Journal of the Egyptian Society of Parasitology, Vol.43, No.2, August 2013
J. Egypt. Soc. Parasitol., 43(2), 2013: 555 – 560

Short communication:

SEVERE ACUTE RESPIRATORY SYNDROME (SARS) CORONAVIRUS: POSSIBLE RE-EMERGENCE OF THE ASIAN-GLOBAL NOVEL THREAT

Generally speaking, there is an observational consensus by Scientists that the potentially fatal viruses of influenza are spreading and behaving more aggressively when they arise again by time to their new mutant forms, like: the pandemic influenzas, swine flu and bird flu. Similarly, this novel coronaviruses seems to be re-arising after a long period of dormancy since 2003 - when it was contained - by crossing countries from the Far East, again. Recently, new cases in China and Saudi Arabia (Middle-Eastern form) are confirmed to be rising and this can be a warning of its re-emergence as a red flag sign or a global alert. Researchers said Middle East Respiratory Syndrome

(MERS) is even more deadly than SARS and is easily transmitted in healthcare environments.

Historically, This mysterious puzzle started without a name, origin ,or cure when, an outbreak of SARS in South China (Guangdong) in November 2002, and the patient, a farmer, was treated in the First People's Hospital of Foshan ,then spread to Hong Kong and nearly became a pandemic, as, within weeks, SARS spread from Hong Kong to infect individuals in 37 countries across all 4 continents (Asia, Europe and the Americas) in early 2003, between November 2002 and July 2003 with 8,273 cases and 775 deaths worldwide (9.6% but can reach 15 % fatality) according to the World Health Organization (WHO).

WHO estimated that the case fatality ratio of SARS ranged from 0% to 50% depending on the age group affected i.e.: Age-stratified ratios were estimated to be <1% in patients < 24 years old, 6% in 25-44 years old, 15% in 45-64 years old, and >50% in elderly > 65 years old .The estimates in Hong Kong were 13% in patients <60 years old, and 43% in those > 60 less than 1% in persons aged 24 years or younger; 6% in persons aged 25 to 44 years; 15% in persons aged 45 to 64 years; and greater than 50% in persons aged 65 years and older .

China had the greatest number (5327) of cases, but its case-fatality ratio was reported as being only 7%. Hong Kong came second with 1755 cases, of whom 17% died. Taiwan, Canada and Singapore followed, and their ratios were 11%, 17%, and 14% respectively .In addition to age, death rates may be affected by other patient factors such as genetic predispositions, the immune status, pre-existing co-morbidities and cardiopulmonary reserve, and by the disease severity which depends theoretically on the viral strain's virulence, viral load and magnitude of the host's immune response. The rates may also be related to other factors such as case selection and volume, facilities and manpower, treatment strategies and regimens.

Areas of the World Affected by SARS: Probable cases of SARS by country, 1 November 2002 -31 July 2003				
Country or Region	Cases	Deaths	SARS cases dead due to other causes	Fatality (%)
China *	5328	349	19	6.6
Hong Kong *	1755	299	5	17
Canada	251	44	0	18
Taiwan **	346	37	36	11
Singapore	238	33	0	14
Vietnam	63	5	0	8
United States	71	4	0	5.6
Philippines	14	2	0	14
Mongolia	9	0	0	0
Macau *	1	0	0	0
Kuwait	1	0	0	0
Republic of Ireland	1	0	0	0
Romania	1	0	0	0
Russian Federation	1	0	0	0
Spain	1	0	0	0
Switzerland	1	0	0	0
South Korea	4	0	0	0
Total	8273	775	60	9.6
(*) Figures for the People's Republic of China exclude the Special Administrative Regions (Macau SAR, Hong Kong SAR) which are reported separately by the WHO.				
(**) Since 11 July 2003, 325 Taiwanese cases have been 'discarded'. Laboratory information was insufficient or incomplete for 135 discarded cases; 101 of these patients died (Source: WHO)				

Epidemiologically, Coronaviruses was known before only to be responsible for simple common cold infections in humans acquired from animals, but this novel forms through molecular: mutations, deletions and recombination; suddenly started and rapidly spreading globally with high morbidity and mortality and without any definitive specific effective treatment. The novel coronavirus was identified as the causative agent of SARS only later on March 2003.

Prognostic Risk Factors: Poor Prognosis more likely with: old age, diabetes, chronic hepatitis "B", and other underlying comorbid conditions, atypical symptoms and elevated LDH (Lactate Dehydrogenase).

The main way that SARS seems to spread directly is by close person-to-person contact and most readily by respiratory droplets (droplet spread) produced when an infected person coughs or sneezes. Droplet spread can happen when droplets from the cough or sneeze of an infected person are propelled a short distance through the air and deposited on the mucous membranes of the mouth, nose, or eyes of persons who are nearby. The virus also can spread indirectly, when a person touches a surface or object contaminated with infected droplets and then touches his or her mouth, nose, or eye(s). Shedding in feces and urine also occurs. Medical personnel,

physicians, nurses, and hospital workers are among those commonly infected. In addition, it is possible that it might spread more broadly through the air (airborne spread) or by other ways that are not now known and needs to be investigated further, right now. Canada and Hong Kong had the most of Clustered cases at that time.

Diagnosis depends through clinical suspicion by exclusion in cases of atypical pneumonias in suspected endemic areas and/or of close contacts to patients presenting with high fever more than $38^{O}C$ ($100.4^{O}F$). Other symptoms may include headache, an overall feeling of discomfort, and body aches. Some people also have mild respiratory symptoms at the outset. About 10 percent to 20 percent of patients have diarrhea. After 2 to 7 days, SARS patients may develop a dry cough. Most patients develop pneumonia. Really, understanding such respiratory illnesses is a challenge as about 40-60% of people with pneumonia will never know what caused the illness, even after much testing. Rapid deterioration in an intensive care setting with intubation and mechanical ventilation in 25% of cases with desaturation after increasing oxygen requirements can be potentially fatal.

The cause of death is mainly from Adult Respiratory Distress Syndrome and Multi-organ failure.

Laboratory Diagnosis: Lymphopenia and possibly thrombocytopenia is likely with elevated Alanine Aminotransferase. High LDH (lactate dehydrogenase) is associated with disease severity and a poor outcome. A RT (Reverse Transcriptase) PCR (Polymerase Chain Reaction Technique) from the nasopharynx in two separate samples as early as the second week, and from serum as early as after one week with diminished sensitivity over time, OR, by an EIA (Enzyme immune assay) for a rising antibody titer, though false positives exist due to Antigenic similarities with other strains of Coronaviruses. Stool samples for PCR remain positive for the longest period of 14 days. Serum and respiratory virus titers as measured by real time RT-PCR correlate higher with worse prognosis. Antibody titers where found high in asymptomatic animal handlers in Southern China.

The imaging by Chest X-Ray can be normal up to an Adult Respiratory Distress Syndrome pattern findings with peripheral mid and lower lung zones, and by CT-scan as diffuse peripheral ground glass infiltrate.

Nowadays, the most efficacious treatment regimen for SARS is still subject to debate. The treatment of coronavirus-associated SARS has been evolving and so far there is no consensus on an optimal regimen for patients with progressive deterioration, intensive and supportive care is of primary importance. In the absence of effective drugs or a vaccine for SARS, control of this disease relies on the rapid identification of cases and their appropriate management, including the isolation of suspect and probable cases and the management of their close contacts. In the great majority of countries, these measures have prevented imported cases from spreading the disease to others, by applying specially regulated infection

control measures and assisted ventilation in a non-invasive or invasive mechanical ventilation when complicated by respiratory failure. It can present with a spectrum of disease severity. A minority of patients with a mild illness recover either without any specific form of treatment or on antibiotic therapy alone.

Currently and unfortunately: due to the lack of long prospective controlled treatment trials only some medications are used on controversial bases primarily in China based on their immuno-modulatory effect like : the trial of a broad spectrum antibiotics on empirical bases early in suspected cases which are known to have immuno-modulatory role as Levofloxacin® (quinolones) or macrolides as Clarithromycin®. Steriods are very controversial and maybe helpful only in some situations. Beta interferon seems promising than Alfa-interferon. Antivirals as: the Ribavirin® (a nucleoside analogue used in hepatitis C), Oseltemavir® (a neuraminidase inhibitor used in influenza A and B), Lopinavir-ritonavir® co-formulation (a protease inhibitor used in HIV treatment), seems all very lacking evidences. Human enriched immunoglobulin and convalescent plasma of recovered patients were also lacking data of strong evidence. Alternative medicine in the form of the traditional Chinese Herbal Medicine was tried and glycyrrhizin, an active component derived from Liquorice roots, are still uncertain.

Prospective potential future treatments rely on developing a vaccine, research on the gene expression profiles and the disease immune profile, advancing the experimental human monoclonal antibodies therapy are all in progress as they may facilitate the diagnosis, monitoring and tailoring of specific immunotherapies

Overall, SARS-CoV comes from the family of viruses that causes the simple common cold in humans. The novel Coronavirus though a relatively rare disease, but mutants are rising and can rapidly spread globally with characteristic rapid deterioration of patients and contacts if not early and promptly managed and contained with proper guidelines and infection control measures and an access to respiratory intensive care centers for assisted ventilation when needed.

Diagnosing those cases is a challenge being a respiratory illness where about 40-60% will never know the microbe even after much extensive testing in cases of pneumonias.

Presently, as of today, cases are rising, during its possible re-emerging phase, most of the nearby countries detected cases so far have been in: Saudi Arabia, where 60 people have been confirmed as having the disease, of whom 42 reported cases have died, those numbers are increasing daily. What about unreported cases who died worldwide or passed undiagnosed due to lack of diagnostic methods, and/or what about transmission by international travellers? This country is hosting millions of pilgrims every year from all-over the world in such gatherings without really able to implement a specialized full infection control process that can help spread that virus easily and it already has spread from the Gulf to France,

Germany, Italy and Britain. Now, Tunisia is a confirmed country to spread the disease. i.e., Global spread is increasing.

The North African (Egyptian) borders represents a potential source or a bridge of infection from the returning travellers to and from the Saudi-Arabian long borders, whom they represent a large number and many of them needs more care and management of their respiratory health arising there or shortly after arrival.

Recommendations

CDC and WHO are the two organizations collaboratively contained the virus before in 2003 but other Authorities are requested for more Collaboration, today. To CDC and WHO websites is a must referral to surveillance guidelines, diagnosis, reporting and public health management of this notifiable illness. CDC had never advised against travel to any region, even during the plague epidemic in Indian in 1994, until the SARS outbreak 2003 which was later lifted over.

On April 22, 2003, even after the cause of SARS was identified as a new coronavirus and the number of cases was leveling off, CDC cautioned about the epidemic, "we have no capacity to predict where it's going or how large it's ultimately going to be…

China, an overpopulated country, where the disease originally started and contained before in 2003, still has re-emergence rising number of cases with fatalities presently, which worth collaboration between Chinese Health authorities, the Saudi-Arabian Health Authorities and the North African Borders (Egyptian) The Public Health Authorities regarding Diagnostic Methods Supply, Standardized Management Protocols by the Quarantine Health Offices a, developing more investigational treatment plans and research projects centers for all aspects of this serious disease.

The greatest risk of the re-emergence of the disease may derive from an animal reservoir or infections transmitted in the laboratory. The appropriate containment measures in diagnostic and research laboratories must therefore be strengthened.

Given the fact that the virus has been isolated before from some animals (Asian palm civet or Musang, or Toddy-cat, *Paradoxurus hermaphrodites* (Pallas, 1777) Order Carnivora. Family Viverridae or "Zabbad Al-Nakheel" (Arabic) used for food in Southern China. The Toddy-cats are widely distributed across South and Southeast Asia particularly India. There are scattered records from Sulawesi, the Moluccas, Timor, and the Aru Islands and they may be present in Papua New Guinea and introduced to Japan in the late 1800s. They occur in a range of habitats up to 2400 m, including evergreen and deciduous forests (both primary and secondary), plantations, suburban gardens, and around human dwellings and settlements. They are nocturnal omnivores, utilizing fruits as a major food source, as well as palm flower sap but also eat all small vertebrates and invertebrates. They are hunted by large cats; like tigers, leopards, reptiles as snakes and crocodiles.

Actually, this animal reservoir was banned by law in Southern China to be used as food since the virus was isolated from its meat in 2003 out-break, and we have to make sure that this law is put into effect.

The active surveillance for clusters of cases of severe respiratory disease must be a priority, especially among health care workers. Such surveillance should include the rapid diagnosis and prevention of other respiratory viruses that cause outbreaks of febrile respiratory disease-notably, influenza.

Surveillance on the part of clinicians is the main key for early detection of any reemergence before it steps back in a community.

Now the questions to be experimentally answered: Are filth flies and/or blood-sucking insect-vectors representing a potential source of infection transmission?

Since the antiviral drugs and steroids are of limited or no value, therefore, no doubt, for human welfare vaccines and experimental monoclonal research being now in a development phase represent the main hope for future specific treatment and thus worth funding for multi-centers investigation.

Vaccination efforts have concentrated on developing antibody (either secretory or systemic, or both) to the surface S glycoprotein, since neutralizing antibody is directed against the receptor-binding portion of this molecule. Still there is controversy about the potential inclusion of the M protein portion as a vaccine component. The following illustrate several vaccines development that is being evaluated: *Macaques immunized with a vaccine constructed of three structural proteins from a prototype strain with adenovirus vectors developed neutralizing antibodies. *DNA vaccine approaches have induced antigen-specific antibody and cellular immune responses, as well as protection in murine models. *Intranasal immunization of monkeys with an attenuated Para-influenza virus that expressed the coronavirus spike protein resulted in no viral shedding after exposure to the coronavirus.

Monoclonal antibody is another potential approach to prevention. Humanized monoclonal antibodies directed at specific portions of the S-glycoprotein have developed singly or in combination to effectively neutralize virus in vitro and prevent infection in animal models. Examples are: *Human monoclonal antibody to the S1 domain of the spike protein led to potent neutralization of the coronavirus in vitro. *Several widely conserved amino-acids in the receptor binding domain in the S1 region of the S-glycoprotein have been identified that are critical in neutralization of the virus. *A combination of two noncompeting human monoclonal antibodies broadened protection in vitro by reducing immune escape.

Best Regards, We are:

HAZEM H. M. KHALIL (email:hazemkhalil@yahoo.com)
HUSSIEN ZAGLOUL KANDEEL (email:hadoki@hotmail.com)
AYMAN T. A. MORSY (email:aymanmorsy72@yahoo.com)