



Qualitative assessment of risk for spontaneous abortion associated with toxoplasma and rubella: immunity appraisal

ABSTRACT

Background and Objective: Maternal viral and protozoan infections contribute to many complications in early pregnancies leading to spontaneous abortion. The present study was aimed to determine the prevalence of toxoplasmosis and rubella infections in women experienced spontaneous abortion.

Materials and Methods: 692 serum samples were tested for the presence of antibodies for toxoplasmosis and rubella using ELISA techniques. The investigations were carried out in the laboratory of Tripoli Central Hospital from January 2002 to December 2007.

Results: Testing results showed serological evidence of previous infection in 17.6% of tested women for toxoplasmosis and only 4.3% for rubella with co-existence of both infections in only 1.8% of women.

Conclusion: It seems that testing is more useful in excluding rather than establishing etiology. Considering the study outcome, it appears that toxoplasmosis and rubella represent only about one fifth of the total number of spontaneous abortion, this means that there are some other factors involved that have to be identified and deeply studied in order to establish prevention and therapeutic strategies.

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INTRODUCTION

Toxoplasmosis is an infectious disease of worldwide distributions affecting both animals and humans. Toxoplasmosis is caused by the *intracellular* protozoan parasite *Toxoplasmosis gondii* (1). The parasite's definitive host is house cat and certain other felidae. Transmission to humans occurs primarily by ingestion of

undercooked pork or lam meat that contains cysts or by exposure to Oocysts either through direct contact with cat feces or ingestion of contaminated vegetables. The other potential routes of transmission are blood product transmission, organ transplantations and the transplacental route (2).

Acquired toxoplasmosis is usually asymptomatic and benign (3). In pregnant women, however, the infection acquires a special significance as the parasite may enter the fetal circulation through the placenta and cause congenital toxoplasmosis (2). Several

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studies have shown that the risk and severity of congenital toxoplasmosis are greatest when acquired during the first three months of pregnancy (4-6). The consequences of congenital toxoplasmosis range from spontaneous abortion and prematurity to generalized and neurological symptoms which often involve ocular complications (7,8).

Rubella is a small spherical enveloped virus, 55-60 nm in diameter, and is the only member of the genus Rubivirus of the family Togaviridae (9). The virus contains a single positive stranded 42s RNA molecule and only one serotype is known. Infection with Rubella virus (German measles) in children and adults is a self-limiting, mild disease characterized by an erythematous rash, mild upper respiratory symptoms and sub occipital lymphadenopathy (10). After recovery, the individual is immune to subsequent infection with rubella. Primary infection of a pregnant woman however, particularly in the first trimester of pregnancy, may result in a high risk of fetal infection with severe complications (11).

In our study we have chosen these two microorganisms because recently they have been accused of causing most of the spontaneous abortion. The present study, therefore, aims to detect the presence of antibodies to *Toxoplasmosis gondii* and rubella in women who experienced spontaneous abortion, in order to document the prevalence of toxoplasmosis and rubella infections and their relation with spontaneous abortion.

MATERIALS AND METHODS

The study was conducted at Tripoli Central Hospital during the period 2002 to 2007 and included 692 women who suffered spontaneous abortion and attended the Department of Obstetric and Gynecology of the hospital. The age of the women ranged between 16-35 years and parity between one and five. 5 ml serum samples were collected from each woman at

the time of abortion and stored at 4°C until analysis. The samples were serologically tested to detect the presence of antibodies to *Toxoplasmosis Gondii* and/or Rubella using the enzyme linked immunosorbent assay (ELISA) techniques according to the manufacturer's instructions (12,13).

RESULTS AND DISCUSSION

Table 1 and Table 2 show the results into three groups according to the type of antibodies present with the prevalence in percent of each disease.

The first group; the negative group with negative antibodies for both IgM and IgG with a prevalence of 36% for toxoplasmosis and 6.5% for rubella infection. This result indicates that there was no previous exposure to *Toxoplasma gondii*, or rubella virus. These women therefore are the non-immune group and they are presumed to be susceptible to a primary infection. A negative result, however, does not eliminate the possibility of recent infection with the serum being tested before the appearance of the IgM antibodies. (14-16). This group of women has to follow strict measures to avoid infection with toxoplasma, since there is no available vaccine. However, these women have to be immunized with rubella vaccine before they become pregnant again.

The second group; the positive group for IgM antibodies with a prevalence of 17.6% for toxoplasmosis and 4.3% for rubella infection or 1.8% for coexistence of both infections. This indicates acute or recent infection with seroconversion may have occurred, i.e., later, both IgM and IgG antibodies are positive. For this group the infection with toxoplasma, rubella or both could be the causative agent for the spontaneous abortion (15,17). In this group we found that the incidence for the newly infected cases is relatively low (4.3%) compared with toxoplasmosis, which is

Table 1: Prevalence of toxoplasmosis, rubella infections or both in women with spontaneous abortion in percentage

Groups	Toxoplasmosis	Rubella	Toxoplasmosis and Rubella
Total No.	245 cases.	277 cases.	170 cases
Group 1	Negative cases: 36%	Negative cases: 6.5%	
Group 2	New Infections: 17.6%	New Infections: 4.3%	New Infections: 1.8%
Group 3	Old Infections: 45%	Old Infections: 89%	

Table 2. Seroprevalence of IgG and IgM antibodies in cases of Toxoplasmosis and Rubella

Groups	Cases for both organisms	IgM/IgG	Remarks
Group 1	Negative cases	Negative/Negative	Non-immune
Group 2	New Infections	Positive/Negative or Positive/Positive	Acute or recent. infection
Group 3	Old Infections	Negative/Positive	Immune

threefold high. Positive rubella-specific IgM antibodies indicate acute or recent infection. The detection of these antibodies therefore is very important for the serological diagnosis of both congenital and primary postnatal rubella infection as they can lead to severe birth defects. The absence of virus-specific IgG antibodies, is indicative of the risk of detection in newborn infants. Acute or recent infection with seroconversion can occur, i.e., later, both anti-IgM and IgG antibodies are positive. In our study, the incidence of Infection with both *Toxoplasma gondii* and Rubella in the same time is very low i.e. 1.8 %.

The third group; in this group the presence of negative IgM and positive IgG antibodies with a prevalence of 45% for toxoplasmosis and 89% for rubella infection, indicates that there was prior exposure at some undetermined time to *Toxoplasma gondii* or Rubella infection. Theoretically, these women are immune against *Toxoplasma gondii* and the probability that the parasite *Toxoplasma gondii* could disseminate because of the decrease in the immunity during pregnancy, is something of speculation and could not

be proved, therefore the immune state of the pregnant women as immunocompromised cases should be studied. Meanwhile, negative IgM and positive IgG rubella antibodies indicate of immunity against rubella infection. Natural infection leads to life-long immunity and in our study most of the tested women (89%) were previously infected and have immunity to subsequent infection with rubella virus. These groups of pregnant women have antibodies which cross the placenta and protect the newborn. Therefore, an old infection with rubella as causative agent for miscarriage is very low.

There are many reasons related to spontaneous abortion other than toxoplasmosis which represents only 17.6% if we eliminate the old infected group which shows negative IgM and positive IgG. This group should be theoretically immunized; on the other hand the incidence of rubella infection which could be responsible is only 4.3%. The immunity should be studied at the onset of each disease and other factors should be studied in relation to the host defense.

Considering primary prevention further research is required to examine the effectiveness of health information strategies.

Also prevention through immunization of rubella negative women is extremely beneficial. If not available other preventive instructions should be followed to protect pregnant women from unsuspected problems.

Strategies for treatment should be carefully set although it appears that there is still no conclusive evidence showing to what extent treatment following screening reduces the risk of congenital infection or severe impairment. Also there is no consensus on the most appropriate treatment strategy because in some countries There is no clear evidence that intensive treatment protocols were beneficial. The European Multicentre Study on Congenital Toxoplasmosis (EMSCOT), was unable to demonstrate a beneficial effect of the timing or type of prenatal treatment on the risk of mother to child transmission, but could not exclude a clinically important effect (18). The findings of some studies are somewhat contradictory and causis controversy. We believe that the strains of toxoplasma in Libya should be studied to identify new strains and the possible mutations which may have an effect on their behavior and virulence.

In conclusion, it seems that testing is more useful in excluding rather than establishing etiology. Considering the study outcome, it appears that toxoplasmosis and rubella represent only about one fifth of total number of spontaneous abortions, this means that there are some other factors involved that have to be identified and deeply studied in order to establish prevention and therapeutic strategies.

REFERENCES

1. Tamma P. Toxoplasmosis. *Pediatr Rev* 2007;28:470-471.
2. Lynfield R, Eaton RB. Teratogen update. Congenital Toxoplasmosis. *Teratology* 1995;52:176-180.
3. Jones JL, Muccioli C, Belfort RJr, Holland GN, Roberts JM, Silverira C. Recently acquired *Toxoplasma gondii* infection, Brasil. *Emerg Infect Dis* 2006;12:582-587.
4. Adesiyun AA, Gooding R, Ganta K, Seepersadsingh N, Rainsewak S. Congenital toxoplasmosis in two health institutions in Trinidad. *West Indian Med J* 2007; 56:166-170.
5. Nowakowska D, Stray-Pedersen B, Spiewak E, Sobata W, Malafiej E, Wilczynski J. Prevalence and estimated incidence of toxoplasma infection among pregnant women in Poland: a decreasing trend in the younger population. *Clin Microbiol Infect* 2006;12:913-917.
6. Jumaian NF. Seroprevalence and risk factor of toxoplasma infection in pregnant women in Jordan. *East Mediterr Health* 2005;11:45-51.
7. Tan HK, Schmidt D, Stanford M, Teär-Fahnehje, Ferret N, Salt A, Gilbert R: European Multicentre Study on Congenital Toxoplasmosis (EMSCOT). Risk of visual impairment in children with congenital toxoplasmic retinochoroiditis. *Am J Ophthalmol*2007;144:648-653.
8. Abudher A., Elsaid, M., Zahra,S., Elkatib, A. Toxoplasmosis in pregnant women and newborn babies. *Infectious & Endemic Diseases Scientific Conference, Tripoli, Libya, May 2007, pp 17. (Abstract)*
9. Best JM. Rubella. *Semin Fetal Neonatal Med* 2007;12:182-192.
10. Vander Straten MR, Tyring SK. Rubella. *Dermatol Clin* 2002;20:225-231.
11. De Santis M, Cavaliere AF, Straface G, Garuso A. Rubella infection in pregnancy. *Reprod Toxicol* 2006;21:390-398.
12. Voller A., Bidwell DE., Barlett A, Fleck DG, Perkins M., Olandehin B. A microplate enzyme immunoassay for toxoplasmosis antibodies. *J Clin Pathol* 1976;29: 150-153.
13. Volk W. A. *Essentials of Medical Microbiology. Second Edition pp.729. J.B. Lipincott Company, Philadelphia, 1982.*
14. Montoya JG, Huffman HB, Remington JS. Evaluation of the immunoglobulin G avidity test for the diagnosis of toxoplasmic lymphadenopathy. *J Clin Microbiol* 2004; 42::4627-4631.
15. Kaul R, Chen P, Binder SR, Detection of immunoglobulin M antibodies specific for *Toxoplasma gondii* with increased selectivity for recent acquired infections. *J. Clin. Microbiol* 2004;42:5705-5709.
16. Petersen E, Borobio MV, Guy E, Liesenfeld O, MeroniV, Nassens A, *et al.* European multicenter study of the LIAISON automated diagnostic system for determination of *Toxoplasma gondii*-specific immunoglobulin G (IgG) and IgM and the IgG avidity index. *J. Clin. Microbiol* 2005; 43:1570-1574.

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17. Wilson M, Mcauley JB. Clinical Use and Interpretation of Serologic Tests for *Toxoplasmosis gondii*. Standard M36-A. NCCLS, Waune, 2003.
18. European multicentre study on congenital toxoplasma: Effect of timing and type of treatment on the risk of mother to child transmission of toxoplasma gondii. Br J Obstet Gynaecol 2003;110:112-120.