

## ABSTRACT

### **Influence of *Toxoplasma* Infection on Pregnancy Outcome through Gamma Interferon (IFN $\gamma$ ), Activation of Caspase 3 and Apoptosis of Placental Cells**

*A laboratory experimental study on pregnant Balb/c mice inoculated by tachyzoites of RH strain *Toxoplasma gondii**

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Mechanism of pregnancy failure in toxoplasmosis it is still not fully understood. Increase of IFN $\gamma$  production, caspase-3 activation and apoptosis of placental cells due to infection of virulent strain of *Toxoplasma gondii*, are assumed to be some possible mechanisms. Eighty female BALB/c mice were monogamously mated, then divided into four dose groups, and injected intra-peritoneally by 10, 50, 100 tachyzoites of RH-strain of *Toxoplasma gondii* and PBS (control) respectively, on D9 post-mating (p.m). Effects of treatments were observed on D12 p.m. and D15-16 p.m., represented second and third period of pregnancy respectively. Peritoneal tachyzoites were counted under Neubauer counting slide. Plasma IFN $\gamma$  levels were examined by ELISA technique. Expression of caspase-3 on immuno-histochemistry and apoptotic index of trophoblast and decidua cells on HE and Apoptag stainings, were observed and counted under light microscopings from 20 fields of 1000 magnifications.

This study showed that toxoplasmosis in pregnant mice decreases number of litters. ANOVA and Path Analysis showed that decreasing number of litters was influenced by duration of infection, increase of plasma IFN $\gamma$  level, caspase-3 activation and apoptotic index of trophoblast cells ( $p < 0.05$ ), but not by dose of inoculation, number of peritoneal tachyzoites, caspase-3 activation and decidual apoptotic index ( $p > 0.05$ ). Plasma IFN $\gamma$  level was influenced by number of intraperitoneal tachyzoites and duration of infection ( $p < 0.05$ ) but not by dose of inoculation ( $p > 0.05$ ). Plasma IFN $\gamma$  level influenced activation of caspase 3 and apoptotic index of trophoblasts ( $p < 0.05$ ), but not deciduas ( $p > 0.05$ ). Number of tachyzoites did not influence apoptotic index of trophoblast and decidual cells ( $p > 0.05$ ). Apoptotic index of trophoblast was significantly higher than decidual cells. All of those were only found on the third period of pregnancy or 6-7 days post inoculation.

This study suggested that mechanism of pregnancy failure in toxoplasmosis is more indirectly immunobiochemical aspect rather than directly parasitological aspect. Decreasing number of litters due to IFN $\gamma$  overproduction as response to acute RH strain infection, suggested that there are still many possible molecular and cellular mechanisms that could not be explained in this research, and need more studies. Increase of trophoblast apoptosis initiated by activation of caspase 3, is led by role of macrophages accumulated at or near implantation site. Pregnancy failure in toxoplasmosis is more initiated by fetal part rather than maternal part.

**Key words:** *Toxoplasmosis, IFN $\gamma$ , caspase-3, trophoblast, apoptosis, pregnancy.*