LITERATURE REVIEW

On 31st December 2019, Wuhan health commission in the Hubei province of the Republic of China notified the National Health Commission, China CDC and WHO of a cluster of 27 cases of pneumonia of unknown etiology [1]. These patients presented with a constellation of symptoms such as fever, dyspnea, dry cough, and radiological findings showed bilateral lung glassy opacities. Furthermore, the public health office traced all these 27 cases to Huanan Seafood Wholesale Market which trades live species of bats, snakes, pangolins, and badgers [1]. Multiple intrinsic variables led to rapid early transmission dynamics, and this made Wuhan the flashpoint of the pandemic. In 2018, Wuhan had a documented population of 11.08 million, this made Wuhan one of the top five most populated cities in China [2]. Wuhan's large population density and proximity of the marketplace that sold live animals made it the epicenter for the human-animal interface. Additionally, the lack of early containment due to the inability to accurately trace the history of exposure in the early patient cases contributed to the rapid rate of spread in Wuhan. This eventually precipitated into the WHO declaring this viral pneumonia as an outbreak on 30th January 2020. On 11th March 2020, due to the global logarithmic expansion of the cases the coronavirus disease 2019 (COVID-19) was declared as a pandemic by the WHO.

SARS-CoV2 is from the beta Coronavirus family, it is a positive-sense, single-stranded RNA, enveloped virus that is 50-200 nm in diameter [3]. The genomic RNA is 30 Kb, one vital encoded structural protein is the Spike Glycoprotein (S) that consists of three S1-S2 heterodimers that bind to angiotensin-converting enzyme 2 (ACE2) receptor on type II pneumocyte [3,4]. The other surface protein such as the hemagglutinin-esterase (HE) dimer is shown in Figure *1*. The entry of SARS-CoV-2 into the type II pneumocyte is via endocytosis and then multiplies in the cytoplasm. The high protein manufacturing stress induced upon the type II pneumocytes leads to apoptosis. Additionally, the RNA from the SARS-CoV-2 acts as a pathogen-associated molecular pattern (PAMP) and will be recognized by the pattern recognition receptor or toll-like receptors. This leads to a chemokine surge which causes neutrophil migration and activation. This leads to the destruction of the alveolar-capillary walls. At a microscopic level, this leads to a loss in the interface between the intra-alveolar space and the surrounding stroma. Therefore, fluid leaks through and fills into the alveolar sacs.

The origin of the SARS-CoV-2 genome has been linked to bats akin to the SARS-CoV-1 and MERS-CoV viruses [5]. Interestingly, the SARS-CoV-2 whole-genome aligned with the genomes of viruses (Bat-CoV and Bat-CoV RaTG13) in

Rhinolophus affinis species of Yunnan province with 96% similarity [6]. As seen previously in SARS-CoV-1 and MERS-CoV viruses that undertake residence in the intermediate hosts shown in Figure *2*, it was suspected that in SARS-CoV-2 pangolins were the natural reservoir. This was based on the analysis of the genome contig alignment of SARS-CoV-2 like CoV (Renamed: Pangolin-CoV) harbored in the lung tissue of two dead Malayan pangolins [7]. This Pangolin-CoV's whole genome had 91.02% similarity with SARS-CoV-2 and 90.55% similarity with Bat-CoV RaTG13 [8]. Proteomic analysis revealed that the S1 subunit of Spike glycoprotein (S) was more closely related to that of SARS-CoV-2 compared to BaT-CoV RaTG13. Furthermore, five amino acid residues of the S protein of SARS-CoV-2 interacting with the ACE2 receptor are identical in Pangolin-CoV [8]. Contrastingly, only four amino acid residues are identical in the S protein of BaT-CoV RaTG13. Interestingly, both Pangolin-CoV and BaT-CoV RaTG13 have lost the furin recognition motif, vital to the S1/S2 cleavage [8]. This putative furin recognition sequence is still intact within the SARS-CoV-2. A compilation of all these findings portrays that pangolins are the intermediate hosts for SARS-CoV-2.

Modes of transmission traced in an imported case are through droplet transmission, fecal-oral route, conjunctiva and fomites [10, 11]. Additionally, local transmission can be traced back to the patient's bodily fluids such as respiratory droplets, saliva, feces, and urine [11]. The virion is stabilized at lower temperatures, i.e., 4°C has higher survival than 22°C [12, 13]. As SARS-CoV-2 virions are shed throughout the clinical course, patients with COVID-19 can spread the infection prior to symptom presentation, during the symptomatic course and during the clinical recovery period. Additional considerations must be made regarding the residence time of the SARS-CoV-2 virion on surfaces. The half-life of SARS-CoV-2 in aerosols, copper, cardboard, stainless steel, and plastic are 1.5 h, 1 h, 3.4 h, 5.6 h, and 6.8 h, respectively. The viable residence time of SARS-CoV-1 in aerosols, copper, cardboard, stainless steel, and plastic are 3 h, 4 h, 24 h, 48 h, and 72 h, respectively [14].