

EMERGING DISEASE OF COVID-19 PROBLEMS ANALYZED VARIOUS HYPOTHESIS USING EXPERT SYSTEMS

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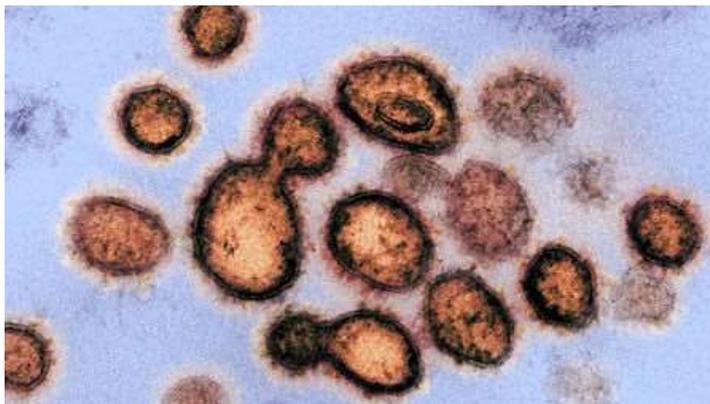
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Abstract: This Current pandemic of COVID-19 is challenging scientific community with lot many hypothesis. The clinical and epidemiological conclusions of COVID -19 are still uncertain due to its higher transmission rate. From all the corners of the world is sharing their understandings on COVID-19 but the interpretation of those understandings is still ambiguous. There is an urgent need for the scientific community for imperative discussion of those hypothesis on COVID-19. In this prospective discussion we analyzed various hypothesis on COVID-19 with existing clinical facts. Including clinical management, epidemiology and controlling strategies. In addition to that to make services effective and achieve the scalability and efficiency with help of machine learning algorithms and techniques.

Keywords: COVID-19, Clinical management, epidemiology, controlling strategies etc.,

I.INTRODUCTION

Coronavirus Disease (COVID-19) is an irresistible ailment brought about by novel corona virus which is emerged from Wuhan, China in the month of December 2019. The clinical introduction of extreme intense respiratory disorder coronavirus malady (SARS-CoV2-Causative infection) takes after viral pneumonia. This enveloped positive RNA virus shows lower respiratory symptoms including cough, shortness of breathing and fever within 11.5 days post infection. This ongoing pandemic attributed to > 200,000 mortality, > 1,962,235 infected cases and widespread to > 200 nations. It witnessed the world needs more scientists who can effectively translate their expertise, the findings and projections at this time undoubtedly help the scientific community to relay further. However, these projections may lead a kind of uncertainty about COVID-19 that will cause misrepresentations of risk to common community. Hence, the hypothesis and clinical opinions on this infection are taken for prospective discussion with available facts.



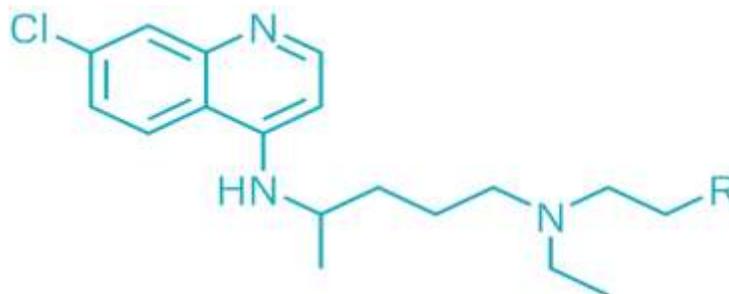
II. CLINICAL MANAGEMENT

2.1 Hydroxychloroquine (HCQ) as a game changer

Since from outbreak of COVID-19 this drug played global political responses of unconceivable proportions. The president of United States shown his trust of HCQ for his people using ready for retaliation. This molecule exhibits blocking replication of enveloped viruses including coronavirus at late stage by interfering pH dependent steps of viral entry. Effective concentration 50 (EC₅₀) value of 6.25 micromole of HCQ at 24 hrs was reported to have a promising effect on COVID-19 prevention in *in vitro* experiments. Mode of action perhaps blocking endosomal maturation in intermediate stages of endocytosis which leads to failure in transport of virions to releasing site. Other than direct antiviral potentials, HCQ may possess anti-inflammatory potentials in autoimmune conditions.



It plays vital role in attenuating release of pro-inflammatory mediators. Further, HCQ treatment shows viral nasopharyngeal carriage clearing of SARS-CoV-2 in coronavirus patients in three to six days. Single dose of 800mg of HCQ provides more than higher level of EC₅₀ at lung fluids. However, FDA suggested 200mg for 22 days were found to be effective in prevention of lung damage of COVID-19 patients. Antimalarial agents most commonly produce cardiotoxicities including cardiomyopathy, atrioventricular block and majorly in the case of HCQ produces QT prolongation which is potential indicator of *torsade de pointes*.



Chloroquine, R = H
Hydroxychloroquine, R = OH

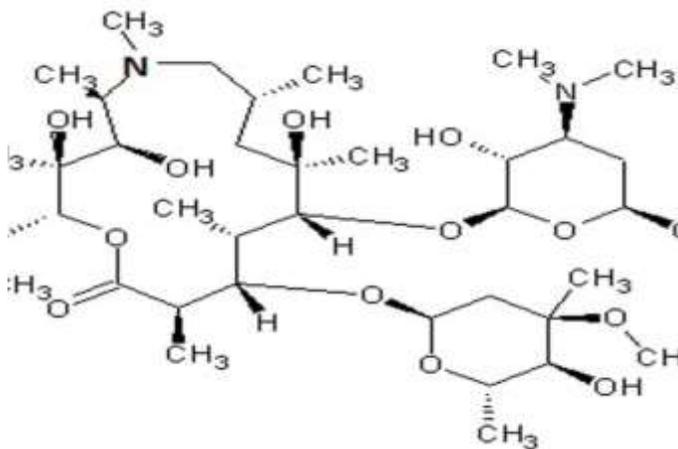
There are two trials in progress in Shanghai Public Health Clinical Center and University of Oxford which are currently in the process of recruiting patients with COVID-19. Indian council of medical research expresses that there is no satisfactory results attained with HCQ for COVID-19 patients. On the other hand United States and Brazil appreciate India's decision of exporting HCQ. However, more trials are the only way to decide the safety and efficacy of HCQ further.

2.2 Azithromycin with chloroquine

The pharmacokinetics of azithromycin and chloroquine does not have any interactions as such. Further, chloroquine is also a well-known candidate for phase IV potassium channel repolarization delay. Hence, it has increased chance of prolongation of QT intervals. Further, the genetic polymorphism plays crucial role in the release of cytochrome P450 enzyme 2D6 (CYP2D6), a metabolizing enzyme of Chloroquine. This will allow the chance of suspect of death reports from Africa and Arizona due to chloroquine. However, there is no evidence of Azithromycin and/or chloroquine for fetus toxicity.



On the other hand there should be Azithromycin and/or chloroquine optimization need for their employability in COVID-19 therapy for pregnant patients; else it will negatively impact the course of the disease. Chloroquine may augment the inflammatory response due to T-helper cell proliferation.



On the other hand, the immunomodulatory effect of chloroquine may give a great prescribing push for COVID-19. However, more robust randomized trials needed for proving the effect.

2.3 Ayurveda's Immunity Boosting

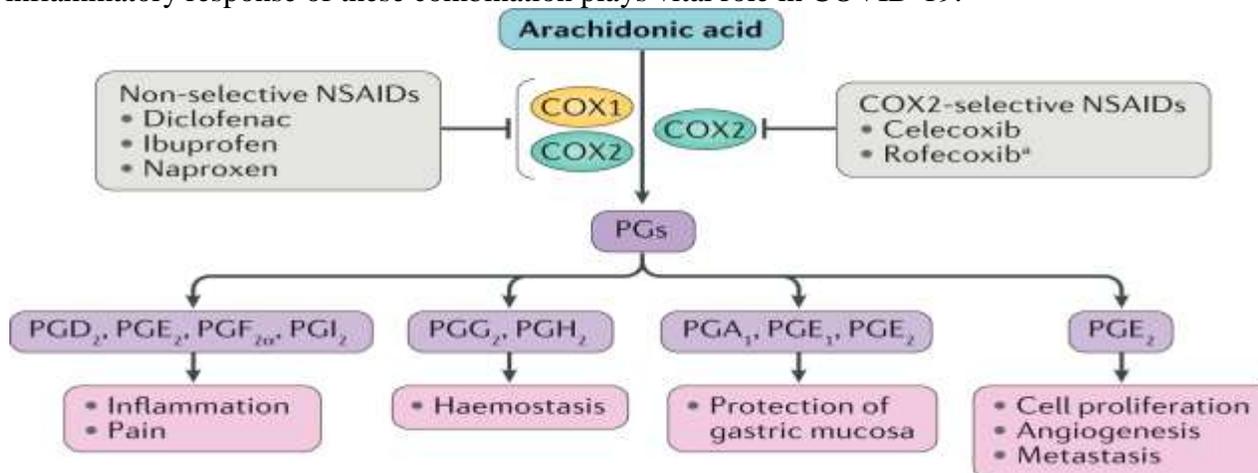
The global ayurveda's birth place INDIA's Ministry of AYUSH recommend few care rules for preventive wellbeing measures and boosting resistance with uncommon reference to respiratory wellbeing. These are bolstered by Ayurvedic writing and logical distributions. The practices include, consuming *chyavanprash* (A herbal immune booster) 10 g and/or drinking herbal tea contain basil, cinnamon, black pepper and dry ginger for two to three times a day.



Further, golden milk (Milk with, turmeric) also suggested by many Ayurveda literature against viral infections. However, these suggestions are chiefly employed to feel symptomatic relief and boosting immunity needs more evidences against COVID-19. Further, these Ayurveda supplements can be suggested along with ongoing other system of medicines.

2.4 Antiviral with NSAIDs

Traditionally NSAIDs were used for flu like fever in clinical practice. Indomethacin exhibits promising anti-viral property against coronavirus, by interfering with viral multiplication. The cyclooxygenase inhibition effect helps to block viral RNA synthesis at cytoprotective dose of Indomethacin which was demonstrated *In vivo* and *In vitro* experiments. However, the augmented evidences suggest that children treated with NSAIDs for viral infections produces emphysema which may lead to lethality in case of lower respiratory tract targeting disease like COVID-19. Naproxen shows potential interference in RNA synthesis process with influenza infections, selective JAK-STAT signaling inhibitors like baricitinib, fedratinib, and ruxolitinib were reported for effectiveness in elevated interferon- γ cases of COVID-19. Combining Baricitinib with antivirals is consciously practiced for COVID-19 due its favoring pharmacodynamics property. Further, aberrant host inflammatory response of these combination plays vital role in COVID-19.



2.5 Africa's response and herbal remedy for COVID-19

The East African nation Ethiopian Ministry of Innovation and Technology and Ministry of Health has reported that they stepped up to the plate and build up "another medication" for COVID-19 as a team with a group of customary meds specialists. The essential worry of the pundits from academic network is that dread of driving people in general to accept the treatment against crown is low hanging natural product however. In any case, the starter information, logical clarification about the adequacy and averageness of the supposed inhibitors by the researchers. The legislature of Zimbabwe accepts home grown treatment can be the response to the dangerous coronavirus. Henceforth, the legislature has approved botanists to treat coronavirus patients. Be that as it may, clinical specialists have asked the legislature to adhere to WHO rules on the most proficient method to contain the infection. Madagascar's leader has embraced a dubious "supernatural occurrence fix" to handle the coronavirus. There is no logical proof however that the home grown cure is successful. Likewise, Burkina Faso will make face covers required as of April 27, however they're still difficult to find.

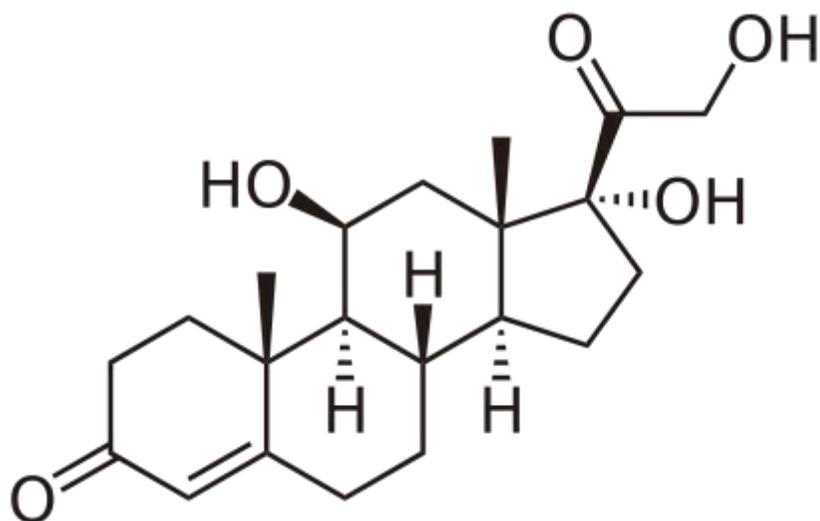


2.6 Off label antivirals

Majority of antiviral agents administered immediately after symptoms of COVID to reduce viral load in respiratory secretions from 5-6 days to up to 14 days. Further, antivirals can be also prescribed as prophylactic purpose to reduce the risk of contact infection. The off label claim of lopinavir/ritonavir combination along with oseltamivir relatively shown good recovery in COVID-19 related pneumonia in few cases in china. The influenza agent favipiravir also reported effective in current pandemic. Radiological investigations on favipiravir (600 mg twice daily) plus interferon treated subjects shown greater viral shedding. Remdesivir an anti-Ebola agent also prescribed for MERS and SARS in cells. But, there is no concrete evidence for its therapeutic ability. Though there are few studies with off label COVID-19 claims but with this minor populations and lack of randomization in available trials. Further, the available studies have not considered the stage and differences in severity of the disease as well as the differences in age of the two groups. Hence, this lead lack of blinding of outcomes to the researchers all cast doubt on the findings.

2.7 Corticosteroids

Generally corticosteroids are mostly effective in controlling immunopathological damage but simultaneously produce viral rebound in most of respiratory viral diseases. Higher viral RNA load was reported with SARS-CoV patients treated with corticosteroids. Latest study with COVID-19 pneumonia early and low dose of corticosteroid therapy for short duration of 2-4 days reported with earlier improvement of clinical symptoms.



COVID -19 patients who received corticosteroids for earlier symptoms were reported for requirement of mechanical ventilation and renal replacement therapy. A definitive truth of viral burden increase upon corticosteroids organization is notable in past episodes of Middle East respiratory disorder (MERS) and serious intense respiratory condition (SARS).



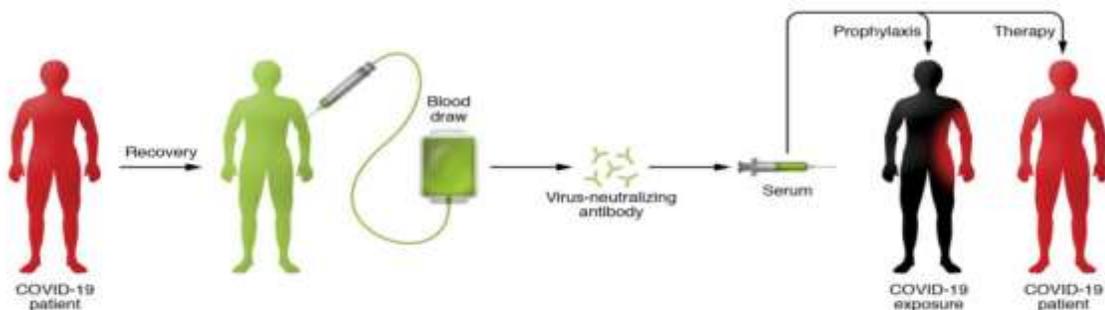
2.8 Cuba's interferon alpha-2b

HIFN-2b atom is a glycoprotein comprising of 166 amino acids with O-glycosylated threonine at position 106. Enlarged confirmations proposed that HIFN alpha-2b thwarting JAK-STAT signal transduction by hindering extracellular sign managed kinase (ERK) mitogen ERK kinase (MEK) pathway. Youthful and moderately aged COVID-19 patients may not requires HIFN-2b attributable to their great invulnerable conditions. In any case, matured patients who are defenseless to terrible insusceptibility maybe require HIFN-2b for keeping away from complexities. South America and African nations have plan to begin HIFN-2b inoculation to accomplish prior control of COVID-19.



2.9 Convalescent Plasma Therapy

Convalescent plasma (CP) therapy, played significant role in past decades as classic adaptive immunotherapy in counteraction and treatment of numerous irresistible illnesses. The proficiency in treatment of SARS and MERS and H1N1 pandemic is notable. In any case, the CP treatment couldn't show criticalness in Ebola infection sickness, maybe nonattendance of information of killing immune response titration for defined examination. Primarily the extent of CP treatment for COVID-19 may be promising because of virological similitude with SARS and MERS. Pilot examines recommended likely restorative impact in lessening viral burden by killing antibodies for serious patients. Be that as it may, numerous populace randomized path are justified at the soonest to make CP as promising.



III.EPIDEMIOLOGY

3.1 Elderly are more Prone

More established grown-ups are at higher hazard for growing increasingly genuine difficulties from COVID-19 ailment. Specialists report old individuals' raised danger of genuine disease and demise from the new coronavirus: Covid-19 executes an expected 13.4% of patients 80 and more established, contrasted with 1.25% of those in their 50s and 0.3% of those in their 40s. The casualty rate for individuals more than 80 from COVID-19 is practically 15% as per information from China. The principle motivation behind why more seasoned grown-ups are at higher hazard is that they don't have as solid an insusceptible framework so they are increasingly helpless against irresistible infection. The other motivation behind why more established individuals are progressively inclined to casualty from COVID-19 is that they are bound to have conditions,

for example, coronary illness, lung malady, diabetes or kidney ailment, which debilitate their body's capacity to battle irresistible ailment.

3.2 Co-morbidities vs COVID-19

The quantity of comorbidities is an indicator of mortality in COVID-19. Diabetes has been accounted for to be a hazard factor for hospitalization and mortality of the COVID-19 contamination. An investigation in 52 concentrated consideration patients uncovered that diabetes was comorbidity in 22% of 32 non-survivors. In another investigation of 173 patients with extreme illness, 16.2% had diabetes, and in further investigation of 140 hospitalized patients, 12% had diabetes. When looking at concentrated consideration and non-serious consideration patients with COVID-19, there seems, by all accounts, to be a twofold increment in the occurrence of patients in escalated care having diabetes. Mortality is by all accounts about triple higher in individuals with diabetes contrasted and the general mortality of COVID-19 in China. To be sure, individuals with diabetes are a high-chance gathering for extreme ailment. Eminently, diabetes was additionally a hazard factor for serious sickness and mortality in the past SARS, MERS coronavirus diseases and the extreme flu A H1N1 pandemic in 2009.

Diabetic patients are at expanded danger of diseases including flu and inconveniences, for example, optional bacterial pneumonia. This is in all probability since they have weakened resistant reaction to disease both corresponding to cytokine profile and to changes in insusceptible reactions including T-cell and macrophage actuation. Poor glucose control disables a few parts of the resistant reaction to viral disease and furthermore to the possible bacterial auxiliary contamination in the lungs. Almost certainly, huge numbers of the patients with diabetes in China have been in poor metabolic control when contaminated by COVID-19.

Notwithstanding diabetes, the other most normal comorbidity COVID-19 is hypertension. Out of 1,590 COVID-19 cases in an across the country examination in China almost 17% was seen as hypertensive cases. The seriousness of the ailment was additionally answered to be higher for hypertensive cases contrasted and those non-hypertensive cases. It was likewise proposed that comorbidities, for example, COPD, other cardiovascular and renal maladies, and harm inclined to unfriendly clinical results in patients with Covid-19. In any case, the quality of relationship between various comorbidities and the anticipation was less steady when contrasted and the writing reports.

It has been all around acknowledged that some comorbidities as often as possible exist together. For example, diabetes and COPD oftentimes exist together with hypertension or coronary heart ailments. Accordingly, patients with existing together comorbidities are bound to have less fortunate standard prosperity. Critically, it was confirmed that the fundamentally heightened danger of poor guess in patients with at least two comorbidities as contrasted and the individuals who had no or just a solitary comorbidity. The classification and number of comorbidities ought to be considered while anticipating the forecast in patients with Covid-19.

3.3 Vaccination against tuberculosis prevents mortality

The WHO clears with its explanations that no proof that Bacille Calmette-Guérin immunization (BCG) ensures individuals against contamination with COVID-19 infection. However, this tubercular vaccine reported effective against leprosy with non-specific immunity boosting, the common logic behind is both are mycobacterial infections. The correlation of BCG vaccinated COVID-19 positive cases suggested that fall in mortality and morbidity and may be played vial role in controlling this pandemic. BCG vaccinated mice shown increased IFN- γ production from CD4+ cells, this so called trained immunity produces epigenetic changes. Including increasing secretion of pro-inflammatory cytokines. This may drive the scientific community like to tempt to pronounce the statements BCG vaccine as "silver bullet". Further, we observe the slow spreading rate of COVID-19 in BCG vaccine mandate countries. But another 90 days may require to have strengthen this statement. The COVID-19 data of south Asia and Africa may be contributed to lower

number of testing. Additionally, there are couple of trials are registered for BCG for COVID-19 the results of these trials may give us better conclusion.

3.4 SARS-CoV-2 cross immunity to south Asians, Africans, and South Americans

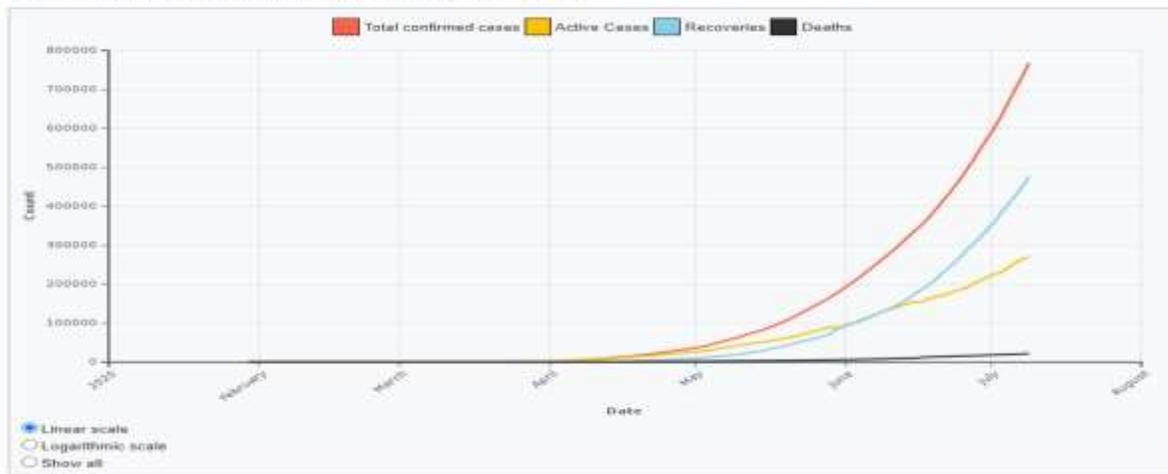
The spike protein of SARS-CoV, HCoV-NL63 and SARS-CoV-2 possess quite similar in structure among them. The hypothesis of antibody dependent enhancement in south Asians, due to previous exposure of Dengue and Zika virus is may be the reason of slow in doubling rate of COVID-19 in South Asians. But this statement not ends unless this pandemic completes its turn. Other observations on slow spreading of COVID-19 in South Asia, Africa and South America make us to suspect cytokine storm. But this is too early to conclude. The pandemic is not over yet.

IV.EVALUATION CRITERIA

Daily samples tested



Total confirmed cases, active cases, recoveries and deaths



		Predicted class			
		Yes		No	
True Class	Yes	True Positive (TP)	False Positive (FP)	False Negative (FN)	True Negative (TN)
	No	False Positive (FP)	True Positive (TP)	True Negative (TN)	False Negative (FN)

Accuracy – Performance of classifier – $TP + TN / TP + TN + FP + FN$

Precision – Exactness of Classifier – $TP / TP + FP$

Recall – Completeness of classifier – $TP / TP + FN$

V.CONCLUSION

Numerous understandings and hypothesis from various parts of the world signifies clearly, that the COVID is yet to be understood by scientific community. However, researchers are continuously working for vaccine development for this ongoing pandemic. Majorly CHINA, INDIA and AMERICA are actively participated in vaccine development race. Our understanding suggests that this pandemic deemed to be over in 12 to 30 months in this world. At all the outset we have to live with COVID-19 and this is “not the first nor the last”.

Future enhancements to this work include the adaptation of the proposed model in the various domains. Our proposed a deep learning algorithms automatically to detect and classify the Corona disease using datasets.

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