

Serological detection of *Toxoplasma gondii* in chronic renal failure patients and in renal transplant recipients

Thesis

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ABSTRACT

Toxoplasma gondii antibodies were detected serologically in 78 patients with renal disease using ELISA technique. Patients were classified according to renal status; chronic renal failure not undergo haemodialysis group (19 cases), chronic renal failure undergo haemodialysis (30 cases), renal transplant recipient (29 cases), compared to 13 cases in control group. Seropositivity for anti-*Toxoplasma* IgG & IgM antibodies were 36.8% & 10.5% in renal failure patients not undergo haemodialysis, 56.7% & 16.7% in patients undergo haemodialysis and 69% & 24.1% in renal transplant recipients versus 23.1% & 0% in control group with statistical significant difference for anti-*Toxoplasma* IgG antibodies only.

KEY WORDS: *Toxoplasma gondii*, renal, haemodialysis, transplant, ELISA, IgG & IgM antibodies.

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LIST OF ABBREVIATIONS

| | |
|--------------|--|
| AIDS | Acquired immune deficiency syndrome |
| APCs | Antigen presenting cells |
| AU | Arbitrary Units |
| CA | Circulating antigens |
| CAT | Computerized axial tomography |
| CFT | Complement fixation test |
| CGMC | Comparative IgG profiles between mother and child test |
| CIEP | Counter-current Immune Electrophoresis |
| CMI | Cell mediated immune response |
| CNS | Central nervous system |
| CRF | Chronic renal failure |
| CT | computed tomography |
| DCs | Dendritic cells |
| DT | Sabin-Feldman dye test |
| ELIFA | Enzyme-linked immunofiltration assay |
| ELISA | Enzyme linked immunosorbent assay |
| ES | excretory/ secretory |
| ESRD | End-stage renal failure |
| GRA | Granular proteins |
| HIV | Human immune deficiency virus |
| HRP | Horseradish peroxidase |
| HS | Highly Significant |
| HSP | heat shock protein |
| IDO | Indolamine-2,3dioxygenase |
| IEL | Intraepithelial lymphocytes |
| IFA | indirect fluorescent antibody assay |

| | |
|-------------------------|---------------------------------------|
| IFAT | Indirect fluorescent antibody test |
| Ig | Immunoglobulin |
| IHAT | Indirect haemagglutination test |
| IL | Interleukin |
| ISAGA | IgM Immunosorbent agglutination assay |
| IU | International Units per milliliter |
| LA | Latex agglutination test |
| M | Macrophages |
| MAT | Modified direct agglutination test |
| MIC | Microneme |
| mRNA | Messenger ribonucleic acid |
| NK | Natural killer |
| NO | Nitric oxide |
| NS | Non-Significant |
| PAS | Periodic acid-Schiff positive |
| PCR | Polymerase Chain Reaction |
| PMNs | Polymorphonuclear leukocytes |
| PV | Parasitophorous vacuole |
| PVM | PV membrane |
| RNI | Reactive nitrogen intermediates |
| ROI | Reactive oxygen intermediates |
| S | Significant |
| SAG | Surface antigen |
| SMX | Sulfamethoxazole |
| <i>T. gondii</i> | <i>Toxoplasma gondii</i> |
| TE | Toxoplasmic encephalitis |
| Th | T-helper |
| Thp | T-helper precursor cells |
| TMB | Tetramethylbenzidine |

| | |
|-------------|--------------------------------------|
| TMP | Trimethoprim |
| TNF | Tumor necrotic factor |
| TSPs | <i>Toxoplasma</i> serologic profiles |
| W | Week |
| Y | Year |

INTRODUCTION AND AIM OF THE WORK

Introduction and Aim of the work

Toxoplasma gondii is a ubiquitous protozoan parasite that is estimated to infect one-third of the world's human population (*Weiss and Dubey, 2009*).

Toxoplasmosis can cause fetal infection if it is acquired during pregnancy, with unpredictable manifestations in the fetus and neonate (*Foulon et al., 2000*). Within immunocompetent humans, toxoplasmosis is benign and self limiting (*Barbosa et al., 2008*). Whereas, toxoplasmosis is a major opportunistic infection that may lead to morbidity and mortality in immunocompromised individuals (*Lin et al., 2000 and Meeka et al., 2001*).

Chronic renal failure patients suffer from impairment of cell mediated immunity either due to uremia or due to interventions used in their therapy, including dialysis and transplantation with subsequent immunosuppressive therapy and multiple blood transfusions (*Pesanti, 2001*).

Immunocompromised hosts with T cell defects include AIDS patients, patients with hematological malignancies (especially Hodgkin's disease and other lymphomas), organ transplant recipients, and patients receiving immunosuppressive therapy with corticosteroids and cytotoxic drugs (*Weiss and Dubey, 2009*).

Toxoplasmosis in these patients usually occurs as a consequence of the recrudescence of a latent infection acquired before the onset of immune suppression. However, it may occur also due to recently acquired acute infection with the parasite (*Montoya et al., 2001*).

Human beings can be infected with *Toxoplasma gondii* (*T. gondii*) by ingestion or handling of undercooked or raw meat (mainly pork and lamb) containing tissue cysts or water or food containing oocysts excreted in the faeces of infected cats or exposure to infected cats (*Cook et al., 2000, Dubey et al., 2002 and Bahia-Oliveira et al., 2003*). Direct human-to-human transmission include transplacental transmission from mother to her fetus (*Reis et al., 2006*). It also include transmission of *T. gondii* by organ

transplantation from a seropositive donor to a seronegative recipient in heart, heart-lung, kidney, liver, and liver pancreas transplantations. Although rare, *T. gondii* can also be transmitted via blood or leucocytes from immunocompetent and immunocompromised donors (*Montoya and Liesenfeld, 2004*).

Toxoplasmosis demonstrates various clinical manifestations. In immunocompetent individuals, toxoplasmosis is generally asymptomatic, however, it sometimes manifests with fever, malaise, headache, myalgia, asymptomatic lymph node enlargement, and chorioretinitis when it locates in the eye (*Montoya et al., 2002*). In immunocompromised patients, *T. gondii* may cause encephalitis, pneumonitis and myocarditis as manifestations of toxoplasmosis. These infections are usually fatal if not recognized and treated (*Weiss and Dubey, 2009*).

Clinical signs are non-specific and insufficiently for a definite diagnosis because toxoplasmosis mimics several other infectious disease (*Remington et al., 2001*).

Diagnosis of toxoplasmosis in humans is usually made by serological, histological, and molecular methods, or by some combination of the above (*Montoya et al., 2002*). The direct recovery of *Toxoplasma gondii* from biological samples is often impracticable. Consequently, serological diagnosis represents the most widely used approach for defining the stage of infection (*Sensini, 2006*).

In clinical practice, serological tests are routinely employed to detect immunoglobulin M (IgM) and immunoglobulin G (IgG) specific antibodies, including indirect immunofluorescence and immunoenzymatic tests (enzyme – linked immunosorbent assay (ELISA), with the latter showing higher sensitivity and specificity (*Remington et al., 2004*).

Aim of work:

- Study prevalence of seropositivity for anti-*Toxoplasma* antibodies (IgG and IgM) in patients with chronic renal failure and renal allograft recipient using enzyme – linked immunosorbent assay (ELISA) technique.