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CORONAVIRUS [COVID -19] -A SCOPING REVIEW

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ABSTRACT

The 2019 Novel Corona virus infection (COVID 19) is an ongoing public health emergency of international significance. The novel COVID-19 coronavirus Initially observed in the Wuhan province of Following reports of patients with unexplained pneumonia at the end of December 2019 in Wuhan, China, now fatly spreading around the world. There are significant knowledge gaps in the epidemiology, transmission dynamics, investigation tools and management. In this article, we review the available evidence about this disease**.** As this pandemic is very new and very less scientific material is available on the topic**.** The causative agent was identified as coronavirus (SARS-CoV-2), and the 2019 novel coronavirus disease was named COVID 19 by the World Health Organization. the severe acute respiratory syndrome coronavirus (SARS-CoV-2) at the genomic and transcriptomic level. In a short time following the outbreak, it has been shown that, similar to SARS-Cove, COVID-19 virus exploits the angiotensin converting enzyme 2 (ACE2) receptor to gain entry inside the cells. Here, we investigate the density of the expression levels of ACE2 in the CNS, the host−virus interaction and relate it to the pathogenesis and complications seen in the recent cases resulting from the COVID-19 outbreak. it is important to consider potential plausible mechanisms by which hypertension or hypertension medications might influence COVID-19 severity. The mechanisms underlying the purported association between COVID-19 severity and hypertension are not clear, but some evidence points towards a pathogenic role for the renin–angiotensin system (RAS), as it is tied directly to both viral transmission and hypertension.

KEYWORDS: Immune system against Covid-19, Genetic Recombination in Coronaviruses, Epidemiology and Pathogenesis, Virus isolation, Collection of specimens for laboratory diagnosis, RT-PCR.

1. INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a respiratory disease which will spread from person to person. The virus that causes COVID-19 may be a novel coronavirus that was first identified during an investigation into an epidemic in Wuhan, China. And it's a Broad Spectrum antiviral Niclosamide.[1,2] COVID-19 is presumably developed from bat origin coronaviruses. Coronaviruses (Coves) are an outsized family of viruses that cause illness starting from the cold to more severe diseases like Middle East Respiratory Syndrome (Merson) and Severe Acute Respiratory Syndrome (SARS-Cove). a completely unique coronavirus (no) may be a new strain that has not been previously identified in humans.[3] Coronaviruses are zoonotic, meaning they're transmitted between animals and other people. Detailed investigations found that SARS-Cove was transmitted from civet cats to humans and MERS-Cove from dromedary camels to humans.[4] Several known coronaviruses are circulating in animals that haven't yet infected humans. Coronaviruses are large, enveloped, positive-stranded RNA viruses. they need the most important genome among all RNA viruses.[5] The genome is packed inside a helical capsid formed by the nucleocapsid protein and further surrounded by an envelope. the viral envelope are a minimum of three structural proteins: the membrane protein and therefore the envelope protein are involved in virus assembly, whereas the spike protein mediates virus entry into host cells. On 30 January 2020, the planet Health Organization (WHO) declared the outbreak a Public Health Emergency of International Concern. The WHO recommended that the interim name of the disease causing the present outbreak should be 2019-nCoV acute respiratory illness.[6]

1.1. Immune system against Covid-19

Cytokines produced by T-helper (Th) lymphocytes regulate immunity and inflammation. Th1-type cytokines are microbicidal and proinflammatory and chiefly include gamma interferon (IFN-γ), interleukin (IL)-1α, IL-1β, IL-6 and IL-12. In contrast, Th2-type cytokines are anti-inflammatory and comprise IL-4, IL-10, IL-13 and reworking protein beta (TGF-ß). In pregnancy, the attenuation in cell-mediated immunity by Th1 cells thanks to the physiological shift to a Th2 dominant environment contributes to overall infectious morbidity by increasing maternal susceptibility to intracellular pathogens like viruses.[7,8,9] In contrast,

patients with COVID-19 demonstrated activation of both Th1 and Th2 immunity over similar periods within the disease course, culminating within the presence of IFNγ and IL-1β additionally to IL-4 and IL-10. Additionally, elevated levels of IL-6 (which may be a predominantly Th1 response), is related to a significantly increased risk of mortality in COVID-19 patients.[10,11] Marine studies of influenza have demonstrated that pregnancy increases influenza- 253 related pathology via disrupted viral clearance, increased pulmonary IL-6, IL-1α, and G-CSF 254 expression and enhanced physiological stress within the lungs, influenced by changes in prostaglandin and progesterone levels.[11] However in COVID-19, a variety of immune 256 responses has been described, and early adaptive immune responses could also be predictive of milder disease severity.[7]

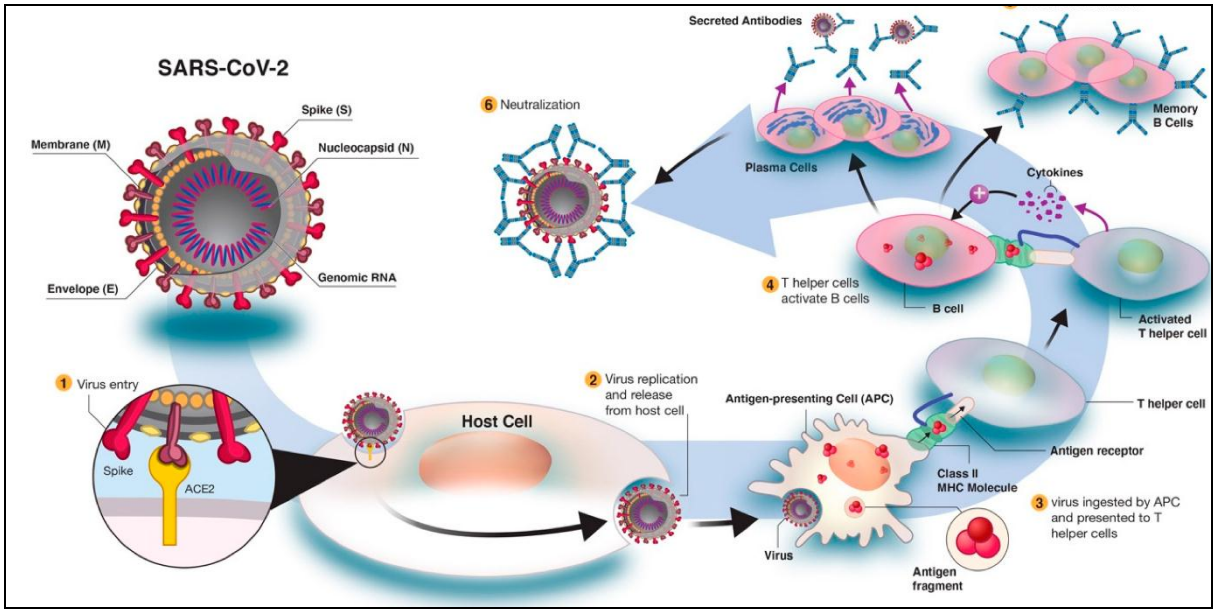


Fig. no.1: Mechanism of Immune system against Covid-19.

1.2. Genetic Recombination in Coronaviruses

The major reason for recombination could also be at the replication step within the virus life cycle. During replication, a group of subgenomic RNAs is generated, increasing the homologous recombination rate among closely related genes from different lineages of CoVs or other viruses by template switching.[12] Concurrently, circulating CoVs in multiple host species likely contribute to increases within the rate of recombination events. However, the precise mechanism of genetic recombination in CoVs remains unclear: recombination site 'breakpoints' within the viral genome the crossing point of the recombinant genes between two distinct viral strains or genotypes appear to be random, as different recombinant strains have different breakpoints.[13]

1.3. Epidemiology and Pathogenesis

The majority of the cases reported early were associated with exposure at the Wuhan Seafood Wholesale Market where an outsized sort of vertebrate and invertebrate animals, wild caught and farm raised, were sold. it's been postulated that bats are the first source and spread to humans occurred possibly via transmission from wild animals illegally sold within the market.[14,15,16,17] ACE2, found within the lower tract of humans, is understood as cell receptor for SARS-CoV and regulates both the cross-species and human-to-human transmission Isolated from the broncho alveolar lavage fluid (BALF) of a COVID-19 patient have confirmed that the SARS-CoV-2 uses an equivalent cellular entry receptor, ACE2, as SARS-CoV. The virion S-glycoprotein on the surface of coronavirus can attach to the receptor, ACE2 on the surface of human cells S glycoprotein includes two subunits, S1 and S2 S1 determines the virus-host range and cellular tropism with the key function domain − RBD, while S2 mediates virus-cell membrane fusion by two tandem domains, heptad repeats 1 (HR1) and HR2.[18,19,20,21] Spread from One person-to anathor person happens among close contacts (about 6 feet) mainly via respiratory droplets through contact with mucosa of mouth, nose and possibly eyes. A familial cluster of cases from Shenzen and Vietnam provided the primary evidence suggesting such human to human transmission.[16] After membrane fusion, the viral genome RNA is released into the cytoplasm, and therefore the uncoated RNA translates two polyproteins, pp1a and pp1ab, which encode non-structural proteins, and form replication-transcription complex (RTC) in double-membrane vesicle.[17] Continuously RTC replicate and synthesize a nested set of subgenomic RNAs, which encode accessory proteins and structural proteins. Mediating endoplasmic reticulum (ER) and Golgi, newly formed genomic RNA, nucleocapsid proteins and envelope glycoproteins assemble and form viral particle buds. Jan. 3, 2020, 44 cases were reported to the WHO.[14]

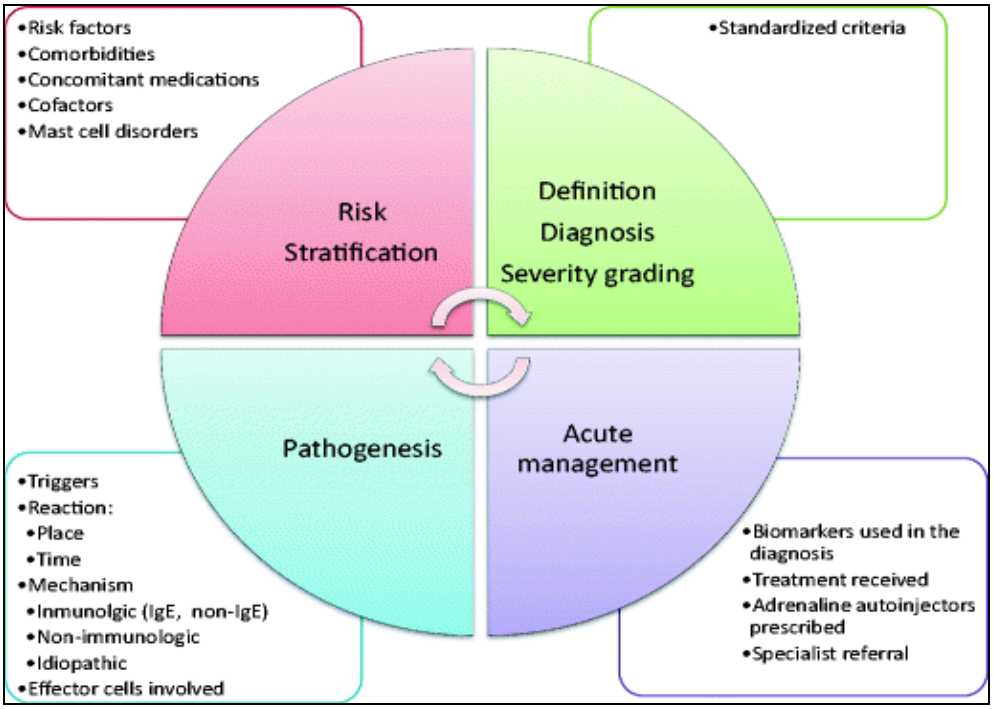


Fig. no. 2: Epidemiology and Pathogenesis of COVID-19.

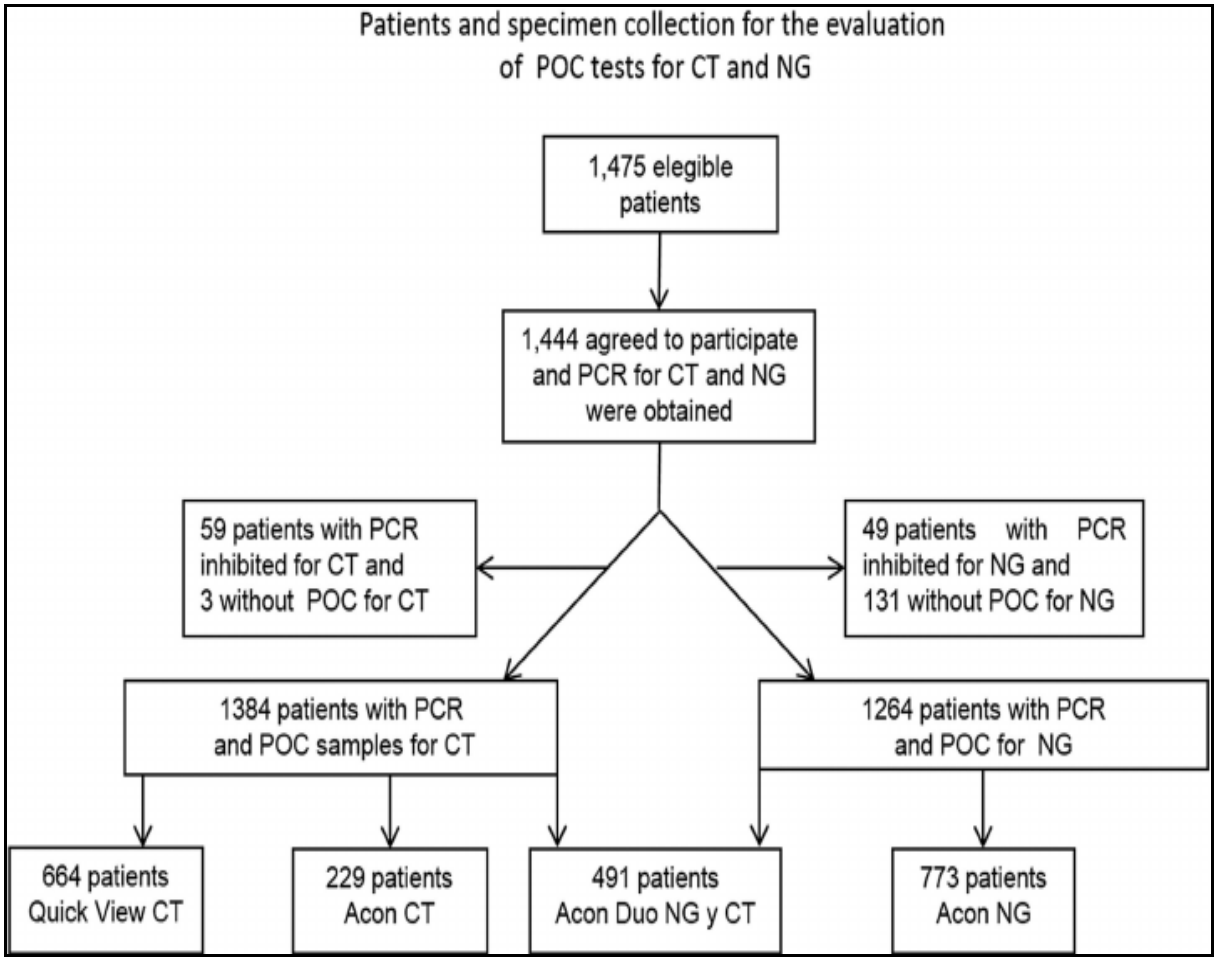
1.4. Virus isolation

The virus was isolate d from nasopharyngeal and oropharyngeal samples from putative COVID-19 patients. Oropharyngeal samples were diluted with viral transfer medium containing nasopharyngeal swabs and antibiotics (Nystadin, penicillin-streptomycin 1:1 dilution) at 1:4 ratio and incubated for 1 hour at 4°C, before being inoculated onto Vero cells. Inoculated Vero cells were cultured at 37°C, 5% CO2 in 1× Dulbecco's modified Eagle's medium (DMEM) supplemented with 2% fetal bovine serum and penicillin-streptomycin. Virus replication and isolation were confirmed through cytopathic effects, gene detection, and microscopy. Viral culture of SARS-CoV-2 was conducted during a biosafety Level-3 facility consistent with laboratory biosafety guidelines of Korea Centers for Disease Control and Prevention.[22]

1.5. Collection of specimens for laboratory diagnosis

Collect blood cultures for bacteria that cause pneumonia and sepsis, ideally before antimicrobial therapy. don't delay antimicrobial therapy to gather blood cultures. Collect specimens from the upper tract (URT; nasopharyngeal and oropharyngeal), where clinical suspicion remains and URT specimens are negative, collect specimens from the lower tract. when readily available (LRT; expectorated sputum, endotracheal aspirate, or bronchoalveolar lavage in ventilated patient) for SARS-CoV-2 testing by RT-PCR and bacterial

stains/cultures. In hospitalized patients with confirmed COVID-19, repeat URT and LRT samples are often collected to demonstrate viral clearance.[11] The frequency of specimen collection will depend upon local epidemic characteristics and resources. For hospital discharge, during a clinically recovered patient two negative tests, a minimum of 24 hours apart, is suggested. Both URT and LRT specimens are often tested for other respiratory viruses, like influenza A and B (including zoonotic influenza A), respiratory syncytial virus, parainfluenza viruses, rhinoviruses, adenoviruses, entero viruses (e.g. EVD68), human metapneumovirus and endemic human coronaviruses (i.e. HKU1, OC43, NL63, and 229E). LRT specimens also can be tested for bacterial pathogens, including Legionella pneumophila.[23,24]



1.6. Reverse Transcriptase Polymerase Chain Reaction (RT-PCR)

A primer is attached to the 3 prime end of a single strand of viral RNA Deoxynucleoside triphosphates are added stepwise creating a DNA copy of the viral RNA. The single strand of DNA is separated and double-stranded complementary DNA (cDNA) is prepared copies of which are synthesized using primers and DNA polymerase Step 6 can be repeated many

times, doubling the numbers of DNA molecules created each time; 30 steps, for example will yield 230 (i.e. 1,073,741,824) or about 109 molecules An immunoassay has also been described, but it has a high false omission (or exclusion) rate Efforts are currently being made to develop and implement an immunoassay for antiviral antibodies to determine whether infection has previously occurred.[25] The RNA transcripts of SARS-CoV. The primer and probe sequences used for RNA-dependent RNA polymerase gene detection were: 5′GTGARATGGTCATGTG- TGGCGG-3' (Forward), 5'CARATGTTAAASACACTATTA GCATA-'3 (Reverse) and 5'CAGGTGGAACCTCATCAGGAGATGC-3' (Probe in 5-FAM/3'- BHQ format) and the primer and probe sequences used for E gene detection were: 5'ACAGGTACGTTAATAG- TTAATAGCGT-3' (Forward), 5'ATATTGCAGCAGTACGCACACA-3' (Reverse) and 5'A-CACTAGCCATCCTTACTGCGCTTCG-3' (Probe in 5-FAM/3'- BHQ format). A 25-µL reaction was setup that contained 5 µL of RNA, 12.5 µL of 2 × reaction buffer provided with the Agpath IDTM 1 step RT-PCR system (Thermo Fisher Scientific, Waltham, USA), 1 µL of 25 × enzyme mixture, 1 µL of forward and reverse primers at 10 pM, and 0.5 µL of each probe at 10 pM. Reverse transcription was performed at 50°C for 30 minutes, followed by inactivation of the reverse transcriptase at 95°C for 10 minutes. PCR amplification was performed with 40 cycles at 95°C for 15 seconds and 60°C for 1 minute using an ABI 7500 Fast instrument (Thermo Fisher Scientific)[6] As RT-PCR is a quantitative method where the amplification of DNA is detected in real-time, the determination of viral load in COVID-19 is theoretically possible. The practical limitations of RT- PCR testing include the need for a biosafety level-2 (BSL-2) facility, a requirement for kits with specific reagents and primers, the need to maintain a cold chain (as the specimens require storage at 2 – 8 C) and the use of strict, validated protocols for testing consequently, countries with resource limitations or acute spikes in the numbers of suspected cases may not be able to meet these demands.[26,27]

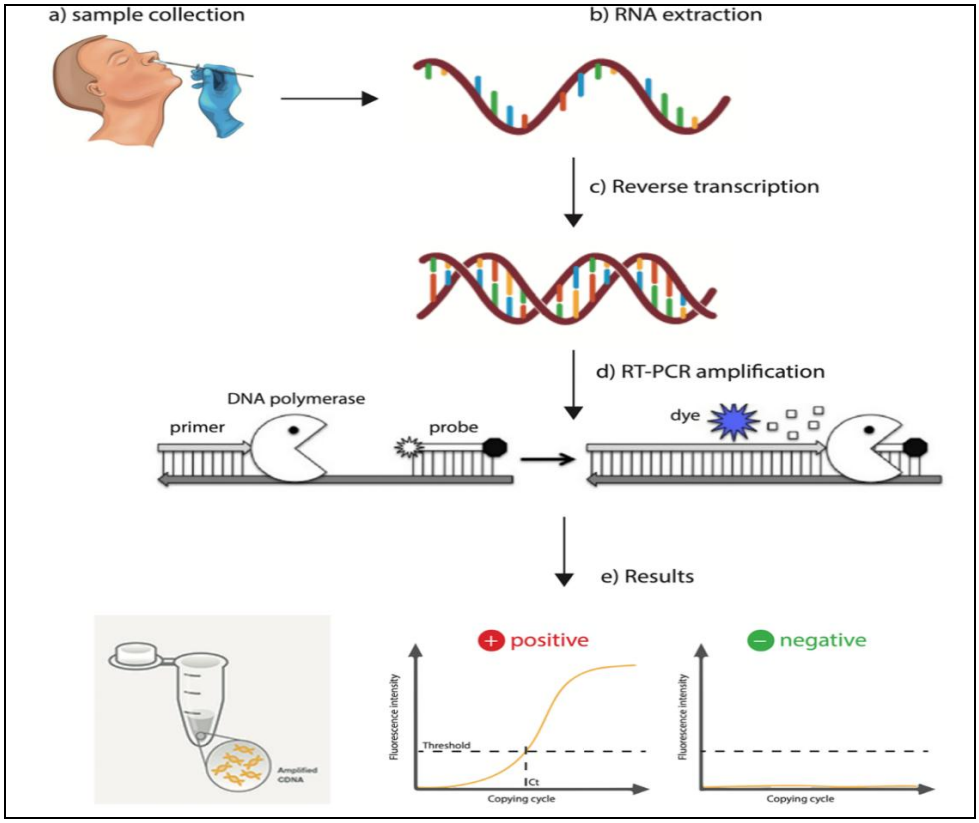


Fig.no. 3: Procedure for RT-PCR.

1.7. Detection of coronavirus in plasma

Each 80 µL plasma sample from the patients and contacts was added into 240 µL of Trizol LS (10296028; Thermo Fisher Scientific, Carlsbad, CA, USA) in the Biosafety Level 3 laboratory. Total RNA was extracted by Direct-zol RNA Miniprep kit (R2050; Zymo research, Irvine, CA, USA) according to the manufacturer's instructions 50 µL elution was obtained for each sample. 5 µL RNA was used for real-time RT-PCR, which targeted the NP gene using AgPath-ID One-Step RT-PCR Reagent (AM1005; Thermo Fisher Scientific).[28,29] The final reaction mix concentration of the primers was 500 nM and probe was 200 nM. Real-time RT-PCR was performed using the following conditions: 50°C for 15 min and 95°C for 3 min, 50 cycles of amplification at 95°C for 10 s and 60°C for 45 s. Since we did not perform tests for detecting infectious virus in blood, we avoided the term viraemia and used Anaemia instead. Anaemia was defined as a positive result for real-time RT-PCR in the plasma sample.[30]

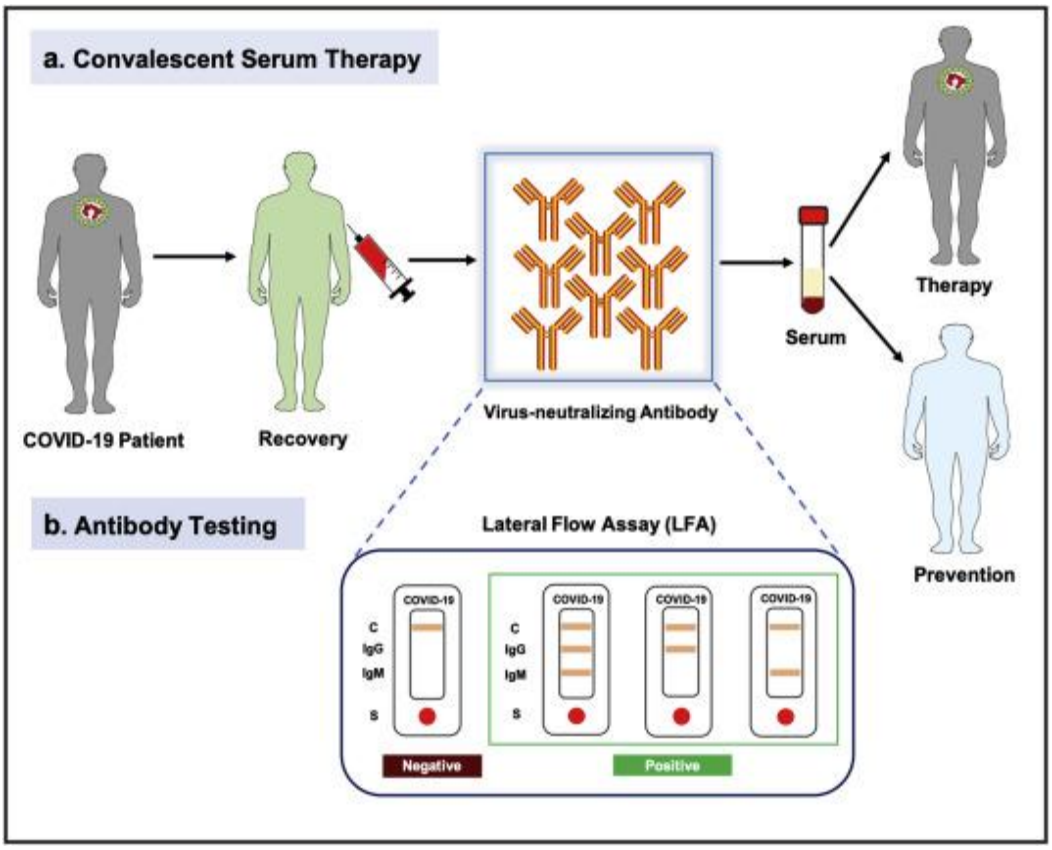


Fig.no. 4: Detection of coronavirus in plasma.

2. CONCLUSION

Insights into the Pathophysiology, Transmission dynamics, Clinical features & management of this virus developing. It is highly transmissible infection but mortality is less compared to SARS and MERS. The cerebral damage may complicate a COVID-19 infection, it appears that it is the widespread dysregulation of homeostasis caused by pulmonary, renal, cardiac, and circulatory damage that proves fatal in COIVD-19 patients. COVID-19 can take a lead in causing death long before systemic homeostatic dysregulation sets in. Although cases are primarily in China, it is highly likely that there will be additional global spread of the virus. It is important to be vigilant about the spread of the disease and be able to provide rapid implementation of outbreak control and management measures once the virus reaches a community.

3. CONFLICT OF INTEREST

All authors have participated in (a) conception and design, or analysis and interpretation of the data; (b) drafting the article or revising it critically for important intellectual content; and (c) approval of the final version.

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