/5327).[7] These countries were the earliest to be affected by SARS, with the onset of symptoms of the first probable SARS case on 16 November 2002 in China, 15 February 2003 in Hong Kong, 23 February 2003 in Vietnam and Canada, and 25 February 2003 in Singapore and Taiwan. The World Health Organization (WHO) raised a global health alert on an outbreak of a severe form of atypical pneumonia on 12 March 2003 and this new disease was called SARS on 16 March 2003.[17]

Nosocomial transmission from unrecognised SARS patients preceded and was largely responsible for subsequent community transmission. Transmissibility of the virus was highest after 5 days of the onset of symptoms.[18] A 1-week delay in the implementation of infection control precautions would nearly triple the size of the epidemic and increase the expected duration of the epidemic by 4 weeks.[19] Hence, it is crucial to control the outbreak at its earliest stages to ensure that healthcare facilities do not become the epicentres of SARS transmission in any community.[6] Early detection of SARS through HCW surveillance and immediate isolation of new cases are keys to minimising transmission. If HCWs are inadvertently exposed, unprotected, to a SARS patient during aerosol-generating procedures (e.g., cardiopulmonary resuscitation, endotracheal intubation, bronchoscopy, diagnostic sputum induction and open airway suctioning), they should be quarantined for 10 days before they can return to work.[3,6] HCWs with other unprotected exposures need not be removed from patient care but symptom surveillance should be continued. Transmission of the disease has not been documented from asymptomatic and convalescent cases,[20] and subclinical SARS is not an important feature of the disease.[21]

The effective protection of HCWs is of utmost importance, as they are needed to look after the patients. Furthermore, if HCWs fall victims to SARS, there may be tremendous adverse consequences on staff morale and performance. A self-administered questionnaire among frontline HCWs found that 57% experienced significant psychological stress during the SARS crisis. One of the most prevalent fears was the danger to their personal health. Adequate protective facilities and equipment were found to be paramount in alleviating this fear.[22] In an epidemic, healthcare personnel and facilities are already stretched. We must prevent the attrition of healthcare professionals or the closure of health facilities.[4,23]

Clinical Course

The patients are usually hospitalised on the 3rd to 5th days of the onset of symptoms.[4,24-26] Clinical deterioration occurs in the 2nd week, with recovery or death in the 3rd week.[26-28]

Intensive care unit (ICU) admission rates reported by different case series range from 13.8% to 45.5%,[4,24-34] with an estimated average of 20% to 30%.[20] In a complete cohort in Singapore, 20.2% of SARS patients required ICU care,[35] and the maximum daily number of patients in the designated national SARS ICU was 22.[36]

About 13.8% to 26.1% of patients were mechanically ventilated.[20,24,27,29,33-37] Such critically ill patients are usually transferred to the ICU on days 8 to 10 of illness.[4,25,26,28] The median lengths of ICU stay and hospital stay in these ICU patients were 14.5 (inter-quartile range, 7 to 22) days and 23.5 (range, 15 to 36) days respectively.[28]

SARS patients were hospitalised towards the end of the first week of the onset of symptom, and transferred to the ICU in the second week. There was a 1-week lead-time to prepare ICU manpower and facilities, and provide rapid refresher education and training on the use of personal protective equipment (PPE). Strict adherence to infection control practices was essential in breaking the chain of transmission. It is important that such training programmes and mask fitting be carried out during "peacetime."

About 1 in 5 patients required ICU care. This number is helpful in projecting ICU manpower and bed requirement. The number of ventilators required could be projected from the percentage who required mechanical ventilation.

Criteria for ICU Admission

There is a tendency to transfer such ill patients earlier to ICU for closer monitoring so that intubation, when indicated, can be performed electively by fully protected HCWs.[30] Criteria for ICU admission included[4,26,28]

- Clinical: respiratory rate >35/min or progressive respiratory failure,

- FiO_2 requirement >0.5 via face mask,
- Intubation: SpO_2 <90% on 100% non-rebreather mask or respiratory fatigue (rising $PaCO_2$, sweating, tachycardia, tachypnoea, feeling of exhaustion), and
- Inotropic support.

Using the above criteria for ICU admission, 51% to 85% of SARS ICU patients eventually required mechanical ventilation. It is crucial that potential ICU patients be transferred early so that intubation can be done electively, in a controlled and safe environment.

Complications

In the ICU cohorts, at least 80% had acute lung injury (ALI)/acute respiratory distress syndrome (ARDS).[4,25,26,28] Other complications observed in ICU patients included secondary pneumonia (52%),[29] barotrauma (13% to 34%),[4,26,28] septicaemia (26%),[28] deep vein thrombosis (24%),[28] acute renal failure (5% to 20%),[4,25] acute myocardial infarction (16%),[38] pulmonary embolism (15%)[28] and cerebrovascular accident (10%).[39]

Based on the incidence of various complications, we could project the amount and type of medical supplies and equipment needed in an outbreak.

Predictors of Poor Outcome

Children have a shorter and milder illness with good outcomes.[20,40-42] In a Hong Kong case series, there were no fatalities among children but 2 required assisted ventilation.[42] None of the children in Singapore required ICU care and there were no fatalities. There was no evidence of vertical or perinatal infection.[20]

Data from Hong Kong and Singapore estimated that the mortality for patients below 60 years was 8.4% to 13.2%, and 43.3% to 50% for those aged 60 years or older.[24,28]

Predictors for ICU admissions are comorbidities (especially diabetes mellitus and heart disease), advanced age, peaked LDH and high absolute neutrophil counts.[20,27,29] These factors, as well as male gender, APACHE II score ≥15, pulse methylprednisolone, tachycardia and elevated creatine kinase, also predict mortality.[4,20,24,27-30,33,43] Autopsy findings have reported that rising total white counts and neutrophils were associated with clinical deterioration to ALI/ARDS.[38]

Mortality rates of mechanically ventilated SARS patients ranged from 44.8% to 48% at 28 days after ICU admission, and 51.7% at 8 weeks.[4,20] When the ventilated SARS patients were followed till their discharge from the hospital, the mortality rate was 64%.[44] These mortality rates are similar to the mortality rates of ARDS patients requiring mechanical ventilation.[45] Autopsy studies confirmed that severe hypoxaemic respiratory failure in SARS was a form of ALI/ARDS.[33,38,43,46,47]

The global case fatality was 9.6%.[7] Patients usually died or recovered in the third week. In a huge outbreak, when ICU facilities are overwhelmed, withdrawal of therapy may have to be considered in the fourth week for patients with poor prognostic factors who are not improving with intensive care.

Treatment

Randomised placebo-controlled treatment trials were not available because of the sudden emergence of SARS and its rapid spread. As no drug interventions of proven or prophylactic value have been established,[48] treatment is essentially symptomatic and best supportive care.[49] However, pulse methylprednisolone 250 mg/day to 500 mg/day, for 3 to 6 days, has been reported to have some efficacy in a subset of patients with "critical SARS,"[49-52] i.e., critically ill SARS patients with deteriorating radiographic consolidation, increasing oxygen requirement with PaO_2 <10 kPa or SpO_2 <90% on air, and respiratory distress (respiratory rate of 30/min).

Infection Control

Most transmission occurs as a result of direct patient contact or exposure to large respiratory droplets, although airborne spread cannot be ruled out.[6] Standard precautions (Tables 1 and 2) should be practised for all patients in all healthcare facilities to ensure a high level of protection to patients, HCWs and visitors.[53,54] Infection control precautions for SARS in various case scenarios have been detailed by the WHO.[55]

As mask fitting takes time, this should be done for all HCWs upon starting work. The staff should be reminded that tight-fitting masks do not confer effective protection in bearded individuals. Periodic checks on staff proficiency in their use of PPE should be carried out.[56]

Besides respiratory and contact precautions, the Communicable Diseases Centre recommends airborne infection isolation whenever possible for SARS patients. However, in the event of a large outbreak, there may not be

Table 1. Standard Precautions for All Patients[53]

• Hand washing and antisepsis (hand hygiene)
• Use of PPE when handling blood, body substances, excretions and secretions
• Appropriate handling of patient care equipment and soiled linen
• Prevention of needlestick/sharp injuries
• Environmental cleaning and spills-management
• Appropriate handling of waste

PPE: personal protective equipment

Table 2. Appropriate PPE During Procedures and Patient-care Activities that may Generate Splashes or Sprays of Blood, Body Fluids, Secretions or Excretions[54]

• High-efficiency masks where possible; alternatively, use surgical mask.
• Clean, non-sterile gloves when entering patient's room.
• Clean, non-sterile long-sleeved cuffed gown when entering patient's room if envisaging substantial contact with patient, environmental surfaces or items in patient's room.
• Face shield or goggles

PPE: personal protective equipment

enough isolation rooms. One alternative to constructing new airborne infection isolation rooms is the creation of a "SARS unit" where SARS patients could be cohorted (Figs. 1 and 2).

One of the advantages of a dedicated SARS unit is that it would allow the concentration of certain resources and equipment, such as portable X-ray and computerised tomogram machines, thereby reducing the risk of fomite transmission. In the designated national SARS hospital in Singapore, a satellite computerised tomogram scan facility was set up near the SARS ICU. Secondly, SARS patients can be segregated from non-SARS patients and a certain number of staff can be designated to care for SARS patients, reducing the risk of nosocomial transmission to non-SARS patients and HCWs. Lastly, infection control practices, such as the careful monitoring of compliance with precautions and entry screening, would be better carried out and monitored.[6]

Fig. 1. Conversion of the 6-bed high-dependency room into a SARS cohort ICU room. Note the creation of a temporary partition, consisting of swing door with viewing glass window, at the original open entrance. The door remains slightly ajar (arrow) when there is negative pressurisation of the patients' room.

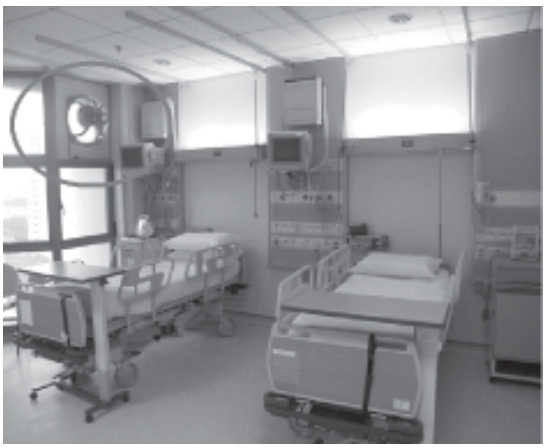

Fig. 2. An industrial exhaust fan (circle) was installed at the window to create negative pressure in the converted SARS cohort ICU.

Banning or restricting visitor access to healthcare facilities, and limiting new elective admissions to hospitals in communities where transmission was occurring helped limit the number of individuals who might have been otherwise exposed to SARS.[6] Staff could also be redeployed from other facilities where activities had been scaled down or closed, to look after SARS patients.

Patients should be educated to practice frequent hand washing, especially after touching their faces. A surgical mask or facial tissues should be used to cover their noses and mouths to help contain respiratory droplets and secretions. Waste receptacles and hand hygiene supplies should be easily accessible.[6]

In the absence of vaccines and effective anti-viral drugs against SARS-CoV, general preventive public health measures are very effective in preventing the transmission of SARS in the community.[14,57] These include:[2,14,36]

- Early case detection e.g., daily temperature monitoring during outbreaks,
- Rapid isolation,
- Effective contact tracing,
- Quarantine of exposed persons,
- Surveillance of fever clusters and atypical pneumonia, and
- A dedicated ambulance service to transport all possible cases to a SARS-designated hospital.

Asymptomatic individuals have not been reported as a source of infection.[20,21] The key to control seems to have been the prompt diagnosis and appropriate isolation of febrile individuals with pneumonia not responding to standard therapy or undifferentiated fever without an alternative diagnosis.[58] The Ministry of Health (Singapore) implemented a post-epidemic surveillance system for SARS in all hospitals and nursing homes on the following:[59]

1. Patients with atypical pneumonia.
2. Patients with persistent unexplained fever >72 hours and travel history to a previously SARS-affected area.
3. Patients who died suddenly with unexplained acute respiratory symptoms.
4. Fever clusters of healthcare staff and patients.

The Electronic Notification System (ENS) was launched on 1 January 2002.[60] This is a web-based application that allows medical practitioners and laboratory personnel to submit on-line notifications of infectious diseases in a rapid and secure fashion to the relevant surveillance agencies. Such real-time notification is especially important in times of disease outbreaks so that prompt and appropriate public health measures can be instituted to control the spread of infectious disease.

Epidemiological surveillance is one of the key components of a cost-effective system of prevention, early recognition and control of healthcare-associated infections (HAIs). The Ministry of Health (Singapore) has also established a system of surveillance and response to HAIs with requirements for reporting by both public- and private-sector acute care hospitals.[61]

International collaboration among the world's scientists, clinicians and public health experts, aided by electronic communications, greatly contributed to our understanding of SARS, in terms of aetiological agent, mode of transmission, clinical spectrum, treatment strategies and outcome.[14] Such rapid sharing of information provides the scientific basis for recommendation of control measures, treatment and adjustment of case definition.

Conclusions

In any infectious disease outbreak, the chain of transmission must be broken to bring the epidemic under control. Otherwise, the expansion of medical facilities can never keep up with the escalating demands. It is important for everyone to practise public health consciousness such as hand and respiratory hygiene, including cough etiquette.[18]

Unrecognised SARS is an important source of transmission in healthcare settings and communities. The world has to maintain its vigilance against the recurrence of outbreaks from environmental sources or laboratories. Global efforts and co-operation are required to control devastating pandemics as our world is miniaturised by rapid air travel.[1,5,14]

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