Omaima El Tahir et al., Clin Pediatr OA 2018, Volume 3
DOI: 10.4172/2572-0775-C2-011

Integrating host genetic variants in clinical prediction rule for hearing loss after childhood bacterial meningitis: A model renewing study

Omaima El Tahir, A M van Furth, S A Morré, S Ouburg and **M W Heymans**
VU University Medical Center, Netherlands

Statement of the Problem: Sensorineural hearing loss is the most common severe sequela in survivors of childhood bacterial meningitis. In the past, we developed a validated prediction model to identify children at risk for post-meningitis hearing loss based on clinical factors. As genetic variation in host immune response genes is also associated with susceptibility to and severity of bacterial meningitis, the purpose of this study is to determine host genetic risk factors to improve the performance of the prediction model.

Methodology & Theoretical Orientation: The generated data of 471 Dutch Caucasian survivors of childhood bacterial meningitis genotyped for four single nucleotide polymorphisms (SNPs) in three different genes involved in pathogen recognition and inflammation were used to improve the prediction model. Genetic data were included during model construction and performance of the model was compared to the original model by likelihood ratio tests and the area under the curve (AUC) of the receiver operating characteristic curves.

Findings: Addition of genetic predictors significantly improved the performance of the new model compared to the original clinical prediction rule (increase of AUC from 0.85(95% CI 0.78-0.91) to 0.91 (95% CI 0.84-0.97). Independent predictors for hearing loss were *S. pneumoniae*, presence of ataxia during illness, CSF glucose level≤0.6 mmol/L, duration of symptoms before admission >2 days, TLR4+896 A>G and TLR9-1237 T>C.

Conclusion & Significance: Including host genetic factors during model construction results in a significantly improved prediction model for post-meningitis hearing loss in children. Prediction of outcome using host genetic risk factors and clinical variables may contribute to better understanding, timely intervention and thereby appropriate follow-up of children after bacterial meningitis. Future studies should focus on additional value of other SNPS and investigate SNP combinations (SNP traits) in larger cohorts but also assess applicability of the model.

Recent Publications

1. De Jonge R C, Sanders M S, Terwee, Heymans M W, Gemke R J, Koomen I and Spanjaard (2013) Independent validation of an existing model enables prediction of hearing loss after childhood bacterial meningitis. PLoSOne 8(3):e58707.
2. Sanders M S, de Jonge R C, Terwee CB, Heymans M W, Koomen I, Ouburg S, Spanjaard L, Morre S A and Van Furth A M (2013) Addition of host genetic variants in a prediction rule for post meningitis hearing loss in childhood: a model updating study. BMC Infect Dis. 13:340.
3. Sanders M S, van Well G T, Ouburg S, Morre S A and van Furth A M (2011) Genetic variation of innate immune response genes in invasive pneumococcal and meningococcal disease applied to the pathogenesis of meningitis. Genes Immun. 12(5):321-34.
4. De Jonge R C, van Furth A M, Wassenaar M, Gemke R J and Terwee C B (2010) Predicting sequelae and death after bacterial meningitis in childhood: a systematic review of prognostic studies. BMC Infect Dis. 10:232.
5. Koomen I, Grobbee D E, Roord J J, Donders R, Jenneskens-Schinkel A and van Furth A M (2003) Hearing loss at school age in survivors of bacterial meningitis: assessment, incidence, and prediction. Pediatrics 112(5):1049-53.

Biography

Omaima El Tahir has completed her Graduation in Biomedical Sciences and a Master's degree in Medicine both at VU University in Amsterdam. She has her expertise in the role of host genetic variants in susceptibility, severity and outcome of childhood bacterial meningitis, aiming to create prediction tools for complications of bacterial meningitis integrating both clinical and genetic biomarkers because it is still a life-threatening infectious disease. She also aims to provide more insight into the possible very long-term sequelae which could have a significant impact on subsequent health state of childhood BM survivors during young adult life. Her area of research interest are pediatric infectious diseases, genetic disorders, immune deficiencies

o.tahir@vumc.nl