Hepatitis C Genotype 4 NS5A Protein: A New Study Determining Combination Therapy Drug Resistance in Saudi Patients

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Hepatitis C Virus (HCV) has transformed from a silent disease to become a threat to the world, with approximately 170 million people infected globally. Although HCV genotype 4 (HCV-4) is the cause of approximately 20% of hepatitis C infection worldwide, it is poorly studied. In Saudi Arabia, in particular, there are limited studies. The standard treatment of HCV-4 infection is the Pegylated Interferon and Ribavirin (PEG-IFN/RBV) combination therapy. However, only 60% of patients respond to the treatment, because the role of the NS5A protein, which contains the interferon sensitivity-determining region in HCV-4 infections, is unclear. This study examines the NS5A protein of HCV-4 isolates from 90 Saudi patients, and analyzes the association between NS5A protein mutations and treatment resistance. We utilized direct sequencing approach and advanced sequence analysis software. The data showed that there is a significant association between NS5A protein mutations, at the last 157 amino acid, particularly at positions 331aa (Cys40Arg), 352aa (Val61Iso), 405aa (Iso114Val), 407aa (Val116Ala) and treatment outcome in subgenotype 4a (P value ≤ 0.05). However, HCV subgenotype 4d showed no significant association between NS5A protein and treatment outcome. Furthermore, the response rate in our population was 58% responders and 42% non-responders. The finding provides a new insight into HCV-4 among affected Saudi population where the knowledge is lacking. In fact, finding a correlation between the HCV NS5A protein mutation(s) and the treatment outcome could be used as a predictor of treatment response, and avoid exposing them to unnecessary side effects.