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Review Article

SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS TYPE 2 OMICRON VARIANT OUTBREAK IN INDIA: TIME TO ALERT

PRITHIVIRAJ NAGARAJAN[1]*, JAYANTHI KUMAR[2], ANUSHEELA HOWLADER[3], SATHEESH KUMAR SABAPATHY[4], MUTHU GOPAL[5], LEENA RAJATHY PORT LOUIS[6], SARAVANAAVEL KUMAR[7]

[1]Multi-Disciplinary Centre for Biomedical Research, Aarupadai Veedu Medical College & Hospital, Vinayaka Mission's Research Foundation (Deemed to be a University), Puducherry-607 403, India. [2]Directorate of Indian System of Medicine and Homeopathy, Government of Puducherry, Puducherry, India. [3]Department of Microbiology, Aarupadai Veedu Medical College & Hospital, Vinayaka Mission's Research Foundation (Deemed to be University), Puducherry-607 403, India. [4]SRL limited, Department of Molecular Biology, New Avadi Road, Kilpauk, Sreerosh Renaissance, Chennai, Tamil Nadu, India. [5]Model Rural Health Research, Primary Health Centre, Tirunelveli, Tamil Nadu, India. [6]Department of Pharmacology, Aarupadai Veedu Medical College & Hospital, Vinayaka Mission's Research Foundation (Deemed to be University), Puducherry-607 403, India. [7]Department of Microbiology, Aarupadai Veedu Medical College & Hospital, Vinayaka Mission's Research Foundation (Deemed to be a University), Puducherry-607 403, India. Email: prithivinaga@gmail.com

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ABSTRACT

Early 2022 saw an outbreak of the coronavirus severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) variant known as Omicron, which has become more contagious than the previous variants of concern alpha, beta, and gamma variants, and it shares many mutations. Still, so far, Omicron transmission has exceeded many borders worldwide compared to other kinds of SARS-CoV-2; there has been a significant increase in the number of confirmed cases globally, and it is re-emerging currently in India. The World Health Organization, the Centers for Disease Control and Prevention (CDC), the Ministry of Health and Family Welfare, and other research institutions, as well as worldwide international press media provided data on "Omicron" outbreaks in India. Our review recorded information about the prevalence and clinical characteristics of the Omicron variant of SARS-CoV-2 from November 24, 2021, to January 17, 2022. Our highlights will talk about its global transmission, characteristics, and impact on vaccine efficiency, and possible strategies to prevent and overcome the spread of the Omicron variant.

Keywords: Omicron, Severe acute respiratory syndrome coronavirus type 2, Prevalence, Outbreak, Clinical characteristics.

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INTRODUCTION

According to the World Health Organization (WHO) statistics, approximately 161,000 confirmed cases of Omicron have been recorded worldwide [1]. The original severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) virus, detected in late 2019, has mutated, leading to the appearance of several variants. To prioritize monitoring and research, the WHO has classified these variants into three categories: Variants of concern (VOCs), variants of interest, and variants under monitoring (VUMs). The preceding four VOCs were alpha (B.1.1.7), beta (B.1.351), gamma (P.1), and delta (B.1.617.2) [2]. On November 26, 2021, the WHO approved a new type named Omicron (B.1.1.529) as the fifth VOC, instantly raising global panic. This review will go over Omicron global transmission, the timeline of outbreaks in India, characteristics, and the impact on vaccine efficacy for the Omicron variant.

OMICRON EMERGENCE

Many websites have been set up to track pandemic case confirmation mortality and record recovery data hourly. nCOVID-19 has spread to over 150 countries. At present, there are nearly 330,183,256 confirmed cases, 5,561,065 mortalities, and over 268,517,341 recoveries as of January 17, 2022. On November 24, 2021, the WHO received the first report of the B.1.1.1.529 variant. The day after receiving the information, the WHO classified it as VUM and renamed it the Omicron variant (B.1.1.529). Two days later, the WHO classified the Omicron variant as a VOC, the shortest lag time yet recorded to reclassify a variant from VUM to VOC and raise significant public concerns. Within days of its discovery in Africa, Omicron spread to other countries. The variant has not stopped spreading to other countries and regions. As of January 17, 2022, the Omicron variant strain was detected in approximately 77 countries, with most occurrences in the United Kingdom, South Africa, Botswana, Hong Kong, Israel, Belgium, and Italy. Omicron positive events have also been reported in the United States [3] and India [4]. The UK recorded the first fatality linked to the novel Omicron variant strain [5]. The origin of the new Omicron variant is as yet unknown, and it appears to be spreading to other countries and regions. It is currently unclear how effectively the Omicron variant may be transmitted from one person to another. Due to the displacement of the delta variant as a consistently circulating form of SARS-CoV-2, the threat of the Omicron variant's high transmissibility can be feared [6]. The rapid rise in Omicron cases in South Africa, with more cases reported in a single day, is linked to the spread of Omicron around the world.

OMICRON OUTBREAKS IN INDIA

Our current review focuses on Omicron outbreaks in India. New cases of Omicron are suspected and detected in India due to the virus's spread between human-to-human transmissions, especially by Omicron affected international air travellers and carriers from other countries. According to the Ministry of Health and Family Welfare (MoHFW), the total number of confirmed Omicron cases in India is 8209, of which 5100 are active cases, one is mortality, and 3108 are cured. In Omicron, which has spread over 77 nations, younger- and middle-aged people are infected more than in the previous variants. In addition, we have recorded India's state-wise and daily-wise confirmed cases, as given in Figs. 1a and b until January 17, 2022. We also illustrated the timeline events of Omicron in India (Fig. 2) in the present scenario.

GENERAL CHARACTERISTICS OF OMICRON

The characteristics of Omicron are remarkably similar to the victims' nCOVID-19 infections, although some general characteristics are

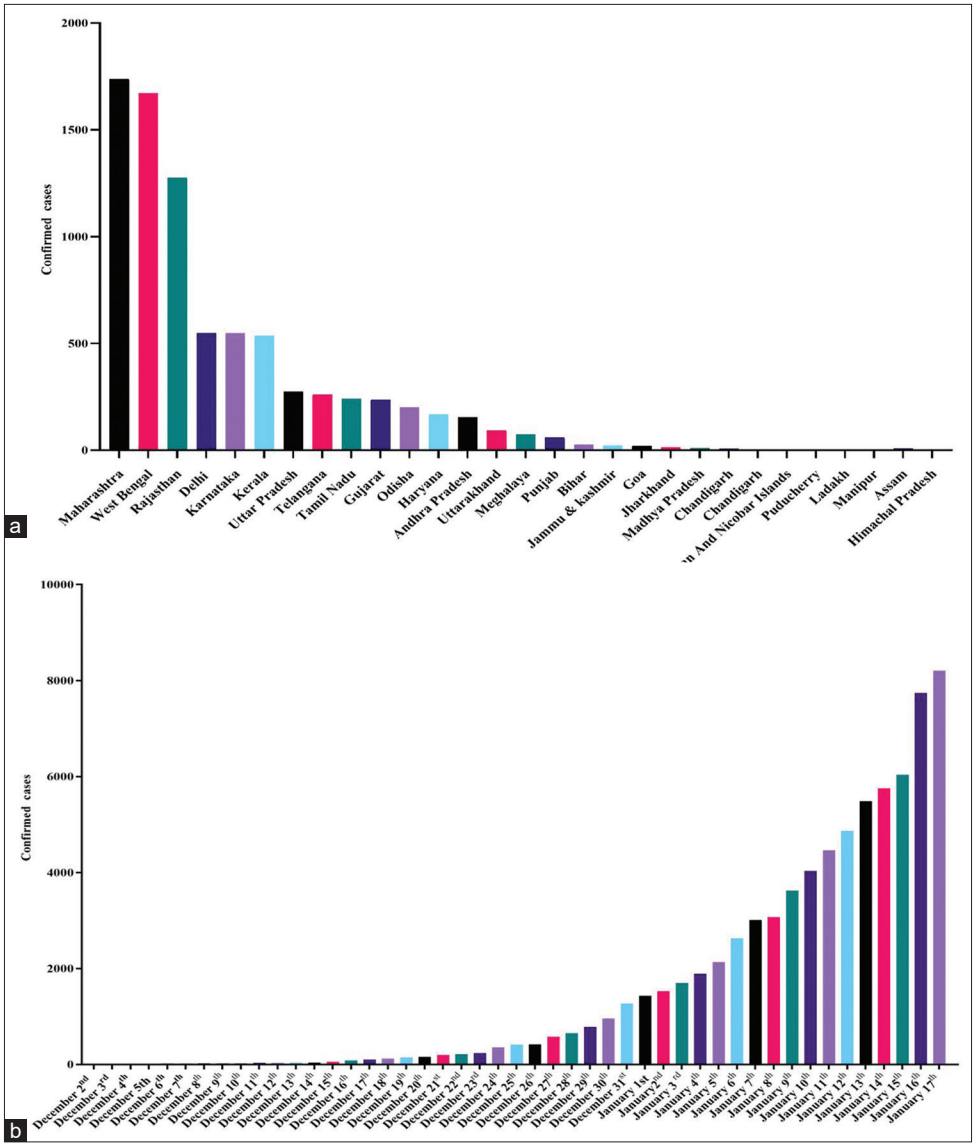

Fig. 1: (a) Number of Omicron confirmed cases in India as state-wise. (b) Daily-wise confirmed case of Omicron from December 2021 to January 17, 2022. Data were illustrated according to the MoHFW Omicron disease daily dashboard

described in Table 1. At present, the mechanisms of Omicron human pathogenesis are poorly understood and yet to be reported, and they are probably similar to the nCOVID-19 variant characteristics [7]. Compared to the previous Delta and COVID-19, the new Omicron variant had significant modifications in spike proteins. The delta variant (B.1.617.2) contains eight mutations in the spike protein, while the Omicron variant (B.1.1.529) contains 32 mutations. The delta variant was discovered in India, along with eight other mutations, earlier in 2021 and has spread rapidly [8]. The primary clinical characteristics of Omicron symptoms are fever, chills, generalized myalgia, malaise, drowsiness, and confusion. Mild symptomatic cases are manifested by low fever, sore throat, running nose, joint pain, and muscle aches, which are almost similar to COVID-19 symptoms [9]. In critical issues, gastrointestinal symptoms of vomiting, diarrhea, nausea, pain in the abdomen, and renal failure features are shared, and the severe infection progresses to the acute lower respiratory syndrome [10].

RNA viruses are known to change and evolve rapidly to adapt to and survive in a changing environment. The most worrying feature of the Omicron variation is its constellation of more than 50 mutations, of which about 30 are in the spike protein [11]. Several non-synonymous mutations were observed in the spike protein at positions H69, V70, G142, V143, Y144, and N211, of which 69/70 deletions failed to target the S-gene [12]. Fig. 3a depicts the schematic diagram illustrating the domain arrangement of the 32 spike proteins found in Omicron, which has more mutations than any other variety of delta, COVID-19, which includes the following: A67V, T95I, Y145D, G339D, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, D614G, Y5H, D614G, Y5H, T547K, P681H, N764K, D796Y, N856K, Q954H, N969K, and L981F [13]. Of these, mutations at H655Y, N679K, and P681H in the S1S2 furin cleavage site of the omicron variant may be associated with increased transmissibility. A P681H mutation was also identified in the alpha variant [13]. As reported in the delta variant, mutations in Q498R and N501Y increased the binding affinity for ACE2 [11]. This mutation has been suggested to increase SARS-CoV-2 infectivity [14]. Although the spike protein gene is currently the target of most existing vaccines, this variant may be more able to evade prior immunity than the earlier delta form, according to the researchers. It should also be noted that the spike receptor-binding domain is the genuine viral entity that recognizes the ACE2 receptor to mediate virus entry. Fig. 3b depicts the cryo-EM structure of the SARS-CoV-2 Omicron spike protein in a complex with human ACE2. In addition, Omicron also has the N679K and P681H mutations near

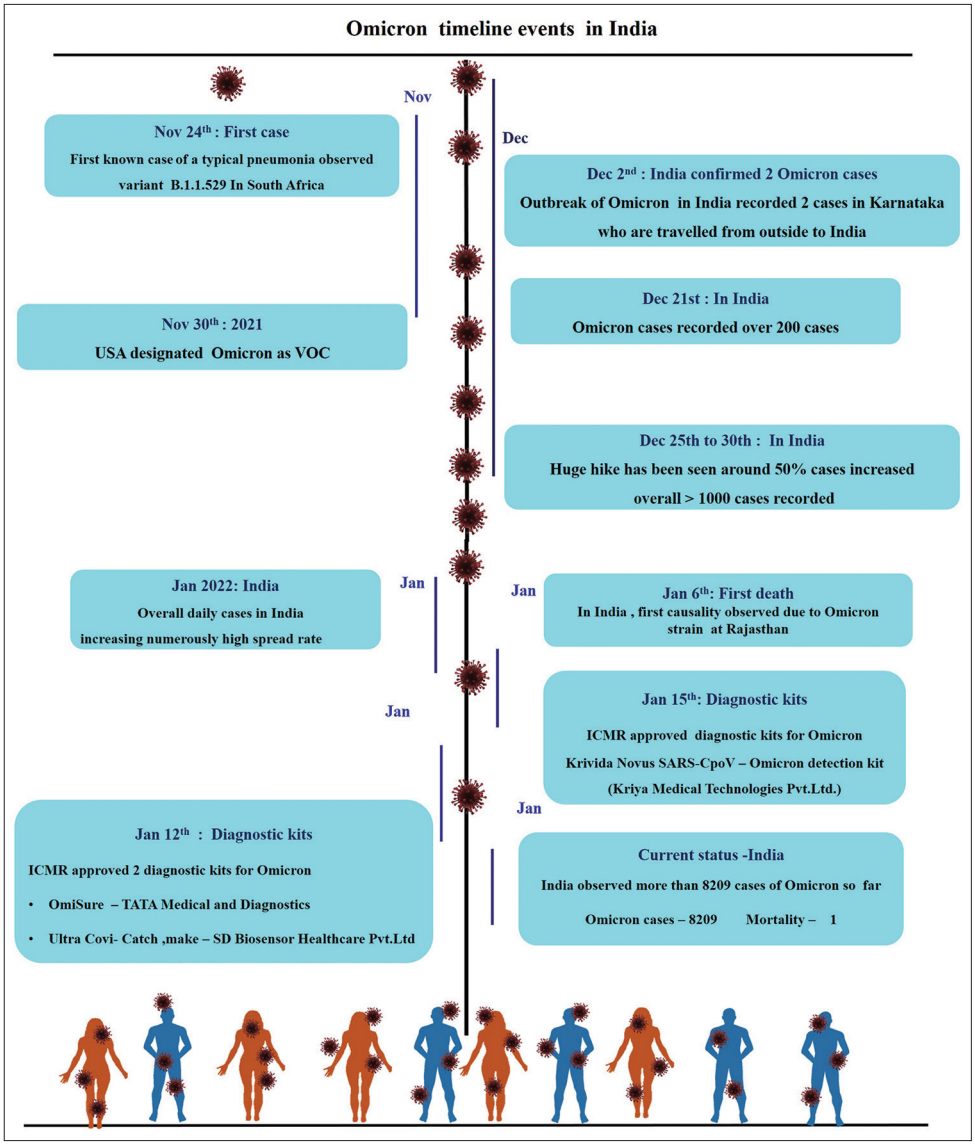

Fig. 2: Time line events of Omicron in India

the furin cleavage site, which incorporate basic amino acids around the furin cleavage site and facilitate cleavage of the spike at S1 and S2, leading to increased fusion and virus infection [15,16]. Due to this, scientists and virologists were concerned that the Omicron (B.1.1.529) variant had an unusual number of mutations compared to the other variants. We have tried to figure out how those genetic changes work together.

PREVENTION OF OMICRON VARIANTS

Once Omicron is suspected or confirmed, clinical specimens of blood, sputum, nasal secretions, bronchoalveolar lavage, tracheal aspirate, and an oropharyngeal or nasopharyngeal swab are collected from infected patients for RT-PCR analysis to target the specific S dropout genes [23]. In hospitalized patients, repeated samples from serum and the lower and upper respiratory tract are highly recommended by RT-PCR analysis [24]. Another method of Omicron diagnosis is by chest CT scan for lung involvement, and many clinicians suggest CT scan as a more sensitive and effective method for diagnosis [25]. High-resolution computed tomography is recommended for determining disease severity in SARS-CoV-2 patients [25]. At the moment, the specific features of the Omicron variant are unknown. As a result of the spike mutations found in other VOCs, it's a massive issue that Omicron might be able to spread more quickly and be capable of fighting off the antibodies currently used to treat it. Furthermore, the early identification ICMR has approved a list of testing laboratories all over India that help to detect and prevent the spread of disease during a pandemic situation. At present, laboratories are dedicated to viral diagnostics, and INSACOG Genome Sequencing Laboratories are committed to identifying and monitoring existing Omicron or any new variants. Using whole-genome sequencing, early and frequently will help us better understand and map the changing strategies of circulating variants. To successfully overcome the problem in India and decrease the risk of the Omicron outbreak, maintain public health prevention measures, such as wearing masks, regular ventilation, maintaining physical distance, and washing hands. These strategies efficiently prevent the spread of other variants and help deal with the Omicron variant.

ENCOURAGING VACCINES IN INDIA

According to some estimates, Omicron's rapid spread in South Africa could start a wave of new pandemics across the world. However, the significance of this variant and what it symbolizes for the current pandemic is still unknown. According to specific estimations, the Omicron distribution in India may be quite different from other

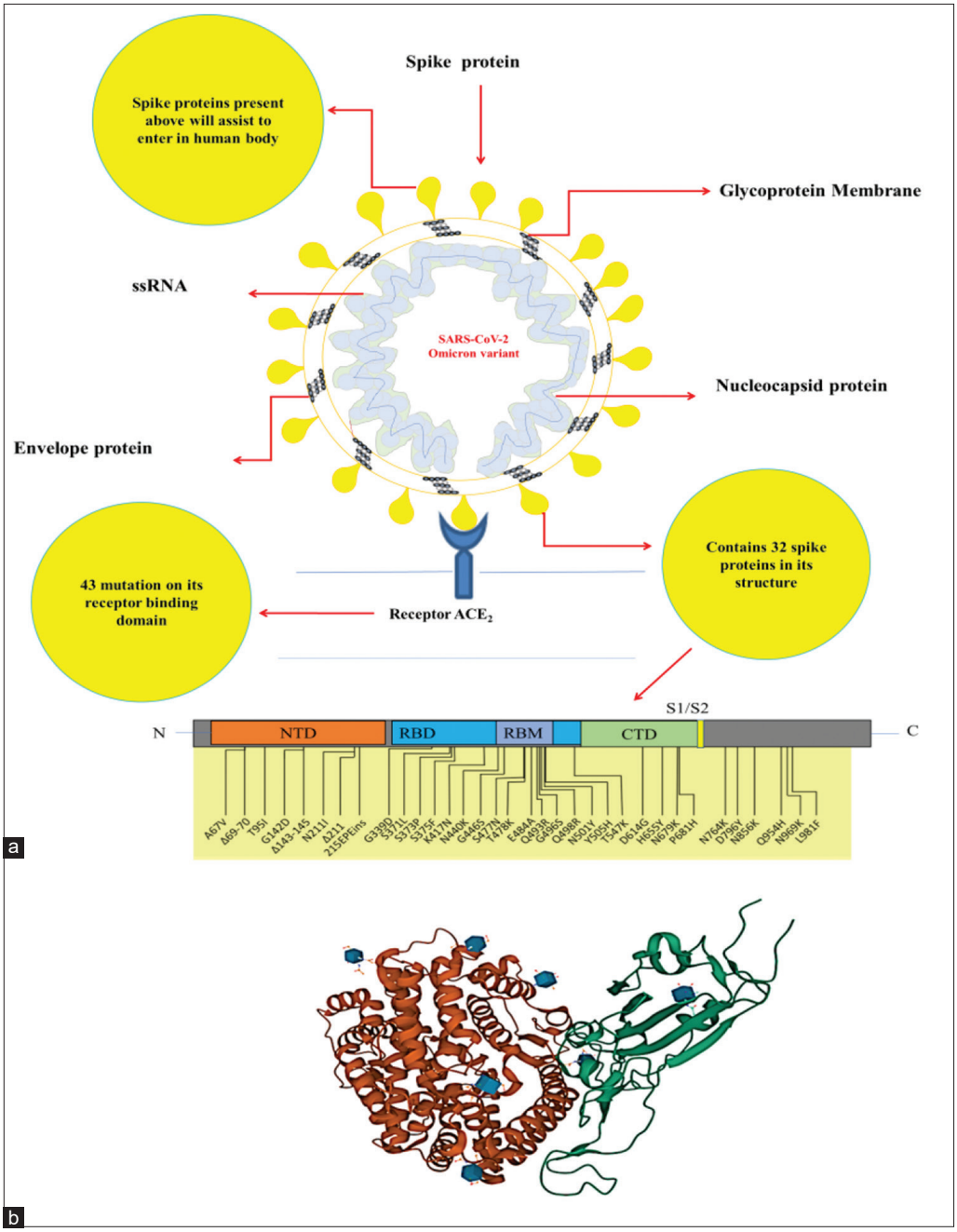

Fig. 3: (a) The schematic diagram illustrating the domain arrangement of the 32-spike protein found in Omicron (b) The Cryo-EM structure of Omicron spike protein in complex with human ACE_2

countries. According to the worldwide data population, fully vaccinated and partially vaccinated globally are shown in Fig. 4. Just 65% of India's population are fully vaccinated [26]. This percentage is much lower than the global average of 84% [26]. Omicron may spread quicker in India, highlighting the urgent need to increase vaccine coverage. Despite the FDA-approved COVID-19 vaccines' reduced efficacy against variant viruses [27-33], they have been shown to protect against significant illness, hospitalization, and death [34-36]. Based on the findings of several studies showing that, a supplemental booster dose of the COVID-19 vaccine can restore and even improve vaccine effectiveness [37]. It has been a long time since India last made a billion doses of the vaccine, but now it can analyze about one million samples every day [38]. In addition, adding an extra boosting dose of the COVID-19 vaccine to the vaccination program could undoubtedly help control the Omicron spread and infection [39].

DEVELOPING NOVEL VACCINES WITH NEW VARIANTS

In addition, there is much speculation about whether the current COVID-19 vaccination can protect against the Omicron variant due to the new wave brewing globally. The treatment for HIV, SARS, and MERS infections is accomplished using antiviral medications such as lopinavir-ritonavir and ribavirin [40]. The United Kingdom government has suggested and authorized Zewoodi, also known as Sotrovimab, as a medicine to combat the new strain [41]. The Medicines and Healthcare Products Regulatory Agency says that both Xevudy and Sotrovimab are effective at treating mild-to-moderate COVID-19 and Omicron infections in people who are at high risk of getting the disease [41]. According to the most recent studies, existing COVID-19 vaccinations offer less protection against the Omicron variant than other VOCs [42]. Meanwhile, sera from vaccinated people demonstrated about 40% lower neutralization power against the Omicron variant than the SARS-CoV-2 wild type [43]. These findings imply that the existing COVID-19

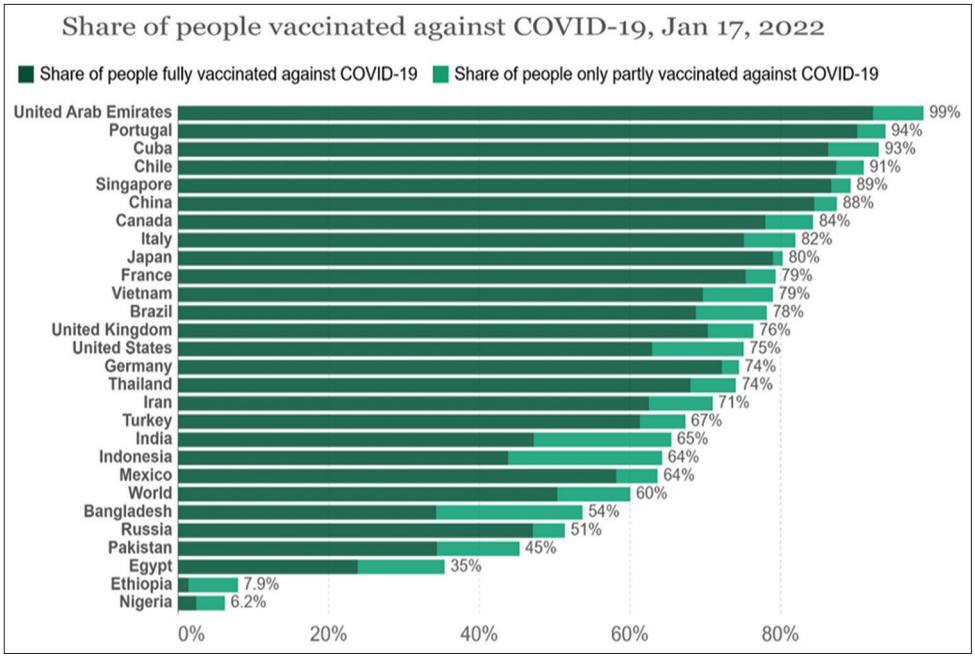

Fig. 4: World wide data of fully vaccinated and partially vaccinated for COVID-19

Table 1: General characteristics of Omicron

Characteristics	Omicron
Biological characteristics [17,18]	
Virus	Single standard RNA
Origin	All SARS Originated from Bats, Civet cats, Omicron originated from Gauteng, South Africa
Transmission	Omicron variant is more transmissible than previous strains especially Nosocomial, respiratory, Airborne, and Zoonotic Transmission* and Aerosol droplets through human to human
Spike protein	Contain 35 mutation on the spike protein
Dominance	Both male and female
Age of infected individuals	Children to adult (9 – more than years)
Incubation periods	2–3 days
Spread mode	Peak
Incidence	During (Nov – Jan) winter season
Clinical characteristics [19-21]	
Head ache	Mild
Joint Pain	Mild
Fever	Moderate
Chillness/Rigors	Moderate
Malaise	Mild
Generalized Myalgia	Moderate
Drowsy	Mild
Pulmonary characteristics [14,22,23]	
Cough	Moderate
Shortness of breath	Mild
Abdominal pain	Mild
Nausea and Vomiting	Mild
Dyspnea	Mild
Diarrhea	Mild
Pneumonia	Further investigation is required
Hemoptysis	Further investigation is required
Acute Renal failure	Further investigation is required

vaccine may be less effective against the Omicron variant than others. Since there is no vaccine for Omicron, vaccines for SARS-CoV-2 variants, which include Omicron, are used as a preventive measure to make the disease less severe and less likely to kill [44].

However, three critical concerns remain unanswered:

1. Will this variant lead to more severe and fatal diseases?
2. Will prior vaccination protect against this new variant?
3. Will previous medicines be effective against this new variant?

The Pfizer vaccination's effectiveness nearly halved from February to October, dropping 86–43%. The Moderna Vaccine's efficacy fell from 89% to 58%, while the J&J vaccine's effectiveness fell from 86% to 13% [33]. If necessary, vaccine manufacturers such as Pfizer and BioNTech need to modify their mRNA vaccination doses for the Omicron strain to manage the condition effectively [45]. Pfizer wants to produce a vaccine kit unique to the Omicron strain of the virus and is also expected to identify escape variants in its data within 2–6 weeks [46]. Research is being carried out on-site by AstraZeneca/Covishield in Botswana and Eswatini, with the company saying that their current vaccination platform enables them to uncover new Omicron mutations. Wilhelm *et al.* [47] examined *in vitro* tests using sera collected from double BNT162B2 and double mRNA 1273-vaccinated individuals. The neutralization potential against Omicron was reduced 11.4 and 20-fold compared to the control groups, respectively. The use of sera from ChAdOx1-vaccinated people resulted in no significant neutralizing effect. In addition, the Omicron variant was not neutralized by the monoclonal antibodies imdevimab and casirivimab, which were also further tested in future studies. Unauthorized information suggests Moderna developed two multivalent vaccination candidates: mRNA-1273.211 has numerous mutations seen in both Omicron and beta variants, while mRNA-1273.212 contains mutations present in Omicron, beta, and delta variants, respectively [43,44]. The efficacy of both candidate vaccines against the Omicron variant should be further investigated [48,49]. Since vaccination efficacy for the Omicron variant had likely declined due to mutations, the CEO of Moderna developed a strategy to investigate three booster options and create an Omicron variant-specific booster dose to improve immunity [50]. Due to the rapid spread of Omicron, the US Centers for Disease Control and Prevention (CDC) approved adult booster doses of the Pfizer BioNTech and Moderna vaccines [50]. Globally, the WHO is actively collaborating with researchers to investigate the transmission, severity, and effectiveness of Omicron vaccines and the availability of clinical trials for the disease. Table 2 shows the list of vaccines approved in India by the WHO. Furthermore, more research is still needed to find out how well COVID-19, Omicron, and other variants in India work.

Table 2: List of vaccines approves in India for COVID-19 by the WHO

S. No	Vaccine type/platform	Name of the vaccine	WHO approved	No of the approved countries	Reference
1	Non-replicating viral vector	Oxford/AstraZeneca: AZD1222	Yes	127	Voysey *et al*. [51]
2	Non-replicating viral vector	Serum Institute of India: Covishield	Yes	47	Voysey *et al*. [51]
3	Inactivated	Bharat Biotech: Covaxin	Yes	12	Thiagarajan *et al*. [52]
4	DNA	Zyduscadila, ZyCoV-D	No	1	Momin *et al*. [53]
5	Non-replicating viral vector	Gamaleya, Sputnik V	No	74	Baraniuk *et al*. [54]
6	Protein subunit	Serum Institute of India COVOVAX (Novavax formulation)	No	2	Serum Institute of India Pvt. Ltd. [55-57]

IMPLEMENTING AUTHORITIES' RECOMMENDATIONS

Preventing COVID-19 infection is still the best strategy. The WHO has suggested that countries improve their ability to monitor and sequence SARSCoV2 variants to better understand them. Adding whole genome sequences to public databases like GISAID may help find new mutations and variants. Global networks should explore epidemiological surveys, social assessments, public health efforts, diagnostic processes, immunological reactions, etc. [37]. A hospitalized patient's clinical data may help doctors formulate treatment recommendations using the WHO COVID-19 Clinical Data Platform. The CDC, in collaboration with public health organizations in the United States, increased surveillance for S gene target failures [13]. On December 9, 2021, the MoHFW announced the list of countries from which visitors to India must face additional procedures, including post-arrival testing, including the UK, Israel, Hong Kong, Tanzania, several European countries, Zimbabwe, and New Zealand [38]. Thermal screening is advised for all passengers on arrival at the airport or railway station. In the case of a negative COVID-19 test, passengers will have to complete a 7-day home quarantine with testing on day 8, followed by 7 days of self-monitoring. If passengers are tested positive, samples should be sent to the INSACOG laboratory for whole-genome sequencing to determine the type of virus variant. On arrival at the airport, 5% of all passengers from non-risk countries will be tested for the Omicron variant. Monitoring COVID-19 hotspots, increasing testing, and improving health infrastructure, including samples for whole-genome sequencing, are some of the steps that should be taken. Indeed, vaccination is the key strategy to reduce COVID-19 morbidity and mortality.

CONCLUSION

Since December 2019, the globe has been fighting the nCOVID-19 pandemic. The origin, structure, pathogenesis, and symptoms of the Coronavirus have been studied over the past 2 years. The new Omicron strain has more infectious epidemiological and biological characteristics and has put human lives in danger globally in the past 2 months. In this pandemic, researchers, doctors, and frontline workers are doing an outstanding job. Officials in both the public and commercial sectors must work together to address this growing medical problem. Cough, fever, widespread myalgia, and acute fatigue are Omicron symptoms that should be isolated and evaluated promptly. Effective FDA-approved vaccination, treatment, and management standards will benefit sophisticated health care workers. Globally, the WHO receives daily reports of new SARS-CoV-2 strains. In India, Omicron therapy did not increase severity or mortality. Governments, NGOs, pharmaceutical and biotechnology businesses, and educational and health institutions should launch regional public awareness campaigns to contain the pandemic. To successfully overcome the problem in India and decrease the risk of the Omicron outbreak, maintain public health prevention measures, such as wearing masks, regular ventilation, maintaining physical distance, and washing hands. These strategies efficiently prevent the spread of other variants and help deal with the Omicron variant. In addition, to reduce the burden of disease internationally, global health authorities must quickly stop outbreaks of this re-emerging infection. The early diagnosis and timely quarantine during a pandemic can help reduce viral spread.

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AUTHORS' CONTRIBUTIONS

Prithiviraj Nagarajan, Jayanthi Kumar, and Satheesh kumar conceived the idea and planned the study. Leena RajathyPort Louis and Saravanaavel Kumar collected the data, made the figures, and devised the initial draft. Anusheela Howlader and Muthu Gopal reviewed, finalized, and approved the final version of the manuscript for submission.

ETHICAL CLEARANCE

Ethics approval was not required for this systematic review.

STATEMENT OF DATA AVAILABILITY

The datasets included in this study are available on request from the corresponding author**.**

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None.

CONFLICTS OF INTEREST

None.

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