

# Detection of Genetic Alteration of Polymerase Protein of Hepatitis B Virus Strain C2 Isolated From Bangladesh



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## Abstract

The changes in polymerase gene of Hepatitis B virus (HBV) is increasing rapidly. HBV/C2 strain predominating with the frequent molecular changes in Bangladesh. Herein, the pattern of the changes of polymerase protein of HBV/C2 is reported. The strains isolated in 2017 comprise several amino acid substitutions and were found phylogenetically distinct from the strain isolated in 2000. The rapid changes of the protein due to change in genetic makeup may bring HBV disaster in near future.

**Keywords:** Hepatitis B virus sub-genotype C2; Polymerase; Phylogeny

## Introduction

Hepatitis B virus (HBV) belongs to the *Hepadnaviridae* family with a unique partially double stranded DNA [1,2]. Since the existence, HBV renders a gradual genomic changes due to the lack of some regulatory systems such as proof-reading activity of polymerase enzyme during replications [3]. Currently, HBV has been reported to have ten genotypes and multiple sub-genotypes [4]. Globally, more than 2 billion people have been infected by HBV and above 300 million are chronically infected annually [3,5]. Bangladesh also bears a high rate of HBV infection, some of which were reported to cause liver cirrhosis and hepatocellular carcinomas [3].

Among the HBV types, sub-genotype C2 (HBV/C2) are the most prevalent in Bangladesh, which was reported to cause most of the chronic infections in previous studies [6]. From the literature, HBV/C2 is also responsible to cause liver cirrhosis and other liver complications frequently [7]. Furthermore, the treatment of this strain is also getting difficult due to the resistance to the antiviral. Resistances to the antiviral are commonly due to the mutations in the polymerase gene as the antiviral drugs neutralize infections based on the inactivation of viral polymerase protein [3]. However, information about the pattern of changes in the polymerase protein of HBV is scarce. Hence, in this study, we determine the Genetic changes of HBV/C2 polymerase protein sequences isolated in Bangladesh

## Materials and methods

Polymerase protein sequences of 15 HBV/C2 strains were collected from NCBI Gen Bank. The sequences were then analyzed bio informatically for amino acid substitutions using Bio Edit version 7.1.9 [8] and the sequence, BAL45466 (documented to be isolated in 2000) was used as reference strain. Furthermore, phylogenetic analysis of the sequences with an out group sequence of sub-genotype A1 (AUF49588) was performed using MEGA6 [9]. The accession numbers of the sequences used in this study were AUR80750, AUF49609, AUF49574, AUF49526, AUF49505, AUF49498, AUF49450, AUF49412, AUF49386, AUF49379, AUF49372, AUF49365, AUF49333 and AUF49319

## Results and Discussion

Analysis of the HBV/C2 polymerase protein sequences from Bangladesh using Bio Edit revealed some common substitutions different from the reference sequence of HBV/C2 strain isolated in 2000. The substitutions include E73D, N81H, Q85K, E93Q, Y95F, T101V, A137T, K143Q, S196P, C213S, L218F, K229Q, L232M, R234M, S237P, S242I, P249S, R253Q, H267N, D281V, H305Q, F321L, Q327K, T340S, H355Y, N359H, I437L, N468I, L613Q, I615L, V624I, S663A, H683N and R713Q. These substitutions are the fates of the genomic changes in last 17 years, some of which may have potential medical significance to

be responsible for drug resistance. Furthermore, phylogenetics analysis with the sequences rendered a close relationship between the sequences isolated in 2017 and a distinct difference with the reference strain isolated in 2000 (Figure 1). The inter-

difference between the isolates of 2000 and 2017 may indicate a possible evolution of the strain, which may rise extensively in near future.

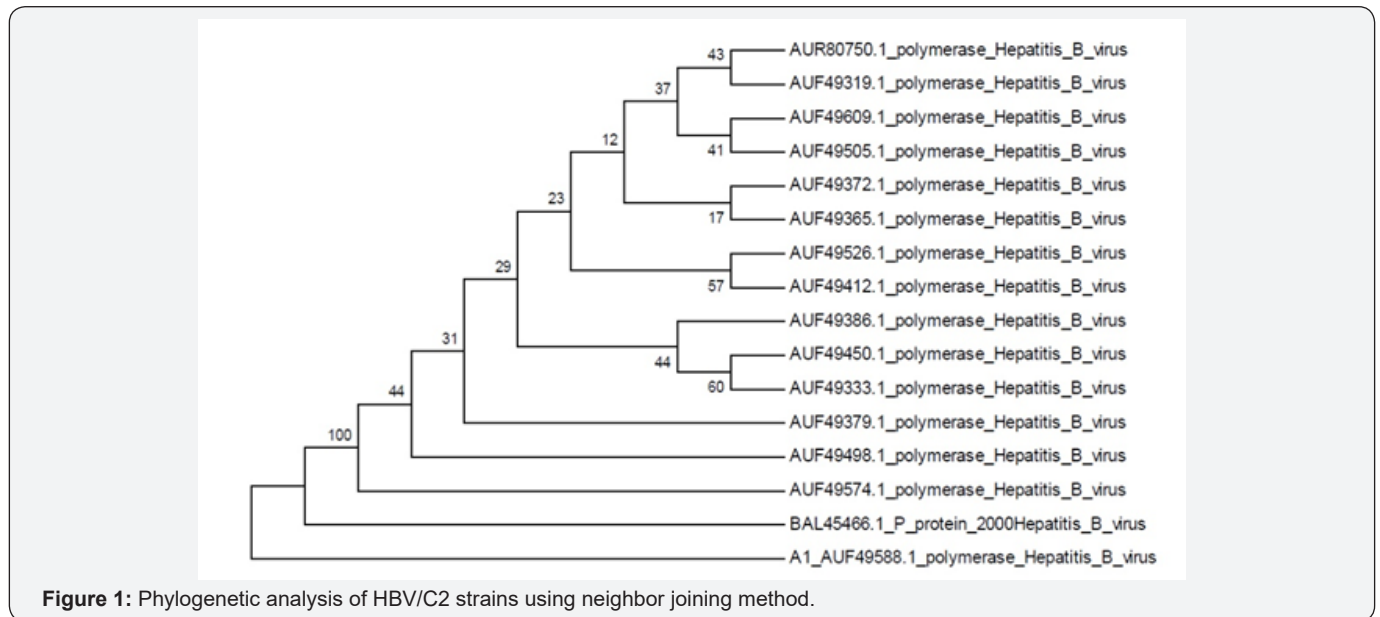


Figure 1: Phylogenetic analysis of HBV/C2 strains using neighbor joining method.

### Conclusion

In conclusion, the genetic diversity of HBV/C2 strains is quite frequent compare to others near inheritance. The drastic changes in amino acid compositions in the genome may denote another evolution of the strain which may bring the disease burden more complicated in future.

### Data Availability

The HBV/C2 strain polymerase protein sequences were retrieved from NCBI Gen Bank and are described in methods section.

### Conflict of Interest

The authors declare no conflict of interest.

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