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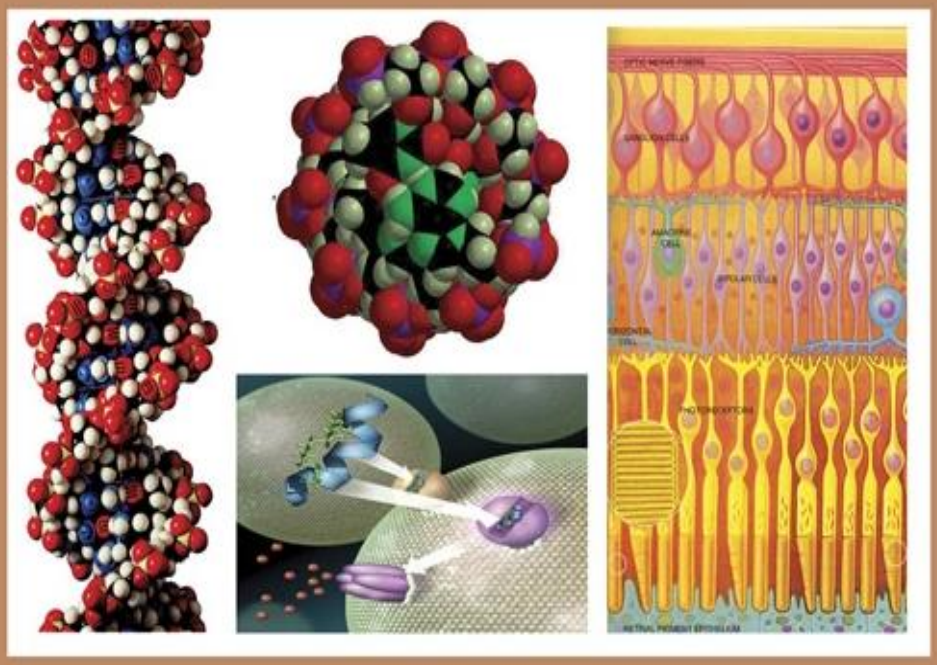

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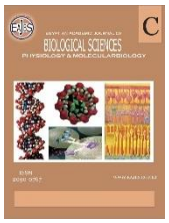

Mini Review; Role of Changes in SARS-CoV-2 Spike Protein and Its Human Interaction

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ABSTRACT

The world has been in a state of a pandemic for more than a year, and humanity is suffering great losses. Millions of people have died, and countries have been in proper lockdowns to stay safe which has led to greater economic and social loss. the virus that turned the world over is referred to as the SARS COV 2 virus commonly known as the coronavirus. The Aim of this review was to determine the mutation(s) in the sequence of the spike protein of the SARS-CoV-2 that might be favoring human-to-human transmission.

INTRODUCTION

The world has been in a state of a pandemic for more than a year, humanity is suffering great losses. Millions of people have died, and countries have been in proper lockdowns to stay safe which has led to greater economic and social loss. the virus that turned the world over is referred to as the SARS COV 2 virus commonly known as the coronavirus. Coronaviruses are RNA viruses that can infect animals and humans, causing respiratory and intestinal infections. SARS-CoV-2, MERS-CoV, and a new coronavirus (SARSCoV2 [2019nCoV]) are all members of the Coronaviridae family and the Beta coronavirus genus. SARSCoV2 is currently being studied in greater depth. It is known that it's not the virus that interacts directly with the human gene and causes the infection, but the spike protein of the SARS-COV-2 virus that binds the human gene and leads to the infection. This study will focus on the interaction between the spike protein and the human gene which is resulting in such an infection. As there have been multiple studies by now and vaccines being introduced in the market as well, the virus is well studied but new strains of the virus are evolving causing more severe infections and leading to more deaths. This study will be based on the analysis of these evolving strains, the primary strain, and how they have evolved in causing more lethal infections. As there have been multiple studies by now and vaccines being introduced in the market as well, the virus is well studied but new strains of the virus are evolving causing more severe infections and leading to more deaths. This study will be based on the analysis of these evolving strains, the primary strain, and how they have evolved in causing more lethal infections.

The serum will be collected from participants and the questionnaire will be constructed including demographic data, camel breeding status, previous affecting with MERS cov, signs and symptoms present, duration of illness, and management during hospital staying and after release treatment. The sample size will be calculated according to the software available for this issue. Ethical approval will be obtained from the university of Hail ethical committee, and all participants will be asked to sign ethical consent. Data will be analysed using SPSS software.

KEY Words; COVID-19 (Coronavirus disease), SARS-COV-2, Vaccine, RBD (receptor binding domain), Human angiotensin-converting enzyme (ACE2) receptor

Literature Review:

The recently emerging infectious disease known as Coronavirus is spreading across the world at an increasing rate. COVID-19 (Coronavirus disease) has become a global pandemic. The virus itself was discovered to be caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This belongs to the β coronavirus family. Currently, it is known as the 7th coronavirus that had affected or infected humans, with four of these 229E, NL63, OC43, and HKU1 known to have very mild symptoms of a cold. The remaining three, SARS-CoV, SARS-CoV-2, and MERS-CoV can cause severe symptoms and can further be fatal. The fatality rate for SARS-CoV and SARS-CoV-2 is 10% and 5%, respectively with the highest fatality rate of 37% is accounted for MERS-CoV (Huang *et al.,* 2020; Akisawa *et al.,* 2021).

Since the scale of the global epidemic is rising and there is a prediction that the number of infected persons can reach up to 1 billion shortly. Hence, a huge number of studies and clinical trials had been launched on COVID-19 to treat it. Recent vaccination programs have been able to reduce the effect by a specific percentage, however, there is no evidence from the current outcomes that can fully treat COVID-19 and stop the spread of the epidemic. Therefore, it can be said that the vaccination program needs to focus on developing specific therapies for COVID-19 that can target various SARS-COV-2 proteins under development which is discussed later.

DISCUSSION:

The SARS-COV-2 is a single-stranded RNA-enveloped virus, in which the metagenomic next-generation sequence approach had been applied to characterize the entire genome. The bp in the length is 29881 followed by encoded 9860 amino acids. The gene fragments express structural and non-structural proteins where the S, E, M, and N genes encode the protein structure, and the non-structure proteins like 3-chymotrypsin-like protease, RNA-dependent RNA polymerase, papain-like protease, are often coded by the ORF region.

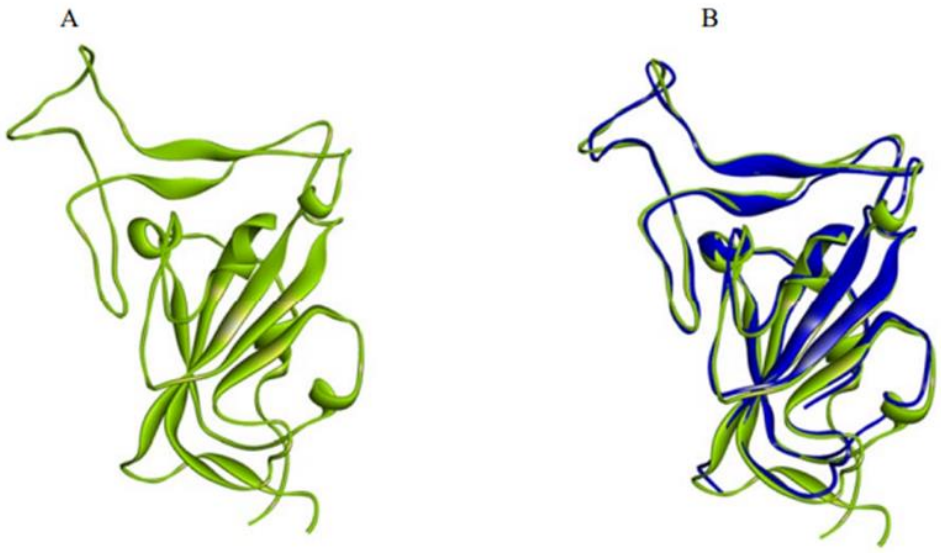

Fig. 1: Spike protein of *Rhinolophus sinicus* (A) and the merge between spike of *Rhinolophus sinicus* and SARS-CoV(B).The merge image show a high level of structural similarity in both protein, suggesting a similar pattern of interaction with the receptor.

A huge number of glycosylated S protein cover the surface of SARS-CoV-2 and can in fact bind to the host cell receptor known as angiotensin-converting enzyme 2 which mediate the viral cell entry. As soon as the S protein binds with the receptor, the TM protease serine 2, which is a type 2 TM serine [protease located at the host cell membrane would allow the virus entry into the cell and then activate the S protein. As soon as the virus had entered the cell, the viral RNA is released and the polyproteins are then translated from the RNA genome, and transcription and replication of the viral RNA genome occur by the protein cleavage and also from the assembling of the replicase transcriptase complex. Furthermore, the viral RNA is replicated and the structural proteins are further synthesized, packaged, and assembled in the host cell, after that these viral particles are released.

Moreover, these proteins are quite crucial to the viral life cycle and often provide potential targets for any drug-related therapy. The SARS-CoV-2 S protein is highly conserved in all human coronaviruses and is also involved in reception recognition, the virus's entry to the host cell, and viral attachment. Because of their indispensable function, it represents one of the vital targets for the COVID-19 vaccine and its therapeutic research.

The S protomer in the virus consists of S1 and S2 subunits where S1 is used to mediate binding to the host cell receptor and S2 is used for the fusion of the viral envelope. Furthermore, the RBD (receptor binding domain) of the S1 goes through a large rigid body motion to bind with the ACE2. However, in the closed state, all the RBDs of the S trimmer are facing the downward position which makes the binding surface inaccessible to the ACE2. Switching any of these RBDs into a semi-open intermediate is quite capable to expose the binding surface of ACE2 and hence, stabilize the RBD in the up position where it can attach and bind itself again (Priya & Shanker, 2021).

Octenyl, the reason by which this virus becomes more dangerous is when the S protein binds to the human angiotensin-converting enzyme (ACE2) receptor, as mentioned before. These binding generate homodimer integral membrane protein that is present in the epithelial cell of vital organs such as the intestine, lungs, heart, and kidney. Furthermore, the ACE2 protomer consists of the N-terminal peptidase domain (PD), which binds with the RBD of the S protein using the serine protease that can separate the S1 and S2 subunits. The latter

exposes the fusion peptides that insert the host membrane and allow for the fusion of the viral membrane.

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