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Correspondence

Reduced severity of SARS-CoV-2 infection by Kappa variant of interest (B.1.617.1) in a healthcare worker post-vaccination from Gujarat, India

Sir,

After the year long wait for the COVID-19 vaccine, India had initiated the vaccination against COVID-19 from January 16, 2021. Two vaccines, namely COVAXIN™ (BBV152, Bharat Biotech, India) and Covishield (ChAdOx1 nCoV-19, Oxford-AstraZeneca, UK manufactured by Serum Institute of India), are administered as part of the vaccine roll-out programme in India[1]. Post-vaccination breakthrough cases are now being reported at various time points all over the world including India[2-4]. Experts across the globe are trying to evaluate the COVID-19 vaccine effectiveness in the real world outside the clinical trial setup. Here, we present a case of SARS-CoV-2 infection in a healthcare worker post-COVID-19 vaccination (ChAdOx1 nCoV-19), having the Kappa variant of interest (VOI) B.1.617.1.

A 41 yr old male[†], doctor by profession, presented to a tertiary care hospital in Vadodara district, Gujarat, India, in March 2021 with symptoms of dry cough and mild fever of two days duration. There was no history of breathlessness, abdominal discomfort, loss of smell, headache, neurological symptoms or other significant complaints and no history of clinically significant underlying comorbidities. The patient was a healthcare worker involved in the management of COVID-19 patients admitted to his hospital. None of his family members had similar complaints. He was vaccinated with ChAdOx1 nCoV-19 and was administered the second dose one week before the onset of the symptoms. On examination, he was febrile, vital parameters were stable and SpO_2 was 99 per cent. His chest computerized tomography (CT) scan showed severity index of 0/25 with a few subcentimetric and enlarged peritracheal and perivascular lymph nodes which were not radiologically significant.

His clinical specimens [throat swab (TS) and nasal swab (NS)] were obtained and tested positive for SARS-CoV-2 by real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) (*N* gene-16, *RdRP* gene-16, *E* gene-16)[5]. He was admitted to the hospital, kept under isolation and managed symptomatically. On admission, his haemoglobin was 14.6 gm/dl, normal total leucocyte counts and platelet counts. His random blood sugar levels were 142 mg/dl, normal coagulation profile, liver and kidney function test. The acute phase markers were normal including serum ferritin (117 ng/ml), D-Dimer (268 ng/ml), lactate dehydrogenase was (355 U/l) and interleukin-6 (0.50 pg/l). The patient remained admitted to the hospital in isolation ward till complete resolution of his symptoms (7 days) and was followed up on outpatient department basis subsequently for a period of eight weeks.

The TS, NS and serum samples were referred to the Indian Council of Medical Research–National Institute of Virology (ICMR-NIV), Pune, for confirmation and also for genomic sequencing. The study was approved by the Institutional Biosafety Committee and Institutional Human Ethics Committee of ICMR-NIV, Pune, under the project entitled 'Molecular epidemiological analysis of SARS-CoV-2 circulating in different regions of India' (20-3-18N).

The serum sample was screened for anti-IgG against the spike (S1) protein, receptor-binding domain (RBD) and nucleocapsid (N) protein (Lab care diagnostics, Mumbai, India) of SARS-CoV-2 using ELISA with optical density (OD) cut off of 0.2[6]. Anti-IgG antibodies were detected by both the assays with the OD of 0.725 (1:3200 titre) for S1-RBD and 0.408 (1:50 titre) for N protein. The serum was also

[†]Patient's consent obtained to publish clinical information

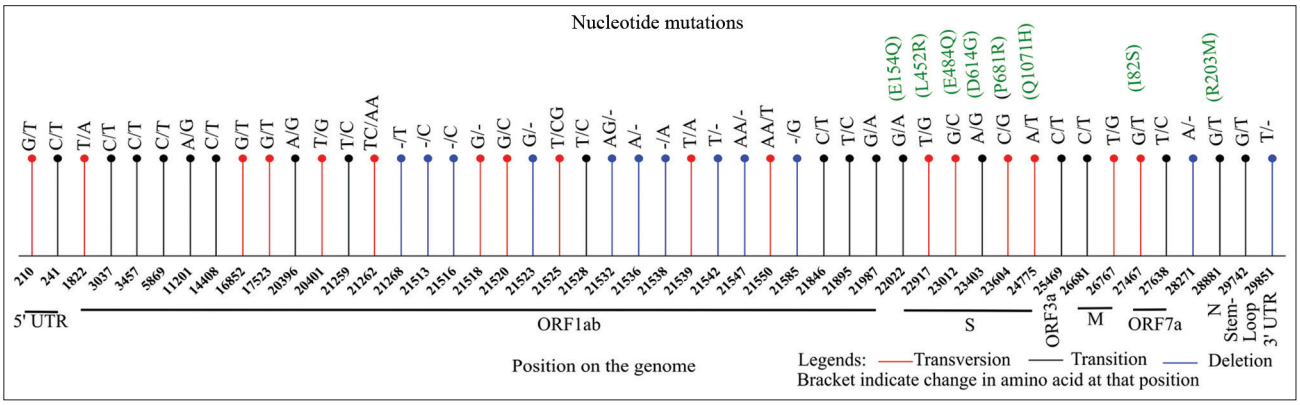

Figure. Nucleotide variations in the clinical sample of the case were observed using Base Variant analysis of the CLC Genomic Workbench 20.0.04 in comparison to the Wuhan Hu-1 (accession number: NC_045512.2). The transitions are marked with black coloured lines; transversions are marked with red-coloured lines and deletions with blue coloured lines. The amino acid changes specific to the Kappa variant of investigation B.1.617.1 in the spike protein region are mentioned in green. Nucleotide and amino acid changes are marked with single letter denotion. '/' indicates the replacement sign.

positive for anti-SARS-CoV-2 IgG antibodies by whole antigen SARS-CoV-2 human IgG antibody ELISA with O.D of 0.311 (cut-off 0.2) and P/N value of 3.24[7].

To characterize the SARS-CoV-2, next-generation sequencing (Illumina, California, USA) was performed as described earlier[8]. Reference-based mapping was done with Wuhan Hu-1 (accession number: NC_045512.2) using CLC genomics workbench 20.0.4 (Qiagen, USA), which retrieved 99.79 per cent of the SARS-CoV-2 genome. The B.1 lineage carries D614G mutation (aspartic acid is replaced by glycine at the 614th position of the spike protein) whereas sequences of B.1.617.1 pangolin lineage showed spike mutation with double mutation belonging to G clade [as per the Global Initiative on Sharing All Influenza Data (GISAID) classification- *https://www.gisaid.org/*]. The double mutation refers to specific changes that are denoted by E484Q (glutamate is replaced by glutamine at the 484th position of the spike protein) and L452R (substitution of leucine with arginine at the 452nd position). However, the non-synonymous changes were also observed in spike protein including E154K (glutamate is replaced by lysine at the 154th position of the spike protein), P681R (proline is replaced by ariginine at the 681th position of the spike protein) and Q1071H (glutamine is replaced by histidine at the 1071th position of the spike protein) (Figure).

The genomic surveillance has been instrumental in the detection of VOI/variants of concern (VOCs). Among these cases, VOC, Alpha (B.1.1.7), Beta (B.1.351), Delta (B.1.617.2) and Gamma (P.1) had already been detected in the country[9,10]. The emergence of the B.1.617 lineage created a grave public health problem in India with a second wave in India. B.1.617 lineage evolved further to generate sub-lineages B.1.617.1, B.1.617.2, B.1.617.3[11]. Nearly 60-80 per cent clinical samples from Maharashtra State in India were reported to have the VOI B.1.617.1[12]. However, this case was reported from Gujarat, indicating the spread of Kappa variant to other parts of India. Breakthrough cases would normally be asymptomatic to mildly symptomatic post-vaccination. However, with the presence of the new VOCs and VOIs, along with the rapid mutations in the spike protein, particularly at the amino acid positions 438-506, could make them highly infectious by increasing the transmissibility. These variants have the ability to evade natural immunity or vaccine-induced immunity, which is a serious concern.

The present case had got SARS-CoV-2 infection even after completing two doses of the vaccination. However, the patient had mild symptoms, required no oxygen support and recovered completely within seven days of the infection due to Kappa variant. This short and mild course of the illness demonstrates the effectiveness of the vaccines in preventing moderate/severe disease and mortality. Similar findings of reduced disease severity in post vaccinated individual have been reported by Gupta *et al*[4]. Sapkal *et al*[13] have reported that vaccinated individuals contracting SARS-CoV-2 infection even due to variants show a significant boost in the neutralizing antibody (NAb) titres induced by the infection. Yadav *et al*[14] reported that the NAb titres against B.1.617 in COVAXIN recipients which was comparable to the NAb titres of recovered naturally

infected cases. A major limitation of our study was that we were unable to assess fully the effectiveness of the immune responses, especially by doing the NAb titres due to low volumes of the serum samples available at the time of infection. Further, the NGS data generated were limited to the machine specificity and sensitivity.

The findings in our study have implications for the role of vaccination in response to COVID-19 considering the infection by the new variant post-vaccination and effectiveness to prevent severity and morbidity.

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