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A METHODICAL REVIEW ON OMICRON -A NEW VARIANT AS A DRUG DEVELOPER

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ABSTRACT: In mid-November 2021, the new OMICRON variety was first discovered in South Africa. As of today, the OMICRON version already appeared on December 15, 2021. Around 77 countries are affected, with the bulk of cases originating in the United States, India, the United Kingdom, and South Africa. OMICRON-positive instances were also reported. The first mortality associated with the novel COVID-19 mutation was reported in the United Kingdom. Recently, a sister variant of OMICRON, 21L or BA.2, has also been discovered. Due to its enormously high number of mutations, viewed enhancement in immune evasion and transmissibility, OMICRON was developed as a new variant of concern (VOC) by the WHO on 26 November 2021. On a global pandemic scale, positive selection of SARS-CoV-2 mutations appears to have begun in late 2020. Since then, the virus has been evolving on two fronts: immune evasion and enhanced transmissibility, as expressed by Delta. This review elaborates the effects of drugs in the management of OMICRON.

INTRODUCTION: On November 11, 2021, Botswana reported the first sequenced omicron case was reported in Hong Kong, and a few days later, another sequenced case was reported in a visitor from South Africa [1]. Following the revelation that the novel variant was connected to an S-gene target failure on a specific PCR assay, the researchers set out to find out more about it. Due to a 69–70del deletion, similar to the alpha version, many sequences from South Africa followed [2]. Although there are likely unexplained examples in numerous locations throughout the world before then, In South Africa, the first case of omicron was diagnosed in a patient with Covid-19.

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November 9, 2021. In the week leading up to the identification of COVID-19 in South Africa, there were an average of every day, 280 COVID-19 instances are reported. Omicron rose to 800 instances per day the next week, thanks in part to increased surveillance [3]. COVID-19 cases are rapidly spreading in the Gauteng region of South Africa; the fourth wave's early doubling time is faster than the previous three waves, as seen in the key concerns with omicron are whether it is more contagious or severe than other VoCs and whether it can get around vaccine protection.

Although there is currently a dearth of definitive immunological and clinical evidence, we can extrapolate from what we know about omicron mutations to generate preliminary estimates of transmissibility, severity, and immune evasion. Omicron possesses a few deletions and over 30 mutations, some of which (e.g., 69–70del, T95I, G142D/143–145del, K417N, T478K, N501Y, N655Y, N679K and P681H) overlap with those

seen in the alpha, beta, gamma, or delta VoCs. Increased transmissibility, stronger viral binding affinity and antibody escape have all been linked to these deletions and alterations. Other Omicron mutations that have been linked to higher transmissibility and influence binding affinity [4, 5]. Importantly, the implications of the majority of the remaining omicron alterations are unknown, leaving a lot of questions about how the whole set of deletions and mutations may affect viral behavior and vulnerability to natural and vaccine-mediated immunity [6].

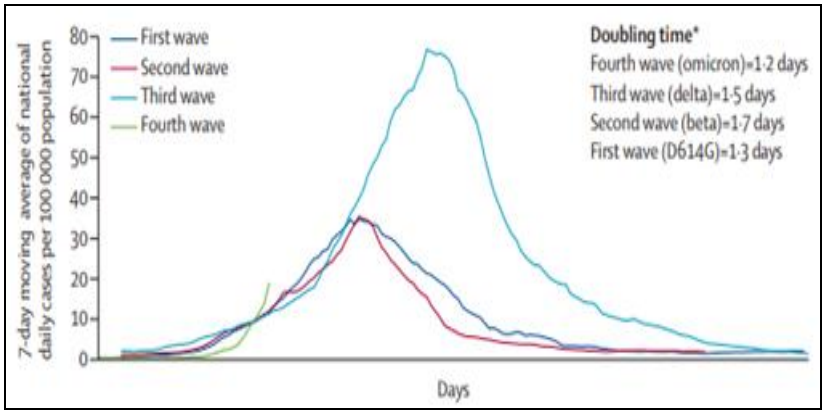

FIG. 1: SARS-COV-2 CASES IN FIRST, SECOND, THIRD AND FOURTH WAVES, GAUTENG PROVINCE OF SOUTH AFRICA. *Doubling time for the fist 3 days after the wave threshold of ten case per 100,000 population. 7 days moving average case per 100,000population up dec1, 2021. Data are from the Department of Health, Government of south Africa.

Omicron: A Choice of Varient of Concern: RNA viruses are known to mutate fast and evolve to adapt and survive in changing environments. The most worrying feature is the constellation of more than 50 mutations in the OMICRON variation, of which roughly 30 mutations are in the spike protein. The more worrisome are the 15 mutated sites in the receptor-binding domain (RBD) that interact with human cells before cell entry, possibly enhancing transmissibility.

A large number of non-synonymous mutations were observed in the spike protein at positions H69-, V70-, G142-, V143, Y144-, N211- of which 69/70 deletions resulted in the failure of the S-gene target. Other substitutions in the spike protein are A67V, T95I, Y145D, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, and L981F. Of these, mutations at H655Y, N679K, and P681H in the S1-S2 furin cleavage site of the OMICRON variant might be associated with increased transmissibility. Mutations at Q498R and N501Y in combination increased the binding affinity to ACE2 as reported in the delta variant [7]. Mutations at ORF1a (NSP6) are K856R, S2083-, L2084I, A2710T, T3255I, P3395H, L3674-, S3675-, G3676-, and I3758V. Deletions at L3674-, S3675-, and G3676- are speculated to aid in innate immune evasion by compromising the cell's ability to degrade viral components. Mutations at ORF1b are P314L and I1566V; at ORF9b are P10S, E27-, N28- and A29-, three deletions at E31-, R32- and S33- and substitutions at P13L, R203K, and G204R are reported in the nucleo-capsid protein. The Envelope gene has only one mutation at T9I and the Matrix gene has mutations ate D3G, Q19E, and A63T [8].

Analysis of spike protein sequences revealed two sub-clades of OMICRON, that is, sub-clade 1 having a low sequence frequency with mutations at 417K, 440N, and 446G site and sub-clade 2 with mutations at 417N, 440K, and 446S sites and found globally at high frequency [9]. Many of the mutations in OMICRON are common with the Delta variant of SARS-CoV-2 however; a large number of additional mutations may increase the infectivity of this novel variant which needs to be studied [10].

Omicron its Molecular Elucidation: Omicron mutant has been identified to possess 32 amino acid changes in the spike (S) protein. Some of the mutations that are present in the receptor-binding domain (RBD) of the Omicron variant have been shared by other SARS-CoV-2 variants that evolved previously.

These mutations are K417N, E484K, N501Y, D614G and T478K (ecdc.europa.eu). In the spike protein, RBD is composed of 319-541 residues of the S1 subunit. The K417N mutation (lysine to asparagine substitution) is shared between Omicron and Beta variants. The mutation at residue 484 in which the glutamic acid is substituted to lysine (E484K) is found in both Beta and Gamma variants [11]. Whereas in Omicron the mutation at 484 is E484A, the residue glutamic acid is mutated to alanine. The E484A mutation in the Omicron might be an important mutation that was present as E484K **Fig. 2** in the Beta and Gamma variants. In the Gamma variant the E484K mutation had the ability to cause reinfection. This might be due to substituting a negatively charged, hydrophilic residue (glutamic acid) with a positively charged and relatively high hydrophilic amino acid (lysine). In the Omicron variant, the mutation of a hydrophilic amino acid (glutamic acid) to a hydrophobic amino acid (alanine) might alter the interaction between RBD and human angiotensin converting hACE2. The N501Y mutation (asparagine to tyrosine) present in the Omicron variant was also detected earlier in the Alpha, Beta and Gamma variants. N501Y was identified to have a stronger binding affinity, since it is one of the contact residues in RBD. The D614G mutation (substitution of aspartic acid to glycine) located in the S1 subunit of the Omicron variant is shared by Alpha, Beta, Gamma, and Delta variants. Relative to Alpha, Beta, and Delta SARS-CoV-2 variants Omicron has a 5.5 to 11 time's higher mutations rate in the receptor-binding motif (RBM). Among all the mutations, the crucial mutations in the RBM of the Omicron variant are T478K, E484A, Q493R and N501Y. Yi *et al*11 showed that substituting the residues at five different positions P499, Q493, F486, A475 and L455 of the SARS-CoV-2 spike RBM increases the affinity to receptor binding [12]. Therefore, the Q493R might increase the affinity to bind the hACE2. Delta variants share the T478K mutation (threonine to lysine) found in Omicron. Several crucial mutations in the S protein of RBD and S1 subunit of the Omicron variant are shared by other SARS-CoV-2 variants. Henceforth, the virulence and infectivity features of the Omicron variant might be either surpassing the Alpha, Beta and Delta variant reciprocally or in a transitional phase between the variants.

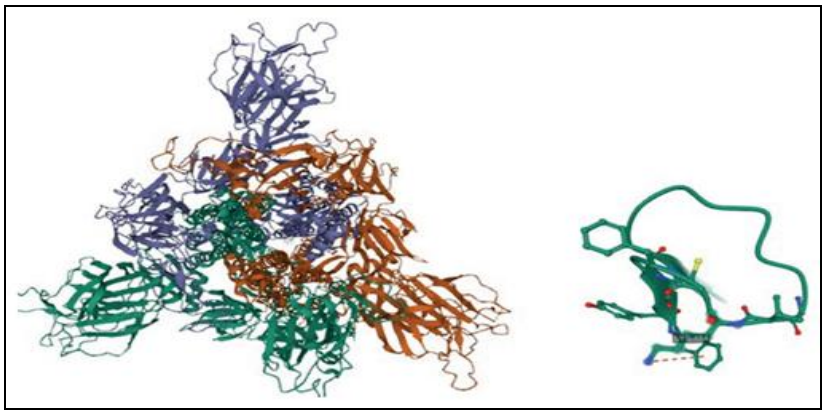

FIG. 2: SARS-COV-2 BETA VARIANT SPIKE PROTEIN IN OPEN STATE ALONG WITH E484K (7VX1 – WANG, Y.F., XU, C., WANG, Y.X., HONG, Q., CONG, Y. CONFORMATIONAL DYNAMICS OF THE BETA AND KAPPA SARS-COV-2 SPIKE PROTEINS AND THEIR COMPLEXES WITH ACE2 RECEPTOR REVEALED BY CRYO-EM. DOI: 10.1093/NAR/GKAB314)

Omicron Variant Infection and Vaccine Efficacy Views: According to the World Health Organization (WHO), no research has shown that the OMICRON version is more harmful than other VOCs. Concerns about the virus's high transmissibility, virulence, increased risk of reinfection, and decreased efficiency of current diagnostics, vaccines, and therapies have yet to be addressed. Chen *et al* [13]. The effect of 15 RBD mutations on the OMICRON infectivity and efficacy of existing vaccinations was predicted using an artificial intelligence (AI) model (TopNetmAb). Mutations at the N440K, T478K, and N501Y positions give ten times, two times, and ten times more infectivity to OMICRON, respectively, than the original SARS-CoV-2 and Delta variants. In South Africa, a study of 35,670 reinfections among 2.8 million positive cases indicated considerable population-level evidence of prior immunity evasion. This suggests that the

OMICRON mutation is involved in recovered persons' infections [14, 15]. When evaluated against a panel of human sera collected from convalescent COVID19 patients, the OMICRON (pseudo typed) construct had an ED50 of 66, indicating an 8.4-fold reduction in neutralization [16]. Whether OMICRON will be able to avoid detection. It's still up for debate whether vaccines cause immunity. However, in South Africa, the abrupt increase in OMICRON positive and rising hospitalization rates are cause for alarm and require additional investigation [17]. In the absence of an OMICRON variant-specific vaccine, the existing licensed (FDA/EUA) vaccines will continue to be used to minimize illness severity and death from the currently circulating SARS-CoV-2 variations, including OMICRON. WHO is working together with researchers from around the world to assess the transmissibility, severity, and effectiveness of OMICRON vaccinations and the diagnostic tests that are now available.

Because most currently available vaccines target the spike protein gene, this variant may have a higher chance of evading past immunity than the delta variant. The main worry with today's vaccines is that their efficacy is deteriorating. The spike protein gene is the target of most of the currently available vaccines; therefore, this variant may have a greater potential to escape prior immunity than the previous delta variant. The prime concern over the current vaccines is their decreasing effectiveness against COVID-19 throughout a period of time against COVID19 Pfizer's vaccination efficacy plummeted nearly in half from February to October, from 86 percent to 43 percent, Moderna vaccine 2 | THAKUR AND RATHO from 89 percent to 58 percent, and J&J vaccine from 86 percent to 13 percent [18].

In the AI-predicted model, the prominent E484A mutation in OMICRON's RBD and others such as K417N and Y505H lowered the efficacy of Eli Lilly mob cocktail and Celltrion Ab Regdanvimab. According to preliminary studies, this variety appears to have a higher risk of reinfection and limited antibody-mediated neutralization. Wilhelm *et al.* [19]., utilizing sera from double BNT162b2 and double mRNA1273 vaccinated people, demonstrated an 11.4 and 20 fold loss in neutralizing ability against OMICRON *in-vitro*. Using sera from ChAdOx1 vaccines, no neutralizing effectiveness was detected. The decreased neutralizing efficiency of vaccine-elicited sera against OMICRON revealed reduced T cell-mediated immunity. Further monoclonal antibodies, imdevimab and casirivimab, failed to neutralize the OMICRON version. Vaccination producers, such as Pfizer and Biotech, are willing to adjust their mRNA vaccine doses for the OMICRON strain if necessary to deal effectively with the novel OMICRON variant[20]. Pfizer planned to create a custom vaccine against the OMICRON variant and expected to find an escape variant in 2–6 weeks using their data[21]. AstraZeneca claims that their current vaccine platform allows them to identify novel mutations in OMICRON and is doing on-site research in Botswana and Eswatini. Due to a mix of changes, the vaccine efficacy for the OMICRON version has likely decreased, according to the CEO of Moderna.

As a result, the company has devised a strategy to test three booster possibilities as well as develop an OMICRON variant-specific booster dose for boosting decreasing immunity [22]. Following the unexpected development of new OMICRON cases worldwide, the US Centers for Disease Control and Prevention allowed adults to receive the Pfizer BioNTech and Moderna vaccine booster shots. Without strong evidence and research, it will be too early to comment or draw any conclusions on vaccine efficacy with the OMICRON variant.

Indian Response to Omicron Variant: India completed 1 billion vaccination doses and increased its testing capability to 1 million samples per day [22]. The existing Virus Research Diagnostic Laboratory for viral diagnosis and INSACOG labs for genome sequencing is already in place for identifying and monitoring the current OMICRON or any novel variant. Understanding circulating variations and tracing their evolving strategy will be aided by early and active surveillance and whole genome sequencing. Following the COVID-19 guidelines, such as social distancing, hand cleanliness, mask wear, and immunizations are still the most significant factors in preventing viral transmission.

Omicron-Led Third Covid Wave: According to a new IISc-ISI modeling study, the peak of the third

Covid-19 wave will vary from mid-January to mid-February, depending on the state. According to the report, the curve could begin to flatten by the beginning of March. A new modelling study by IISc-ISI predicts that the Omicron-triggered third wave of Covid-19 in India will peak in January-end and February, with daily cases reaching 10 lakh. Professor Siva Athreya, Professor Rajesh Sundaresan, and a team from the Indian Institute of Science (IISc) and the Indian Statistical Institute (ISI) in Bengaluru conducted the study based on Omicron transmissibility rates. According to the report, the peak of the third corona wave in India might occur in the last week of January, with effects beginning in the first week of February. It does, however, state that different states will have different peaks.

The peaks of T various states will be different. The peak of the third wave will occur in several states between mid-January and mid-February. The Covid-19 curve for India could start flattening by the beginning of March, according to the report.

Depending on the percentage of persons vulnerable to the virus, the model predicts a high in Delhi by mid-January or the third week and a peak in Tamil Nadu in the last week of January or the first week of February. The prediction was made based on previous infections and vaccination, which leaves a small percentage of the population vulnerable to the new variation. According to the model, 30 percent, 60 percent, or 100 percent of the population is vulnerable.

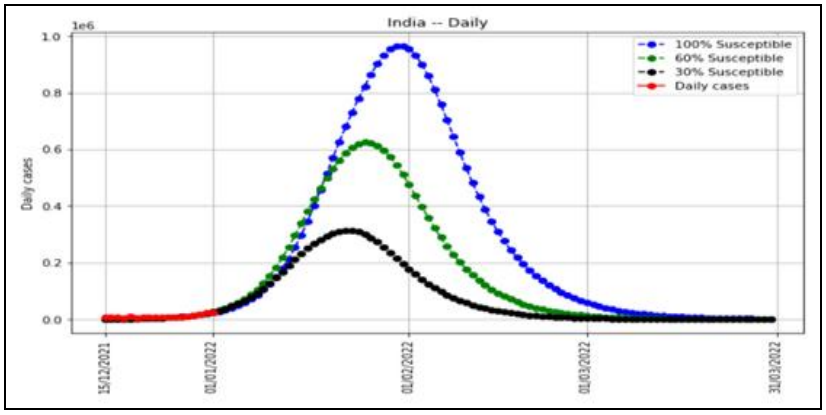

FIG. 3: DEPICTING THE PERCENTAGE OF SUSCEPTIBILITY OF VIRUS

During the peak, the number of daily cases in India might reach around 3 lacks, 6 lacks, or 10 lacks, depending on the percentage of persons who are vulnerable to the virus.

Since, the end of December, India has seen an increase in corona cases. The union government, on the other hand, is not pushing for a new wave. According to a study conducted by researchers at the Indian Institute of Technology (IIT), Kanpur, the third wave of the Covid-19 pandemic in India could peak on February 3.

Last month, the National Covid-19 Supermodel committee anticipated that the third wave of coronavirus will strike India in February, and that the daily Coronavirus caseload in India would rise until the Omicron Variant overtook the Delta Variant as the main variant. Tracker Covid-19According to India, a tracker built by researchers at the University of Cambridge, new infections will begin to surge in the last week of December, and India will likely see a period of exponential growth in daily cases. It went on to say that the high growth phase will be brief.

In this phase, Cases will continue to rise in the following period, although at a slower and slower rate. Since, December 31, India has seen a significant increase in Coronavirus infections, with daily cases jumping by five times and the active caseload increasing by three times in the last seven days. According to data assessed by the Union Ministry of Health and Family Welfare, the number of instances with Omicron Variant has doubled since December 31 [23].

Omicron and Statistical Report Up-to-date: The research report used the data of the first and second waves in India, and the current rise in cases triggered by omicron in various countries, to predict a possible third wave in the country.

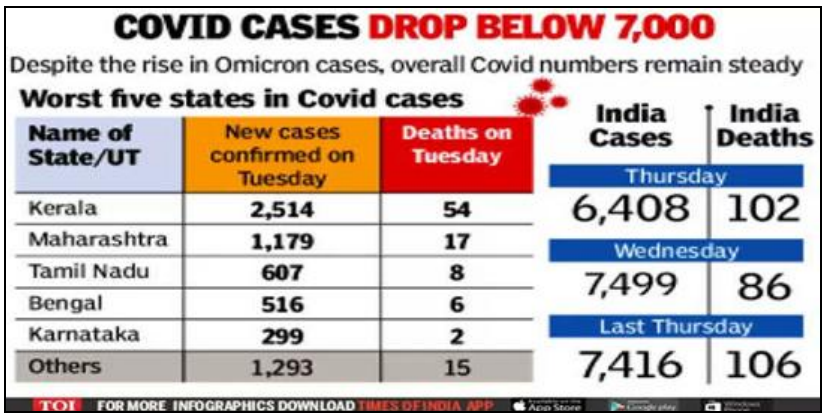

FIG. 4: DEPICTING THE STATISTICAL REPORT OF OMICRON

The researchers said that the study "suggests cases reach peak value after 735 days from our initial observation date. Which is January 30, 2020, when India reported its first official case of COVID-19.So, the cases start rising around December 15,201, and the peak of the third wave will occur on Thursday, February 3, 2022". The research team drawn from the Department of Mathematics and statistics, IIT Kanpur comprises Sabaraparshad Rajeshbhai, Subhra Sankar Dhar and Shalabh. The researchers said the key question after the first and second waves of COVID19 was "Will the third wave also arrive and, if yes, then when". To unravel the puzzle, the team used a statistical method based on fitting a mixture of Gaussian distributions. "After plotting the daily cases per million of all other countries and matching the graphs with India, the top 10 countries with the best match are chosen as the training dataset. The Top 10 countries are US, UK, Germany, France, South Africa, Russia, Israel, Spain, Zambia and Zimbabwe are the closest matching countries for which the daily cases data follow very similar Pattern's to India [24].

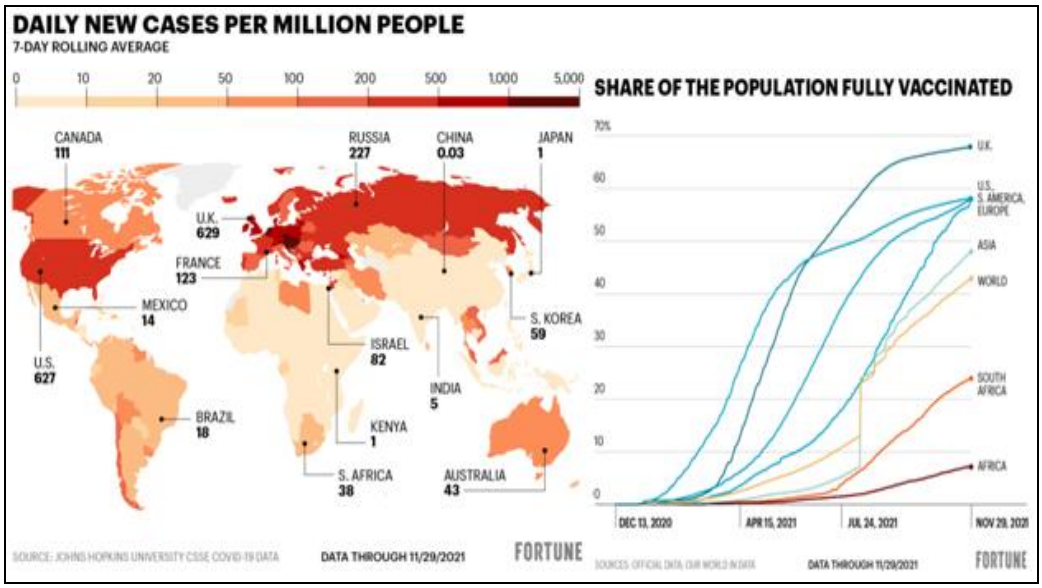

FIG. 5: COVID INFECTIONS ARE RISING AGAIN AS THE OMICRON VARIANT EMERGES IN NEARLY 20 COUNTRIES

As depicted in **Fig. 5**, While Europe, along with Russia and the United States, remains a virus hotspot three weeks into the "fourth wave" new cases in South Africa, the country where the Omicron variety was initially found, have grown dramatically, up 432 percent from two weeks earlier. (South Africa still has significantly fewer cases per capita than the United States, European countries, and Australia.) New cases have also increased dramatically in France (175%), Spain (112%), and Portugal within the same time period (107 percent). Over the last two weeks, the number of new cases reported daily in the United States has increased by 10%.

On the other hand, vaccination rates continue to be woefully inadequate worldwide. When it comes to the appearance of Omicron, which the WHO promptly labelled a "variant of concern" last week, a number of African countries that struggled to get vaccines for much of the pandemic are especially vulnerable.

While vaccination rates vary across Africa, according to Our World in Data, which collects data from local governments, just 7.2 percent of the continent's population has been fully vaccinated against COVID [25].

Clinical Outcomes: In the article released by MedRxiv on clinical outcomes in Omicron-infected patients (B.1.1.529) Southern California has a SARS-CoV-2 variant. From November 30, 2021 to January 1, 2022, they analysed Clinical and epidemiologic data from cases in the Kaiser Permanente Southern California healthcare system that tested positive for SARS-CoV-2 infection, utilizing S gene target failure (SGTF) as a surrogate for Omicron infection as determined by the ThermoFisherTaqPathComboKit assay. In cases with Omicron and Delta (non-SGTF) variant infections, they usedto compare time to any hospital admission and admissions related to new-onset respiratory symptoms, ICU admission, mechanical ventilation, and mortality, Cox proportional hazards models were used. To compare the lengths of hospital stays among patients with Omicron and Delta variant infections who were admitted. We used parametric competing risk models [26].

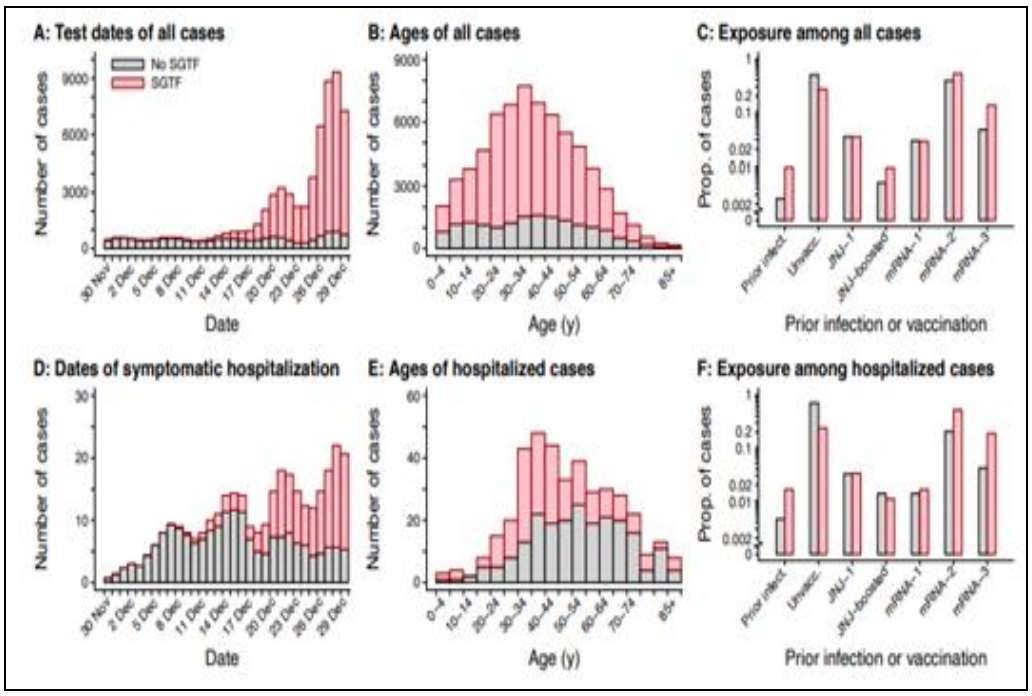

FIG. 6: DESCRIPTIVE CHARACTERISTICS OF SITUATIONS WHERE SGTF AND NON-SGTF SAMPLES WERE FOUND (A) TEST DATES FOR ALL CASES ANALYZED (TRUNCATED AT DECEMBER 29, 2022 TO ACCOMMODATE 1 DAY JITTERING); (B) AGE DISTRIBUTION OF ALL CASES ANALYZED; (C) EXPOSURE HISTORY (PRIOR DOCUMENTED INFECTION AND VACCINATION) AMONG ALL CASES ANALYZED; (E) AGE DISTRIBUTION OF CASES WITH SYMPTOMATIC HOSPITALIZATIONS; (F) EXPOSURE HISTORY (PRIOR DOCUMENTED INFECTION AND VACCINATION) AMONG CASES WITH SYMPTOMATIC HOSPITALIZATIONS. DETECTIONS WITH AND WITHOUT SGTF (INTERPRETED AS A SURROGATE FOR SARS-COV-2 OMICRON VARIANT INFECTION; RESPECTIVELY) ARE REPRESENTED BY PINK AND GREY BARS. THE TOTAL NUMBER OF SAMPLES PROCESSED ON THE RT-PCR TAQPATH COVID-19 CORRESPONDS TO THE TOTAL NUMBER OF SAMPLES PROCESSED. THIS IS A HIGH-THROUGHPUT COMBO KIT THAT DOES NOT REPRESENT ALL CASES

There were 88,576 positive SARS-CoV-2 detections among plan members examined as outpatients at KPSC between November 30, 2021 and January 1, 2022, with 69,279 (78.2%) ascertained using the ThermoFisherTaqPath COVID-19 Combo Kit, allowing SGTF determination. Among those who were admitted to the hospital during the study period, 457 of the

1,721 people infected with SARS-CoV-2 were tested with the ThermoFisherTaqPath COVID-19.Combo Kit is a set of two items. SGTF was found in 52,297 (75.5 percent) of the 69,279 positive specimens examined with this assay, including 235 of them. Inpatient patients accounted for 51.4 percent of the 457 individuals tested. The total number of patients with SGTF as well as the proportion of patients with SGTF, is both high. Except for the week following the Christmas vacation on December 25, findings increased continuously throughout the research period. When determining the amount and fraction of Regional laboratories, the Thermo Fisher was used to process samples. The COVID-19 Combo Kit from TaqPath has been discontinued **Fig. 5**. For instances with SGTF, the average time of follow-up was 5.5 days. Infections caused by the SGTF took 15.8 days, while infections caused by the non-SGTF took 15.8 days. SARS-CoV-2 isolates were found in 1,477 affected patients. The Omicron variation was found in all SGTF samples (382/382) and was chosen for sequencing across the study period. The Delta variation was found in 1,092 out of 1,095 non-SGTF samples (99.7 %;), confirming the interpretation of the results. Infections of SARS-CoV-2 with and without SGTF are classified as Omicron and Delta variant infections, respectively [27].

Vaccination and Booster Dose: Pfizer and BioNTech have started a study to see how well an Omicron-based COVID-19 vaccine works in adults aged 18 to 55. BioNTech and Pfizer worked together to develop the Pfizer-BioNTech COVID-19 Vaccine, based on BioNTech's patented mRNA technology. In the United States, the European Union, the United Kingdom, Canada, and other countries, BioNTech holds marketing authorizations, emergency use authorizations or equivalents (jointly with Pfizer) and other nations. Submissions will be made to seek regulatory clearance in countries where emergency use authorizations or equivalents were initially obtained.

There will be a total of 1,420 participants in the trial, divided into three cohorts:

Cohort #1 (n=615): Participants received two doses of the current Pfizer-BioNTech COVID-19 vaccine 90-180 days before enrollment; participants will get one or two doses of the Omicron-based vaccination in the study.

Cohort #2 (600 People): 90-180 days before to enrollment, participants received three doses of the existing Pfizer-BioNTech COVID-19 vaccination; in the study, participants will get one dose of the current Pfizer-BioNTech COVID-19 vaccine or the Omicron-based vaccine. Cohort #3 (n=205): Participants who have never been vaccinated will get three doses of the Omicron-based vaccine.

In what Manner is the Vaccine Given: The vaccine will be administered as a muscle injection.

Primary Series: The vaccination is given in a two-dose series, three weeks apart, to those aged 5 and up. Individuals 5 years of age and older who are determined to have specific types of immuno-compromise may get a third primary series dosage at least 28 days after the second dose.

Dose of Booster: Individuals 12 years of age and older may get a single booster dose of the vaccine at least 5 months after completing a primary series of the Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY® (COVID-19 Vaccine, mRNA). Individuals aged 18 and above may receive a single booster dose of the vaccination.

Important Health and Safety Information: If you have any of the following conditions, you should not obtain the vaccine:

- Previous dosage of this vaccine caused a serious allergic response had a significant adverse reaction to any of the vaccine's ingredients.
- Individuals should disclose all medical conditions to the immunization provider, including if they:
- Have any Allergies
- Have had myocarditis (inflammation of the heart muscle) or pericarditis (inflammation of the lining outside the heart) feel feverish.
- If you're taking a blood thinner or have a bleeding disorder.

- ❖ Are immunocompromised or on an immune-suppressing medication.
- ❖ Are expecting a child, plan to have a child, or are breastfeeding. Have been vaccinated against COVID-19 for the second time.
- ❖ Have you ever passed out after receiving an injection. It's possible that the vaccine won't protect everyone.

Side Effects have been Documented Include:

- ✓ The vaccine has a small probability of causing a serious allergic reaction.
- ✓ A significant allergic reaction would likely happen within minutes to an hour of receiving a vaccination dose. As a result, vaccination providers may advise people to stay at the location where they received the vaccine thereafter for monitoring.
- ✓ Difficulty breathing, swelling of the face and throat, a fast heartbeat, a nasty rash all over the body, dizziness, and weakness are all signs of a severe allergic reaction.
- ✓ If someone has a severe allergic response, they should dial 9-1-1 or go to the nearest emergency room.
- ✓ Some persons have developed myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the membrane around the heart).

Males under the age of 40 are more likely than females and older males to have got the vaccine. Symptoms appeared in most of these persons within a few days of receiving the second vaccine dosage. The chances of this happening are extremely slim. If somebody experiences any of the following symptoms after taking the vaccine, they should seek medical help right away:

- ❖ Chest discomfort.
- ❖ Breathing problems.
- ❖ Feeling like your heart is racing, fluttering, or thumping.

The vaccine has also been linked to the following negative effects:

Severe allergic reactions; non-severe allergic reactions such as rash, itching, hives, or swelling of the face; myocarditis (inflammation of the heart muscle); pericarditis (inflammation of the lining outside the heart); myocarditis (inflammation of the heart muscle); myocarditis (inflammation of the heart muscle); myocarditis (inflammation of the heart muscle); myocarditis (inflammation of the Pain at the injection site, fatigue; headache; muscle discomfort; chills; joint pain; fever; injection site swelling; injection site redness; nausea; feeling sick; swollen lymph nodes (lymphadenopathy); decreased appetite; diarrhea; vomiting; arm pain; fainting after receiving the vaccine.

These aren't all of the vaccine's possible negative effects. Serious and unexpected adverse effects may emerge. Clinical trials are still being conducted to determine the vaccine's potential negative effects. Contact your immunization provider or healthcare professional if you have any bothersome or persistent adverse effects. Data on the use of this vaccination in combination with other vaccines has yet to be submitted to the FDA. Individuals who are considering receiving this vaccination in combination with other immunizations should talk to their doctor about their alternatives [28].

Moderna Vaccine: Thousands of clinical studies have been conducted, dozens of vaccines and novel chemicals have been developed, and hundreds of authorized medications have been investigated for efficacy against COVID-19 in the last two years. More research is ongoing, particularly in light of the Omicron outbreak and the virus's potential to adapt.

Take a peek. Moderna Doses First Patient in Omicron-Specific Vaccine Phase II Trial. The first patient was dosed in the Phase II study of Moderna's Omicron-specific booster vaccination candidate. Adults aged 18 and up will be enrolled in the trial, which will include two cohorts: those who received the two-dose Moderna series at least six months ago and those who received the two-dose primary series plus a 50-microgram booster dose. Atleast three months ago of the first vaccine Each cohort is expected to have around 300 participants [29].

The Hope is Optimism: Since, December 2019, the whole world is dealing with different variants of SARS-CoV-2 and experienced 1st and 2nd waves of the COVID-19 pandemic. However, few nations are still struggling with 3rd wave due to the Delta variant. Amid this, the emergence of a new OMICRON variant THAKUR AND RATHO | 3 might negatively affect humankind's life and livelihood.

The untiring efforts of scientists, medical professionals, front-line workers, and policymakers associated with handling this pandemic are praiseworthy. A big boon is a better understanding of SARS-CoV-2 and its variants, its origin and structure, pathogenesis, and associated symptoms in different categories of patients in the last 2 years. Availability of effective FDA- approved vaccines, treatment, and management regime, better diagnostic and treatment infrastructure, and trained health care staff may facilitate in handling the novel OMICRON variant possibly in a better way [30].

Further Updates on Omicron: This section contains a summary of the current best available evidence (as of 20 January 2022) regarding the potential impact of the Omicron variant.

C.1. Epidemiology Incidence: The Omicron variation has been found in 171 countries as of January 20, 2022. In most nations, the variation has surpassed Delta, increasing in cases across the board. COVID-19 case incidence continues to rise worldwide, with a 20% weekly increase in week 2 (10-16 January 2022) compared to the previous week. However, the global pace of increase appears to be slower, given that week 1 (3–9 January) saw a 55 percent increase compared to week 52 (27 December 2021–2 January 2022).

The South-East Asia Region and the Eastern Mediterranean Region, with 145 percent and 68 percent increases in case incidence, respectively, recorded the largest increases in case incidence during week 2. In the African Region, however, a reduction of 27% was reported following a peak in week 52, 2021. The huge increase in the South-East Asia Region is primarily due to an increase in the number of cases in India, which reported 1 594 160 million new cases last week compared to 638 872 the week before (a 150 percent increase). Morocco (46 104 new cases versus 31 701 new cases, a 45 percent rise), Lebanon (45 231 new cases vs. 38 112 new cases, a 19 percent increase), and Tunisia (45 231 new cases vs. 38 112 new cases, a 19 percent increase) reported the largest numbers of new cases in the Eastern Mediterranean Region (39 487 vs. 13 416 new cases, a 194 percent increase).

The increase in weekly case incidence in the WHO European Region has moderated, with a 10% increase in week 2 compared to 31% in week 1 (2–9 January 2022). Differences do exist; however a few nations in Western Europe are starting to witness a fall or plateauing; many Eastern European and Central Asian countries are seeing significant growth rates, with Kazakhstan seeing the largest rises in week 2.

Transmission: Compared to Delta, Omicron exhibits a considerable growth advantage, higher secondary attack rates, and a larger observed reproduction number. In all countries with sufficient sequence data, an analysis of GISAID data using a previously published methodological approach [31] shows a growth rate advantage of Omicron over Delta, translating to a pooled mean transmission advantage (i.e. relative difference in effective reproduction numbers) of 189 percent (95 percent confidence interval: 162 percent – 217 percent) across epidemiological contexts under the assumption of an unchanged generation time. Early data for a shorter Omicron generation time [32] implies the transmission advantage may be lower; for a 20% shorter generation time, the estimated pooled mean transmission advantage of Omicron over Delta is 163 percent (139 percent – 186 percent) [33-35].

Studies on transmission in Omicron's transmission advantage is further substantiated. Household secondary attack rates for Omicron, for example, are always higher than Delta: 13.6 percent (95 percent CI: 13.1 percent -14.1 percent) vs. 10.1 percent (95 percent CI: 10.0 percent -10.2 percent) in the UK [36], and 31% vs. 21% in Denmark [37]. Immune avoidance appears to represent a big part of Omicron's transmission advantage, but there's also the possibility of higher intrinsic transmission fitness [38].

While evidence of immune evasion against infection and vaccine-derived immunity exists (see subsequent sections), more data is needed to better understand the relative contributions of intrinsic enhanced transmission fitness and immune evasion in explaining transmission dynamics. There's evidence that the Omicron variation infects human bronchus tissue faster and more efficiently than Delta [39] and outperforms Delta in terms of virulence. The transmission advantage of Omicron is further demonstrated.

Household secondary attack rates for Omicron, for example, are consistently higher than Delta: 13.6 percent (95 percent CI: 13.1 percent -14.1 percent) vs. 10.1 percent (95 percent CI: 10.0 percent -10.2 percent) in the UK [36], and 31% *vs.* 21% in Denmark [37]. Immune avoidance appears to be a large portion of Omicron's transmission advantage, although increased intrinsic transmission fitness is also a possibility [38]. While there is evidence of immune evasion against infection and vaccine-derived immunity (see the sections below), more data is needed to understand better the relative contributions of intrinsic increased transmission fitness and immune evasion in explaining transmission dynamics. There's evidence that the Omicron variant infects human bronchus tissue more quickly and effectively than the Delta variant [39].

CONCLUSION: We presently have limited information on the Omicron form, and further research is needed to understand this variant's danger properly. We believe that only time and surveillance will provide us with further information on the disease's transmissibility, vaccine efficacy, and severity based on our previous experiences with Alpha and Delta. Protective measures and immunization will continue to be crucial in battling the new variant's spread and averting future waves of severe COVID-19 infections and deaths. Omicron emerged in a country with insufficient immunization coverage, which is no accident. Indeed, the finding of this new strain emphasizes the importance of widespread immunization. The severity of Omicron *vs*. Delta variant infections has been measured in two ways: the risk of progression to severe endpoints among confirmed cases and the risk of progression to acute respiratory symptoms among those first diagnosed before symptoms begin. While the discovery of reduced previous evidence of enhanced transmissibility of Omicron variant infections in association with illness severity is good, as well as immune evasion from past infection and vaccination is worrying. The Omicron variant's rapid dissemination over a short period has resulted in exceptional COVID-19 outbreaks in our research population and elsewhere worldwide. High infection rates in the population have overburdened healthcare systems, potentially leading to many hospitalizations and deaths.

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