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Phyloevolutionary analysis of delta variant of SARS-CoV 2 in Nigeria

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Abstract

***Background & Aims*:** The evolution of SARS-CoV-2 from its inception created a need for phyloepidemiological approaches to provide unanswered questions regarding the viral emergence and evolvement of various mutated strains. Unfortunately, there is an absolute dearth of information on the evolution of the delta variant strain in Nigeria. This study investigated the phyloepidemiology of the delta variant of SARS-CoV-2 in Nigeria.

***Materials & Methods*:** A total of 33 complete genomic sequences of the SARS-CoV-2 delta variant (B.1.617.2) from Nigeria, India, United Arab Emirates (UAE), United States of America (USA), Canada, United Kingdom (UK), China, and the reference sequence were retrieved from the GISAID EpiFlu™ on the 11th of August 2021**.** The sequences were selected based on the most visited tourist destinations of Nigerians (USA, UK, China, UAE, India, and Canada). The evolutionary history was inferred using the maximum likelihood method based on the general time-reversible model. Finally, a phylogenetic tree was constructed to determine the common ancestor of each sequence.

***Results*:** The phylogenetic analysis revealed that the delta strain in Nigeria clustered in a monophyletic clade with other Nigeria strains with its root from the reference Wuhan sublineage. Nucleotide alignment also showed a 99% similarity indicating a common origin of evolution.

***Conclusion*:** Our findings revealed that the current outbreak of the delta variant of SARS-CoV-2 infection in Nigeria stemmed from a genetic mutation that shared a consensus similarity with the reference SARS-CoV-2 human genome from Wuhan and was not imported from other countries as widely reported.

Keywords: Delta Variant, Genome Sequence, Phyloevolution, SARS-CoV-2

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Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has been rapidly evolving in the form of new variants. At least eleven known variants have been reported (1).

SARS-CoV-2, like other viruses, keeps mutating, a process in which genetic information of the virus changes because of repeated copying errors. These mutations result in new variants, some of which can spread more quickly or cause more severe symptoms of covid-19 disease and a higher fatality rate (2).

The Delta variant (Phylogenetic Assignment of Named Global Outbreak (Pango) lineage designation B.1.617.2), first detected in India, was designated a variant of concern by the World Health Organization (3). Much focus has turned to the Delta variant, which was first detected in India and has recently increased in prevalence globally (4).

The Delta variant currently seems to be displacing all other variants, including the highly dominant and contagious Alpha variant, in numerous countries across the globe (4).

The spike protein mutations make the Delta variant the "fastest and fittest" variant yet, according to the WHO. The disease caused by this variant might also exhibit different symptoms than other viral mutations. Those with the Delta variant often complain of headaches, sore throat, and a runny nose, replacing cough and loss of taste or smell like the most common symptoms (5).

Phyloepidemiological approaches have provided specific insight into understanding the emergence and evolution of infection (6).

The evolution of SARS-CoV-2 from its inception created a need for phyloepidemiological approaches to provide unanswered questions regarding the viral emergence and evolvement of various mutated strains. Unfortunately, there have been no reports on the evolution of the delta variant of SARS-CoV-2 in Nigeria. Thus, the study objective was to investigate the phyloepidemiology of the delta variant of SARS-CoV-2 in Nigeria.

Materials & Methods

Retrieval of Nucleotide Sequence and Alignment tool:

A total of 33 complete genomic sequences of SARS-CoV-2 delta variant B.1.617.2 lineage and that of reference SARS-CoV-2 were retrieved from the GISAID (http://www.epicov.org) and NCBI (http://www.ncbi.nlm.nih.gov) respectively on the 11th of August 2021.

Sequences retrieved were those from Nigeria, China, India, USA, UAE, UK, and Canada based on the travel history of Nigerians and location of the first detection of SARS-CoV-2 delta variant B.1.617.2 lineage (Table 1).

Table 1. Characteristics of the SARS-CoV-2 delta variant B.1.617.2 lineage genomic sequences retrieved for this study

Country	Accession no	Date of collection
Nigeria	EPI_ISL_3314967	20/07/2021
Nigeria	EPI_ISL_3314971	18/07/2021
Nigeria	EPI_ISL_3314972	17/07/2021
Nigeria	EPI_ISL_3314961	19/07/2021
Nigeria	EPI_ISL_3314963	21/07/2021
India	EPI_ISL_3315877	05/2021
India	EPI_ISL_3315881	05/2021
India	EPI_ISL_3315879	05/2021
India	EPI_ISL_3315878	05/2021
India	EPI_ISL_3315880	05/2021

UAE	EPI_ISL_3048171	23/06/2021
UAE	EPI_ISL_3048168	23/06/2021
USA	EPI_ISL_3332190	02/08/2021
USA	EPI_ISL_3332192	02/08/2021
USA	EPI_ISL_3332354	23/07/2021
USA	EPI_ISL_3332352	20/07/2021
USA	EPI_ISL_3332191	01/08/2021
Canada	EPI_ISL_3255959	24/06/2021
Canada	EPI_ISL_3255960	24/06/2021
Canada	EPI_ISL_3256972	05/06/2021
Canada	EPI_ISL_3255938	24/06/2021
Canada	EPI_ISL_3255961	25/06/2021
UK	EPI_ISL_3314942	31/07/2021
UK	EPI_ISL_3314943	31/07/2021
UK	EPI_ISL_3314944	26/07/2021
UK	EPI_ISL_3314945	28/07/2021
UK	EPI_ISL_3314941	31/07/2021
China	EPI_ISL_3305848	17/07/2021
China	EPI_ISL_3305850	18/07/2021
China	EPI_ISL_3305852	19/07/2021
China	EPI_ISL_3305851	18/07/2021
China	EPI_ISL_3305849	17/07/2021
China	NC_045512.2	

Evolution analysis:

Multiple sequence alignment was done to obtain the conserved and polymorphic regions using MAFFT (http://www.mafft.cbrc.jp/alignment) and CLUSTAL W on MEGA X. An evolutionary divergence analysis was done, and a phylogenetic tree was constructed to determine the common ancestor of B.1.617.2 strain from different locations and comparative analysis of strain in different clades.

Results

Evolutionary History:

The evolutionary history was inferred by using the Maximum Likelihood method and the General Time Reversible model. The bootstrap consensus tree inferred from 50 replicates is taken to represent the evolutionary history of the taxa analyzed. Branches corresponding to partitions reproduced in less than 50% of bootstrap replicates are collapsed. The percentage of replicate trees in which the associated taxa clustered together in the bootstrap test (100 replicates) are shown next to the branches. Initial tree/trees for the heuristic search was/were obtained automatically by applying Neighbor-Join and BioNJ algorithms to a matrix of pairwise distances estimated using the Maximum Composite Likelihood (MCL) approach and then selecting the topology with a superior log-likelihood value. A discrete Gamma distribution was used to model evolutionary rate differences among sites (5 categories (+G, parameter = 0.0746)). The rate variation model allowed for some sites to be evolutionarily invariable ([+I], 60.69% sites). This analysis involved 33 nucleotide sequences. Codon positions included were 1st+2nd+3rd+Noncoding. All positions containing gaps and missing data were eliminated (complete deletion option). There were a total of 25,836 positions in the

final dataset Sequence. The maximum likelihood tree is shown in Figure 1.

The result showed that three strains from Nigeria formed a clade with more than 70% similarity, although two others were outgroups.

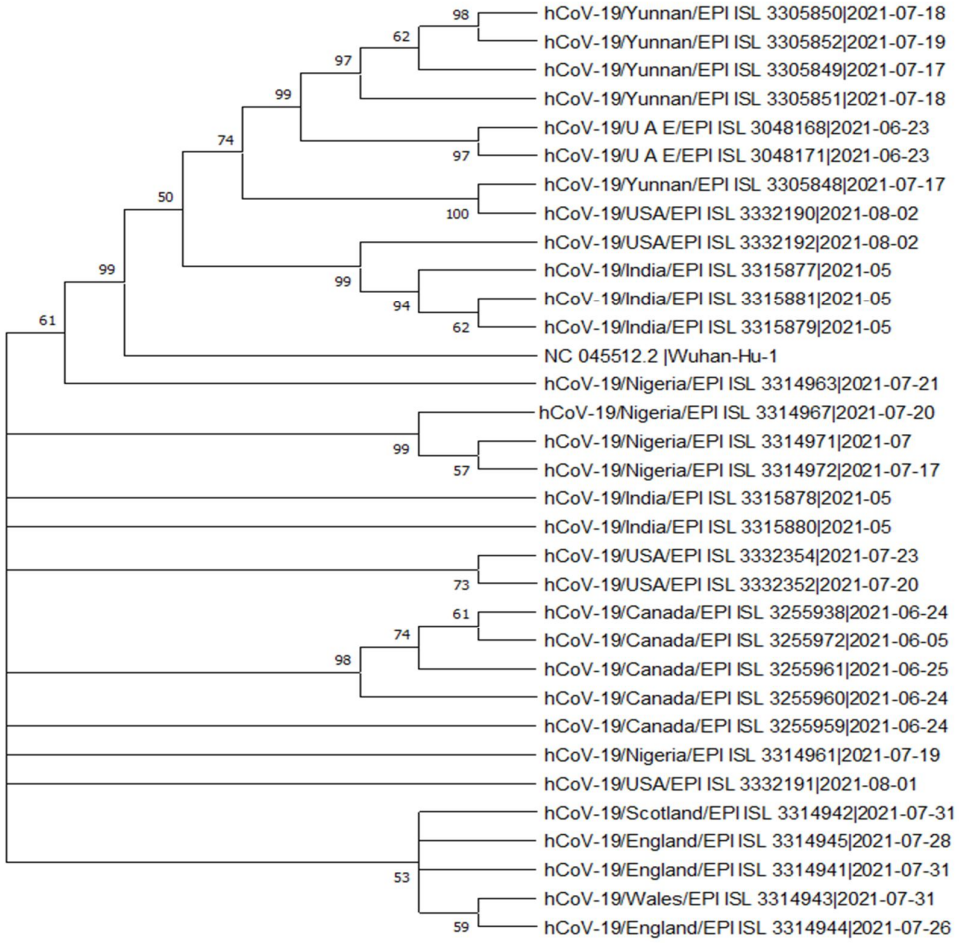

Fig. 1. Maximum Likelihood Tree of Delta variant of SARS-CoV-2. Sequences were aligned using MAFFT and tree reconstruction using MEGA 5.0

Discussion

The pattern of SARS-CoV-2 genetic mutations to variants of concern (VOC) within a population provides more insight into adopting a better approach to managing Covid-19 through prevention of the spread of infection and appropriate vaccination programs. Reports on genetic mutations of SARS-CoV-2, particularly its spike protein genes, to new variants since the virus was first detected have been documented (7-9). As peculiar to many RNA viruses, SARS-CoV-2 exploits various mechanisms to produce new variants, thereby ensuring its survival, and contributing to its transmissibility and virulence. The new variants have been classified by the United States Center for Disease Control (US-CDC) (2021), depending upon transmissibility and disease severity, to a variant of concern (VOC) or variant of interest (VOI). The delta variant (B.1.617.2) of SARS-CoV-2 is a variant of concern that has been shown to be associated with high transmissibility estimated to be about 60% more than the alpha variant of SARS-CoV-2 (10). The alpha variant, in turn, is more transmissible

than the wild-type SARS-CoV-2 [11]. Furthermore, mutations in the spike protein genes of delta variant confer on it partial immune escape (12), and this has been linked with disease severity associated with infection by this variant.

Multiple sequence analysis and phylogeny of SARS-CoV-2 delta variant (B.1.617.2) in this study show that three out of five taxa from Nigeria are in the same clade. Although there are two out-groups, none of the taxa from Nigeria forms a clade with those of the sequences from other countries that were studied. Additionally, phylogeny reveals that one of the out-groups is a close relative to the three taxa that formed a clade. Sequences of all the taxa show significant similarities with the reference sequence from Wuhan, where the virus was first detected.

Cases of delta variant of SARS-CoV-2 infection in Nigeria were believed to have stemmed from a single introduction of this variant into the country through a traveler from India. However, our study shows that the delta variant of SARS-CoV-2 in Nigeria arose from mutation of existing variants and was not an imported case. This is consistent with studies that revealed mutation of SARS-CoV-2 to VOC and VOI in other countries (7).

Reports on genetic mutation in the spike protein of SARS-CoV-2 with resultant evolution of the delta variant, creating the second wave of COVID-19 in India (13). The evolution of new variants through genetic mutation, such as the alpha variant (B.1.1.7) in the United Kingdom, Beta (B.1.135) in South Africa, Gamma (P.1) in Brazil, has been reported (14). In the United States of America, there have been reported cases of the evolution of new variants of SARS-CoV-2 (15).

On the contrary, this study also revealed that sequences from the USA and China produced a clade with 100% sequence similarities. Additionally, one other sequence from the USA is in the same clade with three others from India. This buttresses the report of Kannan *et al.* (2021) that the delta variant may have initially been imported to the USA (1).

Conclusion

In summary, based on evolutionary analysis, it can be inferred that the delta variant (B.1.617.2) of SARS-CoV-2 detected in Nigeria stemmed from a genetic mutation of a pre-existing variant of the virus in the country.

Evolutionary study of the origin of this variant could benefit its biological study and establishment of interventions to control its transmission.

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Authors' Contributions

FO, and EI, planned the work and retrieved the data needed for the study. Then, EI, FO, constructed the phylogenetic tree. Finally, FO and EI composed the article. Both authors thoroughly read and approved the final manuscript.

Conflict of interest

There are no conflicts of interest.

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