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Review Article

Delta and Omicron Variants

Isiaka Sanni Oluwasegun*

Department of Optometry and Vision Therapy, Makkah Specialist Eye Hospital Bauchi, Basar International Foundation, Nigeria

***Corresponding Author:** Isiaka Sanni Oluwasegun, Department of Optometry and Vision Therapy, Makkah Specialist Eye Hospital Bauchi, Basar International Foundation, Nigeria.

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Abstract

The purpose of this paper is to review recent studies on Delta and Omicron variants of SARS-CoV-2 as to their symptoms, disease presentation and diagnosis, how they are affecting us and how ocular exposure routes influence disease presentation. Delta and Omicron have similar symptoms that sufferers present with, but shortness of breath is peculiar to the Delta variant and sneezing is not a symptom of Delta but of the Omicron variant infection. PCR and Antigen tests are usually done to diagnose SARS-CoV-2 if the disease is suspected but genomic sequencing (an expensive diagnostic test) is required to diagnose the Delta, Omicron, or the exact SARS-CoV-2 variant. The Delta variant (B.1.617.2) had invaded over 163 nations as of August, 2021 after it was discovered in India in late 2020. The Omicron SARS-CoV-2 variant may be more transmissible but less severe than the Delta variant form. The Delta VOC mostly endangers those who are unvaccinated or just partially vaccinated but the Omicron variant may be associated with increased risk of reinfection. In South Africa, the base of the Omicron variant, children seem to have been affected more with increase in number of hospitalizations among those children under age 5. A few cases of Delta variant infections reported had ocular manifestation including red bloodshot eye and conjunctivitis, but there may be a connection between chronic yet SARS-CoV-2 (Omicron variant) and neuroparalytic keratitis. Further studies into the ocular manifestation of these two VOCs and the susceptibility of the ocular surface as a route of entry may revolutionize our understanding of the two VOCs.

Keywords: SARS-CoV-2; Delta Variant; Omicron Variant; Ocular Surface

Introduction

Severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) was first identified in Wuhan, China in December 2019 with a clinical presentation similar to viral pneumonia and now associated with over 5 million deaths worldwide [1-3]. By early 2020, SARS-CoV-2, also known as coronavirus disease 2019 (COVID-19) was declared a global pandemic and a public health emergency of international concern because of the rapid spreading across the world [1]. The virus is efficiently transmitted from person-to-person (between sick and asymptomatic people) via respiratory droplets and/or airborne droplets and contact with fomites [1,4]. Transmission via aerosol, gastrointestinal and ocular surface may be potential routes and should be considered very seriously [5].

SARS-CoV-2 efficiently exploit vulnerable human host factors for its attachment and entry. The SARS-CoV-2 disease causing mechanism initializes by its viral spike protein binding to the host cell receptor human angiotensin-converting enzyme 2 (ACE2) receptors, ACE2 receptor cleavage by a human transmembrane serine protease 2 (TMPRSS2) to endosomal proteases cathepsins provided, for activation of the viral spike protein that facilitate membrane fusion [6-8]. COVID-19 disease global circulation which is recurring in steady and in rapid succession is powered by the

emergence of variants, particularly the new ones with key mutations in the spike protein receptor binding domain (RBD) that markedly enhance the binding affinity in the RBD-hACE2 [9]. These were classified by World Health Organization (WHO) as Variants of Concern (VOCs) [10]. SARS-CoV-2 disease have a wide range of clinical symptoms, from initial symptoms of fever, cough, and fatigue, moderate to severe respiratory disorder, fast progressive to acute pneumonia disease [11]. COVID-19 diagnosis manifest in a variety of ways, ranging from asymptomatic to severe pneumonia and death. But some patients experienced extra-pulmonary manifestation of SARS-CoV-2 like headache, diarrhea, nausea and vomiting at the onset of their illness [12-14].

Moreover, the Delta variant (B.1.617.2) was detected in India for the first time in late 2020. It has invaded over 163 countries by 24th of August, 2021 and WHO, in June 2021, considered Delta strain as becoming the most prevalent strain in the world [15]. On the contrary, Omicron variant (B.1.529) was detected in the samples collected in Botswana on November 11, 2021, South Africa on November 14, 2021 and named the fifth VOC by the WHO's Technical advisory Group on Virus Evolution (TAG-VE) [16-19].

However, making new vaccines and effective vaccination globally is required to build protective immunity in children as well as adults and should be considered as the way to bring the pandemic to an end, stopping the increased viral replication which often may leads to SARS-CoV-2 variants formation [20].

Nevertheless, since Lu., *et al*. [19] reported that the transmission of SARS-CoV-2 through the eyes must be considered. Hence, this paper reviewed a few studies recently done on Delta and Omicron variant as well as their binding protein expression on the ocular surface and/or how ocular exposure routes influence disease presentation, their symptoms, their diagnosis, and how they are affecting us.

Delta and omicron variant

The Delta variant is classified and/or named the fourth VOC after it was initially classified as Variant of Interest (VOI). The Delta variant mostly attacks those unvaccinated or just partially vaccinated [22]. The Delta variant is characterized by the spike protein mutations T19R, Δ157-158, L452R, T478K, D614G, P681R, and D950N. Several of these mutations may affect immune responses directed toward the key antigenic regions of receptor-binding protein (452 and 478) and deletion of part of the N-terminal domain. P681R is at the S1-S2 cleavage site, and it appears that strains with mutations at that site may have increased replication, which leads to higher viral loads and increased transmission [23].

Omicron is a novel variant classified as the fifth variant of concern. It may be more transmissible and associated with increased risk of reinfection and may cause lower vaccine efficiency because of the unusual large number of mutations which includes those that are known to cause escape from neutralizing antibodies as well as increased binding to the host cell receptor angiotensin converting enzyme-2 (ACE2) [22]. The Omicron lineage has split of three divergent sub-lineages (BA.1, BA.2, and BA.3) but BA.1 spreads rapidly all over the world. The BA.1 Omicron genome encodes 30 amino acid substitutions relative to Wuhan-Hu-1 within the spike glycoprotein, 15 of these amino acid substitutions are in the Receptor-Binding Motif (RBM), the RBD subdomain that is able interacts with the human ACE2 receptor. Six of these mutation (G339D, N440K, N501Y, Q498R S477N, and T478K) boost binding affinity to the human ACE2 receptor. Composite such as N501Y and Q498R may also collectively boost ACE2 binding [21]. Generally, the Omicron RBD binds to the human ACE2 with more than twice the affinity (x2.4) of the Wuhan RBD. Seven of Omicron RBD mutations (E484A, K417N, G4465, G4965, Q493R, Q498R and N501Y) are related to diminish antibody binding, especially in epitopes failure akin to the three fundamental classes of RBD-specific neutralizing antibodies. Three deletions (amino acid 69 - 70, 143 - 145 and 211) and an insertion (at site 214) are also available in the Amino-Terminal Domain (NTD) of the Omicron spike glycoprotein. This deletion can be employed as a useful proxy for the estimation of prevalence in the population by S-gene target failure (SGTF) using the TaqPath™ (Applied Bio-systems, Pleasanton, CA) diagnostic assay. Deletions in proximity to amino acids 143 - 145 have been reported to have effect on a range of NTD - specific neutralizing antibodies [24].

Symptoms

Diagnosis

Delta and Omicron variants are diagnosed with a medical history which captures any recent known exposure to the virus, and/or a physical exam to check for peculiar symptoms stated in the

Symptoms	Delta variant	Omicron variant
Fever	Common	Less Common
Cough	Common	Less Common
Runny Nose	Common	Common
Sneezing	No	Common
Sore Throat	Common	Common
Shortness of Breath	Common	No
Night sweats	No	Sometimes
Chills	Common	Less Common
Headache	Common	Common
Loss of Smell	Very Common	Less Common
Fatigue	Common	Common
How Long Symptoms Take to Show Up	4-5days	2-3days

Table 1: A comprehensive table of possible symptoms and incubation period for Delta and Omicron variant disease presentation [18].

table above. If SARS-CoV-2 is suspected, then these tests below are used to diagnose the virus.

PCR tests (genetic or molecular test)	Antigen test
Results can take hours to up to one week	Results are available in less than one hour
More accurate than an antigen test	Less accurate than a PCR test

Table 2: A comparison of PCR and Antigen test as to accuracy and time needed to get result.

An antibody test may be used to determine if a person had a past SARS-CoV-2 infection, but it is not used to diagnose current infections because it takes up to 3 weeks following infection, for the body to produce antibodies to the virus. However regular SARS-CoV-2 diagnostic tests do not test for variants. Testing for variants requires genomic sequencing, which is expensive and requires state health departments to run the tests which help determine prevalence of a particular variant in that state. The Omicron variant includes 3 descendent lineages (BA.1, BA.2 and BA.3). BA.1 and BA.3 have the 69-70 deletion in the spike protein but BA.2 don't. BA.1 is spreading rapidly and accounts for 99% of sequences submitted to GISAID, of which 95% of Omicron variant sequences reported include a 69-70 deletion in the S gene. Some PCR assays reveals a negative signal for the S gene target because of the presence of the 69-70 deletion in the spike protein. This S-gene target failure (SGTF) gives an impression or genetic marker suggestive of Omicron variant. Moreso, confirmation should be obtained by sequencing for at least a subset of samples to differentiate from the mutation (like L452R mutation) or deletion seen in Delta variant [25,26].

How they are affecting world

The changing immunological composition of the human species give rise to the variants of concern because of the marked changes in the properties of SARS-CoV-2 such as disease transmission and antigenicity. The Delta variant (B.1.617.2) had invaded over 163 nations as at August, 2021 after it was discovered in India in late 2020. Globally, the number of nations reporting SARS-CoV-2 Omicron VOC infections continues to rise, with a total of 352 confirmed cases reported by 27 countries as of December 1, 2021 [27]. Omicron SARS-CoV-2 variant may be more transmissible but less severe than the Delta variant form. According to present evidence, the SARS-CoV-2 Delta VOC is 40%-60% more transmissible than the Alpha (B.1.1.7) VOC and may be associated with an increased risk of hospitalization. The Delta VOC mostly endangers those who are unvaccinated or just partially vaccinated but Omicron variant may be associated with increased risk of reinfection [27,28].

As of 9th of January 2022, the confirmed cases and deaths are more than 304 million and 5.4 million respectively. All regions except Africa reported increased incidence of cases (within the spin of a week) and South-East Asia region being the largest with 418%, then Western Pacific Region (122%), then Eastern Mediterranean Region (86%), then Region of Americas (78%) and then the European Region (31%). African Region had the highest recent increased deaths of 84%, then 26% reported in Region of the Americas [29].

Their effect on children

Omicron variant poses greater risk to children than Delta. SARS-CoV-2 cases in children skyrocketed because of the virulence of Omicron variant and the overall percentage of symptomatic children are increasing, compared to the previous delta variant. Chil-

dren under 5 are especially at risk of getting the infection. "In South Africa, the base of the Omicron variant, children seem to have been affected more with increase in number of hospitalizations among kids under age 5 [30].

Figure 1: A comparison of (A) Delta and (B) Omicron variant spike mutation (Image source: Modified from COVID-19 Genomics UK Consortium) [22].

How they affect vision

A few cases of Delta variant infections reported, had ocular manifestation including red bloodshot eye and conjunctivitis. Other SARS-CoV-2 variants also caused blood shot eyes, pink eye, sore eyes, itchy eyes, blurry vision, dry eye, floaters and/or photophobia [31,32]. Omicron variant appears to be more contagious even among fully vaccinated but cause less serious disease and risk of hospitalization compared to the previously dominating Delta variant. Moreso, there may be a connection between chronic yet SARS-CoV-2 (Omicron variant) and damage to microscopic sensory nerve fibers in the cornea that leads to neuroparalytic keratitis.

Figure 2: A comparison of (A) Delta and (B) Omicron variant mutation in receptor-binding domain (RBD). The mutation is marked in orange color. Delta-RBD has only 2 mutations whereas Omicron-RBD has 15 mutations [22].

With possible inter-individual variability, conjunctival epithelium and cornea may be susceptible to SARS-CoV-2 because the conjunctiva and cornea epithelial cells may be a portal of entry as well as a reservoir for person-to-person transmission due to their expression of ACE2 and TMPRSS2 [33-36].

Conclusion

This review suggests that the two recently discovered VOCs named Delta variant and Omicron variant had emerged to cause havoc to human. Hence, both are of public health and economic importance to the world and should be further studied to know their ocular manifestations and/or the susceptibility of ocular surface as a route of entry for these VOCs. This may revolutionize our understanding of these two VOCs.

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