



Editorial

An evaluation of the 2019 novel coronavirus (COVID-19) disease

A.G. Nerkar^{1,*}, Praneeta Pawale¹

¹Ateos Foundation of Science Education and Research, Pune, Maharashtra, India



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ABSTRACT

WHO (World Health Organization) termed the diagnosed coronavirus as COVID-19. The pandemic outbreak of COVID-19 was manifested by intense acute respiratory system (SARS) and in Middle East known as Middle East Respiratory Syndrome (MERS). An outbreak of pneumonia of unknown aetiology in Wuhan City, Hubei province in China emerged in December of 2019. The virus originated in bats and became transmitted to people through but unknown middleman animals in Wuhan, China. There was not any clinically authorised antiviral drug to be had for use in opposition to COVID-19. However, few extensive-spectrum antiviral pills had been evaluated in opposition to COVID-19 in scientific trials, led to scientific recovery. In the cutting-edge evaluate, we summarize and relatively examine the worldwide emergence and pathogenicity of COVID-19 contamination.

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1. Introduction

The city of Hubei Province of China transmitted the virus to the other parts of the world, and almost all parts of the world were affected in 2019 by novel coronavirus (2019-nCoV) or the intense acute respiration syndrome corona virus 2 (SARS-CoV-2).^{1,2} Coronavirus is one of the important pathogens that mostly goal the human respiratory system. Previous outbreaks of corona viruses (CoVs) consist of the intense acute respiration syndrome (SARS)-CoV and the Middle East respiration syndrome (MERS)-CoV that have been formerly characterised as retailers which might be a first rate public fitness hazard. In past due December 2019, a cluster of sufferers became admitted to hospitals with an preliminary analysis of pneumonia of an unknown etiology. These patients have been epidemiologically having a seafood and moist animal entire sale marketplace.^{3,4} SARS CoV- 2 is related to an ongoing outbreak of extraordinary pneumonia (Covid-2019). More seriously, the epidemic

endured to unfold from China to Europe, North America, and different Asian nations, no matter first rate efforts and more and more humans being cured in China. On January 30, 2020, WHO declared Coronavirus as gobar emergency and in February 2020 as an epidemic.⁵⁻⁷ Coronavirus (CoV) is a big own circle of relatives of super-coiled single-stranded RNA viruses that belong to the Nidovirales order. The order consists of Roniviridae, Arteriviridae, and Coronaviridae families. The Coronaviridae in system of nomenclature of viruses of relatives is subdivided into Torovirinae and Coronavirinae subfamilies. Coronavirinae is similarly sub categorized into alpha-, beta-, gamma-, and delta-COVs.⁸ Their viral RNA genome stages from 26 to 32 kilobases in length. They may be remoted from extraordinary animal species. These consist of birds, stay stock, and mammals which include camels, bats, masked palm civets, mice, dogs, and cats.⁹ The extensive unfold distribution and infectivity of COV make it a crucial pathogen. The repeated emergence and outbreaks of CoVs imply a public health hazard. This indicates the opportunity of animal-to-human and human-to-human transmission of

* Corresponding author.

E-mail address: dragnerkar@gmail.com (A. G. Nerkar).

newly rising CoVs. The ongoing adjustments in ecology and weather make destiny emergence of such infections extra probably.¹⁰

2. Review

2.1. Origin and transmission of SARS-CoV-2

The SARS-CoV-2 is a γ -coronavirus, enveloped in non-segmented super coiled single spiral RNA, (subgenus sarbecovirus, Orthocoronavirinae subfamily).¹¹ Coronaviruses (CoV) has 4 genera, which include α - β - γ - δ -CoV.

1. α - and β -CoV: infect mammals, while
2. γ - and δ -CoV: contaminate birds.

Previously, six CoVs are designated as human-infective virus, amongst several has low pathogenicity, may cause moderate respiration signs such as cold and fever. The different regarded γ -CoVs, SARS-CoV and MERS-CoV cause intense and severe acute respiratory tract infections.¹² Based on virus genome sequencing effects and evolutionary evaluation, bat has been suspected as herbal host of virus beginning, and SARS-CoV-2 is probably transmitted from bats thru unknown intermediate hosts to contaminate people as shown in (Figure 1).

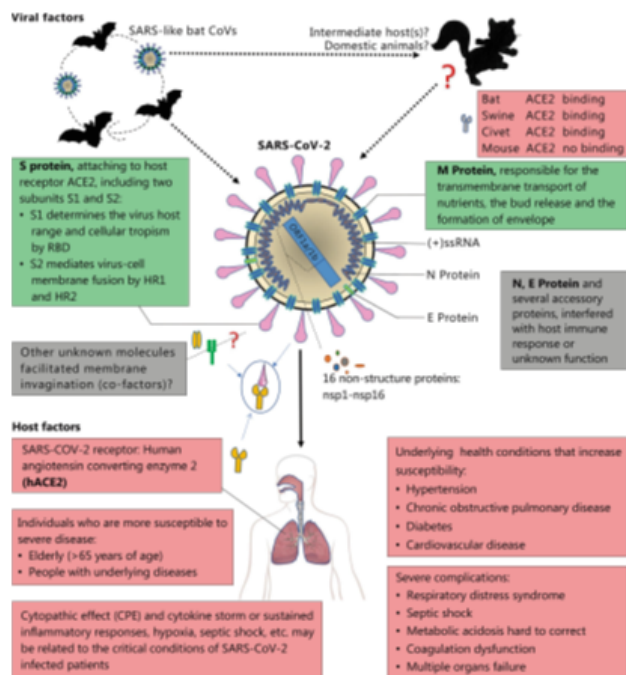


Fig. 1: Viral and host elements that have an effect on the pathogenesis of SARS-CoV-2.

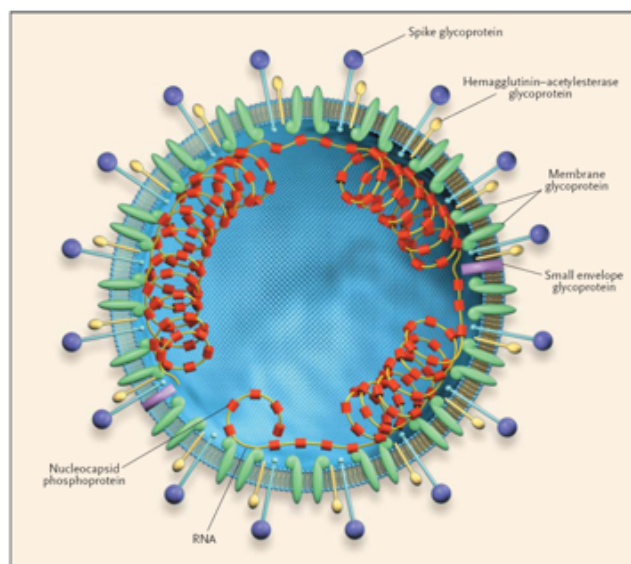


Fig. 2: Structure of the Corona virus virion: (A) Electron micrograph of MHV debris. (B) Schematic of virion. Viral debris include an inner helical RNA-protein nucleocapsid surrounded through an envelope containing viral glycoproteins. Nucleocapsid (N) protein is a phosphoprotein this is complexed with genome RNA to shape the nucleocapsid. Spike glycoprotein (S) paperwork the big glycosylated peplomers which might be feature of corona viruses. M, the transmembrane protein, is fantastically hydrophobic and spans the membrane 3 times. E, a membrane-spanning protein, is a minor element of the membrane. Some organization II viruses specific some other glycoprotein, hemagglutinin-esterase (HE), which has a framework of smaller spikes on virions.

2.2. Structure of virions

2.3. Genome shape of corona viruses

Corona viruses encode 5 structural proteins of their genomes. These are the Spike (S), Membrane (M), Envelope (E) glycoproteins, Hemagglutinin Esterase (HE) and Nucleocapsid (N) protein, (Figure 2) All envelope proteins and N protein is found in all virions however HE is best found in a few beta corona viruses.¹³ In addition to that, it's miles idea the virus debris are huddled collectively because of interplay among those proteins.^{14–16} S Glycoproteins: S Glycoproteins are positioned out of doors the virion and deliver the virion the standard shape. The S proteins shape homotrimers, which permit the formation of sun-like morphologies that deliver the call of Corona viruses.^{17–19} S proteins bind to the virion membrane thru the C-terminal transmembrane areas and additionally they have interaction with M proteins.²⁰ Virions may be certain to unique floor receptors withinside the plasma membrane of the host mobile thru the N-terminus of the S proteins.²¹ M Glycoproteins: M Glycoproteins have 3 transmembrane areas. M proteins are glycosylated withinside the Golgi

equipment.^{22–24} This amendment of the M protein is important for the virion to fuse into the mobile and to make protein antigenic.^{25–27} The M protein performs a key position in regenerating virions withinside the mobile. N protein framework a complicated through binding to genomic RNA and M protein triggers the formation of interacting virions on this endoplasmic reticulum-Golgi equipment intermediate compartment (ERGIC) with this complicated.^{22–29} E Glycoproteins: E Glycoproteins are small proteins which might be composed of about 76 to 109 amino acids. About 30 amino acids withinside the N-terminus of the E proteins permit attachment to the membrane of viruses.³⁰ In addition, coronavirus E proteins play a essential position withinside the meeting and morphogenesis of virions. In one examine coronavirus E and M proteins have been expressed collectively with mammalian expression vectors to shape virus-like systems^{31–33} In some other examine, there has been a substantial lower withinside the cappable of the recombinant mouse hepatitis virus (MHV) and SARS viruses to elicit E protein expression withinside the genome to aid this status.^{34,35} N Proteins: N proteins are phosphoproteins which might be able to binding to helix and feature bendy shape of viral genomic RNA. It performs an crucial position in virion shape, replication and transcription of corona viruses, due to the fact the N protein localizes withinside the replication/ transcriptional vicinity of the corona viruses and the ERGIC vicinity wherein the virus is collected.^{28,36}

2.4. Pathogenesis of COVID-19

COVID-19 is recognized with symptoms inclusive of fever, nonproductive cough, dyspnea, myalgia, fatigue, normal or decreased leukocyte counts, and radiographic evidence of pneumonia,³⁷ which is probably like the symptoms of SARS-CoV and MERS-CoV infections.³⁸ Hence, even though the pathogenesis of COVID-19 is poorly understood, the identical mechanisms of SARS-CoV and MERS-CoV nevertheless can supply us lots of records on the pathogenesis of SARS-CoV-2 infection to facilitate knowledge of COVID-19.

2.5. Coronavirus access and replication

Coronavirus S protein has been mentioned as a substantial determinant of virus access into host cells.³⁹ The envelope spike glycoprotein binds to its cell receptor, ACE2 for SARS-CoV⁴⁰ and SARS-CoV-2,⁴¹ CD209L (a C-kind lectin, additionally known as L-SIGN) for SARS-CoV⁴², DPP4 for MERS-CoV.⁴³ The access of SARS-CoV into cells became to begin with diagnosed to be done through direct membrane fusion among the virus and plasma membrane.⁴⁴ Belouzard et al.⁴⁵ located that a critical proteolytic cleavage event came about at SARS-CoV S

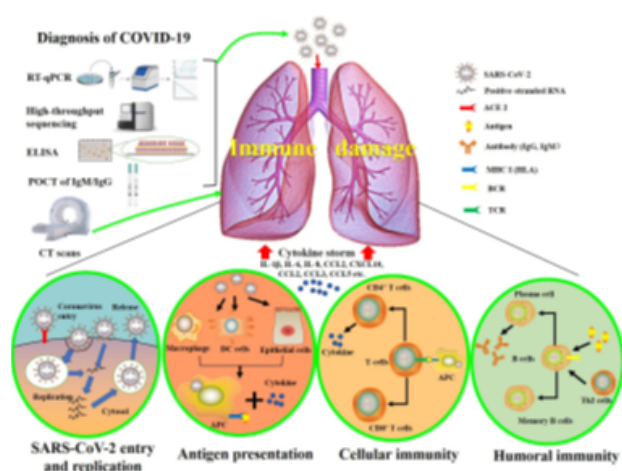


Fig. 3: Diagnosis of COVID-19.

protein at position (S2') mediated the membrane fusion and viral infectivity. MERS-CoV moreover has superior unusual -step furin activation for membrane fusion.⁴⁶ Besides membrane fusion, the clathrin-primarily based totally and unbiased endocytosis mediated SARS-CoV get right of entry to too.^{47,48} After the virus enters the cells, the viral RNA genome is released into the cytoplasm and is translated into polypeptides and structural proteins, after which the viral genome begins off evolved to replicate.⁴⁹ The newly formed envelope glycoproteins are inserted into the membrane of the endoplasmic reticulum or Golgi, and the nucleocapsid is formed thru the combination of genomic RNA and nucleocapsid protein. Then, viral particles germinate into the endoplasmic reticulum Golgi intermediate compartment (ERGIC). At last, the vesicles containing the virus particles then fuse with the plasma membrane to release the virus.³⁹

2.6. Diagnostic techniques for COVID-19

The real-time RT-qPCR for detection of COVID-19 in nasopharyngeal and throat swabs or oropharyngeal swabs has been gold standard for detection of coronavirus disease. For the analysis of COVID-19, even though RT-qPCR is unique, its price cannot be neglected due to the intense outcomes of overlooked analysis. CT scans which in vivo and RT-Qpcr is ex-vivo technique. Out of which RT-PCR being the sensitive, whereas the CT- Scans being auxillary shows ground glass opacities of lung involvement. Of patients inflamed with SARS-CoV-2^{50–53} According to the ones findings, CT scans have a first rate scientific diagnostic cost for COVID-19, specifically within the excessive incidence vicinity of SARS-CoV-2. However, CT scans additionally have a drawback, which include undifferentiations from different viral pneumonia and the hysteresis of unusual CT imaging. The CT imaging should

be additionally accompanied with immunological test such as IgG/ Ig M detection and ELISA assay by kits. The sensitivity of SARS-CoV N-primarily based totally IgG ELISA (94.7%) is extensively better than that of SARS-CoV S-primarily based totally IgG ELISA (58.9%),⁵⁴ however the sensitivity of SARS-CoV-2 IgG/IgM stays to be studied.

2.7. Symptoms

The signs of COVID-19 contamination seem after an incubation duration of about 5.2 days.⁵⁵ The duration from the onset of COVID-19 signs to death ranged from 6 to 41 days with an average of 14 days. This duration is depending on the age of the affected person and standing of the affected person's immune system. It became shorter amongst sufferers >70-years vintage as compared with the ones below the age of 70.⁵⁶ The maximum signs at onset of COVID-19 infection are fever, cough, and fatigue, whilst different signs consist of sputum production, headache, haemoptysis, diarrhoea, dyspnoea, and lymphopenia^{10,56–58} Clinical capabilities found out through a chest CT experiment provided as pneumonia, however, there have been unusual capabilities which include anaemia, acute respiration misery syndrome, acute cardiac injury, and occurrence of grand-glass opacities that caused the death.¹⁰ In a few instances, couple of peripheral ground-glass opacities have been found in subpleural areas of each lungs that probably prompted each systemic and localized immune reaction that caused accelerated inflammation. Regrettably, remedy of a few instances with interferon inhalation confirmed no scientific impact and rather regarded to get worse the circumstance through progressing pulmonary opacities.⁵⁸ It is crucial to notice that there are similarities withinside the signs among COVID-19 and in advance beta coronavirus which include fever, dry cough, dyspnea, and bilateral ground-glass opacities on chest CT scans.¹⁰ However, COVID-19 confirmed a few specific scientific capabilities that consist of the concentrated on of the decrease airway as glaring through top respiration tract signs like rhinorrhoea, sneezing, and sore throat.^{37,38} In addition, primarily based totally on effects from chest radiographs upon admission, a number of the instances display an infiltrate withinside the top lobe of the lung this is related to growing dyspnea with hypoxemia.⁵⁹ Importantly, wherein as affected person inflamed with COVID-19 advanced gastrointestinal signs like diarrhoea, a low percent of MERS-CoV or SARS-CoV sufferers skilled comparable GI misery. Therefore, it's miles crucial to check faecal and urine samples to exclude a ability opportunity path of transmission, in particular thru fitness care workers, sufferers etc.^{37,38} Therefore, improvement of techniques to become aware of the numerous modes of transmission which include faecal and urine samples are urgently warranted for you to increase techniques to inhibit and/or limit transmission and to increase therapeutics

to manipulate the disorder. Current remedy techniques for COVID-19. At present no clinical agent antiviral can be employed for the successful treatment of SARS-CoV and MERS-CoV.⁶⁰ The supportive remedy together with oxygen remedy, conservation fluid control, and the usage of extensive-spectrum antibiotics to cowl secondary bacterial contamination, stays to be the maximum crucial control strategy.¹⁰ According to studies to prevent the pathogenesis of SARS-CoV-2, there are numerous molecular mechanisms available,⁹ thus based on these studies the repurposing of the antiviral agents may be a promising therapy for the healing and treatment of SARS-COV-2.

2.8. Potential healing techniques in opposition to COVID-19

Initially, interferons- $\hat{1}\pm$ nebulization, extensive-spectrum antibiotics, and anti-viral pills have been used to lessen the viral load^{61–63} however, best remdesivir has proven promising effect in opposition to the virus.⁶⁴ Remdesivir best and in mixture with chloroquine or interferon beta extensively blocked the SARS-CoV-2⁶⁴ replication and sufferers have been declared as clinically recovered.^{65–67} Various different anti-virals are presently being evaluated in opposition to contamination. Nafamostat, Nitazoxanide, Ribavirin, Penciclovir, Favipiravir, Ritonavir, AAK1, Baricitinib, and Arbidol exhibited slight effects while examined in opposition to contamination in sufferers and in-vitro scientific isolates.^{65–68} Several different mixtures, which include combining the antiviral or antibiotics with conventional Chinese drug treatments have been additionally evaluated in opposition to SARS-CoV-2 prompted contamination in people and mice.⁶⁵ Recently in Shanghai, in an experiment, blood plasma from covid recovered patients was injected in inflamed patients and shown to have advance recovery.⁶⁹ In a study it was suggested and observed that monoclonal antibody (CR3022) binds with the spike RBD of SAR-CoV-2. The antibody epitope of CR3022 has the advance healing therapeutic index, on individually or in mixture with different neutralizing antibodies for the prevention and remedy of COVID-19 contamination.⁷⁰

2.9. Antibody and plasma remedy

It has additionally been mentioned that there are numerous convalescent sufferers donating plasma in opposition to SARS-CoV-2, simply as SARS-CoV⁷² and MERS-CoV trials.⁷³ It has initial received favourable effects in acute, intense SARS-CoV-2 sufferers. Moreover, it was demonstrated that the technology of recombinant human monoclonal antibody (mAb) is a reasonably has ability to neutralize SARS-CoV. CR3022, a SARS coronavirus-unique human monoclonal antibody, can bind potently with the receptor-binding domain (RBD) of SARS-CoV-2 and

Table 1: Common and potent antiviral drugs.⁷¹

Status	Drugs	Action mode	Anti-infective mechanism	Target diseases
Approved	Lopinavir/ Ritonavir	Protease inhibitors	Inhibiting HIV-1 protease for protein cleavage, resulting in non-infectious immature viral particles	HIV-AIDS, SARS, MERS
Approved, Investigational, Vet approved	Chloroquine	9-aminoquinolin	Increasing endosomal pH, immunomodulating autophagy inhibitors	Malaria, autoimmune disease
Experimental	Remdesivir (GS-5734)	Nucleotide analogue prodrug	Interfering with virus post-entry	Ebola, SARS, MERS (A wide array of RNA viruses)
Investigational	Nafamostat	Synthetic serine protease inhibitors	Prevents membrane fusion by reducing the release of cathepsin B; anticoagulant activities	Influenza, MERS, Ebola
Approved	Ribavirin	Synthetic guanosine nucleotide	Interfering with the synthesis of viral mRNA (a broad spectrum activity against several RNA and DNA viruses)	HCV, SARS, MERS
Approved	Oseltamivir	Neuraminidase inhibitor	Inhibiting the activity of the viral neuraminidase enzyme, preventing budding from the host cell, viral replication, and infectivity	Influenza viruses A
Approved	Penciclovir/Acyclovir	Nucleoside analog	A synthetic acyclic guanine derivative, resulting in chain termination	HSV/VZV
Approved, Investigational	Ganciclovir	Nucleoside analog	Potent inhibitor of the Herpes virus family including cytomegalovirus	AIDS-associated Cytomegalovirus infections
Investigational	Favipiravir (T-705)	Nucleoside analog viral RNA polymerases inhibitors	Acting on viral genetic copying to prevent its reproduction, without affecting host cellular RNA or DNA synthesis	Ebola, Influenza A(H1N1)
Approved, Investigational, Vet approved	Nitazoxanide	Antiprotozoal agent	Modulating the survival, growth and proliferation of a range of extracellular and intracellular protozoa, helminths, anaerobic and microaerophilic bacteria, viruses	A wide range of viruses including human/ animal coronavirus

HIV Human immune deficiency virus, AIDS Acquired immune deficiency syndrome, SARS Severe acute respiratory syndrome, MERS Middle East respiratory syndrome, HCV Hepatitis C virus, HSV Herpes simplex virus, VZV Varicella-zoster virus

has ability to uncomplicate and treat the infections of SARS-CoV.⁷⁴ Other monoclonal antibodies neutralizing SARS-CoV, for the future development of the antibody plasma remedy include m396, CR3014, which might support the prognosis in SARS-CoV-2.⁶⁷

2.10. Future guidelines

Extensive measures to lessen man or woman-to-man or woman transmission of COVID-19 are required to manipulate the cutting-edge outbreak. Special interest and efforts to shield or lessen transmission must be carried out in prone populations together with children, fitness care providers, and aged humans. A guiding principle became posted for the scientific staff, healthcare providers, and,

public fitness people and researchers who're interested by the 2019-nCoV.⁷⁴ The early dying instances of COVID-19 outbreak passed off mostly in aged humans, probably because of a susceptible immune gadget that lets in quicker development of viral contamination.^{58,57} The public offerings and centers must offer decontaminating reagents for cleansing palms on a habitual basis. Physical touch with moist and infected items must be taken into consideration in coping with the virus, specifically retailers which include faecal and urine samples that may doubtlessly function an opportunity path of transmission.^{37,38} China and different nations together with the United States have applied important prevention and manage measures together with journey screenings to manipulate similarly unfold of the virus.⁷⁵ Epidemiological adjustments in

COVID-19 contamination must be monitored taking into consideration ability routes of transmission and subclinical infections, further to the adaptation, evolution, and virus unfold amongst people and viable intermediate animals and reservoirs. Significant wide variety of questions that want to be addressed. These consist of, however aren't confined to, information about who and what number of had been examined, what percentage of those became superb and whether or not this price stays consistent or variable. Very few paediatric instances have up to now been mentioned; is that this because of loss of trying out or a real loss of contamination/susceptibility? Of those which have up to now been examined, what number of have advanced intense disorder and what number of have been examined superb however confirmed no scientific signal of disorder? There are a few primary questions that could offer a framework for which extra unique and precise public fitness measures may be applied.

3. Conclusions

The novel coronavirus originated from the Human seafood marketplace at Wuhan, China wherein bats, snakes, raccoon dogs, palm civets, and different animals are sold, and was transmitted to as much as 213 nations. The zoonotic supply of SARS-CoV-2 isn't showed, however, collection-primarily based totally evaluation recommended bats as the important reservoir. DNA recombination became observed to be worried at spike glycoprotein which diverse SARS-CoV (CoVZXC21 or CoVZC45) with the RBD of some other Beta CoV, as a result might be the purpose for go-species transmission and fast contamination. The researchers are running to increase green healing techniques to address the unconventional coronaviruses. Various extensive-spectrum antivirals formerly used in opposition to influenza, SARS and MERS coronaviruses had been evaluated both on individually or in mixtures to deal with COVID-19 sufferers, mice models, and scientific isolates. Remdesivir, Lopinavir, Ritonavir, and Oseltamivir extensively blocked the COVID-19 contamination in inflamed sufferers. Most importantly, human coronaviruses concentrated on vaccines and antiviral pills must be designed that might be used in opposition to the cutting-edge in addition to destiny epidemics. The symptoms and signs of SARS-CoV-2 prompted COVID-19 are alike influenza and seasonal allergies (pollen allergies). Person affected by influenza or seasonal hypersensitive reaction may show off temperature which may be detected through thermo-scanners, subsequently the man or woman becomes suspected. Therefore, an correct and fast diagnostic package or meter for detection of SARS-CoV-2 in suspected sufferers is required, because the RT-qPCR primarily based totally trying out is costly and time consuming. More so, destiny outbreaks of viruses and pathogens of zoonotic beginning are probably to continue. Therefore, aside from

curtailing this outbreak, efforts must be made to plan complete measures to save outbreaks of zoonotic beginning.

4. Source of Funding

None.

5. Conflict of Interest

None.

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Author biography

A.G. Nerkar, Founder and Director

Praneeta Pawale, Co-Ordinator

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