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Review

Severe acute respiratory syndrome (SARS): A Review

[1]Wajiha Yousuf, [2]Kh Javaid Yusuf and *[2]Samia Iqbal

[1]University of Lahore, IMBB Department.

[2]ULTH, Lahore.

***Corresponding Author E-mail: samiaiqbal988@gmail.com**

Abstract

Severe acute respiratory syndrome (SARS) may be a newly emerged disease that rapidly spread round the world. The disease originated in southern China and a completely unique coronavirus (SARS CoV) has been implicated because the causative organism. the trail this virus took to line up human infection remains a mystery, though preliminary datum to origins in an animal reservoir. Nosocomial transmission of SARS CoV has been a striking feature during this epidemic. The clinical illness is analogous to several acute respiratory infections, although an outsized proportion of patients show a rapid deterioration with respiratory distress towards the top of the second week of illness. The management principles are broadly almost like treating any community acquired pneumonia but the infection control measures take a pivotal role. There's no proven antiviral against SARS CoV. The foremost remarkable feature about the SARS epidemic was the speed with which the worldwide community acted during a coordinated thanks to control it.

Keywords: Community acquired pneumonia, coronavirus, epidemic, SARS, SARS CoV, severe acute respiratory syndrome.

INTRODUCTION

The clinical findings of SARS included common symptoms like intermittent watery diarrhea, dyspnea, cough and fever (Lu et al., 2020). Many symptoms of SARS were similar to MERS like severe atypical pneumonia, but there were some distinct differences. In the case of SARS-hCoV upper respiratory tract was infected (World Health Organization website, 2020). SARS-CoV patients showed the cases of an atypical pneumonia. The initial target of SARS-CoV infection were pneumocytes. When infection prevailed and spread; it caused haemorrhagic inflammation in maximum pulmonary alveoli and lead to multinucleated pneumocytes with microthrombosis and capillary engorgement, formation of hyaline membranes alveolar thickening, desquamation of pneumocytes and diffused alveolar damage (Worldometer website, 2020). The situation of almost 60% of SAR-CoV patients worsened during the second week of infection, and showed symptoms of oxygen desaturation, dyspnoea and persistent fever (Al-Tawfiq et al., 2014). Therefore roughly 20%–30% of patients were afterwards taken to intensive care unit, where mechanical ventilation was incumbent for positive tackling of such SARS-CoV patients (Ketai et al., 2006). An astonishing fact discovered during SARS-CoV outbreak that SARS outbreak was not an inclusive risk factor for infants and children (Das et al., 2016). Clinical symptoms were less severe amongst infants. Children's between the age group (1-12) did not demanded mechanical ventilation and intensive care as their condition was controlled one. This presented an opposing scenario observed for other respiratory infections; considered in worst situations thus referred as "age related burden". But though intensive research was made for it but still the hidden biological mechanism remained vague (Das et al., 2017). In SARS-CoV cases lungs were reported as heavy with the weight range of (650–1200 g), confronted along with a mild pleural effusion having clear serous fluid of limit (50–200 ml on each side), widespread consolidation and noticeable pulmonary oedema was recorded. Whereas in some individuals infected with SARS-CoV; focal haemorrhage was observed. But a unique case with SARS-hCoV was dealt having apical pleural adhesion. In this strange case whereas pleuritis was not obvious.

Moreover in other confirmed cases small and mild pulmonary thromboembolism was prominent. In its respiratory tract hilar or Peribronchial lymph nodes were not inflamed (Antonio et al., 2005). While considering these cases histologically, all ill individuals had pronounced structures called as diffuse alveolar damage (DAD) with distinct hyaline membrane formation and pulmonary oedema. In some locations, it was highly noticed that ill individuals had persistent interstitial thickening, with fibrosis ranging from moderate to mild (Chung et al., 2020). Nonetheless an extremely sparse infiltrate of inflammatory cells primarily in histiocytes were seen, including (lymphocytes and multinucleated forms). Whereas enlarged airspaces were observed, as per similar to focal honeycombing fibrosis. In some cases of SARS-CoV; within exudates; Intra-alveolar organization was noted. In other cases inflicted from SARS-CoV; there was granulation tissues development in airspaces and small airways (Chan et al., 2020). These sort of lesions were commonly located in the subpleural region and normally the composition of cells include histiocytes. The assortment of acute inflammatory exudates presented in the airspaces were observed in few confirmed cases of SARS which had already secondary bacterial infection. Atypical pneumocytes were observed in rare cases, even though it showed the focal distribution. These atypical arrangements involved multinucleated giant pneumocytes with nuclei which were irregularly distributed or pneumocytes with granular amphophilic cytoplasm, prominent eosinophilic nucleoli and huge atypical nuclei (Liu and Tan, 2019). Though, prominent viral inclusions were not obvious. Histologically it was analyzed and as a result concluded that the duration of illness had been positively correlated to the degree of interstitial fibrosis (Spearman correlation, $p = 0.019$). Whereas when the extrapulmonary organs were examined, white pulp lymphoid depletion was observed in spleen which was a common observation in all SARS patients. Some patients were detected positive for necrosis of focal individual muscle fiber with recovering changes. Other than this comorbid situations were recorded as another uncontrolled feature (Cheng et al., 2007).

Earlier cases of SARS showed records that proved as somehow transmission was through human to animal contact at various places such as game markets that were live. Suspicions strongly suggested that zoonotic transmission was possible. Animals primarily believed as reservoirs including; raccoon dogs and Palm civets. Nonetheless, gradually when suspected virus was sequenced and data was received; it was concluded that natural hosts of SARS were bats. Therefore SARS-CoV has animal-human and human-human transmission. This disease was included in the list of zoonotic infectious disease. Additionally, SARS-CoV disease could spread through various methods in rare cases such as animals handling through (wild animals preparing, selling and killing). It could even spread through other uncommon methods like fecal transmission and fomites (Chan-Yeung and Xu, 2003).

The eruption of SARS-CoV was most-probably linked and associated with zoonotic transmission occurred within the China live animal markets. Primarily raccoon dogs and himalayan palm civets were detected as animals which could transmit a SARS-like-CoV infection showing 99.8% nucleotide resemblance towards SARS-CoV amongst humans. Furthermore some wild animals were identified within the areas surrounding Hong Kong. Thus from there; the scientists discovered the SARS-like-CoV amongst horseshoe bats (genus Rhinolophus) of China, that showed a sequence homology at the amount 87%–92% to human SARS-CoV (Ramadan and Shaib, 2019). Therefore it was apparently confirmed that horseshoe bats were the reservoir occurred naturally of the ancestral SARS-CoV. Meanwhile civets served as the intermediate amplification host which caused further spread of SARS-CoV to animal handlers within the Guangzhou wet markets. Therefore when individuals were encountered under positive selection pressures within the human host of SARS-CoV infection. This will lead to the condition when infection automatically showed readily transmission as fast and active spread was permitted. This transmission would have been suggested as human-to-human transmission was referred as successive international dissemination by the Hong Kong index case (World Health Organization website, 2020).

The Patients of SARS; when detected through lab diagnosis step of PCR. For this purpose two specimens were enough inclusively nasopharyngeal and stool. If these specimens facilitation or feasibility was not done; then the similar specimen as taken before, was collected once again in accordance with standardized procedures for two or more days during SARS-CoV illness duration. In this case two or more nasopharyngeal aspirates were preferred. For example if neither first or nor second feasibility occurred then third option was there. This option was for PCR technique for which two dissimilar assays or PCR repeats were done by means of original clinical sample for every trial of testing for diagnosis (Wong et al., 2003).

It was initiated by antibody test which was negative. Afterwards positive antibody test was done on sample obtained from convalescent phase. If this initial step did not form feasibility then fourfold or greater amount of antibody should had obtained during the duration amongst acute and convalescent phase for the sera examined and compared (Paul et al., 2004).

Initially cell culture technique was done for isolation purpose from any SARS-CoV specimen. Moreover; PCR confirmation was also necessary afterwards for adequate results.

The proper PCR method should have contained suitable positive as well as negative controls during each run. Then the PCR technique would have able to produce the desired results.

The proper PCR procedure included one negative control specifically for the extraction procedure whereas one water control for the purpose of PCR runs. One positive control solely was essential for extraction as well as for PCR run. One other condition was necessary for PCR that sample of patient must had been spiked along with a weak positive control for the identification of any inhibitory substances. This step was known as inhibition control. If positive results were achieved then further confirmation steps were even required which included the repeating PCR step by the usage of original sample. If this step was impossible to attain then sample should be preferred to be tested in second priority laboratory (Ko et al., 2004). Thus it would had allowed the second genome region to be amplified. This would gave strong confirmation and would had led to increased test specification.

Laboratory diagnosis and treatment of SARS was not applicable in Pakistan. It was earlier calculated that the health care expenditure for one SARS patient in Beijing was 17150 Chinese Yuan (or about US$ 1886). This would be the cost for 2521 cases in Beijing which included the total treatment costs of US$ 4.8 m. The treatment cost ranged from minimum to maximum was US$ (1500-1886). The laboratory diagnosis cost ranged from US$ (36.04-90.09) (Ajlan et al., 2014).

SARS belonged to species of coronavirus that infected mammals, bats and humans. There were several hundreds of strains of SARS-CoV, all of which known to infect only non-human species. The etiological agent of SARS was SARS-CoV (Ooi et al., 2004).

Classification

(unranked): Virus
Realm: Riboviria
Phylum: Incertaesedis
Order: Nidovirales

Family: Coronaviridae

Genus: Betacoronavirus

Subgenus: Sarbecovirus
Species: Severe acute Respiratory Syndrome-related Coronavirus

Morphology

The features of coronavirus family are the one which were dedicated to morphology of the SARS. These characteristics made SARS viruses as spherical, large, pleomorphic particles having bulbous surface projections that made SARS visibility as corona around the particles in electron micrographs. The size of the SARS virus particles ranged from 80–90 nm. The envelope of the SARS virus while shown in electron micrographs looked like a prominent pair of electron dense shells (Chang et al., 2005).(Figure 1)

The envelope of that virus contained a lipid bilayer in which the (S) spike, (E) envelope and (M) membrane proteins were anchored. The spike proteins were responsible for its bulbous surface projections. The spike protein was the structure responsible for interaction with host cell receptor complement. It was the central borne structure helpful in defining the species range, infectivity and tissue tropism of the SARS virus (Chen et al., 2019).

Inside the envelope, there lied nucleocapsid, which was made by multiple copies of the nucleocapsid protein (N), which were bonded to the (~30) kb RNA genome which was positive-sense single-stranded designed in a continuous beads on string style pattern. Altogether the nucleocapsid, membrane proteins and lipid bilayer defended the virus while it was outside the host (Huang et al., 2020).(Figure 2)

Pathogenesis

Pathogenesis was meant for knowing organ and cell pathology as well as viral dissemination specifically SARS. It involved the most recent research with regard to genetic factors, responded to immune system and receptor interaction, which was helpful for the discovery of cure of SARS-CoV. Below, we discussed the complete pathogenesis in result of SARS epidemic (Xie et al., 2020).

SARS-CoV receptors and ACE2

The receptors of ACE2 and receptors other than this like SARS-CoV which was a metallopeptidase, was detected and a resultant confirmed efficient receptor for SARS-CoV (Wang et al., 2020). Furthermore research had concluded that immuno histochemically staining could had revealed the of ACE2 tissue distribution. When the structure of respiratory tract was analyzed through ex vivo experiments; ACE2 had been recognized on the luminal surface of alveolar epithelium and tracheobronchial (Alhazzani et al., 2020). In overall, the outline of receptor distribution in situ hybridization was similar to infected organs and cells confirmed through RT-PCR. Nevertheless, abundant expression of ACE2 had been observed in smooth muscle cells and endothelial cells of various visceral organs. But ACE2 was confirmed absent in the similar organ. Moreover, out of seven vitro ACE2 expressions in intestinal cell lines, one appeared to be vulnerable to SARS-CoV infection

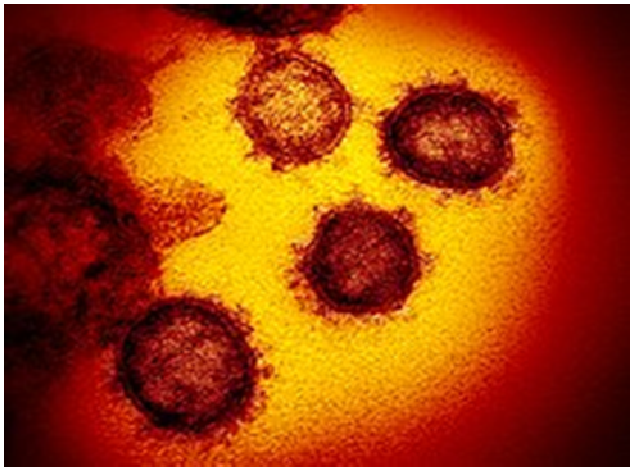

Figure 1. Figure of SARS particle.

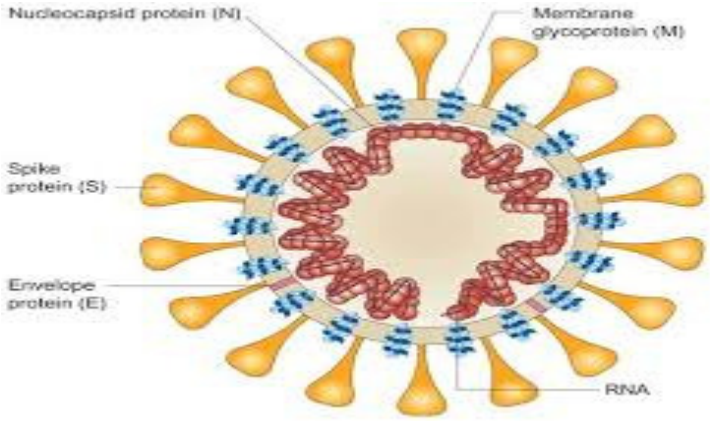

Figure 2. Labelled diagram of SARS.

(Kim et al., 2020). Meanwhile, still, ACE2 was minutely expressed in brain neuronal cells, colonic epithelial cells and immune cells. These observations were reported while making comparisons with confirmed infections cases. These ambiguities lead to conclusion that other mechanisms, co receptors or receptors might took part during the virus and target cells interaction (Mason, 2017). The most recent advanced study through human autopsy had proven that if ACE2 receptors were detected in SARS patients then SARS-CoVs RNA and protein were founded in patients too but these molecules were absent in ACE2-negative cells. Thus we reached to the conclusion by studying pathology that if cells were ACE2 positive then they would had been at risk of developing SARS-CoV infection.

Due to the entrance of SARS-CoV molecules in the respiratory tract epithelium surface, it was observed that this was the most probable and rich location of ACE2 expression other than baso lateral. The primary site of viral departure was apical surface. ACE2 expression in SARS-CoV infected individuals was apparently reliable on proteolytic enzyme cathepsin L. Since in endothelial cells low infection rate was observed; inspite of ACE2 high expression. This feature was due to poor expression of Cathepsin L. Apparently it was assumed that SARS-CoV infection was pH-dependent because cathepsin L was activated at specific pH sensitivity (Bessière et al., 2020).

It was concluded by continuous research on pathology that cathepsin L was variedly expressed on different cell types with respect to difference in viral distribution with justification of ACE2 expression. The alternate SARS-CoV receptors other than ACE2 are dendritic-cell-specific DC-SIGN and Liver/lymph node-specific ICAM3-grabbing non integrin (L-SIGN). L-SIGN expression was largely established in cells of liver sinusoidal and lymph nodes. The IHC is the source of guidelines which suggested that L-sign expression was for endothelial cells and type II pneumocytes. Universally, DC-SIGN expression was seen in specific alveolar macrophages and dendritic cells. Nevertheless, while conducting SARS autopsies of lung tissue, DC-SIGN was specified for expression in

pneumocytes and it was only possible due to SARS infection. In vitro; experiments had confirmed that it did not matter whether cells expression was, L-sign or DC-SIGN, if they were excluding ACE2 then they were only partially or not inclined to SARS-CoV infection. These observations would had led to conclusion that ACE2 receptors were more efficient one as compared to molecules thus were more efficient in causing infection of tolerant cells. Synapse-like structures were responsible for expression of DC-SIGN within dendritic cells. They were meant for transmission of SARS-CoV infection to pneumocytes which were sort of cells particularly vulnerable (Azadeh et al., 2015).

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