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Genetic susceptibility to rheumatic heart disease in three African populations: Egypt, Ethiopia and Mozambique

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Introduction: Rheumatic heart disease (RHD) is a leading cause of incapacity and premature death in Africa among young population. RHD is acquired as a long term outcome of acute rheumatic fever (ARF) that follows Group A β-haemolytic streptococcal (GAS) infections. RHD appears to have a faster and more malignant course among different African populations.

Hypothesis: Higher incidence and possibly severity of RHD in the African population can be contributed to by genetic factors. Detecting these factors may help in prevention and management of the disease by detecting novel therapeutic targets.

Objectives: To identify genetics variants affecting susceptibility to RHD To correlate the genetic risk factors to the clinical phenotype and understand the heterogeneity of the genetic factors in three African populations.

Methods: In a prospective case-control study, 2000 participants will be recruited from three African countries: Ethiopia, Egypt, and Mozambique. Cases group will include 400 patients diagnosed with RHD irrespective of age limitation and 300 non-cardiac controls will be recruited from the general population. DNA samples will be collected from the participants to execute next generation sequencing, a combination of whole genotyping array to their DNA samples, targeting mainly polymorphism patterns of related genes, e.g. IL1RA,αTGFβandTNFIL -10, and their pathophysiological impact on immune response. High resolution analysis will be applied to correlate the participant's genetic features and pre-existing clinical data's as some studies have shown a relation between the genetic variability and expected outcome. The control group genetics and clinical history will be compared to the cases result in order to understand the real impact of newly discovered genetic patterns on immune response and RHD disease progression. Finally, suggested hypothesis will be justified based on conditional logistic regressions.

Expected value of the study: Several previous studies have strongly suggested a relationship between genetic factors and RHD A systematic review and meta-analysis of 435 twin pairs from six independent studies was showed that ARF high heritability, estimated at 60% across all the studies (Engel et al., 2011). The RHD Gen network and molecular epidemiology of streptococcus pyogenes (Bongani., 2016) is currently conducting a project under H3 Africa to identify genetic susceptibility & resistance to RHD. Another recent study on RHD genetics across the pacific regions identify a novel susceptibility signal in the immunoglobulin heavy chain (IGH) is associated with a 1.4-fold increase in the risk of RHD (Tom Parks et al.,2017). The current proposal aims to extend these studies by providing more data, specific to three African populations, using state of the art Next generation sequencing and collaborating with colleagues working in the same field in an attempt to enhance efforts of fighting the epidemics of RHD across the developing countries.

Speaker Biography

Helen Befekadu is medical doctor at Addis Ababa University Cardiac center Ethiopia. She received doctor of medicine at the age 23 and specialized in pediatric and child health and master of public health with great distinction from same university at the age of 26years in 2015 enable to get the academic rank for assistant professor. Following, currently she is attending a joint fellowship program in pediatric cardiac intensive care and cardiology in Egypt, Magdi yacoub heart foundation since November 2016. Her international experience includes presenting posture in European society of Cardiology 2016, Rheumatic heart disease conference in Cairo 2107, and Cardio Alex conference in 2017. In addition to the clinical studies, she is highly dedicated and passionate in research activities / evidence-based medicine particularly focus to genetics of cardiovascular disease in general and in the process of application for Rheumatic heart disease genetics PhD program after completion of joint clinical fellowship studies.

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