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Genetic, biochemical, and immunological determinants of viral resistance to interferon alpha 2b combination therapy of HCV 3a infected Pakistani patients

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Background: Current study deals with viral determinants of HCV response to interferon (IFN) alpha 2b including virus genotype, viral load, quantitative dynamic changes, and mutations in NS5A-ISDR, age, gender, ALT, IL-8, and TNF-alpha levels.

Methods: All parameters including biochemical tests, viral load and genotyping were studied before and after the completion of treatment. Out of 39 patients 26 (67%) were end of treatment responders, while 13 (33%) patients were virological non-responders. 13 responders and 13 non responders of NS5A-ISDR2209-2237 region were amplified by region specific primers followed by sequencing.

Results: Out of 26 isolates, only 03 non responder isolates (23%) showed low to intermediate level mutations within the NS5A-ISDR region including A2209E, N2210D, L2211M, L2212F and Q2215L. Among them were two males and one female. No highly mutant isolate was observed in the study. Strong associations were observed among NS5A-ISDR mutations and before treatment normal ALT levels with mean value of 28+8 U/L ($p=0.028$), viral load of <8x105 IU/ml, high levels of IL-8 2972±238 pg/ml, $p<0.05$ and TNF-alpha (174±7pg/ml, $p=0.01$). Phylogenetic analysis suggests that our isolates are clustered with United Kingdom GQ356209.1, India GQ275355.1, China HQ639942.1, Spain AF339252.1, Thailand HM042073, France AF320789.1 and GQ300882.1and GU294484.1 Pakistani isolates.

Conclusion: Low viremia in non responder mutants showed that these mutations may play important role in virus resistance but may not play significant role in virus replication. No association has been observed with ISDR mutations and non response to interferon alpha 2 b combination therapies but presence of mutations in ISDR of NS5A protein in non responders may be correlated with low pre treatment viral load, low initial ALT levels, high pre treatment IL-8 and TNF alpha values.

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