Diagnostics and biomarkers

OC - (8277) - IDENTIFICATION OF NEW CEREBROSPINAL FLUID AND BLOOD-BASED BIOMARKERS FOR THE DIAGNOSIS OF TUBERCULOUS MENINGITIS IN CHILDREN

Manyelo, Masilo Charles (South Africa)¹; Solomons, Regan S (South Africa)²; Walzl, Gerhard (South Africa)¹; Chegou, Novel N (South Africa)¹

1 - Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa; 2 - Department of Paediatrics and Child Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa

Background: Tuberculous meningitis (TBM) is the most severe form of extrapulmonary tuberculosis (TB). It mostly affects young children and results in high morbidity and mortality, mainly due to diagnostic delay. There is an urgent need for new tests for the earlier and accurate diagnosis of the disease. We previously identified a 3-marker CSF biosignature (VEGF, IL-13, and LL-37) with potential to diagnose TBM. In the present study, we show that cerebrospinal fluid (CSF) and blood-based biosignatures may be useful in the diagnosis of TBM.

Methods: CSF and serum samples were consecutively collected from 47 children that were admitted to the Tygerberg Academic Hospital in Cape Town, South Africa, on suspicion of having TBM. Using a multiplex platform, the concentrations of 69 host markers were evaluated in the CSF and serum samples from all the study participants, followed by statistical analysis to ascertain the usefulness of these biomarkers as diagnostic candidates for TBM disease.

Results: Out of the 47 study participants, 23 (48.9%) were finally diagnosed with TBM and 6 (12.8%) were infected with HIV. Several CSF and serum biomarkers showed potential individually as diagnostic candidates for TBM as ascertained by area under the receiver operator characteristics curve (AUC). However, the main findings of our study were the identification of a four-marker CSF biosignature which diagnosed TBM with an AUC of 0.97 (95% CI, 0.92-1.00), and a 3-marker serum biosignature which diagnosed TBM with an AUC of 0.84 (95% CI, 0.73-0.96). We also validated a previously identified 3-marker CSF biosignature (VEGF, IL13 and LL37) in the study.

Conclusion: CSF and serum biosignatures may be useful in the diagnosis of TBM in children. Our findings require further validation in larger, multi-site studies after which the biosignatures may be incorporated into point-of-care diagnostic tests for TBM.