Title:	Effect of IFN-γ +874 T/A polymorphism on clinical manifestations of dengue: a meta-analysis
Authors:	Kaur, Gaganpreet (/jspui/browse?type=author&value=Kaur%2C+Gaganpreet) Gupta, Kajal (/jspui/browse?type=author&value=Gupta%2C+Kajal) Singh, Anjali (/jspui/browse?type=author&value=Singh%2C+Anjali) Kumar, Nirmal (/jspui/browse?type=author&value=Kumar%2C+Nirmal) Banerjee, Indranil (/jspui/browse?type=author&value=Banerjee%2C+Indranil)
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Abstract:	Dengue virus (DENV) is a mosquito-borne RNA virus, which infects nearly 3.97 billion people every year in the tropical and subtropical regions of the world. DENV infections can range from unrecognizable illnesses to a spectrum of clinical manifestations such as dengue fever (DF), and more severe and potentially lethal dengue hemorrhagic fever (DHF). The variability of clinical manifestations induced by DENV can be attributed to a variety of extrinsic and intrinsic factors including virulence of the DENV strains and host genetic factors influencing the immune response. Interferon gamma (IFN-γ) is one of the critical immunomodulators implicated in DENV infection, and recent case–control association studies examined the role of +874 T/A polymorphism (rs2430561) of the IFN-γ gene in dengue clinical outcomes. Since the results of the association studies on DENV infection and IFN-γ +874 T/A polymorphism were inconsistent, we performed a meta-analysis to derive a more precise estimate of the association. Searching the databases until 15 March 2020, we identified five studies with a total of 1412 subjects (582 cases and 830 controls), which were included in this meta-analysis. The pooled odds ratio (ORs) with corresponding 95% confidence intervals (CIs) were calculated to evaluate the strength of the association. Pooled data indicated significant association of the TT genotype with DENV infection (DI), DF, and DHF in the recessive model TT vs AT+AA: OR (DI) = 1.47, 95% CI (1.10–1.97), P = 0.01; OR (DF) = 1.40, 95% CI (1.00–1.94), P = 0.04, OR (DHF) = 1.73, 95% CI (1.05–2.86), P = 0.03, and the genotype contrast TT vs AT: OR (DI) = 1.70, 95% CI (1.18–2.47); P = 0.005, OR (DF) = 1.72, 95% CI (1.12–2.66), P = 0.014, OR (DHF) = 1.76, 95% CI (1.01–3.06), P = 0.046. The genotype contrast AA vs AT showed significant association with the milder form of dengue (DF), OR (DF) = 1.60, 95% CI (1.07–2.41), P = 0.023, but not with the severe form (DHF). Taken together, this meta-analysis indicated that both the homozygous genotypes conferred risk to dengue, albeit with varied clinical outcomes, and revealed a protective role of the heterozygous genotype against DENV infection.
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