The role of interferon-gamma release assay in the diagnosis of toxoplasmosis in pregnancy

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**Background:** The differential diagnosis between seroconversion and false IgM positivity in a pregnant woman with a suspected *Toxoplasma gondii* infection (IgG negative, IgM positive) is often difficult. It is further complicated by the fact that therapy with Spiramycin, given every time IgM are found to be positive, can delay IgG production and mask seroconversion. Previously immunized women only respond with IFN-γ production to a new antigenic stimulation in vitro. The aim of this study was to develop an experimental Interferon Gamma Release Assay (IGRA) that is able to measure the production of IFN-γ by whole blood T-cells sensitized with *T.gondii* antigens, and to demonstrate its clinical utility in order to solve the diagnostic dilemma of pregnant women found IgG negative and IgM positive with conventional screening tests for toxoplasmosis.

**Material/methods:** Blood samples in Lithio-Heparin tubes of 104 pregnant women were collected between January 2010 and December 2015. All samples were tested for the presence of anti-Toxoplasma IgG and IgM with LIAISON® XL Toxo IgGII/IgM, ETI-ToxoA® (DiaSorin, Saluggia, Italia), VIDAS®TOXO IgG II, Toxo-ISAGA® IgM (Biomerieux Marcy l'Etoile Francia), LDBIO-TOXO II IgG WB (Lione, Francia). Among these, 90 samples were IgG negative and IgM positive. 14 samples of pregnant women with proven past infections were included as positive controls. All women were on Spiramycin regimen. Samples were incubated for 24h with *T. gondii* antigen (Diasorin Saluggia Italy...
), after incubation samples were centrifuged and the supernatants were tested with QuantiFERON®-ELISA (Cellestis Limited, Victoria, Australia) for measurement in IU (International Units) of IFN-γ production.

**Results:** 56 out of 104 women seroconverted during gestation (true positive) and 48 did not even after therapy discontinuation. By means of a ROC curve the Cut-Off value was determined to be 0.74 IU, allowing us to discriminate between early infection and false IgM positivity with a sensitivity of 81% and a specificity of 92%. In the 4 cases of congenital infection both the mother and the newborn resulted positive with the IGRA test.

**Conclusions:** Given the relevant sensitivity and specificity, the IGRA test for the diagnosis of toxoplasmosis in pregnancy for women with suspected seroconversion (IgG negative, IgM positive), even if undergoing treatment, is a reliable tool. Coupled with conventional tests, it allows clinicians to have increased diagnostic confidence and to administer treatment only in truly affected patients avoiding useless anxiety in women who are not affected.