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Short Communication

Serological status of childbearing-aged women for *Toxoplasma gondii* and cytomegalovirus in northern Kosovo and Metohija

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Abstract

Introduction: *Toxoplasma gondii* and cytomegalovirus (CMV) are pathogens associated with congenital anomalies. **Methods:** Serum was collected from 79 reproductive-age women and tested for IgM and IgG antibodies to *T. gondii* and CMV. **Results:** Seropositivity for *T. gondii* was detected in 24.1% of women and CMV in 96.2%. High seropositivity for CMV was found for all ages. The highest seropositivity for *T. gondii* was observed among older participants. **Conclusions:** *T. gondii* remains an important pathogen owing to low seropositivity.

Keywords: *Toxoplasma gondii*. Cytomegalovirus. Serological status. Women of reproductive age.

Toxoplasma gondii and cytomegalovirus (CMV) are among the TORCH (*T. gondii*, rubella virus, CMV, and herpes simplex viruses) group of pathogens associated with congenital anomalies. In pregnant women, most TORCH agents cause mild illness in the mother but can have serious consequences for the fetus. According to available statistics, 2%–3% of all congenital anomalies are due to prenatal infections[1,2]. *T. gondii* is an obligate intracellular protozoan capable of causing subclinical infection in immunocompetent patients. Congenital transmission occurs during acute toxoplasmosis in seronegative mothers when tachyzoites present in the blood cross the placenta and infect the fetus[3,4].

CMV is one of the most common causative agents of viral intrauterine infections, with incidence of 0.3%–2.4% of all live births[5]. Although CMV in infants may occur as a result of reinfection or reactivation during pregnancy (i.e., nonprimary infection), the risk of perinatal infection and subsequent adverse consequences of primary infection, including long-term disability, is much higher than that related to nonprimary infection[6]. Both *T. gondii* and CMV usually cause asymptomatic or mild maternal infections, which markedly decrease and often prevent the possibility of clinical diagnosis. However, both prevention and treatment of infection with these pathogens are possible. Early detection, including prenatal screening, is the foundation of clinical success[7]. Serological status of reproductive-age women provides valuable information on immunity, which may help identify women at risk and contribute to preventing congenital infections caused by these agents. Therefore, further studies in this subpopulation of women in Kosovo and Metohija are warranted. To our knowledge, the population at risk of infection by these agents in this area has never been identified, making the present investigation highly beneficial. We aimed to estimate seroprevalence among women of reproductive age in northern Kosovo and Metohija and define populations at risk of infection with these pathogens.

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In this cross-sectional study, conducted between December 2011 and December 2012, the sample comprised 79 women of reproductive age. Participant age ranged from 20 to 43 years (mean, 30 years; standard deviation, 6 years). Participants included women with a normal or poor obstetric history (history of intrauterine fetal death, intrauterine growth retardation, stillbirth, or habitual abortion) who were patients in the Department of Gynecology and Obstetrics of the Health Centre in Kosovska Mitrovica. All participants completed a questionnaire comprising demographic information (age, place of residence, occupation, education level) and obstetric/gynecological history. In addition, serum samples taken from all participants were tested for the presence of IgM and IgG antibodies to *T. gondii* and CMV. Serological testing was performed using an enzyme-linked immunosorbent assay (ELISA) (EUROIMMUN, Lubeck, Germany) at the Institute for Public Health in Kosovska Mitrovica. All samples were tested for *T. gondii*; however, one participant was known to be CMV-positive, so 78 samples were tested for CMV.

Collected data underwent descriptive analyses, including relative numbers (structure indicators). In addition, the chi-square and Fisher's exact test were used for hypothesis testing. All statistical analyses were conducted using IBM SPSS version 21 (IBM Corp., Armonk, NY, USA). The significance level was set at 5%.

T. gondii seropositivity (positive results for IgM/IgG antibodies) was detected in 19 (24.1%) women. IgM and IgG antibodies were found in 9 (11.4%) and 15 (19%) serum samples, respectively. Findings of European studies involving reproductive-age and pregnant women reveal a wide range in *T. gondii* seroprevalence, from 21.5% in Italy[8] and 29.1% in Croatia,[5] to 48.6% in Albania[9]. In our study, only 24.1% of women had anti-*T. gondii* antibodies, which is lower than the 33% reported for the entire Serbian territory[10]. These variations in seroprevalence are attributable to environmental (climate, rainfall, temperature, type of soil, altitude) and maternal (education level, hygiene, nutritional status, dietary habits, and contact with cats) characteristics. For example, it has been established that high altitude does not favor sporulation and existence of oocytes; *T. gondii* prevalence is lower at higher altitudes[11,12].

Our analyses revealed CMV seropositivity in 96.2% (75/79) of participants. IgM and IgG antibodies were present in 12 (15.4%) and 72 (92.3%) serum samples, respectively. Total CMV seroprevalence in reproductive-age women differs among countries and across regions. In Europe, CMV seroprevalence varies between 30% and 88%. Pregnant women in Ireland have some of the lowest (30.4%) CMV seroprevalence worldwide[13]. However, pregnant women in Turkey have very high (up to 100%) CMV seropositivity rates[14]. In Croatia, IgG seroprevalence of 75.3% for CMV was reported by Vilibic-Cavlek et al[5]. In our study, 96.2% CMV seropositivity was noted, which is much higher than that observed in some parts of Europe[13] but is nearly equal to the seroprevalence noted in Turkey[14]. In addition, seropositivity in pregnant women was even higher (97.6%). Such high CMV seroprevalence may be associated with low hygiene standards among the population of Kosovo and Metohija.

In our investigation, participating women were classified into four age groups: 20–25, 26–31, 32–37, and 38–43 years. Authors of many published studies have noted that seroprevalence for *T. gondii* increases with age, which can be explained by the cumulative effect of exposure to the parasite. As is well known, once created, IgG antibodies remain for life[5,11,15]. According to the present study results, seropositivity for *T. gondii* was also increased with age, whereby 22.7% of women aged 20–25 years were seropositive, compared with 45.5% in those aged 38–43 years. These results show that in northern Kosovo and Metohija, the youngest women have the highest risk of acquiring primary toxoplasmosis during pregnancy. High CMV seropositivity (> 90%) was detected in all age categories. Moreover, seropositivity for both tested causative agents did not significantly vary by age ($p = 0.67$).

It is noteworthy that 37 (46.8%) of the 79 women in our study resided in the countryside and the remaining 42 (53.2%) lived in the city. Authors of numerous studies have discussed the disparity in *T. gondii* seropositivity between women in rural and urban areas[5,12]. The same trend was noted in this investigation, as 29.7% of women from rural areas were seropositive compared with only 19.1% of those living in cities. This finding is attributed to the greater exposure of rural residents to cats, which often live in or around houses and thus have an important role in the *T. gondii* life cycle, whereby oocytes are often buried in soil with cats' bodily waste. In rural areas, women are more likely to acquire toxoplasmosis owing to higher exposure while gardening, farming, and working with animals. Moreover, consumption of homemade meat products, particularly sausages, is another likely factor contributing to the higher prevalence of toxoplasmosis among women from rural areas.[5]

Among the 78 women tested for CMV, 35 (44.9%) were from the countryside and the remaining 43 (55.1%) resided in the city. Similar to findings of other studies[5], seropositivity for CMV in the present study was also higher in rural areas than in cities (97.1% vs. 95.3%). This slight disparity can be explained by the low socioeconomic status and lifestyle of the rural population. In rural areas, people usually live in large families with many children and relatives comprising one household[5]. When examined by place of residence, differences in seropositivity to the tested pathogens were not significant (*T. gondii*, $p = 0.27$; CMV, $p = 1.00$).

When participants were grouped according to educational attainment, 52 (65.8%) of women tested for *T. gondii* and 50 (64.1%) of those tested for CMV had a secondary-level education, in line with the educational level of the general population. Only two participants (representing 2.5% of the *T. gondii* and 2.6% of the CMV seropositive groups) had a primary-level education; the remaining 25 (31.7% vs 33.3%) participants had a university degree. Further analyses revealed that differences in the serological status of participants based on educational attainment were not significant (*T. gondii*, $p = 0.46$; CMV, $p = 0.37$), even though lower *T. gondii* seropositivity was observed among highly educated women (20%) in comparison with women who had secondary- (25%) and primary-level (50%) educations. As occupation is related to educational

attainment, the highest *T. gondii* seropositivity was noted among housewives (40.9%), followed by students (30%), and women holding other occupations (10.7%).

Close contact with small children is also a risk factor for CMV transmission, as infected children excrete the virus in high concentrations over a long period through urine and saliva[5,14]. Consequently, we examined seropositivity in women who have contact with children for professional reasons in comparison with that of women working in other occupations, which revealed no significant differences.

The initial sample was also separated by pregnancy status; 43 (54.4%) of the 79 women tested for *T. gondii* were pregnant, corresponding to 42 (53.8%) of 78 tested for CMV. *T. gondii* seropositivity was noted in 8 (18.6%) pregnant women, and 41 (97.6%) were CMV seropositive. It is noteworthy that 75.9% of women tested were *T. gondii* seronegative, and only 18.6% of pregnant women in this sample had antibodies to this pathogen. This high percentage of seronegative women of reproductive age and low percentage of seropositive pregnant women can indicate increased risk of acquiring primary *T. gondii* infection during pregnancy. *T. gondii* seropositivity among nonpregnant women was slightly higher than that among pregnant women (30.5% vs. 18.6%, $p = 0.22$) whereas CMV seropositivity was similar in both groups (94.4% vs. 97.6%, $p = 0.59$) (**Tables 1 and 2**). In our study, no significant differences in seropositivity were noted between women with normal and poor obstetric histories, irrespective of the pathogen (*T. gondii*, $p = 0.26$; CMV, $p = 0.24$) (**Table 3**). Bearing in mind the small number of participants, these results should be interpreted with caution. Further research involving a larger group of participants is necessary, to clarify our observations.

High CMV seropositivity among reproductive-age women in northern Kosovo and Metohija indicates that most of this population is not at risk of primary infection by this virus during pregnancy. However, due to relatively low *T. gondii* seropositivity, raising awareness about this important pathogen is essential, as it can cause harm to the fetus and neonate. In addition, the lowest *T. gondii* seropositivity was observed among younger women, who are likely planning pregnancy. Prenatal screening and education of seronegative pregnant and young women planning pregnancy are needed, to prevent intrauterine infections caused by these pathogens.

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Conflict of Interest: The authors declare no conflicts of interest.

TABLE 1: Serological status for *Toxoplasma gondii* and patient characteristics.

Variables	Characteristics	Tested N (%)	Seropositive (IgG and/or IgM) N (%)	*p*-value
Residence	Village	37 (46.8)	11 (29.7)	0.27
	City	42 (53.2)	8 (19.1)	
Education	Primary	2 (2.5)	1 (50.0)	0.46
	Secondary	52 (65.8)	13 (25.0)	
	University	25 (31.7)	5 (20.0)	
Pregnancy	No	36 (45.6)	11 (30.5)	0.22
	Yes	43 (54.4)	8 (18.6)	

TABLE 2: Serological status for cytomegalovirus and patient characteristics.

Variables	Characteristics	Tested N (%)	Seropositive (IgG and/or IgM) N (%)	*p*-value
Residence	Village	35 (44.9)	34 (97.1)	1.00
	City	43 (55.1)	41 (95.3)	
Education	Primary	2 (2.6)	2 (100.0)	0.37
	Secondary	50 (64.1)	47 (94.0)	
	University	26 (33.3)	5 (19.2)	
Pregnancy	No	36 (46.2)	34 (94.4)	0.59
	Yes	42 (53.8)	41 (97.6)	

TABLE 3: Serological status for *Toxoplasma gondii* and cytomegalovirus, and obstetric history.

	Obstetric history	Tested N (%)	Seropositive (IgG and/or IgM) N (%)	*p*-value
Toxoplasma gondii	Normal	41 (51.9)	12 (63.2)	1.00
	Poor	38 (48.1)	7 (36.8)	
Cytomegalovirus	Normal	39 (50.0)	36 (48.0)	1.00
	Poor	39 (50.0)	39 (52.0)	

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