

Clinical and demographic features of SARS-COV-2 variants of concern (VOC): B.1.1.7 and B.1.617.2 At a tertiary care hospital in Southern Rajasthan

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Abstract

Introduction: As the global severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) pandemic expands, genomic epidemiology and whole genome sequencing are being constantly used to investigate its transmissions and evolution.

Aims and Objectives: To ensure that best use is made of the whole genome sequencing programmes for SARS-CoV-2 results, in improving public health. Analyze and establish a correlation of demographic features and vaccination status with clinical outcome of VOC's.

Material and Method: 478 samples (December 15, 2020- June 15, 2021) were shortlisted as per state government policy of sample selection criteria for genome sequencing, packed in triple layer according to standard transportation protocol and sent to the National Public Health Laboratory (NPHL) for whole genome sequencing.. The data collected by us were analyzed and correlated with the results of whole genome sequencing, shared by the NPHL to enhance public health impact of the variant identified.

Observation and Results: In our study we found 92% of B.1.617.2 (Delta) variants and 8% of B.1.1.7 (Alpha) variant. We found significantly high mortality (25%) in age group > 60 years compared to other age group (20-40years, 40-60years) with Delta variant (p value < .05). We also found that Delta variant is significantly more transmissible (p value < .05) than Alpha variant. Mortality was significantly higher among unvaccinated patients having co-morbid conditions rather than vaccinated patients having co-morbid conditions with delta variant (p value <0.05).

Conclusion: B.1.617.2 (Delta) variant has emerged as a common VOC among SARS-COV-2 patients in southern Rajasthan. Vaccination has a very high level of protective role in decreasing mortality, especially old age patients with associated co-morbidities among Delta variant.

Keyword:SARS-COV-2, variant of concern, whole genome sequencing, pre-existing medical condition

Introduction

All viruses, including SARS-CoV-2, the virus that causes COVID-19, change over time. Most changes have little to no impact on the virus properties. However, some changes may affect the virus's properties, such as how easily it spreads, the associated disease severity, or the performance of vaccines, therapeutic medicines, diagnostic tools, or other public health and social measures ^[1].

As the global severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) pandemic expands, genomic epidemiology and whole genome sequencing are being constantly used to investigate its transmissions and evolution. Whole genome sequencing was undertaken to identify possible new variants and scale the fitness of current circulating strains ^[2].

So far, there are four globally recognized variants of concern (VOC): Alpha or lineage B.1.1.7 (UK), Beta or lineage B.1.351 (South Africa), Gamma or lineage P.1 (Japan/Brazil), and Delta or lineage B.1.617.2 (India) ^[3, 4, 5, 6].

Alpha or lineage B.1.1.7 emerged in September 2020 in Southeastern England. Due to its enhanced transmissibility, it quickly spread worldwide and it is reported, as of 1 June 2021, in 160 countries. In February 2021, Public Health England (PHE) recognized B.1.1.7 as a new VOC-Alpha ^[7].

As of June 2021, more than 60 countries reported cases caused by a newly recognized variant-lineage B.1.617 (also known as G/452R.V3) and its three sublineages, the first two detected in December 2020 and the third detected in February 2021 in India ^[3]. However, it has since become evident that only sublineage B.1.617.2 is associated with greater public health risk, which is why it is now the only sublineage of B.1.617 that is recognized as VOC-Delta ^[8].

Our study consists of implementation of the clinical and demographic features of SARS CoV-2 virus variants (VOC), which were identified in Southern Rajasthan since December 2020, to support and augment the public health strategies in a tertiary care hospital in Southern Rajasthan by proper analysis of available data.

Material and method

This is an analytical cross sectional study in the department of microbiology RNT Medical College, Udaipur, Rajasthan from 15th December 2020 to 15th June 2021. Total (233427) nasopharyngeal samples were processed for RT PCR test for COVID 19, among them (60236) samples were found positive.

Those samples which were selected and collected for RT PCR diagnostics are typically also appropriate for sequencing ^[9]. Nasal swabs, throat swabs and saliva have been found to have high viral loads shortly after symptom onset and for up to 25 days afterwards ^[10, 11, 12].

Sample Collection

1. Both Oropharyngeal and Nasopharyngeal swabs were collected in a single VTM tube.
2. 1 ml VTM was immediately aliquoted and stored at -80°C of every sample (to eliminate contamination chances during processing) Remaining sample was sent for RTPCR testing.
3. Aliquots of those samples who found Positive for COVID 19 on RT PCR were stored separately.
4. Among these positives, Isolates for whole genome sequencing were selected ^[13].

Sample selection criteria

1. As per the State Government directives, samples from international travelers and 5% of random surveillance samples from the positive cases with Ct value <30 including those from clusters, mild/moderate/severe and deceased cases were selected for whole genome sequencing of COVID-19 ^[13].
2. **Inclusion criteria:** Participants who were identified as B.1.1.7 and B.1.617.2 variants

were included in the study.

3. **Exclusion criteria:** There were no exclusion criteria.
4. As a part of active genomic surveillance, whole genome sequencing (WGS) was performed by the National Public Health Laboratory (NPHL) “Council of Scientific and Industrial Research Institute of genomics and Integrative Biology (CSIR-IGIB), Delhi”.
5. Among (60236) positive samples, n=478 samples (December 15, 2020- June 15, 2021) were shortlisted as per state government policy of sample selection criteria for gene sequencing, packed in triple layer according to standard transportation protocol and sent to the CSIR-IGIB, Delhi for whole genome sequencing^[13].

Data collection

Clinical information was extracted from the medical record submitted by the patient after taking informed consent, by using a standardized patient requisition form. Data regarding clinical outcome of patients was collected at 14th day from the last onset of illness. The data collected by us were implemented, analyzed and correlated with the results of whole genome sequencing which were shared by the IGIB, Delhi to enhance public health impact of the variant identified. Available metadata were in terms of age, gender, VOC type, pre-existing medical condition, vaccination status and clinical outcomes (hospitalization, recovery and death).

Data analysis was done by Fisher Exact Test Statistics for 2×2 contingency table. All statistical tests were two-sided, and p-values <0.05 considered statistically significant.

Observation and results

The present study consisted of 478 sequenced samples among which 100 samples were reported as VOC in southern Rajasthan from 15th December 2020 to 15th June 2021.

Table 1: Distribution of variant of concerns in our study group

Variant of concern	Number	Percentage
B.1.617.2(Delta)	92	92
B.1.1.7 (Alpha)	8	8
Total	100	100

In our study 92 samples were found positive for B.1.617.2 (Delta) variant and only 8 samples were of B.1.1.7 (Alpha) variant.[Table 1, Figure 1].

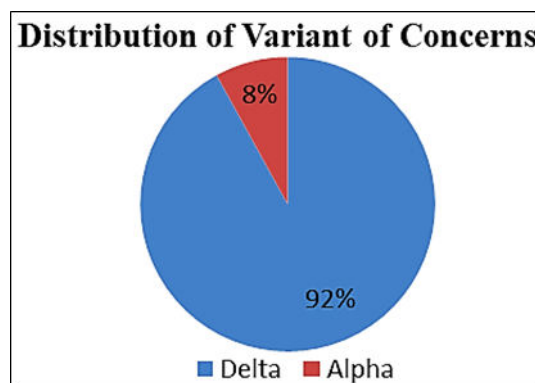


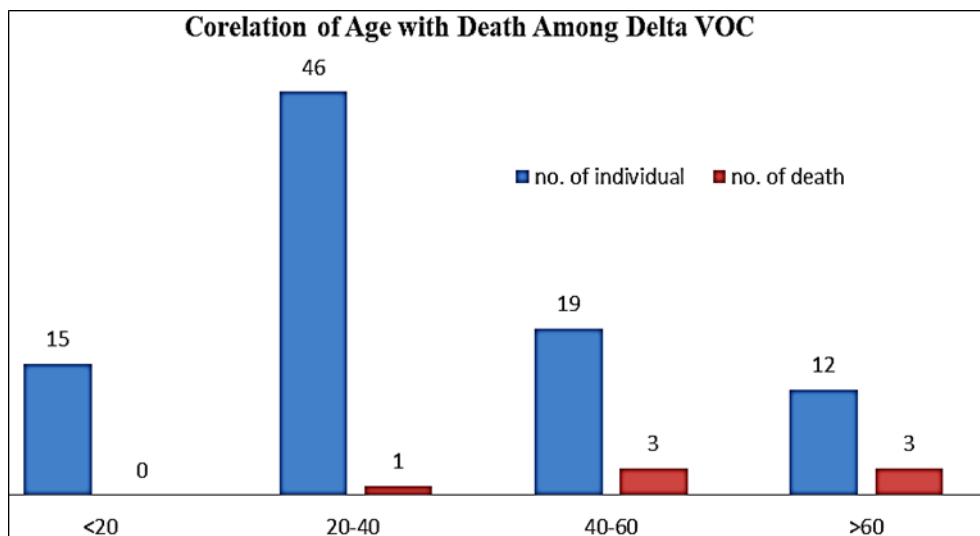
Fig 1

Table 2: Age distribution among identified VOC's and their correlation with clinical outcome

Age in Years	N=Total no of individual	Variant of concern	No. of individual consisting	Death Due to SARS-COV-2		
				No. of death	Total no. of death	% of total no of death
<20	15	Delta	15	0	0	0
		Alpha	0	0		
20-40	51	Delta	46	1	1	2
		Alpha	5	0		
40-60	22	Delta	19	3	3	14
		Alpha	3	0		
>60	12	Delta	12	3	3	25
		Alpha	0	0		
Total	100		100	7		

The chi-square statistic is 7.3696. The *p*-value is .025102. The result is Significant at $p < .05$

In our study group no death reported in age group below 20 years. In 20-40 years of age group 2% death reported, among 40-60 years of age group 14% death occurred and 25% death reported in patients of > 60 years. All reported deaths were from B.1.617.2 (Delta) variant. No death reported in patients identified with B.1.1.7 (Alpha) variant. The chi square relationship between age group and death were found significant among Delta variant ($p < 0.05$). [Table 2, Figure 2].

**Fig 2****Table 3:** Transmission of infection among family members in both variants

Variants of concern	Total no. of VOC	Family member infected		No one infected	
		No.	%	No.	%
B.1.617.2 (B.1.617.2(Delta))	92	76	82.6	16	17.4
B.1.1.7 (Alpha)	8	3	37.5	5	62.5
Total	100	79	79	21	21

The chi-square statistic is 9.0272. The *p*-value is .00266. Significant at $p < .05$ among 92 B.1.617.2 (Delta) variants identified, 82.6% (76) patients were having history of contact transmission of infection to one or the other family member whereas only 37.5% (3) people have history of transmission of infection from 8 B.1.1.7 (Alpha) variants positive patients. The findings were statistically significant ($p < 0.05$). [Table 3, Figure 3].

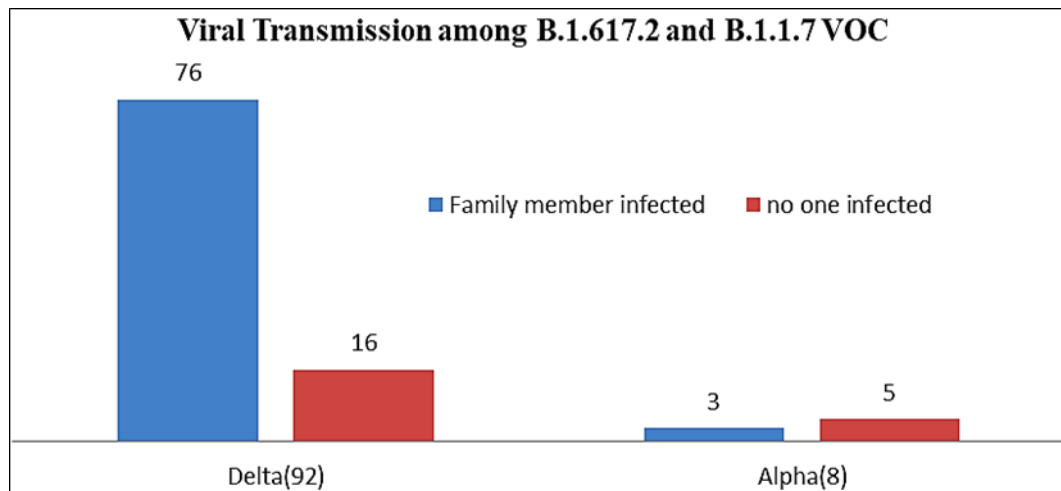


Fig 3

Table 4: Association of premedical condition, vaccination status and death with VOC's

VOC	No	Pre-existing medical condition(PMC)	No.	Vaccination status	No.	Death No.	P value
B.1.617.2 (B.1.617.2(DELTA))	92	PMC	15 (16.3%)	vaccinated	10 (66.6%)	1	<0.002 S*
				unvaccinated	5 (33.3%)	5	
		Non PMC	77 (83.69%)	vaccinated	26	0	1 NS*
				unvaccinated	51	1	
B.1.1.7 (ALPHA)	8	PMC	0	-	0	0	-
		Non PMC	8	vaccinated	1	0	1 NS*
				unvaccinated	7	0	
TOTAL	100				100	7	

*S-significant, *NS-Non Significant

In our study we found that among 92 patients of B.1.617.2(Delta) variant, 16.3% (15) patients were having certain co-morbid conditions like diabetes, hypertension, heart disease etc., Among those (15) patients, 66.6%(10) patients were vaccinated with one death reported and 5 (33.3%) unvaccinated patients with all 5 patients died. These findings were statistically significant ($p < 0.05$). Only one death reported among those patients who neither have any premedical conditions nor vaccinated. No death reported in patients from which B.1.1.7 (Alpha) variants (8%) were identified.[Table 4]

Discussion

Global surveillance of SARS-CoV-2 genetic sequences and related metadata contributes to the COVID-19 outbreak response.

In our study we found 92% of B.1.617.2 (Delta) variants and 8% of B.1.1.7 (Alpha) variant among VOCs identified (Table 1, Figure 1). Delta variant is predominating over Alpha variant in this study group. Similar data has been obtained by various other researchers [14, 15].

In our identified VOC's 60% were male patients and 40% were females. We found significantly high mortality (25%) in age group > 60 years, then 40-60 years (14%) and 20-40 years (2%) among B.1.617.2(Delta) variant of concern (p value < 0.05) (Table 2, Figure 2). The reason behind increased mortality among old age (>60 years) must be, the associated co-morbid conditions which make them more vulnerable of becoming sick and hospitalized and eventually death. Biswas *et al.* 2020 and O'Driscoll *et al.* 2021 also reported high mortality among older age group in Covid 19 cases [16,17].

In our study we found that B.1.617.2 (Delta) variant is significantly more transmissible (p value < .05) than B.1.1.7 (Alpha) variant (Table 3, Figure 3). This might be the cause of

predominating Delta variant over Alpha variant. Results were found to be similar in study done by Public Health England, Dagnanar J, Peacock, T.P *et al.*^[18,19,20].

We found that the mortality was significantly higher among unvaccinated patients having co-morbid conditions with B.1.617.2 (Delta) variant rather than vaccinated patients having co-morbid conditions with Delta variant (p value <0.05) (Table 4). Studies from various parts of the world also reported higher mortality among unvaccinated patients associated with certain co-morbidities^[14, 21, 22].

We did not find any significant difference in mortality among patients not associated with co-morbid conditions with their vaccination status in both the variants (Table 4).

Conclusion

It is evident from the present study that B.1.617.2 (Delta) variant has emerged as a common VOC among SARS-COV-2 patients in southern Rajasthan. Delta variant is highly transmissible which makes it dominating over B.1.1.7 (Alpha) variant. Vaccination has a very high level of protective role in decreasing mortality, especially old age patients with associated co-morbidities among Delta variant. There is an urgent need to develop and strengthen vaccination policy, to prevent mortality due to Delta variant of concern among patients having co-morbid conditions. The accelerated integration of genome sequencing into the practices of the global health community is a must if we want to be better prepared for the future threats. We hope this guidance will help pave the way for that preparedness.

Limitation: This is the clinical data based study, as the sequencer was not available in our setting it could not possible to analyze gene mutations among variants. In this era of viral diseases it is the necessity of time that genome sequencing facility of viruses should be available in at least tertiary care levels so that more research work can be done on various variants which would help in making public health strategy. As we did not get patients having co-morbidities in B.1.1.7 (Alpha) variant so we could not comment on mortality among them.

Ethical consideration: The Investigation Protocol was reviewed and approved by the Institutional Ethics Committee.

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