Title:	Role of gene polymorphisms in susceptibility to viral infections and drug response in human populations
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Abstract:	HCV infection is of growing global concern due to high incidence of morbidity and mortality. Current therapy for chronic hepatitis C is based on a combination of peg-IFN and RBV given for 24-48 weeks based on the type virological response shown by the individual. Mostly, the medications are poorly tolerated and result in low response rates. It has been reported that SNP, in the IL28B gene may affect drug-response to the combined treatments of peg-IFN and RBV in HCV-infected patients, but the data were inconclusive. To resolve the controversy, we conducted a systematic meta-analysis to evaluate the role of SNPs present near to IL28B gene, rs12979860, rs8099917, rs12980275 and a dinucleotide variant ss469415590 in response to the dual drug therapy in HIV-HCV co- infected patients. We included 45 studies published before June 30, 2018 with a total of 9119 subjects (3992 cases and 5127 controls). OR and 95% CI were used to assess the strength of the association. Our results indicated a significant association of all the four polymorphisms considered with the SVR in all HCV genotypes of the HIV co-infected patients, receiving peg-IFN and RBV. The Odds ratio in the recessive models in rs12979860 was OR =3.26 [95% CI (2.77, 3.84)]; P<0.0001, rs8099917 with an OR = 3.78 [95% CI (2.81, 5.07)]; P<0.0001, rs12980275 with an OR = 2.96 [95% CI (2.22, 3.94)]; P<0.0001, and ss469415590 an OR = 3.50 [95% CI (2.37, 5.16)]; P<0.0001. Other genetic models like allele contrast, homozygote contrast, dominant model and additive models were also tested. Our results based on the subgroup analyses on HCV subtypes reveals that out of all HCV subtypes, the hardest to treat is HCV 1 following HCV 4 following HCV 2 and 3.In the case of rs12979860, CC genotype predisposes individuals to responding well with therapy, and ranges to individuals with CT, whereas the TT genotype predisposes them responding poorly with the therapy. Overall, our meta-analysis suggests a significant association of the IL28B gene polymorphisms rs12979860, rs8099917, ss469415590 and rs12980275 with the treatment response to peg-IFN and RBV in patients infected with HCV and HIV in the clearance of HCV as the treatment outcome.
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