2019-n-CoV Novel Coronavirus: The foremost reported coronavirus pandemic in history

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Abstract:
In December 2019, a Corona Virus disease (COVID-19) outbreak has spread in Wuhan city of Hubei province of China. The causative organism of the infectious disease was found to be severe acute respiratory syndrome (SARS CoV2) and was declared as pandemic by the World health Organisation (WHO) on 11 March 2020. It has been observed that COVID-19 is of zoonotic genesis found from the studies on infected patients, those who were closely in contact with the wet market of the Wuhan region. The genomic studies have shown that SARS CoV-2 is somewhat similar to severe acute respiratory syndrome (SARS) bat viruses, so it could be assumed that bats could be the precursors. The source of transfer of infection to the humans is unknown but the infection transfer amongst the humans is widely confirmed. The disease outcomes of SARS and MERS are known at a particular level but, limited knowledge is accessible for 2019-n-CoV. As of now, this infectious disease COVID-19 has become a global health warning. To combat this disease and to supress its transmission, various general treatments and steps have been taken. Till now no anti-viral drug or vaccine is available in the market to fight against COVID-19. However, some of the multi-national companies are regularly working and are performing clinical trials on different drug candidates. This review aims to discuss the influx pathway, epidemiology, its transmission, treatment approaches currently in use and its future perspectives. The review might prove to be useful and have some impact on the knowledge of the people to fight against 2019-n CoV.
Keywords: COVID-2019, 2019-n-CoV, Influx Pathway, Epidemiology, Treatment Approaches.

Introduction:

Nearly in future whole world is affected by novel corona virus (2019-n-CoV) infection, that has become the fifth pandemic in history after the flu of 1918. Starting with December 2019, where patients diagnosed with pneumonia were admitted to hospitals in the Hubei province of Wuhan, China were linked with animal and seafood market in Wuhan. These patients showed symptoms like cough, fever and dyspnea. The genomic studies revealed that the causative agent for this spread is the novel corona virus. World Health Organization (WHO) on 12 January 2020 named this disease the corona virus disease 2019 (COVID 2019).[1]

The coronavirus has single strand Ribo Nucleic Acid (RNA) and belongs to coronavirinae subfamily. From the literature survey it has been calculated that Corona Viruses (CoVs)

causing human infections are of six types and is sub categorized into two groups of moderate and exceedingly pathogenic CoVs. [2,3] The moderate CoVs being OC43, NL63 and HKUI cause infections in upper region of respiratory tract in range of 10-30% in humans, whereas exceedingly pathogenic CoVs being Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) cause infections in lower respiratory tract that leads to pneumonia. [4]

The clinical signs of 2019 – CoVs, SARS CoV and MERS CoV has shown some similarities, that can range from asymptomatic illness to serious respiratory diseases, the speedy widespread of novel corona virus makes it a crucial global health warming. The present review expresses the functioning of the virus around the globe, its epidemiology, the pathway of inflow in the host cells, its impersonal demonstration and also the treatments which are presently utilized.

The intention if this review is to offer practical grip in the awareness of 2019-n-CoV a novel virus that has become a global health warning and to set up the successful procedure to fight the 201-n-CoV in nearly future.[4,5]

Classification of virus

Coronaviruses (COVs) belongs to one of the biggest families of viruses existing in nature called *Coronaviridae* and the order is *Nidovirales,* On the basis of genomic classification of viruses the family *Coronaviridae* is further classified into two sub families named *Torovirinae and Coronavirinae.* Further, *Coronavirinae* embraces four subdivisions called *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus* and *Deltacoronavirus*. Among all subgroups these two subdivisions the *Alphacoronavirus* and *Betacoronavirus,* causes infection in the mammals only and are accountable for causing respiratory tract infections in humans as well. The group of *Betacoronavirus* is further classified into five subgroups among which two of them named *Nobecovirus* and *Hibecovirus* does not cause infections in humans.The other three divisions *Merbecovirus*, *Sarbecovirus*, and *Embecovirus* are responsible for causing infections in humans. *Merbecovirus* contains MERS-CoV and *Sarbecovirus* contains SARS-CoV and are the two vital zoonotic CoVs (Table 1).

Table 1: Classification of Coronaviruses in Humans (According to NCBI) (https://www.ncbi.nlm.nih. gov/taxonomy)

Family	**Subfamily**	**Groups**	**Subgroups**	**Species**
	Torovirinae		Hibecovirus	*Human coronavirus HKU1*
		Alphacoronavirus	Embecovirus	*Betacoronavirus 1*
			Setracovirus	*Human coronavirus NL63*
			Nobecovirus	
Coronaviridae				
		Betacoronavirus	Sarbecovirus	*SARS-CoV*
			Merbecovirus	*MERS-CoV*
	Coronavirinae		Unclassified Betacoronavirus	*2019-n-CoV*
		Gammacoronavirus		

		Deltacoronavirus		

This new coronavirus so called 2019-n CoV that has become a global threat is still regarded as unclassified *Betacoronavirus*, but as discussed earlier show 80% of similarities with the bat SARS-like CoV. In contingent to this, the International Committee on Taxonomy of Viruses called it severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Morphology and Genome Structure

The 2019-n-CoV is a spherical, covered and large sized particle with about 120nm in diameter the covering of this virus under electron microscope appears as a pair of dense electron shells in the micrograph presentation.[6] The covering of virus is composed of a lipid bilayer which accommodates the membrane (M), envelope (E) and spike (S) the protease. **(**Figure 1**)** The genomic sequence of CoVs is one dimensional, with single-stranded RNA (+ssRNA) that is (~30 kb in size) and has a 5' Capped end, it is poly adenylated at the 3' end having minimum six open reading frames (ORFs) and other subsidiary genes. The RNA genesis contains around 29,891 nucleotides (Gene Bank accession number MN908947). The terminal 5' is about two third of the genome that contains two ORFs named as ORF 1 and ORF 2, encoded as polyproteins pp1a and pp1ab, which are further cleaved into 11 and 16 proteins which are non-structural. The proteins are fixed in the viral polymerase form and into other non-structured proteins that are involved in synthesis of RNA. All these proteins incorporate. [7,8]

The spike (S), envelope (E), membrane (M), and nucleocapsid (N) fixed in the one third of 3' terminal of the genome. The gene that is of utmost importance and can prove to be one of the successful candidates for producing vaccine is gene S that is responsible for the binding of receptors to the specific host.

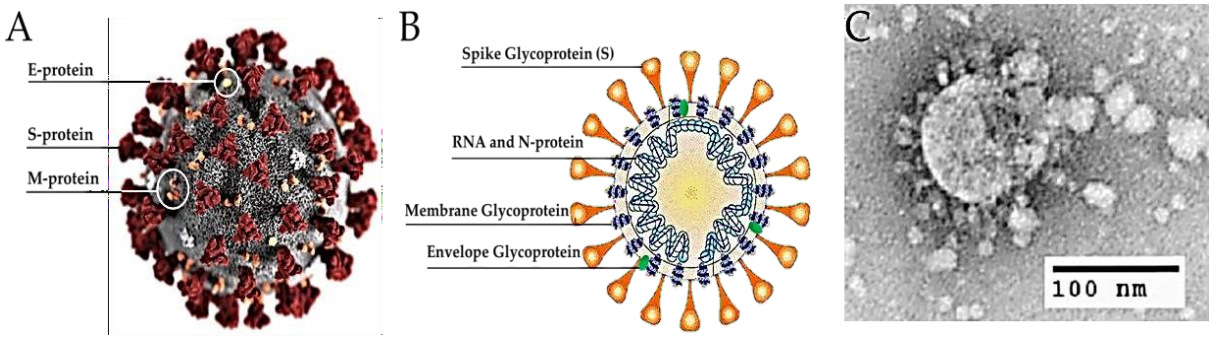

Figure 1: Structure of 2019 n-CoV

Influx Pathway 2019-nCoV of into the Host Cells

Recent reports of literature showed that of around 80% of similarity is seen between SARS-CoV genomic sequence and 2019-n-CoV by WHO, which indicates that 2019-n-CoV works with the same procedure utilising angiotensin converting enzymes 2 (ACE 2) receptor to cause infections in human body cells. The spikes on the surface of coronavirus act as proteins

and eases the entry of virus in the host cells. Cellular protease is responsible and is required for the binding of virus to the receptor and entering into the cells.[9]

The studies have revealed that some strains of 2019-n-CoV and SARS 76 CoV somehow use the ACE 2 receptor for entering the host cells. The investigation of receptor binding motif (RBM) and some part of receptor binding domain (RBD) that is interlinked with ACE 2, showed that many of essential amino acids remains were left over in 2019-n-CoV for the binding of ACE 2, but no proteins were seen in the SARS CoV and it was concluded that it does not utilizes ACE 2 for entering the host cells instead requires protein S for binding to the ACE 2.[9,10]

It has been proved that the entrance of SARS CoV 2 to the host cell can be blocked via an antagonist TMPRSS2 clinically that is a serine protease. These novel findings have shown significance to the knowledge of Corona Viruses (CoVs) in regards to its transmission, pathogenesis and its treatment strategies.[11]

Epidemiology

Beginning with the outbreak of 2019-n-CoV in Wuhan, Hubei, China in December 2019 the virus exceedingly speeded all through China and in other Asian countries like Africa, America and Europe. According to the latest update of WHO, the total patients with COVID-19 positive cases are…. And deaths worldwide by 17^{TH} May, 2020 are that has led it to as a major global health concern. [12]

The information is gathered from the page of WHO site from the situation report site that is being updated daily and another information source is the worldometer that is updated by the team of researchers and volunteers that provide statistics to all of the population worldwide. [13]

Clinical Features and Transmission

Generally, the incubation period of 2019-n-CoV is from 2-14 days with or without symptoms, sometimes symptoms can arise from 3-7 days, the symptoms mostly are cough and fever along with runny nose, headache and diarrhoea. Within a week with the progression of disease other symptoms like poor digestion, restlessness and respiratory failure may appear. In severe cases symptoms like blood loss, shock and coagulation dysfunction may arise.[14]

Table 3 Represents the clinical findings from the different investigations. The novel virus gets diffused in the form of droplets to respiratory system when infected patients either sneezes or cough. Also, the transmission of the infection could be through close contact and from mother to infants or through breast feeding.

Table 2: Data Features from laboratory confirmed 41 patients with 2019-n-CoV infection.

Characteristics	
Age in Years	49.0 (41-58)
Sex	
Men	30 (73%)

Women	11 (27%)
Exposure to Sea Food Market	27 (66%)
Common Symptoms	
Fever	40 (98%)
Cough	31 (76%)
Fatigue	18 (44%)
Pneumonia	40 (98%)
Less Common Symptoms	
Headache	3 (7%)
Diarrhoea	1 (2%)
Dyspnoea	22 (53%)
Sputum Production	11 (26%)

Diagnosis

Endeavors to control spread of COVID-19, foundation quarantine and detachment measures, and suitably clinically oversee patients all require helpful screening and symptomatic apparatuses. While SARS-CoV-2 is spreading, other respiratory diseases might be more normal in a nearby local area. The WHO has delivered a rule on case reconnaissance of COVID-19 on January 31, 2020. For someone in particular rules, WHO prescribes to initially evaluate for more normal reasons for respiratory disease given the season and area. If an adverse outcome is found, the example ought to be shipped off reference research facility for SARS-CoV-2 recognition. Case definitions can differ by country and will advance after some time as the epidemiological conditions change in a given area. In China, an affirmed case from January 15, 2020 required an epidemiological linkage to Wuhan inside about fourteen days and clinical highlights like fever, pneumonia, and Page 14 of 25 Journal Pre-confirmation 14 low white platelet count. On January 18, 2020 the epidemiological standard was extended to incorporate contact with any individual who had been in Wuhan in the beyond about fourteen day. Afterward, the case definitions eliminated the epidemiological linkage. The WHO has advanced case definitions. Associated cases with COVID-19 are people (a) with extreme intense respiratory contaminations (history of fever and hack expecting admission to clinic) and with no other etiology that completely clarifies the clinical show and a background marked by movement to or home in China during the 14 days preceding indication beginning; or (b) a patient with any intense respiratory ailment and somewhere around one of the accompanying during the 14 days before manifestation beginning: contact with an affirmed or plausible instance of SARS CoV-2 disease or worked in or went to a medical care office where patients with affirmed or likely SARS-CoV-2 intense respiratory sickness patients were being dealt with. Likely cases are those for whom testing for SARS-CoV 2 is uncertain or who test positive utilizing a skillet Covid measure and without research center proof of other respiratory microbes. An affirmed case is unified with a research facility affirmation of SARS-CoV-2 contamination, regardless of clinical signs and indications. For patients who meet demonstrative standards for SARS-CoV-2 testing, the CDC suggests assortment of examples from the upper respiratory lot (nasopharyngeal and oropharyngeal swab) and, if conceivable, the lower respiratory parcel

(sputum, tracheal suction, or bronchoalveolar lavage). In every country, the tests are performed by research centers assigned by the public authority.[15]

Treatment approaches

As per today there exists no FDA approved vaccine or treatment for 2019-n-CoV. The two institutes which are regulating and leading the funding of research and response of 2019-n-CoV are National Institutes of Health (NIH) and National Institute of Allergy and Infectious Diseases (NIAID). Also, European Medicines Agency (EMA) and Medicines and Healthcare Products Regulatory Agency (MHRA) are set up for progressive treatments against 2019-n-CoV. Some companies are trying to reutilize the already approved drugs that are somewhat effective against similar CoVs in the previous times.[15]

The clinical studies from the plasma and stem cell studies of patients those who were treated and recovered from 2019-n-CoV were investigated. Additionally, various multinational companies are working for development of vaccine for market use and it has been observed that within the 12-18 month of time slot the vaccine will be ready for supply to the market Table 4.

Although, fewer approaches have been proposed that prevents the additional spread of the virus and manages 2019-n-CoV. The foremost and important one is the isolation of the suspect, keeping the particular patients in isolation and detection of severe and acute patients as soon as possible. The patients should be regularly checked for the symptoms and should be given common treatments like maintaining of their electrolyte balance in body, resting and supportive medicines.

Other treatments like anti-viral therapeutics such as, nebulizing with interferon-α2b and Ritonavir/Lopinavir (200mg/50mg). Some candidates like Nitazoxanide, AAKI, Penciclovir and Barcitinib shoed effective results when investigated clinically. Antibiotics are used as supportive therapy and overuse should be avoided.

The discussed approaches tend to reduce the virus load, but the drug candidate Remdisvir has produced a positive impact on the virus spread, thus this drug either alone or in combination with the chloroquine or interferon beta has blocked the replication of SARS-CoV 2 and has treated the patient clinically.

Table 3: Treatment Strategies for COVID-19

S. No	**Drug**	**Classification**	**Inventor**	**Therapeutic Use**	**Report**
1	Remdesivir	Antiviral	Gilead Sciences	Treatment for Ebola and Marburg virus infections	Phase 3 clinical trial
2	Convalescent plasma	Immunoglobulin		Treatment for Ebola virus infection	FDA approved
3	Favilavir	Antiviral agent	Fujifilm	Against	Phase 3

			Toyama Chemical and Zhejiang Hisun Pharmaceutical	many RNA viruses	clinical trial
4	Hydroxychloroquine (Plaquenil) and chloroquine (Aralen)	Quinoline	Anti-malaria	Ongoing	

Instructions to put a stop on 2019-n-CoV

The introduction of vaccine for the treatment of 2019-n-CoV novel corona virus infection into the market will take time. So, for the time being it is of keen importance to stick to the guidelines on social distancing, timely hand washing and disinfecting the living areas like homes and workplaces.

Various reports of 2019-n-CoV infected patients confirms that this infection is more threating and easily spreadable as compared to other corona viruses. Similar to the other CoVs, it is believed that this virus can remain active in air up to 3 hours. On plastic it can last long for 72 hours. On stainless steel the life of this virus is 48 hours, on cardboard is 24 hours and 4 hours on copper. However, the property of this virus is to get multiplied within the body even if the patient is asymptomatic and can be passed from one to another person. WHO and other welfare organisations have given some guidelines for the prevention of COVID-19 that includes:

i) Wearing a mask or covering of mouth or nose when coughing and sneezing.
ii) Maintaining of at least 6 feet distance from other persons.
iii) Washing of hands frequently especially in the case when contact with someone.
iv) Do not touch your mouth, nose and face repeatedly

Moreover, WHO has given and released biosafety guidelines in relation to 2019-n-CoV. All researchers and healthcare workers should wear N95 and FFP3 masks and protective kits when around COVID-19 patients. For normal population wearing of mask is one criterion to prevent infection. Another factor includes use of disinfectants like 70% ethanol, use of sodium hypochlorite as a bleaching agent, 0.5% of hydrogen peroxide. Other agents such as quaternary ammonium compounds, chlorohexidine digluconate, benzalkonium chloride can be used on recommendations in required quantity. [5,16]

Some assumptions also suggested that hot weather slows the spread of virus and WHO continuously recommends the all official guidelines. Even then it is too early to conclude that whether the virus interacts with hot weather, but the spread of other CoVs is slower in warmer weather.

Omicron SARS-CoV-2 variant

On Nov 25, 2021, around 23 months since the first revealed instance of COVID-19 and later a worldwide assessed 260 million cases and 5·2 million deaths,a new SARS-CoV-2 variation of concern (VoC), omicron,2was revealed. Omicron arose in a COVID-19-exhausted world in which outrage and dissatisfaction with the pandemic are overflowing in the midst of far

and wide adverse consequences on friendly, mental, andmonetary prosperity. Albeit past VoCs arose in a world where normal invulnerability from COVID-19 diseases was normal, this fifth VoC has arisen at a time when immunization resistance is expanding on the planet. The development of the alpha, beta, and delta SARS-CoV-2 VoCs were related with new waves of diseases, at times across the whole world.3 For model, the expanded contagiousness of the delta VoC was related with, among others, a higher viral load,4 longer term of infectiousness,5 and high rates of reinfection, due to its capacity to escape from regular immunity,6 which brought about the delta VoC quickly turning into the worldwide prevailing variation. The delta VoC keeps on driving new influxes of contamination also stays the prevailing VoC during the fourth wave in numerous nations. Worries about lower antibody adequacy in view of new variations have changed our comprehension of the COVID-19 endgame, clarifying the universe of the thought that worldwide immunization is by itself sufficient for controlling SARS-CoV-2 disease.To be sure, VoCs have featured the significance of inoculation in blend with existing general wellbeing anticipation measures, like veils, as a pathway to viral endemicity.7 The previously sequenced omicron case was accounted for from Botswana on Nov 11, 2021, and a couple of days after the fact one more sequenced case was accounted for from Hong Kong in a voyager from South Africa.8 A few arrangements from South Africa followed, later beginning ID that the new variation was related with a S-quality objective disappointment on a particular PCR measure in light of a 69–70del erasure, like that saw with the alpha variant.9 The most punctual known instance of omicron in South Africa was a patient determined to have COVID-19 on Nov 9, 2021, in spite of the fact that it is likely that there were unidentified cases in a few nations across the world before then, at that point. In South Africa, the mean number of 280 COVID-19 cases each day in the week prior to the identification of omicron expanded to 800 cases each day in the accompanying week, part of the way ascribed to expanded surveillance.10 Coronavirus cases are expanding quickly in the Gauteng region of South Africa; the early multiplying time in the fourth wave is higher than that of the past three waves (figure, appendix).10 The chief worries about omicron incorporate whetherit is more irresistible or serious than other VoCs and regardless of whether it can evade antibody security. Despite the fact that immunological and clinical information are not yet accessibleto give conclusive proof, we can extrapolate based on what is had some significant awareness of the changes of omicron to give fundamental signs on contagiousness, seriousness, and resistant getaway. Omicron has a few cancellations and in excess of 30 changes, a few of which (eg, 69–70del, T95I, G142D/143–145del, K417N,T478K, N501Y, N655Y, N679K, and P681H) cross-overwith those in the alpha, beta, gamma, or delta VoCs.8 These erasures and transformations are known to lead to expanded contagiousness, higher viral restricting liking, and higher counter acting agent escape.11,12 Some of the other omicron changes with realized impacts give expanded contagiousness and influence restricting affinity.[11,17] Significantly, the impacts of the greater part of the leftover omicron changes are not known, bringing about a high level of vulnerability concerning how the full mix of cancellations and changes will influence viral conduct what's more helplessness to normal and immunization interceded invulnerability. Distributed Online December 2, 2022.[12,16] Days First wave Second wave Third wave Fourth wave7-day moving normal of public everyday cases per 100000 populace01020304050607080 Doubling time*Fourth wave (omicron)=1·2 daysThird wave

(delta)=1·5 days Second wave (beta)=1·7 days First wave (D614G)=1·3 days Figure: SARS-CoV-2 cases in first, second, third, and fourth waves, Gauteng Province of South Africa *Multiplying time for the initial 3 days later the wave limit of ten cases for each 100000 populace. 7-day moving normal cases per 100 000 populace up to Dec 1, 2021. Information are from the Department of Health, Government of South Africa.10 See Online for reference section,reference section added on Dec 6, 2021Remark www.thelancet.com Vol 398 December 11, 2021 2127The effect of omicron on contagiousness is a concern. If the covering omicron transformations keep up with their known impacts, then, at that point, higher transmissibility is normal, especially due to the changes close the furin cleavage site. Early epidemiological proof proposes that cases are ascending in South Africa and that PCR tests with S-quality objective disappointment are likewise rising. Despite the fact that omicron is probably going to be exceptionally contagious, it isn't yet evident whether it has more noteworthy contagiousness than delta, in spite of the fact that starter signs propose that it is spreading quickly against a scenery of progressing delta-variation transmission and significant degrees of normal insusceptibility to the delta variation. On the off chance that this pattern proceeds, omicron is expected to dislodge delta as the prevailing variation in South Africa. We anticipate information on how this new VoC will affect clinical show. At this stage, the accessible narrative information from clinicians at the bleeding edges in South Africa recommend that patients with omicron are more youthful individuals with a clinical show like that of past variants.13 Although no disturbing clinical concerns have been raised so far, this episodic data ought to be treated with alert given that extreme COVID-19 cases regularly present a few weeks later the underlying indications related with gentle sickness. Insusceptible departure is another worry. In the nonattendance of information on observational immunization adequacy and immune response balance studies on vaccinee sera, primer information from the public PCR testing program could give a few insights. Information on positive PCR tests in individuals with past sure tests propose an increment in instances of reinfection in South Africa. Nonetheless, the expanded utilization of fast antigen tests and fragmented catching of negative results have convoluted the understanding of test energy rates, which have ascended to multiple times the past rate in the previous week. In any case this restriction, the increment in instances of reinfection is in keeping with the safe break changes present in omicron. Despite the fact that there are clashing reports on whether Coronavirus immunizations have reliably held high viability for every one of the four VoCs going before omicron, clinical preliminaries have announced lower adequacy for a few immunizations in transmission settings in which the beta variation is prevailing. Past variations have brought down antibody viability; for instance, the ChAdOx1 immunization was70% successful in forestalling clinical diseases for the D14G variation in the UK, yet this viability diminished to 10% for the beta variation in South Africa.14 However, the viability of the BNT162b2 antibody in forestalling clinical diseases was held across both the D614G and beta variants.14 Given that omicron has a bigger number of changes than past VoCs, the expected effect of omicron on the clinical adequacy of COVID-19 antibodies for gentle diseases isn't clear. Hitherto, most COVID-19 immunizations have remained compelling in forestalling serious COVID-19, hospitalization, what's more passing, for every single past variation, since this viability may be more reliant upon T-cell invulnerable reactions than antibodies. Observational examinations from Qatar(n=231826)15 and Kaiser Permanente

(n=3436957)16 announced antibody adequacy of over 90% in forestalling clinic confirmations during delta-variation transmission, even as long as a half year later immunization. Observational information from the province of New York, USA (n=8834604) showed high antibody adequacy in forestalling serious infection in individuals more established than 65 years, with shifting degrees of security gave by various immunizations—95% for BNT162b2, 97% for mRNA-1273,what's more 86% for Ad26.COV2.S17—with insignificant decreases in security a half year later immunization. As far as diagnostics, the omicron variation is recognizable on generally utilized PCR stages in South Africa.There is not a good excuse to accept that current COVID-19 treatment conventions and therapeutics would no more be viable, with the conceivable special case of monoclonal antibodies, for which information on the omicron variation's weakness are not yet accessible. Critically, existing general wellbeing counteraction measures (veil wearing, physical separating, aversion of encased spaces, outside inclination, and hand cleanliness) that have stayed successful against past variations ought to be simply as successful against the omicron variation. Extrapolations dependent on known changes and primer perceptions, which ought to be deciphered with alert, demonstrate that omicron may spread quick era l so may get away from antibodies more promptly than past variations, in this way expanding instances of reinfection and instances of gentle advancement contaminations in individuals who are immunized. Based on information from past VoCs, individuals who are immunized are probably going to have a much Remark 2128 www.thelancet.com Vol 398 December 11, 2021 lower hazard of serious illness from omicron disease. A blend anticipation approach of immunization Further more general wellbeing measures is relied upon to stay an successful system. [17-28]

CONCLUSION

The current COVID-19 pandemic is clearly an international public health problem. There have been rapid advances in what we know about the pathogen, how it infects cells and causes disease, and clinical characteristics of disease. Due to rapid transmission, countries around the world should increase attention into disease surveillance systems and scale up country Page 19 of 25 Journal Pre-proof 19 readiness and response operations including establishing rapid response teams and improving the capacity of the national laboratory system.

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