ISSN 2692-5877
DOI: 10.46998/IJCMCR.2020.05.000106

International Journal of
Clinical Studies & Medical Case Reports

Mini Review Article

SARS-Cov-2 D614G Spike Protein Mutation is Associated with Potentially Higher viral load in COVID-19 Patients

Ravindra Pratap S*, Dr Surendra Kumar Verma[1]

Department of Pathology, JIPMER, Puducherry, India

[1]Professor (Senior scale Professor), Department of Pathology, JIPMER, Puducherry, India

***Corresponding author:** Pratap Singh, Department of Pathology, JIPMER, Puducherry, India. E-mail: pratapravindra.s@jipmer.edu.in

Received: August 30, 2020 Published: October 01, 2020

Abstract

Severe acute respiratory syndrome- Coronavirus-2 (SARS-COV-2) has undergone several mutations since the Pandemic emerged in December 2019. However only one of these mutations so far singled out as possibly altering SARS-Cov-2 behaviours named as D614 is shift at the amino acid Aspartic acid to Glycaemic shift at position 614 of a protein. Recent studies have shown that D614G mutation in the spike protein of novel coronavirus makes it more infectious, transmissible, and deadly. So far there is no evidence that infection with Severe acute respiratory syndrome- Coronavirus-2 (SARS-CoV-2) containing G614 variants will leads to severe disease and also studies suggest, as the mutation does not change the immunogenic part of the spike protein.

Keywords: COVID-19; SARS-CoV-2; ACE2; Pandemic; D614G mutation; Infectivity; Neutralizing antibodies; pseudovirus; SARS-CoV-2; Spike protein

What is D614G Mutation?

D614G mutation is considered by aspartic acid to glycine shift at the amino acid position 614 of a protein. The RNA codons that codes for aspartic acid and glycine are designed as GAU/GAC and GGU/GGC, respectively. Thus, a single mutation in the RNA codon causing A to G shift can lead to aspartic acid to glycine shift in the peptide sequence of the target protein. Glycine is a nonpolar amino acid with a single hydrogen atom as its side chain; whereas, aspartic acid is a polar amino acid with an acidic side chain. Given the substantial difference between the basic nature of these amino acids, D614G mutation is expected to have significant biological implications [1,2].

Structure of Severe Acute Respiratory Syndrome 2 Coronavirus (SARS-COV-2) And Host Response

SAR-CoV2 is an enveloped, non-segmented, positive sense RNA virus, Its diameter is about 65-125 nm, containing single strands of RNA and provided with crown-like spikes on the outer surface. Structurally, SARS-CoV-2 has four main structural proteins including spike (S) glycoprotein, small envelope (E) glycoprotein, membrane (M) glycoprotein, and nucleocapsid (N) protein and non-structural proteins (nsp1-16), and accessory proteins (ORF3a, ORF6, ORF7a and b, ORF8, ORF10). The spike or S glycoprotein is a transmembrane protein with a molecular weight of about 150 kDa found in the outer portion of the virus. S protein forms homotrimers protruding in the viral surface and facilitates binding of envelope viruses to host cells by attraction with angiotensin-converting enzyme 2 (ACE2) expressed in lower respiratory tract cells. The nucleocapsid known as N protein is the structural component of CoV localizing in the endoplasmic reticulum-Golgi region that structurally is bound to the nucleic acid material of the virus. Because the protein is bound to RNA, the protein is involved in processes related to the viral genome, the viral replication cycle, and the cellular response of host cells to viral infections [3]. During genome replication within the host, the virus acquires genome mutations, which can be passed on to virus progeny in subsequently infected individuals.

What are the implications of D614G mutation in the spike protein of novel coronavirus?

D614G mutation in the viral spike protein occurred at the initial stage of the pandemic, and recent evidence suggests that viruses containing glycine residue at position 614 have now become the most prevalent variant globally. Dr. Bette Korber et al analysed SARS-CoV-2 sequences from 999 patients in the UK. Results showed patients infected with the G614 variant had a higher viral load compared to D614., Korber et al. showed in human cell cultures in a lab dish that the G614 variant displayed increased infectivity than D614. Scientists have found that G614 mutation in the viral spike protein is the most frequently occurring mutation across many geographical locations. As pseudotyped viruses, G614 variants have considerably higher infectious titers than D614 variants. This indicates that spike D614G mutation makes the SARS-2 coronavirus more infectious and that the virus can be transmitted more easily and rapidly from person to person. G614 infections have a higher level of viral RNA and produced higher titers in pseudo viruses from in vitro experiments, results that now seem to be corroborated by others (e.g., Hu et al., 2020; Lorenzo-Redondo et al., 2020; Ozono et al., 2020; Wagner et al., 2020). Still,

these data do not prove that G614 is more infectious or transmissible than viruses containing D614. And because of that, many questions remain on the potential impacts, if any, that D614G has on the COVID-19 pandemic. Moreover, scientists have shown that people infected with the G614 variant have higher viral RNA load in the upper respiratory tract than those infected with the D614 variant. However, D614G mutation is not associated with increased disease severity because D614G mutation is located in the interface between neighbouring spike protein protomers.

Is Spike D614G Mutation Associated With Higher Mortality?

Although there is no evidence showing that D614G mutation is associated with increased COVID-19 severity, a recent study using a phylogenetic tree of more than 4000 coronavirus genomes has claimed that viruses containing D614G mutation are more virulent, and thus, are associated with higher disease-related mortality. The study has speculated that higher viral pathogenicity may be due to mutation-mediated conformational changes in the spike protein, which facilitate the exposure of polybasic cleavage site to cellular proteases [4]. Korber et al. (2020) found that patients infected with viruses containing G614 had higher levels of virus RNA, but not did not find a difference in clinical outcomes. These clinical observations are supported by two independent studies: 175 COVID-19 patients from Seattle, WA (Wagner et al., 2020) and 88 COVID-19 patients from Chicago, IL (Lorenzo-Redondo et al., 2020).

Whether This Mutation also Mediates Neutralization-Escape That May Reduce The Effectiveness of Vaccines?

Drew Weissman et al, to determine whether D614G mediates neutralization-escape that could compromise vaccine efficacy, sera from Spike-immunized mice, nonhuman primates and humans were evaluated for neutralization of pseudo-viruses bearing either D614 or G614 Spike on their surface. In all cases, G614 Spike pseudo virions were moderately more susceptible to neutralization, indicating this is not an escape mutation that would impede current vaccines [5].

References

1. Grubaugh ND, Hanage WP, Rasmussen AL. Making Sense of Mutation : What D614G Means for the COVID-19 Pandemic Remains Unclear. Cell 2020;182:794-5.
2. Ai-Long Huang, Ni Tang, Kai Wang KL. 15 Infectious Diseases (Ministry of. D614G mutation of SARS-CoV-2 spike protein enhances viral infectivity 2020:137.
3. Astuti I. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2): An overview of viral structure and host response. Diabetes Metab Syndr Clin Res Rev 2020.
4. Zhang L, Jackson CB, Mou H, Ojha A, Rangarajan ES. The D614G mutation in the SARS-CoV-2 spike protein reduces S1 shedding and increases infectivity 2020.
5. Eaaswarkhanth M, Madhoun AAl, Al-mulla F. Could the D614G substitution in the SARS-CoV-2 spike protein be associated with higher COVID-19 mortality ? Int J Infect. Dis 2020;96:459-460.

DOI: *10.46998/IJCMCR.2020.05.000106*