

Natural resistance-associated macrophage protein 1 gene polymorphisms are associated with tuberculosis infection in thalassemia patients

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ABSTRACT

Background Thalassemia is a hereditary disorder of hemoglobin that needs regular blood transfusions leading to accumulation of iron in the cell. This iron overload level in macrophage might cause intracellular bacteria, particularly *Mycobacterium tuberculosis* (MTB) to multiply. Polymorphisms in NRAMP1, a metal transporter across the phagosome membrane, play important role in regulating iron, which also needed by MTB. Increased iron in thalassemia patients may have an increased potential risk for TB.

Objective To compare natural resistance-associated macrophage protein 1 (NRAMP1) gene polymorphisms (INT4, D543N, and 3'UTR) in thalassemia patients with and without tuberculosis (TB) infection.

Methods A descriptive, analytical, case-control study with consecutive sampling was performed in pediatric thalassemia patients with TB (n=40) and without TB (n=50). Iron status including serum iron, total iron-binding capacity (TIBC), and ferritin, was compared between the two groups. NRAMP1 genetic polymorphisms were analysed using polymerase chain reaction/restriction fragment length polymorphism (PCR-RFLP). Allelic and genotypic distributions of each polymorphism were assessed for possible associations with TB infection.

Results Mean serum iron and TIBC in thalassemia patients with TB were higher compared to thalassemia patients without TB (mean serum: 166.26 vs. 134.92 $\mu\text{mol/L}$, respectively; $P=0.026$) and (mean TIBC: 236.78 vs. 143.54 $\mu\text{mol/L}$, respectively; $P=0.029$). In thalassemia patients with TB, we observed significantly higher frequency of the C allele in INT4 (10% vs. 2%, respectively; OR=5.44; 95%CI 1.1 to 26.4; $P=0.02$) and the TTTG deletion allele (78.8% vs. 31%, respectively; OR=3.36; 95%CI 1.83 to 6.9; $P=0.0002$) in 3'UTR polymorphisms than in thalassemia patients without TB. There were no significant differences in distributions of the A allele between the case and control groups (16.3% vs. 15%, respectively; $P=0.84$) or the GA genotype (32.5% vs. 30%, respectively; $P=0.79$) in D543N.

Conclusion NRAMP1 polymorphisms are known to be associated with major gene susceptibility to TB, and in our thalassemia patients this association was even more pronounced. Further study on the roles of iron and immunology in TB infection in thalassemia patients is imperative.

Keywords: NRAMP1, iron, tuberculosis, and thalassemia

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