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**Title:** Performance of IP-10, an interferon gamma release assay and tuberculin skin test in children at high risk for tuberculosis infection

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**Body:** Background : Studies propose Interferon- $\gamma$  Inducible Protein 10 (IP-10) as a promising diagnostic marker for tuberculosis (TB) infection, with comparable accuracy to the QuantiFERON-TB Gold In Tube Test (QFT-IT). Aims : We explored the diagnostic performance of IP-10 in paediatric TB infection and compared it with the established QFT-IT and tuberculin skin test (TST). Methods : The study was conducted among 179 children (active TB n=53, latent TB infection n=64, controls n=62; mean age 6.3 $\pm$ 4 years). IP-10 concentration was determined using ELISA, in supernatants from QFT-IT tubes. The diagnostic performance of IP-10 and QFT-IT was evaluated using ROC curve analysis. Agreement between tests was evaluated with the kappa ( $\kappa$ ) statistic. Results : The area under the curve (AUC) for IP-10 -assessed as continuous variable- was 0.79 (95%CI 0.7-0.88). A cut-off point of 1221 ng/ml for IP-10 had 85% sensitivity and 75% specificity to detect active TB. QFT-IT had higher AUC (0.84; 95%CI 0.75-0.93) however the difference did not reach the cut-off point of statistical significance (z=0.86, p=0.19). When introduced as categorical variable, QFT-IT performed significantly better than IP-10 (AUC 0.88, 95%CI 0.83-0.94 vs. 0.77, 95%CI 0.7-0.85 respectively; p=0.01) in detecting TB infection. TST test had equal performance to QFT-IT but it was superior to IP-10. Agreement was substantial between IP-10 and QFT-IT ( $\kappa$ =0.61), between QFT-IT and TST ( $\kappa$ =0.65) and moderate between IP-10 and TST ( $\kappa$ =0.48). Conclusion : IP-10 could be used as an additional TB biomarker, in combination with IGRAs, to increase diagnostic accuracy of TB infection in high risk paediatric populations.