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UNDERSTANDING THE VIROLOGY AND THE IMPACT OF COVID-19 STRAINS ON CHILDREN

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Abstract:
SARS-CoV-2 and COVID-19 both are the types of coronaviruses that firstly outbreak in the seafood market of China, in Wuhan. Epidemiological and clinical characteristics have revealed their morphology, pathology, and transmission. SARS-CoV-2 shows a similarity of about 80% with SARS-CoV and 50% with MERS-CoV. ACE2 (Angiotensin-converting enzyme 2) is the receptor of SARS-CoV-2. By comparing both it has been observed that SARS-CoV-2 is the most severe strain with high mortality rate than COVID-19 although the mode of transmission of COVID-19 is much quicker its pathophysiological impact is still limited. Many cases of COVID-19 infected neonatal babies and asymptomatic children were reported. Mothers suffering from COVID-19 could have complications during giving birth as there were chances of vertical transmission of the virus to the new-borns. Children with gastrointestinal symptoms may suffer from severe disorders and illnesses. Laboratory Reports of COVID-19 infected children have resulted in a decreased level of CD8+, and CD4+ T-cells and higher Lactate dehydrogenase (LDH). This article focusing on future primary strategies and recommendations to overcome the percentage of COVID-19 infected children.

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INTRODUCTION:

In December 2019, a group of people got infected with a disease similar to pneumonia in the seafood market of China, in Wuhan. The patient samples were subjected to the laboratory for genome sequencing which later on, identified as Coronavirus infected patient[1]. The virus was studied by the group of the International Committee on Taxonomy of Viruses named CSG (Coronavirus Study Group) which declared it as an acute severe respiratory syndrome and later on, the World Health Organization stated that disease COVID-19 (Coronavirus disease 2019)[2]. About more than 80,000 cases were confirmed till February 2020 and about 2700 deaths were declared worldwide. This alarming situation spread globally so at the end of January WHO acknowledged it as an emergency health issue. As the issue preliminary reported in the seafood market so it was also expected that some animal species transmitted SARS-CoV-2 to humans[3].Coronavirus and toroviruses are the subdivision of the Coronaviridae family. The coronaviruses that are identified till now are further divided into major four different genera which are: alpha coronaviruses, beta coronaviruses, gamma coronaviruses, and delta coronaviruses. Alpha and beta coronaviruses are considered to cause disease in humans through some uncontrolled intermediate source while gamma and delta coronaviruses cause viral infections in animals especially birds and fishes.

Table.1: Classification of Coronavirus

Genera of Coronavirus	Type	Susceptible
Alpha HCoV-OC43,	HKUI, HCoVNL63, HCoV-229E and HCoV-OC43	Humans
Beta	MERS-CoV ,SARS-CoV and SARS-Cov-2	Humans
Gamma		Fish and birds
Delta		Fish and birds

The six types of coronaviruses were identified that cause respiratory diseases in humans out of which four HKUI, HCoVNL63, HCoV-229E, and HCoV-OC43 are of the alpha type and cause mild respiratory disease in humans while rarely cause severe disease in elders, infants, and children. SARS-CoV, SARS-Cov-2, and MERS-CoV are the type of beta coronavirus[4].

SARS-CoV-2 Properties

SARS-CoV and SARS-CoV-2 both are the severe types of all coronaviruses transmitted from bats through palm civet cat as intermediate host[5]. The similarities between all the genomes of strains are about 80% so all of them are interconnected. SARS-CoV-2 shows a similarity of about 80% with SARS-CoV and 50% with MERS-CoV [6]. Studies have revealed that ACE2 (Angiotensin-converting enzyme 2) present on the cell membrane's surface is the carrier of SARS-CoV-2[7]. SARS-CoV-2 envelope spike protein identifies its entry receptor in the human which is ACE2. This spike clasps on the receptor and the host TMPRSS2 protease break it to expose binding peptides which later on bind with the cell membrane and virus[8, 9] . It favorably prefers to infect epithelial cells of the lungs[10].

In human tissues, ACE2 is articulated so when it is assembled with SARS-CoV-2 it has a diverse influence on the small intestine, lungs, heart, adipose tissue, thyroid, and kidneys[11, 12]. The infection caused by SARS-CoV-2 might show no symptoms or cause little manifestation in the cells of human organs[13, 14]. After the entry into the host cell, SARS-CoV-2 released its RNA into the cytoplasm and takes control over the host's machinery, and started to translate its sequence of nucleotide and, replicate[15]. Studies have revealed that patients susceptible to COVID-19 during their second week of infection suffered CRS (cytokine storm or cytokine release) in their blood that travels through their capillaries, veins, and heart. After 8 days of being susceptible acute cytokine storm is observed which put down the patient towards ventilation elevating its inflammatory factors including interferon γ, tumor necrosis factor α, interleukin γ, IL-5, IL-1β, MCP-1, and IL-8 along with anti-inflammatory factors including IL-10, IL-IRA[16]. Multiple organ failure and ARDS (acute respiratory distress syndrome) are caused by elevated IL-6 inflammatory factor[17]. The main cause of transmission is the respiratory tract as the droplet excreted from the infected patient transmits disease within the incubation period of 2-14 days to a healthy person by directly interrupting its mucous membrane[18]. The fundamental precaution to be taken is hand hygiene, wearing protective tool kits and social distancing. The symptoms observed during the incubation period are cough, fever, sore throat, fatigue, headache, gastrointestinal issues, conjunctivitis, and slight dyspnoea. Chloroquine or

hydroxychloroquine like antiviral medications and respiratory therapy are deliberated as the prime treatments for this disease until the vaccine is not discovered[19]. PCR tool is used to check the samples of the infected patients using bronchoalveolar lavage, tracheal aspirate, and nasal swab. For follow-up and diagnosis, computed tomography results should be considered[20].

SARS Co-V-2 and Aging

The studies revealed that the chances of severe COIVID-19 have been observed in the patients of older age as in the level of interferon γ, tumor necrosis factor α, and lower lymphocyte cell count[21, 22, 23]. The majority of the older age reported cases, were at a time combating with many other diseases about 20% were suffering diabetes,9% coronary heart disease, and 31% hypertension[24]. In older individuals, inflammaging and immunosenescence are preferred as the root of diseases and infirmity[25]. The immunosenescence is the stimulation of the immune response of the person to find a treatment which in older age patient ultimately results in loss of adaptive immune functions while inflammaging is the production of low-grade mediators of inflammation[26]. Both inflammaging and immunosenescence resulted in severe COVID-19 in older age patients. In the developed countries people have major concern towards age profiling and anti-aging drugs so the chances of being susceptible could be reduced[27, 28].

Epidemiological Comparison of SARS and COVID-19

Children suffering COVID-19 had a clear history of being in contact with the infected community while SARS susceptible children had a vibrant history of exposure and were intermittent. Studies revealed the statistical analysis which declared that about 27% of children suffered from COVID-19 and had direct contact with the infected community. Newborn also developed SARS and COVID-19 through mother to baby[29]. The mode of transmission is quite negotiable as some studies have revealed that SARS is transmitted through aerosol which contained digestive tract and virus[30] while other studies revealed that fecal-oral mode of transmission should not be remained unnoticed as some tests showed positive nucleic acid feces test[31]. Although no case has been reported to be transmitted through the digestive tract transmission is quite noticeable in mother-to-baby transmission.

Clinical Analysis and Case Study

The studied cases have declared that newborn babies can be prone to COVID-19 showing common symptoms like cough and fever which were less severe than SARS. The comparison of COVID-19 infected new-borns and SARS infected young children showed that the former had lower outcomes than the latter. This declared that as the age increase the impact of SARS became severe. In some cases, it has been observed that children suffering from gastrointestinal infection symptoms showed severe conditions[32]. In China, in Guangzhou, one death case of a child was reported who was suffering from SARS. The child was suffering from hepatitis about two months ago before being susceptible to SARS. The major cause of his death was declared that the doctor who was treating him was also attending a SARS patient so, within 70 hours the child died[33]. Two other cases of children were reported in China of which one was 10 months old child and the other was 14 years old both of the children died from COVID-19. The former case was a severe case of COVID-19 which led to multiple organ failure. The preliminary symptoms were vomiting and diarrhoea which resulted in sepsis, shock, acute renal failure, and acute respiratory syndrome which ultimately resulted in death within 4 days[34]. When the nucleic acid test was performed out of four 3 were positive furthermore the child who died had no family history of being infected and not even showed symptoms. From this case, it is evident that SARS can have asymptomatic transmission[35]. It is cleared that children who are immunocompromised and immunosuppressant were more vulnerable towards SARS and COVID-19

Neonatal Case Study

There is a less chance of vertical transmission of COVID-19 but still, there were reported three neonatal cases. One died after the mother and caretaker were tested positive, one died within 5 days of his birth as the infant had a fever while the third one died because during pregnancy his mother got susceptible to COVID-19, and within 30 hours of his birth his nucleic acid test result positive[36]. There are rare cases of vertical transmission; the new-born whose mother is susceptible to COVID-19 suffered antagonistic reactions which include respiratory distress, preterm delivery, fetal distress, and even death can occur. The efforts should be made by a multidisciplinary team in the labor room so the survival rate of neonatal could be increased.

Screening Tools of SARS and COVID-19

The individual suffering from SARS and COVID-19 suffered some internal changes which include decreased lymphocytes, malfunctioning of liver, decreased WBCs, and lower cardiac biomarkers. The comparative studies have shown that COVID-19 infected children have higher C-reactive proteins for

SARS infected children[37]. SARS severity and death are interconnected with high lactate dehydrogenase, a higher percentile of neutrophils, and decreased T-cell[38]. COVID-19 infected children also show a substantial reduction of T-cells therefore care should be taken clinically to monitor the biochemical pointers warning at the early stage to avoid the severity.

Pulmonary Imaging of COVID-19 and SARS Infected Children

In the early stages of COVID-19 and SARS disease, the assessment of pulmonary diseases wasn't specified therefore whenever being compared, children suffering COVID-19 and SARS exhibited normal pulmonary functions. It was reported that children infected with COVID-19 haven't shown any symptoms but significant radiographic changes have been recorded while SARS infected children showed unembellished radiographic pulmonary changes along with minor symptoms[39]. It indicated that pulmonary imaging is not a reliable source as the patients were susceptible to the virus but still their X-rays were normal. Chest Computerized Tomography is a more advanced and practicable detection method to improve pulmonary screening.

Treatment Comparison of SARS and COVID-19

Long term studies had reported that adults suffering from SARS shown avascular necrosis AVN of the femoral head in which the supply to bones is interrupted along with pulmonary fibrosis and lungs malfunctioning due to usage of high doses of hormones[40]. The recent report has declared that the usage of corticosteroid hormone as the treatment of COVID-19 should be prohibited as many SARS infected patients were also treated with hormones[41]. To estimate the most operative evidence-based treatment modality, precisely structured randomized clinical trials are required

Immunity

The covid-19 and SARS infected children have reported a significant decrease in the CD3+, CD4+, and CD8+ T-cells in the blood. This interpreted that the immunity of COVID-19 and SARS infected children has been drastically decreased. For an effective diagnosis, further detailed mechanisms need to be investigated. A powerful intrinsic immune system with the potential of antiviral activity named Interferon alpha-beta system (IFNα/β) was introduced but the studies had revealed that SARS blocked the IFN system and also inhibits its regulator efficiently so that IFN system may not be functional and prevent the production of antiviral interferon[42].

Transcription Protein Factor

When the SARS-CoV directly attached with IKK (Ilapak kinas complex) the activity of transcription protein kappa B inhibited which depressed the expression of COX-2(cyclooxygenase 2), which later on interrupted the normal functioning of inflammatory responses and immunity of the body[43]. While the COVID-19 mechanism still needed to be clarified because there are still many queries the probability of all organs to be impaired is equal as ACE2 is equally distributed to lungs, kidney, and intestinal tissues but only lungs tissue damaged whenever the child is susceptible towards COVID-19. Still, there are so many questions related to COVID-19 infecting children that need to be studied clinically.

Discussion and Potential Reasons

The studies have shown so many similarities and differences between SARS-Co-V and COVID-19 observed during clinical treatments and epidemiology. The potential reasons of transmission that have been reported are: 1) because of the mild symptoms children are more susceptible to be infected 2) SARS-Co-V-2 has unique characteristics and morphology 3)false nucleic acid test was reported for nucleic acid detection 4) children who were not showing any symptoms but still got infected which declared that asymptomatic children were ignored. COVID-19 infected children showed mild symptoms of infection, mild pulmonary imaging, the potential reasons understood by the researchers are: 1) children T-cells cross-reacted with SARS-CoV-2 infection as children have more memory T-cells 2) because children are in the developing stage so their body immunity is still developing and defend them inadequately which resulted in less host damage 3) vaccination made body immunity respond more efficient

Future Aspects

Pediatricians have suggested some provisions after a detailed study of COVID-19 and SARS-CoV-2 which concluded that: 1) the transmission of the virus in children with mild symptoms or asymptomatic should be accentuated 2) COVID-19 infected perinatal pregnant woman should be isolated and multidisciplinary team should make sure the survival chances of newborn 3) multidisciplinary approaches should be considered to treat and diagnose COVID-19 infected children 4) Chest computerized tomography should be considered as a more reliable detection method for pulmonary imaging 5) educate people and children about COVID-19 and SARS-CoV-2 and take all precautions especially the use of tool kits and covering of face 6)the extensive use of

hormones should be prohibited. Studies have revealed that during these pandemic young children were also suffering from depression, anxiety, and stress, and that needs to be addressed. Furthermore, still more clinical trials and research is required to study the impacts of COVID-19[44].

CONCLUSION:

Countries that lack pediatric patient data need to state the sternness of disease and its clinical physiognomies as there is inadequate statistics on COVID-19 infected children. China was the first, who got infected with this virus and has improved its evolvement towards the war of COVID-19 but still, there are so many countries that are still trying to control this virus. From clinical characteristics and epidemiology this article, potted the similarities and differences of COVID-19 and SARS infected children. The suggestion provided could help other countries to control and develop all possible preventive strategies to overcome this COVID-19 and SARS.

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