

## Maximum Possible Efforts by which we will Win Over this Deadly Pandemic of COVID-19

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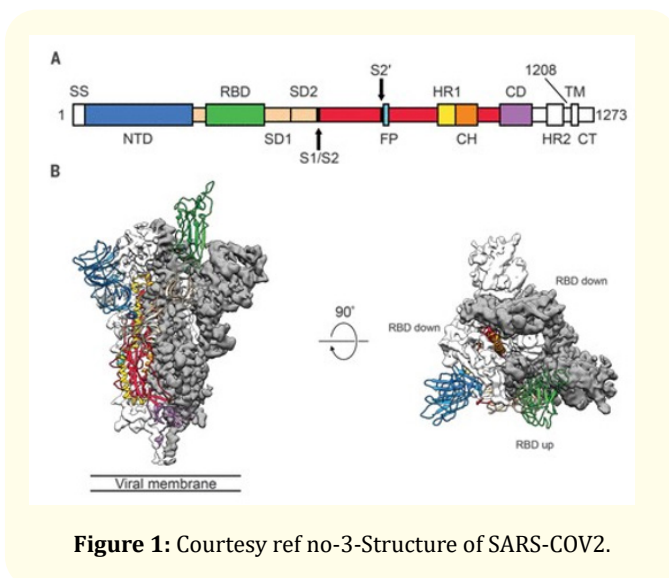
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Currently we are amidst the worldwide pandemic of a new type of Coronavirus (COVID-19) that is going on, and originated from Wuhan, China and has now spread to 140 other countries including Japan, Korea, Italy, USA and UK. The World Health Organization (WHO) declared that COVID-19 has assumed pandemic proportions, causing severe respiratory tract infections (RTI) in humans. Doubtfully this originated from bats and somehow mutated and adapted human transmission [1]. Structurally it is similar to SARS-CoV with The spike (S) glycoprotein of the Corona viruses being a class I viral fusion protein present on the outer envelope of the virion having a key role in viral infection by recognizing host cell receptors and modulating fusion of the viral as well as cellular membranes [2]. The Coronavirus S glycoprotein gets synthesized as a precursor protein made up of ~1300 amino acids which then gets cleaved into an amino (N) terminal S1 subunit (~700 amino acids) as well as carboxy (C) terminal S2 subunit (600 amino acids). 3 S1/S2 heterodimers assemble to develop a trimer spike that protrudes via the envelope. The Cryo-EM structure of the 2019-nCoV spike in the pre-fusion conformation is demonstrated in figure 1 [3].

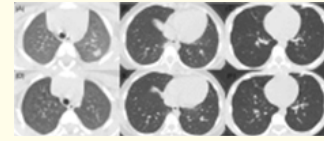
For diagnosis Rapid and proper finding of COVID-19 is important to control outbreaks in the community as well as in hospitals [4]. Mainly Laboratory examination includes nasopharyngeal as well as oropharyngeal swab tests. For identification of patients, by RT-PCR [1]. The commonest symptoms were fever, cough, expectoration, headache, myalgia or fatigue, diarrhea and haemoptysis. Some people might experience Severe acute respiratory syndrome (SARS). Other organs are also susceptible to COVID-19. The single cell RNA-seq data was utilized for evaluating angiotensin converting enzyme 2 (ACE2) expression for telling the potential risk of various human organs to COVID-19 infection. COVID-19 uses the same cell entry receptor like SARS-CoV, ACE2, that regulates both cross-species as well as human-human transmissions. COVID19-infection should be diagnosed with typical chest computed tomography (CT) characteristics in spite of negative RT-PCR results [5]. Of 1014 patients, 59% had RT-PCR positive, while 88% had positive chest CT scans [6]. Coronavirus belongs to the Corona viridae family; hence it does not come as a surprise those imaging findings, which are similar to those of SARS-CoV2 as well as MERS-CoV [1]. Typical CT findings are bilateral pulmonary parenchymal ground glass and consolidative pulmonary opacities, sometimes with a rounded morphology and peripheral lung distribution [1,5]. But in pediatric patients (Figure 2 and 3), Procalcitonin elevation and consolidation with surrounding halo signs were common which were different from adults. It is suggested that underlying coinfection may be more common in pediatrics, and the consolidation with surrounding halo sign which is considered as a typical sign in pediatric patients. Further for investigating the occurrence of olfactory and gustatory dysfunctions in patients with laboratory confirmed COVID-19 infection and further faecal dissemination was proven [7]. Lechien, et al. added in European study, the sudden anosmia or ageusia need to be recognized by the international scientific community as important symptoms of COVID-19 infection [8]. Further Solaimanzadeh, with point of view of early treatment differently, with a perspective on pathophysiology, he tried to emphasize the problems in COVID-19 related to another respira-



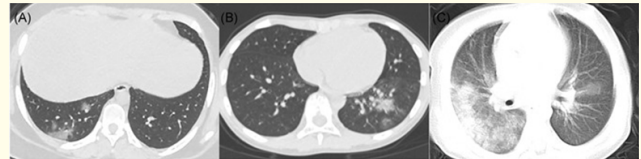
**Figure 1:** Courtesy ref no-3-Structure of SARS-COV2.

tory illness, including high altitude pulmonary oedema (HAPE and how use of acetazolamide, nifedipine and PDE-Inhibitors need to be tried with the view of pulmonary oedema like picture instead of straight intubation and PEEP [9]. Further some speculate that alteration in haemoglobin structure might be there with iron molecule enable to hold oxygen akin to carbon monoxide poisoning [unpublished]. Usual public health measures, that include isolation, quarantine, social distancing as well as community containment, can be utilized for halting the pandemic by applying lessons that we have learnt from SARS [10]. One important finding noted is that. COVID-19 infection has a clustering onset and has chances of affecting older males (average age 51yrs) with comorbidities [11]. Histologic examination of lung biopsy samples revealed bilateral diffuse alveolar damage with cellular fibromyxoid exudates [12]. Further, the apparent reason of >mortality in  $\geq 50$  yr males given by drs from Karnataka is that testes has antigens that do not get exposed to the immune system and hence the immune tolerance in males is poor. Both in China [11], as well as recent New York death reports coming show 60% deaths is in males. Treatment although not known with the virus being novel, drugs tried and in trials have been antivirals like IFN- $\alpha$ , lopinavir/ritonavir as well as ribanivir for treating COVID-19. Darunavir, which is a second generation of HIV1 protease inhibitor. Favipiravir, a new kind of RNA-dependent RNA polymerase (RdRp) inhibitor is undergoing clinical trials for treating COVID-19. Remdesivir, a nucleoside analogue as well as broad spectrum antiviral, also has shown potential benefits in COVID-19. The maximum drug used in recent New York break is remdesivir being tried by WHO in many countries along with Favipiravir, hydroxyl chloroquine, that are under trials by WHO in various countries like favipiravir got legalized in japan [13]. Further Ivermectin an FDA-approved broad spectrum antiparasitic agent [14], was shown to be effective in vitro studies in Vero/hSLAM cells by Leon Cary Moreover in India ICMR has started trials with certain botanical plants besides traditional ayurvedic medicines like turmeric etc. Convalescent plasma transfusion was delivered early following symptoms onset in the therapy of SARS [15]. Till date 3 successful transfers done in USA and 2 in India.

As far as vaccines are concerned with structure of SARS-CoV2 S protein known, might help in the rapid generation Most of the vaccines getting developed for Coronaviruses target the spike glycoproteins or S proteins [16]. But watching the progress with Ebola vaccine that took 3 years still not marketed it seems some companies have skipped animal trials and still as far as reports come not before January 2021 new vaccines will come. As per news Oxford in UK have started some vaccine trials in UK on 22/4/2020. However, seeing the growing increases in pandemic with USA reaching > 7



**Figure 2:** Courtesy ref- 7 - 5yr child with lung involvement- Consolidation with surrounding halo sign was observed.



**Figure 3:** Courtesy ref-8. A, Female, 14 years old. Chest CT showed scattered ground-glass opacities in the inferior lobe of the right lung, located subpleural or extended from subpleural lesions. B, Male, 10 years old. Chest CT showed consolidation with halo sign in the inferior lobe of the left lung surrounded by ground-glass opacities. C, Male, 1 year old. Chest CT showed diffused consolidations and ground-glass opacities in both lungs, with a "white lung" appearance of the right lung. CT: Computed Tomography.

lakh on 20/4/20 and > 40,000 deaths need of early therapy is there (Table 1 and 2). A ray of hope has come from placental expanded cells that Pluristem Diagnostics is conducting in Israel and possibly with it helping immune metabolism and helping in proteins formation might help in preventing severe lung inflammation, renal and other toxicities. Earlier PEX have been used for muscle regeneration in injuries etc [17]. Still lockdown the most intelligent decision taken by our PM. Social distancing remains important till we get over this pandemic. Further some studies are being conducted to see if BCG has any protective effect with compulsory immunization in India, Pakistan, Bangladesh having severe attacks is being studied. Probable explanation might be that these non-specific effects (NSEs) of the Bacille Calmette-Guérin (BCG) vaccine, for instance, implicate adaptive and innate immune mechanisms, with recent evidence suggesting that trained immunity might be a key instrument at play [18]. Collectively referring to the memory-like characteristics of innate immune cells, trained immunity stems from epigenetic reprogramming that these innate immune cells undergo following exposure to a primary stimulus like BCG. The epigenetic changes subsequently regulate cytokine production and cell metabolism and in turn, epigenetic changes are regulated by these effects In India vaccines being produced are also taking advantage of using measles vaccine having compulsion as carrier of Covid virus

antigen so that well tolerated-God willing we will be able to fight with this in time specially with the claims of Pluristens that 100% recovery possible after they did some trials in Israel (unpublished observations).

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