TAKSHASHILA INSTITUTION

TACKLING NEW COVID-19 VARIANTS

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Executive Summary

New variants of SARS-CoV-2 are being routinely identified and evaluated. For example, a new variant named AY.4.2 was detected in a few Indian samples in early November. The clinical manifestation of the former is similar to previous variants; however, its secondary infection rate is higher. Another variant called B.1.1529 (Omicron) with several mutations was first identified in South Africa and has been found in more than 25 countries, including a few cases in India as of 1st week of December 2021. This variant may have increased transmissibility and immune evasion properties and its rapid spread across the world has caused concern.

In addition to new variants, several European countries have also detected a surge in caseloads and some have enforced lockdowns. In India however, there has been a general easing of restrictions of economic and social activities as caseloads are showing a reducing trend. However, in view of the new variants, we propose a framework of permitting economic and social activities based on the extent of vaccination coverage and case load in an administrative unit (state/district) to quickly respond to any surge in cases and prevent further lockdowns.

Introduction

It is natural for new variants of SARS-CoV-2, the causative agent behind COVID-19, to emerge, as infections continue to spread across the globe. Vaccine inequity has created large pockets of populations susceptible to the virus, thus providing SARS-CoV-2 opportunities to grow and mutate. Coupled with this, many countries may not have the necessary infrastructure to detect variants when they emerge. This leads to delayed detection of emerging variants and the further spread of the virus, possibly even to vaccinated populations. It is therefore prudent for India to take measures to detect and protect against emerging variants, even though case numbers in India may be showing a decreasing trend. Below we consider the example of two emerging variants to showcase how strains may differ along with the measures necessary to tackle them.

Details of the new variants

1) Delta (AY.4.2)

AY.4.2 (shortened from B.1.617.2.4.2) is a sub-lineage of the Delta variant, which was responsible for the second wave and is the cause of almost all the new cases in India. However, the frequency of AY4.2 is deemed to be too low for it to be named as a variant of concern at the current time. As the sub-lineage is new, there is limited data available about the changes in its characteristics.

Currently, no difference in clinical symptoms is observed between the Delta variant and its AY.4.2. sub-variant. Though preliminary data show no appreciable increase in severity, there is a possibility that current or further mutations in AY.4.2.'s spike protein may change its severity. Data from the UK Health Security Agency (UKSHA) suggests the possibility of a minor decrease in the fatality rate.

However, AY.4.2 has a 12.2% Secondary Attack Rate (SAR), higher than that observed for other Delta variants that show a SAR of 11.2%. SAR is the probability of an infected member infecting one of her susceptible contacts. A 12.2% SAR means that AY.4.2 shows a 10% increase in infectivity as compared with the preexisting Delta variant.

The sub-lineage has been expanding in the UK since July 2021 and now has been detected in two samples from Karnataka.

A preliminary rapid vaccine effectiveness analysis does not suggest a significant reduction in vaccine effectiveness for AY.4.2 compared to Delta. There is no reason to believe that the sub-lineage escapes detection via the RT- PCR test.

2) Omicron (B.1.1529)

South Africa was the first to report the Omicron variant of SARS-CoV-2. It has now been designated as a variant of concern by WHO. Since its detection, South Africa has reported a steady number of cases. But data is insufficient to comment on the contribution of Omicron to the increased caseload.

Preliminary data suggests that the clinical symptoms exhibited by Omicron are similar to other strains of SARS-Co-V-2. WHO has advised the continued use of Corticosteroids and IL6 Receptor Blockers to manage this infection.

Due to the high number of mutations in the spike proteins, it is being speculated that this variant possesses better cell adhesion and cell entry capabilities leading to a higher rate of infections. Concerns are also being raised about the efficacy of existing vaccines against this variant. Data is insufficient at this time to draw conclusions about vaccine efficacy, chance of reinfection, and severity of symptoms. However, existing vaccines may provide some degree of protection, and in case of infection, might reduce the severity of the course of the disease.

The technical advisory group of WHO in charge of researching SARS-CoV-2 evolution has confirmed that existing RT-PCR based diagnostic tests can detect Omicron. The absence of gene 'S' in this variant, used by some diagnostic RT-PCR tests, can be used to identify Omicron through a PCR test.

Vaccination status and COVID-19 caseload in India

India's vaccination campaign started on January 16, 2021, is being carried out in different phases, with initial priority given to health care workers and adults of the 65+ age group. On May 1, 2021 the eligibility was extended to all adults above 18 years of age. As of November 28, 2021 India has administered 121.9 crore doses of vaccine and fully vaccinated 30.96% of its population, with 56.05% of the population having received at least one dose.

As of November 28, 2021, the states that are lagging behind in vaccination are Jharkhand (29.4%), Uttar Pradesh (32.3%), Nagaland (33.4%) and Punjab (33.6%). Data of all the states of India are summarised in the table below.

State	Percentage of population vaccinated	
	One Dose	Both Doses
Ladakh	96%	77.3%
Jammu and Kashmir	>99%	79.5%
Himachal Pradesh	>99%	92.6%
Punjab	74.4%	33.6%
Uttarakhand	97.5%	64%
Haryana	92.5%	49.6%
Uttar Pradesh	73.6%	32.3%
Delhi	86.5%	54.6%
Bihar	74.9%	36.1%
Rajasthan	84.5%	47%
Madhya Pradesh	92.2%	62.4%
Gujarat	97.1%	72.9%
Chattisgarh	86.4%	49.1%
Jharkhand	63.1%	29.4%
West Bengal	88.7%	40.3%
Odisha	86.5%	48%
Maharashtra	80.7%	42.7%
Telangana	82.3%	41.9%
Andhra Pradesh	85.4%	60.8%
Goa	81.6%	65.3%
Karnataka	94.1%	61.1%
Kerala	89.3%	59.3%

Tamil Nadu	80.8%	44%
Sikkim	>99%	>99%
Meghalaya	55.8%	38.5%
Assam	91.2%	50.8%
Arunachal Pradesh	81%	62.1%
Nagaland	45.1%	33.4%
Manipur	64.9%	43.9%
Mizoram	92.7%	70.4%
Tripura	92.3%	72.6%
Andaman and Nicobar Islands	68.4%	58.2%
Lakshadweep islands	NA	99.2%*

Table summarising the percentage of population vaccinated in each state for the first dose and both the doses. Data obtained from https://www.thehindu.com/coronavirus/
NA - Not available
** As of November 6, 2021. Source: https://www.thehindu.com/news/national/other-states/lakshadweep-close-to-achieving-full-covid-19-vaccination-coverage/article37354016.ece*

The above data show that India needs to ramp up its vaccination drive to ensure more people are fully vaccinated; particularly in states where vaccination rate is poor.

India reported its first COVID-19 case on 30th January 2020. As of November 28, 2021 India has had a total of 34,572,523 coronavirus cases and 468,554 deaths. As on November 27, 2021 India has an active caseload of 107,019, with Kerala accounting for 46.82% (50,109) of the total active cases. Maharashtra and Tamil Nadu account for 11.35% (12,153) and 7.8% (8,418) of active cases respectively.

The daily numbers of the COVID-19 cases reported during late October and November were one of the lowest observed since the pandemic started. Various state governments were in the process of easing restrictions by the end of November 2021, after the end of a series of festivals. Off-line classes in schools for different age-groups have already started in different states. Public transport services in all major cities are back to pre-pandemic timings and frequencies, with only Mumbai restricting local services to fully vaccinated passengers.

But the detection of new variants with a higher transmissibility warrants a rethink of the rate and extent of the easing up of businesses, public transport, and schools across Indian states/ districts.

Recommendations:

1) **Public Health Awareness**: It is evident that pre-existing preventive public health measures continue to be effective against new variants of the virus. But the long duration of the pandemic has led to behavioral fatigue, reducing the chances of people complying with basic public health measures. This was most obviously seen when many spectators were gathered, maskless, to watch the return of international cricket to India. It is important, even for those double vaccinated, to wear masks and practice social distancing to prevent further circulation of the virus. A new government public information campaign to rehash the basics of social distancing, masking up, and personal hygiene is a must.

2) **Easing of COVID-19 restrictions:** The exchequer and private businesses were suffering economic loss due to varying degrees of restrictions on commercial activities. As the current levels of infections are low, the end of November/early December seems like a tempting timeframe to permit commercial activities on a wider scale.

   However, the easing of restrictions, coupled with emergence of new variants, may lead to a sudden rise in infections. Still, lessons from the past have shown that blanket lockdowns and stringent curbs may not be the answer to preventing spread of the virus. Existing vaccines may provide some degree of protection from the new variants of SARS-CoV-2.

   We therefore propose the easing up of restrictions to be proportional to coverage of vaccination and weighted weekly Test Positivity rate (wTPR) in a given state/ district. We also suggest that in the case of any alteration in the vaccination coverage and wTPR of an administrative zone, the extent of permitted economic activities can be altered.

   Different states and districts within one state vastly vary in the degree of vaccination coverage. We believe that our suggestion to link the opening up of business, schools, transport etc. in a

given district to vaccination coverage and wTPR may incentivise local administrations to promote and execute vaccination drives.

Moreover, if a business within a district with low vaccination coverage has a fully vaccinated working force, that business will be permitted to conduct off-line activities while others in the district might not. This may promote private citizens to get vaccinated.

A simple framework as described below can be followed to categorise a district/state into four categories. This will be based on the extent of vaccination coverage amongst their population and wTPR. This will also take into consideration the difference in the percentage of the population partially and completely vaccinated. The following is the four-way categorisation of states/districts.

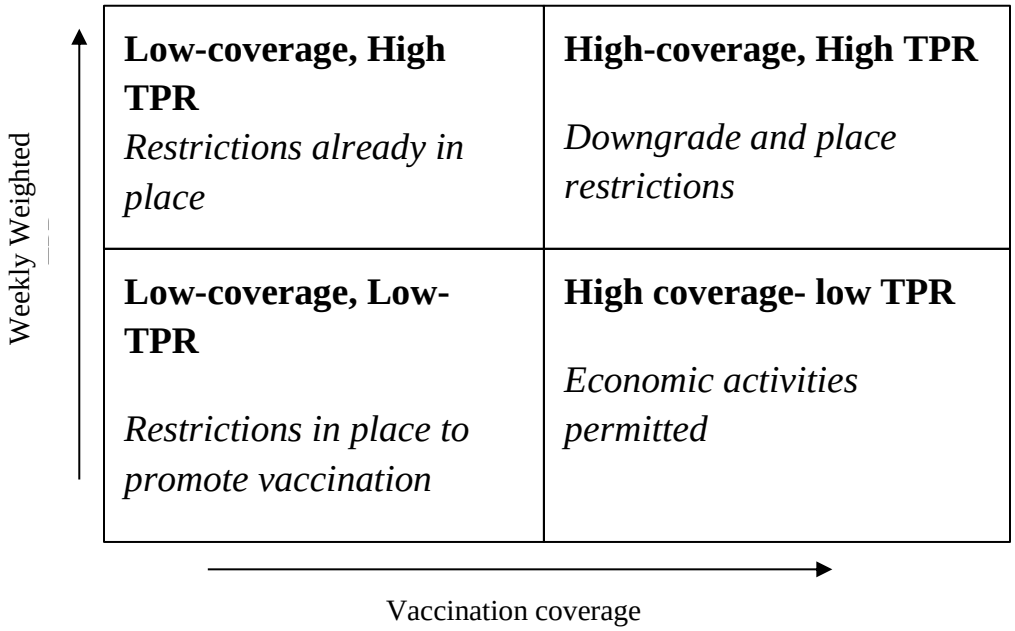
Category Green: A state/district that has vaccinated more than 75% of its population with two doses and a wTPR of less than 5%.

Category Orange 1: A state/district that has vaccinated more than 75% of its population with a single dose but only up to 50% of its population with the second dose and a wTPR of less than 5%.

Category Orange 2: A state/district that has vaccinated between 40 to 75% of its population with a single dose and a wTPR of less than 5%.

Category Red:A state/district that has vaccinated only 40% of its population with a single dose and a wTPR of more than 5%.

Following is a 2X2 framework to visualise the degree of permitted activity in relation to vaccination coverage and Weekly Weighted wTPR as a proxy for caseload.



Based on the above categorisation, the following is the table for permitted economic activities.

Category	Public transport	Offline Schools	Private business
Category Green:	Open to all	Open to children above 7th class	Yes
Category Orange 1	Only for essential workers and fully vaccinated citizens	Only schools with fully vaccinated staff and parents	Only business with fully vaccinated staff
Category Orange 2	Not permitted	Not permitted	Only business with fully vaccinated staff
Category Red	Not permitted	Not permitted	Not permitted

Preliminary data suggest that the existing vaccines are able to offer the same degree of protection to the AY.4.2 variant but are unclear on the efficacy of vaccines against Omicron. Further it is possible that other, as of yet undetected, variants may also emerge and have the capability to escape from immune responses. This may get reflected in a rapid rise in cases.

Therefore, if the wTPR of any administrative zone crosses 5%, that zone will be downgraded to the immediate lower category.

3) Diversification of Vaccines administered in India

Covishied and Covaxin vaccines are the major vaccines being administered in India. Covishield uses an Adenovirus host that expresses a SARS-CoV-2 spike protein while Covaxin uses heat-inactivated SARS-CoV-2 viral particles. The immunity conferred by these vaccines is similar in effectiveness but targets different regions of the SARS--CoV-2 virus.

As seen with recently emerging variants, it is important that India develops a portfolio of vaccines capable of targeting different parts of the virus. For example, even if the mutations in the spike protein of Omicron renders it immune to Covishield, there is a possibility that Covaxin may confer some protection. It would be beneficial if we diversify and expand the vaccines used currently. Such diversification would lead to different areas of the SARS-CoV-2 virus to be targeted and not make the population overly susceptible to particular variants.

Further, In the case of current vaccines displaying reduced efficacy to Omicron, companies using mRNA based vaccines should be able to develop an Omicron specific vaccine in a relatively short period of time

(6 weeks to develop, and 100 days for production). Hence it is important for India to also build capacity in using various strategies of developing vaccines.

4) Reduction in intra-dose interval and booster doses

The existing interval between the 1st two doses of the COVID-19 vaccine in India is 84 to 112 days (12-16 weeks). In light of two new variants of SARS-CoV-2 being reported, it would be beneficial to increase vaccination coverage by reducing this interval to 3060 days (4 to 8 weeks).

Frontline workers and medical personnel composed the group of individuals who first received the COVID-19 vaccine in India. It has been more than nine months since the second dose for this group of individuals. Waning of immunity conferred by any vaccine after six months has been documented. In preparation for a potential surge in cases due to new variants, these groups should be administered booster shots.

5) Permission to conduct home-testing

Rapid antigen-tests are easy to self-administer at home with minimal training. They can serve as a rapid first line of testing and help predict a spike in new cases quicker. RT-PCR tests would remain the gold standard, confirmatory test for COVID-19.

ICMR has approved a Rapid Antigen Test (RAT) kit from Mylab for home usage. ICMR has waived off the Indian validation requirement for other kits approved by the following agencies:

1) United States Food and Drug Administration (USFDA), USA,
2) Pharmaceuticals and Medical Devices Agency (PMDA), Japan,
3) Therapeutic Goods Administration (TGA), Australia, and
4)WHO Emergency Use Listing (EUL) procedure

While these are welcome steps, the use of home testing kits needs to be promoted through various public information campaigns as a cost-effective, quick, easy to use first step in COVID-19 diagnosis.

6) Stringent monitoring at Indian international airports

While the variant of Delta has already been detected in Indian samples, there are no known reports of Omicron being present among the wider Indian population. In light of this, a shutdown of international airports in India seems tempting but would hamper economic activities. A better approach would be to strictly monitor the COVID-19 positive status of incoming passengers and only permit fully vaccinated individuals who have received their last dose a maximum 6 months prior to arrival date, entry into India.

A RT-PCR test with primers that are able to detect the Omicron variant should be employed at airports as an additional precaution.

Conclusion:

In order to prevent a potential wave of infections due to new variants of SARS-CoV-2 we propose a framework to allow permissible economic activities based on the vaccination coverage and wTPR of an administrative unit. We also propose home testing to be promoted to aid the detection of a potential wave of infections as well. In order to increase the coverage of vaccines, we propose to reduce the inter-dose interval and suggest booster shots for frontline workers. We advise against shutting down international airports in India but recommend stringent monitoring of incoming travellers.