The Recent Severe Acute Respiratory Syndrome (SARS) Epidemic – A Critical Review

By

Ike SO[1], Chukwuka CJ[1], Ohanu ME[2] and Ofoegbu EN[1]

[1]Department of Medicine, [2]Department of Medical Microbiology, University of Nigeria Teaching Hospital, Enugu

SUMMARY

Severe Acute Respiratory syndrome (SARS) took the world by storm in the later part of February 2003.It is a syndrome characterized by fever, cough, sore throat , shortness of breath and malaise which may deteriorate very rapidly to respiratory failure and death. The symptoms of SARS are quite similar to those of common cold, malaria and respiratory tract infections all of which are common in our environment. SARS, being a new disease, has as yet neither a definite diagnostic test nor treatment. With the international transmission of SARS first reported in March 2003, it became evident that one did not need to travel to contact the disease. Nigerians travel a lot and our fragile health care facilities may not be able to contain an outbreak of SARS. It is quite fortunate that the country's inadequate health care facilities did not have to face the challenge of a SARS outbreak. Despite this, it is important that necessary facilities be put in place in case of a sudden outbreak of SARS or similar epidemics in Nigeria.

Keywords: *Severe Acute Respiratory Syndrome, Epidemic, Review.*

INTRODUCTION

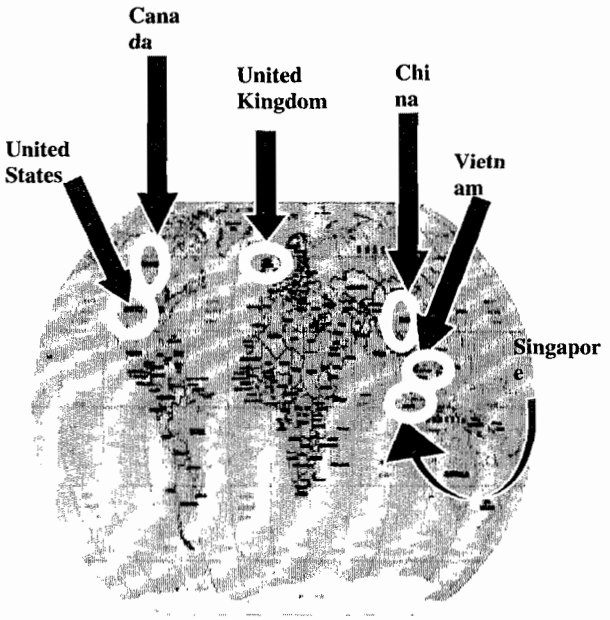

Fig 1: Globally Designated Affected Areas

Severe Acute Respiratory Syndrome is a form of atypical pneumonia which is rapidly progressive and results in hypoxia, respiratory distress syndrome and death in up to 10% of the patients. It is thought to be caused by a corona virus. Initial cases of Severe Acute Respiratory Syndrome (SARS) were recorded in November 2002, in Southern China Province of Guangdong. As at July 3, 2003, when the World Health Organization (WHO) was declaring SARS contained, about 8439 cases had been reported worldwide, fig. 1. It had resulted in about 812 deaths in 29 countries giving a case fatality rate of about 1:11. China alone - Mainland, Taiwan, Hong Kong and Macao Special Administrative Regions - had recorded 7457 cases and 730 deaths (cf 1:11).[1]

The impact of the SARS epidemic on the medical and political world can be captured in the comment of a medical scientist Scott Layne : We are in the age of internet, personal digital

Correspondence Author:
Dr. S.O. Ike, Department Of Medicine
University Of Nigeria Teaching Hospital
Enugu, Nigeria
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assistants, and global positioning devices. We have sequenced the human genome through amazing breakthroughs in science and technology. We also have automated laboratory equipment that can perform the work of thousands of technicians. We have not however, assembled all these readily available parts for the real time surveillance and analysis of new diseases like SARS.[2] The enduring focal lesson from SARS seems to be that whenever unusual disease manifestations are noted, no matter how few, these could serve as pointers to a pattern emerging in the community and should sensitize the clinician to be more alert in reporting the trend. This becomes particularly important as WHO recommends that health care providers should be at alert for a possible seasonal return of SARS.[3]

Global surveillance for SARS instituted by WHO began at the end of February, 2003. The objective was to describe the epidemiology of SARS and to monitor the magnitude and spread of this disease, in order to provide advice on prevention and control. International transmission of SARS was first reported in March 2003 for cases with onset in February 2003. The commencement period of surveillance was then changed to 1 November 2002 to capture cases of atypical pneumonia in China eventually now recognized as SARS.[4]

The surveillance case definitions were based on available clinical and epidemiological data with supplementation by a number of laboratory tests.[5]

SARS is suspected in a person who

1. Presents after 1 November 2002 with history of High fever (>38 ^{0}C); AND
   One or more respiratory symptoms including cough, shortness of breath and difficulty in breathing
2. Died following an unexplained Acute Respiratory Illness (ARI) after 1st November, 2002, but on whom no autopsy had been performed
3. Had close contact (having cared for, having lived with, or having had direct contact with respiratory secretions and body fluids of a person with SARS); Recent history of travel to areas reporting cases of SARS; Residing in an affected area (area in which local chain(s) of transmission of SARS was/were occurring as reported by the National Public Health Authorities)

There is a probable case of SARS if

1. A suspected case has radiographic evidence of infiltrates consistent with pneumonia or Respiratory Distress Syndrome (RDS) on chest x-ray
   OR
2. A suspected case has an unexplained respiratory illness resulting in death, with an autopsy examination demonstrating the pathology of Respiratory Distress Syndrome without an identifiable cause;
   OR
3. A suspected case of SARS that was positive for SARS coronavirus by one or more assays.[6]

A case was excluded if an alternative diagnosis could fully explain the illness.

If an autopsy was conducted and no pathological evidence of RDS was found, the case should be "discarded".

There was a proviso that countries could adapt case definitions depending on their own disease situation.

Although the scourge of the global public health emergency caused by Severe Acute Respiratory Syndrome (SARS) appears to have been contained, the manner of its' appearance, rapidity of spread, case fatality rate, as well as the relative delay in early laboratory diagnosis leave clear learning points for epidemiological surveillance, as well as medical history à la the 1918 influenza epidemic.

The objective of this work is to review the available information on SARS, and to highlight the way forward in case of future SARS and similar epidemics.

CLINICAL FEATURES

The main symptom is fever usually above 38^{o}c associated with dry cough, sore throat, and or shortness of breath. Other usual early symptoms include malaise, body aches,

and headache. These are also the usual symptoms of malaria, common cold, and upper or lower respiratory tract infections. Some patients presented with chest pain (usually pleuritic), rhinitis and productive cough. The features were those of un-resolving rapidly progressing atypical pneumonia. Some of these patients deteriorated rapidly with signs of adult respiratory distress syndrome and hypoxia. These clinical features in a patient who was known to have recently visited areas reporting cases of SARS or was a close contact of someone with SARS, should alert the clinician to the possibility of SARS.

Knowing that close contact includes sitting next to a case or sitting three rows in front of or behind a case in an airplane, makes the problem enormous. Thus at the height of this epidemic, it could have easily spread into several of our towns through one index case who might have been in an airplane with others and they in turn could have spread it to their various destinations without even leaving the country!

NATURAL COURSE/COMPLICATIONS

The incubation period of SARS ranged from 2—10 days at which time the infected person was highly contagious. The patient would be febrile, with flu- like symptoms such as rhinitis, malaise, anorexia, cough and sore throat. These may rapidly progress to severe breathlessness, pleuritic chest pain with deterioration to severe air hunger and death due to respiratory failure in 10% of the patients. The remaining 90% will recover in the first week of the illness.

EPIDEMIOLOGY

The SARS epidemic while it lasted cut across the whole adult population. There was however no reported case of a paediatric SARS. It is not quite clear whether this was due to some form of innate immunity (children being so often exposed to the other infection due to a corona virus –common cold) or merely because for the time it lasted no child was exposed (a remote possibility).

The globally designated affected areas included China, Singapore, Vietnam, United Kingdom, Canada, and United States of America, fig. 2. However, had the epidemic persisted, any country might have been affected because of the ease of traveling around the globe.

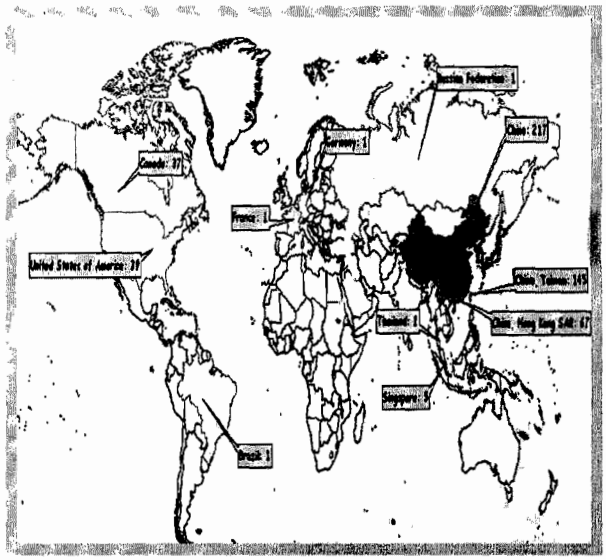

Fig 2: ***SARS: Number of Probable cases as of 3 July 2003 (culled from WHO website)***

Spread of SARS was by heavy (not aerosolized) droplets in close face –to-face contact with patients. Close contact as in having cared for, lived with, or had direct contact with respiratory secretions and body fluids of a person with SARS is also important in transmission of SARS. Close contact includes sitting next to or three rows in front of or behind a case of SARS.

Other routes (example environmental) were entertained, especially during the investigation for the possible cause of a large cluster of SARS cases among residents in the Amoy Gardens Housing Estate in Hong Kong.[7]

Thus improved personal and environmental hygiene would help reduce spread of SARS while overcrowding would increase spread.

AETIOLOGY/PATHOGENESIS

,Data from Global WHO laboratory network involving about 13 laboratories in more than 10 countries consistently isolated a previously unrecognized coronavirus as the causative agent for SARS. This virus was found to cause a cytopathogenic effect (CPE) in VERO cells and FRhK-4 cells, which could be inhibited with serum from SARS convalescent patients.

Electron microscopic pictures and immunofluorescence assays with serum from convalescent patients in cell-culture yielded these coronavirus-like particles.

Human metapneumovirus (hMPV) was found in respiratory specimens and antibodies against hMPV in serum of some SARS patients were regarded as evidence of dual infection with no specific significance for SARS aetiology.[8]

The Center for Disease Control (USA) had sequenced the genome for the coronavirus believed to be responsible for the global epidemic of SARS. The sequence data confirmed that the virus was a previously unknown coronavirus. All of the sequence, except for the leader sequence was derived directly from viral RNA. The genome of SARS coronavirus is 29,727 nucleotides in length and the genome organization is similar to that of other coronaviruses.

Open reading frames corresponding to the predicted polymerase protein (polymerase 1a, 1b) small membrane protein (E) membrane protein (M) and nucleocapsid protein(N) have been identified.

The availability of the sequence data has a positive impact on efforts to develop new and rapid diagnostic tests, antiviral agents and vaccines. It will also facilitate the unraveling of the pathogenesis of this new coronavirus. For now, the pathogenesis is thought to be essentially that of primary atypical pneumonia (PAP) .In PAP the virus can either multiply in the epithelium of the upper and lower respiratory tract damaging the ciliated epithelium or may directly infect the alveoli and cause an intense rapidly fatal alveolitis. Other features of PAP are congested and oedematous lungs, hyperaemic and desquamated tracheobronchial epithelium. There could be myocarditis, pericarditis , encephalitis and polyneuropathy.

DIAGNOSTIC MEASURES

Up to the date of declaring SARS contained worldwide on July 3, 2003 there was still no validated, widely and consistently available test for diagnosing infection with the SARS coronavirus. There was still absence of a rapid and convenient diagnostic test capable of ruling out SARS early in the course of illness, necessitating the retention of clinical and epidemiological basis for the case definitions.[3]

Initial diagnostic measures should include a Chest X-ray ,Sputum gram stain , culture and sensitivity, blood cultures to rule out other possible causes.

Specific tests for the diagnosis of SARS include:

ANTIBODY TESTS using Enzyme Linked Immunosorbent Assay (ELISA) and Immunofluorescence Assay (IFA) would only become positive from the third week of onset of symptoms. By this time the patient may either already be convalescing or is dead

MOLECULAR TESTS Polymerase Chain Reaction (PCR) can detect genetic material of the SARS virus in various specimens (blood, stool, respiratory secretions or body fluids). These tests are very specific but lack sensitivity (so negative test results do not rule out the presence of the SARS virus in patients). Ready to use kits containing primers positive and negative controls have been developed by WHO network laboratories. These are however not readily available.

CELL CULTURES Inoculating cell cultures and growing the virus from specimen such as respiratory secretions, blood or stool, are very demanding tests, though the only means of showing a live virus.[9,10]

TREATMENT

Up to the time the epidemic was declared contained worldwide, no vaccine or other prophylaxis was available. The Global experience was that infection control methods worked well in containing the spread of SARS in hospitals. This includes quarantine for contacts of patients with SARS.

Quarantine for contacts is desirable but may not be feasible in our present day Nigeria. The implication of quarantine strategy is that once a suspected case is identified, all his identifiable contacts in the bus/taxi that brought him to hospital; his home and office contacts should be quarantined! An easier option is to educate the contacts and quarantine them at their various homes. They should be advised to come back to the hospital should they develop any of the symptoms of SARS.

CONTROL AND PREVENTIVE MEASURES

Hospitals should have proper and functional guidelines for the management of SARS patients. All cadres of Hospital staff should be educated on the mode of transmission and the necessity for improved personal sanitation.

There should be a designated SARS waiting room at the point of contact with the patients, for example the General Out Patient or Medical Out Patient Clinics. The staff at these points should be adequately trained to screen patients for SARS. A close-ended questionnaire should be administered to the patients. Those with positive answers should be immediately separated from the rest of the patients into the SARS waiting room and the doctor on duty alerted.

The designated SARS waiting room should be well ventilated, have in stock masks, protective gowns, aprons, gloves, caps, wash hand basins, and running water.

The patient should be assessed by the doctor applying full barrier nursing procedure.

If diagnosed a probable case, the patient will be educated, . masked and sent by a designated ambulance to the SARS isolation facility. Accompanying relatives should be educated and quarantined at home.

The designated ward should be adequately staffed with a team consisting of doctors, nurses, pharmacists, radiographers, laboratory technicians, orderlies - all versed in barrier nursing.

The ward should have:

- Changing rooms for barrier nursing.
- Wash hand basin at every bed side.
- Intensive care facility with Ventilators and piped Oxygen.
- A dedicated laboratory next to the ward.[12]

Treatment is mainly symptomatic **with** empirical therapy against community acquired pneumonia and other symptoms. Thus in our environment, Erythromycin, 2nd and 3rd generation Cephalosporins, and the newer Macrolides would be good choices.

Close monitoring of patients with Oximeters would be imperative so that poor Oxygen saturation will be identified early and adequate treatment instituted.

Anti viral therapy: Oseltamivir, Ribavirin, with or without steroids was a successful treatment modality in many cases.

Mechanical ventilation may be needed in acute severe cases especially if the patient develops respiratory distress syndrome.

Quarantine (Institutional and government based) as discussed above is also a treatment option.

PROGNOSIS

90% of SARS cases usually recovered in 6-7 days[11]. About 10% of the cases progressed to a more severe form of the syndrome.

The Indicators for poor prognosis included

- Age > 40yrs
- Previous existing illness – coronary heart disease, renal impairment, liver disease, diabetes (particularly in Canada)[11]

Mortality among the 10% of cases with poor prognosis was high with the overall case fatality rate at 9%.

WHO Travel Advice[4]

From March 23, 2003 the WHO recommended screening for possible SARS of international travellers departing from places in affected areas, at the point of departure. This subsisted till the containment of the syndrome. This involved answering two or three questions about possible symptoms that a person might have of SARS and about contacts with possible SARS cases. Those with one or more symptoms of SARS and with a history of exposure or who appeared acutely ill were advised to postpone their trips, after assessment, until they felt better.

Individual countries were also at liberty to screen incoming travellers from affected areas with provision for quarantine (where applicable).

LESSONS FROM THE EPIDEMIC

There are as yet many undiscovered pathogens. The onus is on the Medical community to report any unusual pattern of even the common illnesses as soon as they are discovered.

Countries should be encouraged to report any unusual diseases as soon as they occur so that help can be rendered by others where necessary.

The fact that the world is a global village was really brought to fore during the SARS epidemic. Each country knew what was going on in the other countries, and it was thus easy for the WHO to disseminate information as soon as they were available. This aided the quick containment of the epidemic.

If the epidemic had spread to Nigeria, it would have exposed the inadequacy of the health care facilities. Nigeria's borders are quite extensive and porous and routine health checks are usually absent. At the height of the epidemic the Federal Government of Nigeria acquired the instrument to check the temperature of people entering the country from a few of the airports while leaving out the others. The fact of the containment of the epidemic should be seen as an opportunity to prepare adequately for any such recurrence.

Most Teaching Hospitals were mandated to set up SARS committees but there has been no follow up on the report of these committees.

Money should be set aside in the budget for emergencies such as this.

Effort should be made to set up functional and standard laboratories at least one in each geo-political zone.

CONCLUSION

The Severe Acute Respiratory Syndrome (SARS) may have been contained, for now – and we pray for good. It is obvious, however, from the body of knowledge available through the WHO particularly, and other agencies – that there has not been any known specific curative mode for it – except for containment measures. This brings to the fore the high level of suspicion recommended by WHO against a possible seasonal return of SARS.

Here in Nigeria, we should count ourselves fortunate that SARS did not venture into the country except for the solitary case reported by the Federal Ministry of Health. This is because the case fatality rate could have been quite astronomical, since, as highlighted above, there were hardly enough detection and containment measures put on ground.

This may yet be time enough to add to the call for proper equipping of at least a National Centre for Virology to contend with surveillance and mapping of cases such as SARS.

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