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Are Viral Pandemics a New Bane? - Struggle with COVID -19 Pandemic

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ABSTRACT

Between 1940 and 2004 there were 335 emerging infectious diseases (EID) origins reported globally (1). The emerging and re-emerging viruses witnessed in the last decade are mainly (H1N1, H3N2, Ebola virus, Zika virus, SARS, MERS, Nipah virus). Though these outbreaks were controlled but with many flaws like a late response, inadequate resources, no effective vaccines or drugs, etc. Many issues were addressed post outbreaks to plan, and possibly prevent the next global pandemic, but presently the status is questionable. In December 2019 the health care system was severely challenged by the spread of new emerging virus SARS-CoV2 (2). It soon caused a pandemic due to its high human to human transmission rate, generating an unprecedented impact globally. Multiple weapons had been used to fight against the spread of this virus. It started with the public health policies like respiratory etiquette, social distancing, hand hygiene, good sanitation practices, and staying indoors, immediately seconded by the laboratory diagnostics, which helped for the isolation of positive cases and quarantine of high-risk persons. The scope of diagnostic tests evolved a lot in search of a rapid, reliable, and affordable test. Effective drugs and vaccines are still awaited although multiple randomized controlled trials are ongoing. In this review, the previous viral pandemics struggle with diagnostics for COVID-19 and their latest status with the drug and vaccine is covered.

INTRODUCTION:

Viruses and humans

The global population is always at risk of the unexpected emergence of a new and fatal infectious disease with pandemic potential. Medical history has witnessed several contagious diseases and still, the human population continues to be under threat. Viruses are emerging threats, 20th century witnessed three pandemics of influenza virus (H1N1 in 1917-18, H2N2 in 1957-58, and H3N2 in 1968) and in the 21st century COVID-19 is the second pandemic preceded by H1N1 in 2009 (3). Also, multiple outbreaks by other emerging and re-emerging viruses (SARS, MERS, Ebola, Zika, and Nipah viruses) in the last decade had questioned the global preparation to handle them. The MERS outbreak had the highest impact on the human population with a mortality rate of up to 34.4% (4), and all collectively contributed to millions of cases. They have created a great concern, as to date we are without any effective drug or vaccine against these viruses, despite spending millions and conducting multiple united trials by global communities. Therefore these viruses have the potential to cause future pandemics. Moreover, the contribution of research laboratories for new viruses cannot be denied. Millions are affected worldwide, especially the malnourished, weak, and immunosuppressed population, adding to it is poverty, poor sanitation, overcrowding, and environmental degradation in low and middle-income countries. According to WHO, 137 million people in urban centers have no access to safe drinking water, and over 600 million lack sanitation (1). Therefore 'One Health' approach' (integration of human, veterinary, and agricultural medicine) and target surveillance can warn us of early signs of emerging infectious diseases. Therefore pathogens with pandemic potential should be under active global surveillance. This will provide us with a better opportunity to respond appropriately and allocate global resources.

Emergence and spread of SARS-CoV-2

COVID-19 is the first viral non-influenza pandemic declared by WHO on 11th March 2020 (5). COVID-19 chapter, dates back to 31st December 2019, when Chinese authorities informed WHO regarding the cluster of pneumonia cases of unknown origin, in the city of Wuhan in Hubei province. WHO responded to these cluster of pneumonia cases and issued its 1st guidance on 10th January 2020 regarding its reference to other coronaviruses like SARS and MERS. The novel coronavirus (2019-nCoV) was the interim name recommended by WHO in January (6). Soon this virus was reported outside China, the 1st laboratory-confirmed

case was from Thailand. Within a month this virus was also reported from Japan and Singapore, acknowledging this it was declared as Public Health Emergency of International Concern (PHEIC) on 30th January 2020 (7). To be more clear and precise the infection was renamed COVID-19 on 11th February 2020 by WHO (5). The virus was also named, "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)" on 11 February 2020 by the International Committee on Taxonomy of Viruses (ICTV), due to its genetic resemblance to the coronavirus responsible for the SARS outbreak of 2003 (7). Subsequently, understanding the nature of COVID-19, several guidelines were issued by WHO to combat the disease, which included public awareness regarding personal protection (wearing masks and hand hygiene), restricting social gathering, and compulsory social distancing (8). Simultaneously the development of effective and rapid diagnostics, treatment, and the vaccine was stressed. After witnessing the alarming global spread and severity of the outbreak for a month, it was declared as Pandemic on 11th March 2020 by WHO (5).

The graph of COVID-19 confirmed cases, had an increasing trend globally. Millions are affected and thousands have died to date. The status of the COVID-19 cases after 6 months of pandemic (September 2020), is depicted in figures I, II, and III showing both the Global (9) and Indian trends (10).

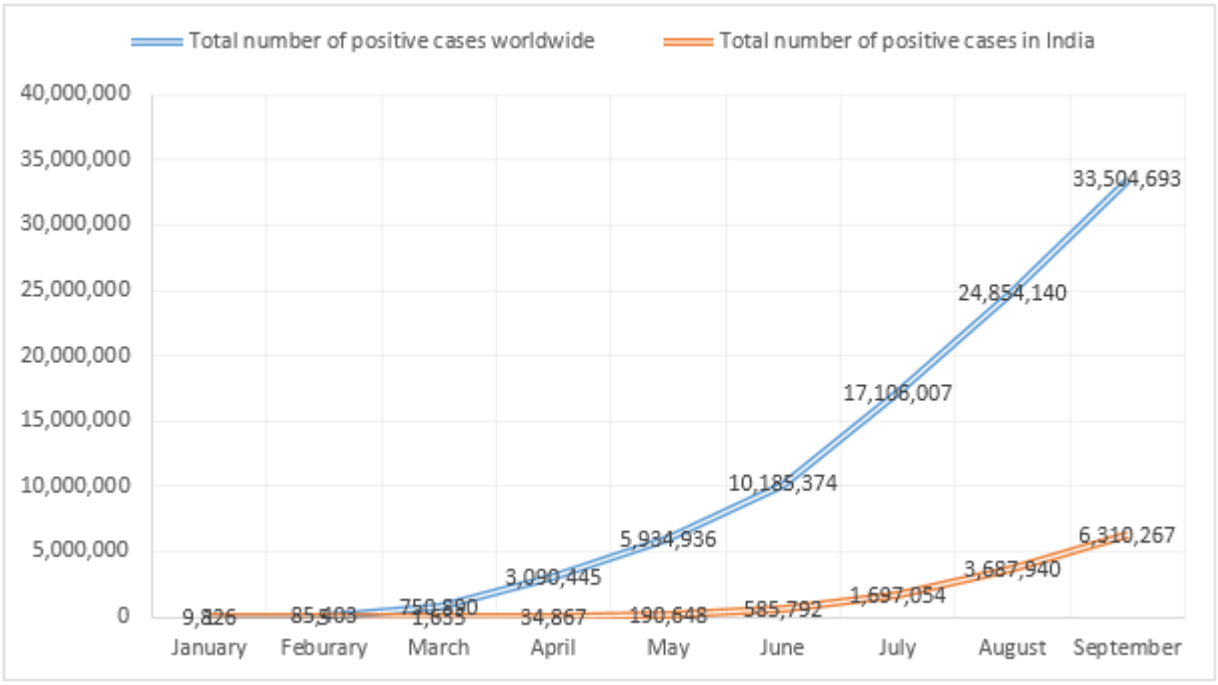

Figure No. 1: Positive COVID -19 cases reported worldwide and in India till September 2020

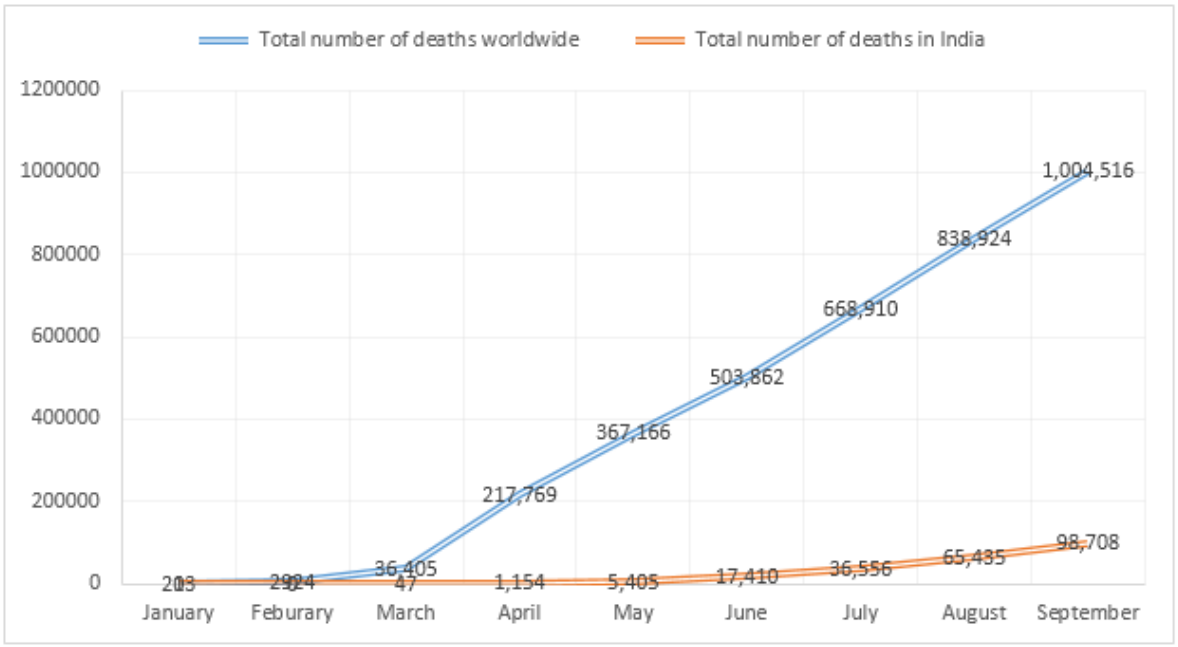

Figure No. 2: Mortality of COVID -19 cases reported worldwide and in India till September 2020

The mortality rate varied worldwide in different regions, it was reported to be highest in April and May (11). The highest mortality rate was reported in the European region up to 9.4% (11), whereas in India the highest mortality was 3.3 % (10). The different behavior of the virus in different regions is still to be understood.

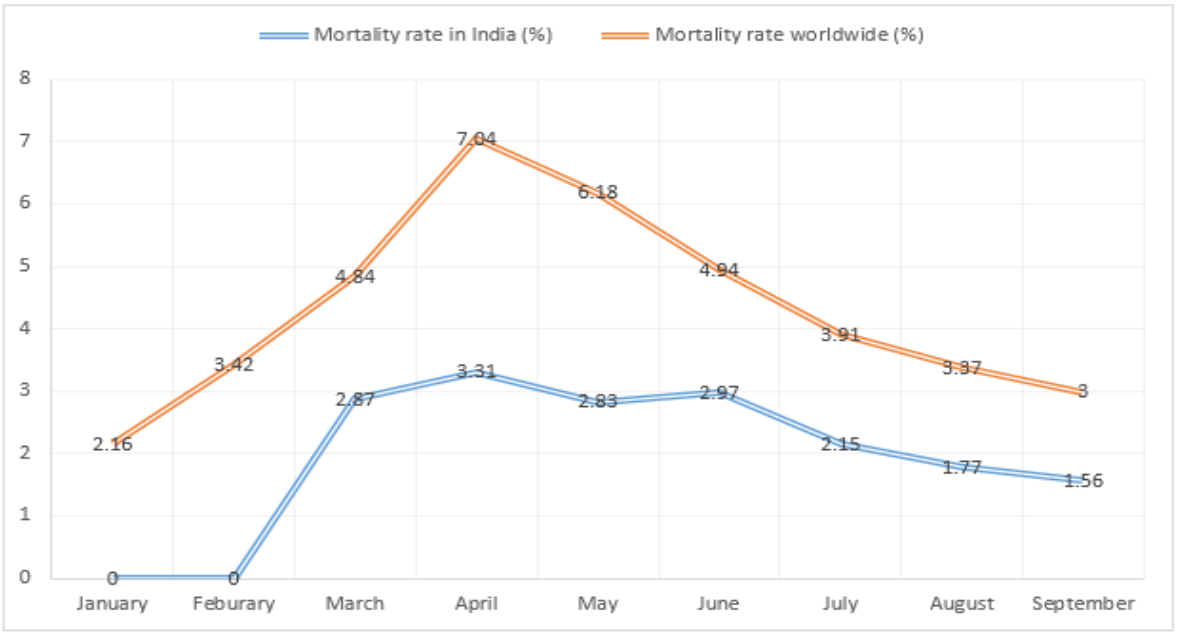

Figure No. 3: Comparison of the Mortality in COVID -19 worldwide and India till September 2020

Though the confirmed cases are rising globally as well as in India, the mortality seems to decrease.

Clinical Presentation of COVID-19 cases

To combat this highly infectious pandemic, early identification of the symptoms is an important aspect. Understanding the pathogenesis of COVID-19 is still evolving. The list of clinical presentation has recently been updated by the Centers for disease control and prevention (CDC) (12) and its degenerative and inflammatory effects on the neurological system have also been decoded. Initially, it was thought to be only the respiratory virus but now symptoms of other systems are also being reported. Clinical symptoms reported are long-standing fever, dry cough and headache being the major symptoms, less commonly there can be loss of smell/taste, dizziness, conjunctivitis, chills, muscle pain, tiredness and now recently 3 more symptoms have been added by CDC i.e. running nose and chest congestion, nausea and diarrhea. The symptoms vary widely in different situations, kids though present with mild symptoms, but at times may have a presentation like Kawasaki disease (12). The elderly are reported to suffer from critical illness and the mortality up to 10% in > 60 years of age (13). The severity with increased mortality also increases in immunocompromised and patients with comorbidities like diabetes mellitus, cancer, prior stroke, and chronic cardiovascular, renal or respiratory disease.

Bundle of diagnostic test used

Given the lack of effective vaccine or treatments, the only currently available strategy to slow the pandemic is through identifying and isolating contagious persons through early and massive deployment of (SARS–CoV-2) testing. In the case of outbreaks, it plays a significant role in the surveillance and containment of the disease. In this ongoing pandemic of COVID - 19, our knowledge regarding the timings and interpretation of various diagnostics used is still evolving. Various diagnostic modalities had been used since the disease emerged. Radiological test (CT-SCAN was first to be used, followed by molecular tests – (RT-PCR, CBNAAT, Trunat) and various serological tests (ELISA, ICT).

Radiology - Computed tomography (CT) of the chest is rapid and the positives findings help in isolating the patients early in the disease. The main features of CT- chest in patients suffering from COVID-19 are Ground-glass opacities (GGOs) and consolidation. Other signs like vascular enlargement, interlobular septal thickening, and air Bronchogram signs are

common for all viral pneumonia (14). Specificity is less as adenoviruses, influenza virus, SARS, MERS, and other viruses of the same family exhibit similar patterns on CT. Positive predictive value is very less, therefore negative findings may give false security and further increase spread. A vast range of sensitivities ranging from 60% to 98% had been reported in the literature (15, 16, 17, 18). Authors of studies with good sensitivities suggest that CT-scan can be used as a primary tool/screening tool for diagnosing COVID-19 in epidemics. This was analyzed by WHO and many methodological limitations were found. All the studies were retrospective, and the study cohort had biased patients (RT-PCR positives) (15,17), no valid gold standard diagnostic was there (usually single PCR was taken), cohort number was very small, co-relation with the clinical presentation was lacking no studies were with asymptomatics, moreover the CT findings varied with the stage of the disease and were not specific. Bernhein et al. (19) has reported that 56% of the early patients had normal CT findings. Another limitation is the transmission of infection to the healthcare professionals, CT scanners may also become potential vectors of infection for the other patients if the machines are not properly sterilized. This is a major challenge in developing countries where mostly only one CT-machine is there in the hospital. Considering all this American College of Radiology (20) on March 22 mentioned the CT scan should not be used as a screening tool or 1st line to diagnose COVID-19.

In imaging apart from CT-scan, studies with X-ray chest and lung Ultrasound are also published. Sensitivities reported with chest X-rays are 64% from Italy (21), 42% from the USA (22), and 69% from China (23). As compared to CT-scan the sensitivity is less and specificity may be high, but the data is very limited to draw any conclusions. Only one study (24) has published the results of Lung USG comparing it with CT-scan. Both these diagnostics need further extensive studies, for reliable data, as they have the advantage of easy sterilization of the equipment.

So far in situations of newer outbreaks, identifying the genetic material in clinical specimens, had been used as the most reliable diagnostic. In the COVID-19 pandemic also RT-PCR soon became the frontline test. Various samples used for diagnosis were nasopharyngeal swabs, oropharyngeal swabs, saliva, and other upper respiratory tract specimens (BAL, Tracheal aspirate, etc.).

Molecular tests - Real-time polymerase chain reaction (RT-PCR) - Various RNA genes were targeted including genes that encode structural proteins and species-specific accessory genes

(1). Structural proteins are nucleocapsid (N1 & N2), helicase (Hel), transmembrane (M), envelope E-gene and glycoproteins spike (S), and species-specific genes are RNA-dependent RNA polymerase (RdRP), open reading frame 1a (ORF1a) and ORF1b and hemagglutinin-esterase (HE) genes (25). These are used in different combinations, provided by different manufactures. Till now, there has been no evidence that any one of the sequence regions targeted offers an advantage over the other for diagnosis. To avoid any cross-reactions and minimize false positives and false negatives at least two molecular targets should be included (one conserved region and one specific region). Various combinations of gene targets are taken by different authorities:- CDC recommends only one step (25): targeting two nucleocapsid protein targets N1 and N2. WHO recommends two steps (26): screening with an E gene assay followed by a confirmatory assay using the RdRp gene. ICMR-NIV Pune guidelines for RT-PCR has two steps (27): Screening is with – E gene and confirmatory is with Orf1b and RdRp gene.

Different manufacturers providing RT-PCR kits are Altona Diagnostics, BGI, CerTest Biotec, KH Medical, Primerdesign, R-Biopharm AG, Seegene, etc, over 500 different kits with approval status are available on ICMR web page (28).

In India initially, ICMR-NIV Pune framed guidelines for the diagnosis of COVID-19, by adopting a two-step strategy using RT-PCR. The screening was done with the *E* (envelope) gene which is specific to the Sarbeco sub-genus and confirmatory run targeted two genes, SARS-CoV-2 specific *RdRp* (RNA dependent RNA polymerase) gene, and *ORF-1b-nsp14* gene. Either of the two genes of confirmatory run showing significant Ct value is confirmed as positive for SARS-CoV-2 (29). Thus the quality of the sample and identification of true positives both were ensured. But this was both, time-consuming and expensive. Thus after analyzing some studies (30, 31) it was suggested that confirmatory run with *ORF-1b-nsp14* gene will be cost-effective and more sensitive as compared to the RdRp gene.

Truenat Beta CoV- Another gene detection based technology is TrueNat (32). It is a microchip-based real-time PCR assay, its advantages being its small size, battery-based, and requires minimally trained staff. It is a chip-based RT-PCR, with semi-quantitative detection of SARS-CoV2 RNA. The target sequence used is the *E gene* for screening and *RdRp* as a confirmatory gene. Its portability facilitates its use in the periphery even with limited resources, closed nature of the instrument, and minimum sample handling add to its advantages. The basic disadvantage is its limited capacity, of the samples tested in one run

(one or two) moreover the cycle run is of 60 minutes, for each step. (latest version is Quattro Real-Time Quantitative micro PCR Analyzer (4 samples can be processed with multiplexing) is under evaluation.

GeneXpert - Continuing with the efforts for expanding the quality diagnostic capacity worldwide, WHO considered GeneXpert machines as a good option for COVID-19 testing. It is a cartridge-based nucleic acid amplification test (CB-NAAT) based on PCR technology and the advantages are, it is being fully automated with 45 minutes cycle time (33). This platform is already in use in the laboratories for testing tuberculosis with laboratory staff being familiar with its use, making its use more convenient. Targets in Cepheid's Xpert Xpress SARS-CoV-2 test are *E gene* and *N2 gene* in the same cartridge.

Loop-mediated isothermal amplification (LAMP) – This technique detects DNA, but with reverse transcriptase, it can be a single step, rapid (30 min), simpler, and highly sensitive diagnostic test (RT-LAMP). This nucleic acid detection method is being explored by many (34, 35, 36) for its practicability in COVID-19 diagnostics. Its high specificity owes to the use of 6 primers targeting 6 sequences, thereby avoiding non-specific amplification of other coronaviruses and respiratory viruses. Its sensitivity is reported to be 80 copies of RNA/ml of sample. Its major disadvantages still to overcome are carry-over contamination and aerosol spread in the environment.

RT-PCR besides having good sensitivity and specificity has some limitations also. It is highly expensive and requires technical expertise therefore cannot be universally available. Turnaround time (TAT) is long and the reported sensitivities also have a wide range. Because of these limitations, other technology-based tests had always been considered as a screening tool.

CRISPER (Clustered Regularly Interspaced Short Palindromic) Cas technology - this technology is being widely used for accurate and rapid diagnostics for infectious diseases targeting either RNA or DNA. CRISPER Cas 12a, Cas 13a, and Cas 13b have been recently applied in detection assays for COVID-19 with good results (37). It is a rapid molecular method that includes isothermal amplification, detection, and visual readout results. Various assays have been developed based on their targets and CRISPER cas –

Table No. 1: Various assays developed based on their targets and CRISPER

ASSAY	Sensitivity	Time	Target	CRISPER Cas	Result readout
DETECTR assay (38)	10-100 copies of RNA/ µL	Approx. 40 min.	E gene and N2 gene	Cas 12a	Lateral flow strips
SHERLOCK (39)	1 molecule / µL	60 min	S gene and ORF gene	Cas 13	Fluorescent visualization
AIOD (all in one dual) (40)	4.6 – 11 copies of RNA/ µL	90 min	S gene and ORF gene	Cas 12a	Fluorescent visualization
CREST (41)	10 copies of RNA/ µL	1-2 hours	Viral RNA	Cas 13	Fluorescent visualization
FELUDA (42)	110 femtomolar	1-2 hours	Viral RNA	Cas9	Fluorescent visualization, Lateral flow strips

Serology tests - Keeping in view the basic goal to test, treat, and track COVID-19 patients, serological diagnostics are being explored. Expecting to be rapid, user-friendly, and cost-effective diagnostics, they are designed to detect either antigen or antibody.

Antibody detection - these tests require the knowledge of the proteins that form the viral coat and to which the host immune system responds for triggering the production of antibodies. Though all the viral proteins elicit some antibody response the main antigens are the spike proteins and nucleocapsid proteins (43). The disease can be determined by detecting either IgM and IgG antibodies or both depending upon the state of infection. IgG ELISA has been done at ICMR-NIV Pune on a trial basis with sensitivity 92.37 % and specificity 97.9 % (44). Immunochromatography also detects IgM / IgG antibodies claiming to be a point of care test but acute infection cannot be confirmed. Though rising titers can confirm present infection still these are not recommended by WHO as a diagnostic test. Antibody response develops only after 2 weeks of infection in the majority of cases, therefore their detection is of significance in estimating the prevalence, attack rate, infection fatality rate in the population which further supports the development of vaccines. Moreover, to answer questions like, how

long the protection lasts after the appearance of antibodies? What is the level of antibodies required for protection? Will they provide lifelong immunity? The status of antibodies at different stages of the disease? Disease surveillance and epidemiological research are encouraged by WHO using these serological tests.

Antigen detection - these are other targets for serological diagnostics. They are the specific proteins that are expressed during the stage when viruses are actively replicating therefore acute/early infection can be diagnosed (45). The test detects antigens qualitatively from the respiratory tract (sputum/throat swab) samples and if the target antigen is present in sufficient quantity, they will bind to the corresponding antibodies fixed on the strip, by immuno-chromatographic technique forming a band. The result depends on many factors - the quality of the sample collected, transportation and storage of the sample, the time of sample collection from the onset of illness, and the concentration of the virus also contribute to its sensitivity. Experience of antigen-based Rapid Diagnostic Tests with other viral respiratory diseases has reported its sensitivity varying from 34% to 80%, therefore 50% of the results reported will be unreliable (45). The test has moderate sensitivity but high specificity. It is recommended by ICMR that positives are reported as positives while symptomatic negatives should be confirmed with RT-PCR before reporting. Detection of Antigen or Antibody, though rapid but both have the disadvantage of false positive and false negative reporting.

These assays could be used as triage tests for isolating COVID-19 positives, thereby decreasing the burden for expensive molecular testing.

Point of care tests (POC) -This long fight with the COVID-19 pandemic has raised the need for rapid simple diagnostics. Currently, most COVID-19 testing is being done in molecular laboratories requiring technical expertise and an expensive set-up. In search of rapid, simple, and reliable diagnostics number of point-of-care tests with different technologies are committed to diagnosing COVID-19. POC tests will increase the diagnostic capacity, further helpful in early isolation and management of the patients. POC tests are both serological and molecular.

Rapid diagnostic tests - detect either antigen or antibody, based on immune-chromatography assays. Antibody detection (kit)– (46) Getein COVID -19 is a one-step POC test for the detection of IgM/IgG antibody in serum, plasma, fingertip blood, or whole blood samples. It is based on the principle of using mixed recombinant 2019-nCoV nucleocapsid protein (N protein) and spike protein (S protein) both conjugated with colloidal gold. Different test lines

are used for coating anti-human IgM and IgG antibody. The antigen-antibody complexes will be captured on different test lines and the positive test is read as red streaks on the test lines in 10-15 min. Antigen detection – viral proteins (antigens) expressed by the COVID-19 viruses are detected in respiratory samples, it is a rapid one step POC test. The test is reported in 30 min.

Molecular POCs - Abbott ID NOW COVID-19 (47, 48) is based on isothermal NAAT and detects viral RNA targeting RNA-dependent RNA polymerase (RdRp) with a claimed LOD of 125 genome equivalents/ml in nasal, nasopharyngeal, or throat swabs. It is a mobile, fastest available molecular POC test. The positive result is obtained in 5 min and the negative result in 13 min. It is authorized under EUA and its small size offers an advantage of it being used in small setups like clinics and physician offices. Its performance had been questioned for its sensitivity in case of low viral load, which was reported to be less than what was claimed.

Other molecular POC tests are GeneXpert and LAMP, their basic methodology is the same as RT-PCR, but various steps are automated reducing the reporting time.

CRISPER is also committed to being a molecular POC test. **FELUDA Covid-19 paper strip Test,** India's CRISPR-based COVID Test has been approved by the Drugs Controller General of India. The result will be available in 2 hours with the cost of only Rs 500 for one test (49).

Treatment and prophylaxis

At this time, there are no specific vaccines or treatments available for COVID-19. A new drug takes years for trials and approval for human use. Therefore available drugs are repurposed. Several drugs have been claimed to be effective, but still many clinical trials are ongoing for evaluating their potential efficacy.

The first drug which was recommended on theoretical evidence was an antimalarial Hydroxychloroquine (50). It got approval under EUA in March 2020. Its acts by decreasing viral polymerases thereby altering various viral processes like assembly, glycosylation, transportation, and release of the virus. Soon it was in controversy for its benefits and side effects, and its use was revoked by the FDA in June 2020 (51). Its use with Azithromycin was identified, but in various randomized control trials it was concluded that the regime does

not improve the outcome of the patient rather it can increase the chances of cardiac toxicities (52).

Remdesivir gained emergency use authorization (EUA) from the FDA on May 1, 2020, based on preliminary data showing a faster time to recovery of hospitalized patients with severe viral disease. It acts by inhibiting the RNA-dependent RNA polymerases (RdRps) causing premature termination of viral RNA transcription. It is administered intravenously, and preliminary data shows that it increases recovery rate, slows down viral replication, decreases the severity of disease and symptoms. It is not FDA approved and has EUA (52).

Favipiravir has a mechanism of action the same as Remdesivir. It is an oral drug and was approved in China in March 2020 for marketing (52).

Lopinavir/ Ritonavir is protease inhibitors having preliminary evidence of their effect, and are still under research and development (52).

Several immunostimulants are also promoted for prophylactic purposes, though no literature is available to support their role.

Other drugs with preliminary evidence are Ivermectin, Nitazoxamide, Colchicine, IL-1, and IL-6 inhibitors. Literature till August 2020 shows that several potential therapies for COVID-19 are at various stages of pre-clinical and clinical research (53). The evidence of the effectiveness of most drugs used is highly uncertain and no data support the benefits and harms of one therapy over another.

Several attempts are being made to design and develop vaccines for SARS-CoV2 infection, basically targeting the spike glycoprotein (54). However, extensive diversity in antigenic variants even within the strains has made vaccine production a big challenge. The vaccine is a real need for the hour, but the need is unmet to date. Researchers and scientists worldwide, are struggling for the breakthrough, as currently immunization is preventing 2-3 million deaths by more than 20 life-threatening diseases globally (55). The efforts of many scientists had resulted in the production of vaccines, which are under trial in many countries. According to WHO, more than 100 vaccine candidates are under development and few are in the human trial phase. Various countries like the USA, UK, Russia, China, and India are actively involved in these trials, the vaccines in phase 3 trials till October 8th (56) are:-

1. **Ad5-nCoV** (Recombinant vaccine), sponsored by CanSino Biologics at Tongji Hospital, Wuhan, China.

2. **AZD1222** (Replication-deficient viral vector vaccine), sponsored by AstraZeneca; IQVIA; Serum Institute of India at The University of Oxford and the Jenner Institute.

3. **CoronaVac** (Inactivated vaccine) sponsored by Sinovac at Sinovac Research and Development Co., Ltd.

4. **JNJ-78436735** (Non-replicating viral vector) sponsored by Johnson & Johnson at Johnson & Johnson.

5. **mRNA-1273** (mRNA-based vaccine) sponsored by Moderna at Kaiser Permanente Washington Health Research Institute.

6. **Inactivated vaccine** sponsored by Wuhan Institute of Biological Products; China National Pharmaceutical Group (Sinopharm) at Henan Provincial Center for Disease Control and Prevention.

7. **NVX-CoV2373** (Nanoparticle vaccine) was sponsored by Novavax at Novavax.

Human vaccine trials are initiated in India (57) with approximately 1000 volunteers at various institutes across the country. Three vaccines have been currently approved for these trials. **COVAXIN** (inactivated whole virion candidate vaccine) by Bharat biotech, **ZyCoV-D plasmid** (DNA vaccine) by Zydas Cadila Healthcare, and **Covishield** by Serum Institute of India. Due to the lack of effective antiviral therapy and vaccines in the present scenario, we need to depend solely on implementing the public policies and infection control measures effectively to lessen the possible risk of uncontrolled spread of the virus.

Psychological and Economic impact

COVID-19 has had a huge psychological impact on everyone including the general public, the patient's positive for COVID-19, and healthcare workers. The general public has lived in constant fear of the disease listening and hearing to the COVID-19 related news being circulated on social media. Patients who came positive have suffered the social stigma of outcasts like that was seen in earlier times with leprosy and tuberculosis. The worst fears have been faced by healthcare workers. Bound by duties, they had to attend to their patients, never knowing who could be the positive one giving them the infection. The fears were not

only for themselves but more for their families, them acting as the infection transmitters. Many healthcare workers even chose to stay in isolation, away from their families for their safety. The rate of depression cases has alarmingly risen in these times leading to an increase in suicides as compared to non-COVID times (58). Its impact has extended to the global economy too. Apart from its effect on jobs and salaries, the global stock market has also suffered dramatically. This crisis had introduced new technologies to sustain with, work from home practices, online teaching, telemedicine, and e-commerce are major victors with Covid-19 pandemic.

CONCLUSION:

Struggle with COVID-19 had been an unexpectedly long experience, for the present generation. This coronavirus pandemic has resulted in the foremost human tragedy, which has affected millions of lives. Responding to the pandemic, the whole world has united in research, framing policies, and implementing them. Governments were compelled to go for lockdown constraining personal freedom and the economy had a hard hit globally. Still, the positive effects cannot be ignored. Restricted traveling and socialization have allowed Mother Nature to replenish and recharge. The rate of road traffic accidents and crime has decreased. People are spending quality time with their family members and the importance of sanitation and hand hygiene is reinforced. The pandemic is a lesson for mankind to rethink their priorities, focusing more on health, as said: “Health is Wealth”. Moreover, the crises have revealed that our health care system including laboratory diagnostics needs to be improved and expanded to cater to the present population, to handle any such situation in the future.

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