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Seroprevalence of anti-TORCH IgG/IgM (*Toxoplasma gondii, Rubella sp,* Cytomegalovirus, Herpes simplex virus 1/2) and associated risk factors in pregnant women in Yaoundé

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Summary: - *Toxoplasma gondii* (TG), Rubella virus (RV), cytomegalovirus (CMV), and herpes simplex virus types 1 and 2 (HSV 1 and 2) are generally mild in immunocompetent adults, but can lead to serious complications for the fetus and newborn when they occur during pregnancy. This study aims to determine the seroprevalence of these infections in pregnant women, commonly referred to by the acronym TORCH, by analyzing their serological profile in IgM and IgG. To achieve this, 83 samples were obtained from two collection sites in Yaoundé from the serological bank of the Microbiology Laboratory of the University of Yaoundé 1 and analyzed. The *One Step Rapid Test* Kit from EVANCARE was used. The survey sheets accompanying the plasma samples were used to associate the risk factors in this population. The results obtained regarding the IgG seroprevalence of TORCH infections in our samples were as follows: Toxoplasmosis IgG 34.9%, Rubella IgG 28.9%, Cytomegalovirus IgG 28.9% and HSV1 IgG 30.1%. Only HSV1 showed an IgM seropositivity (1.2%). These results were totally negative for both HSV2 IgM and HSV2 IgG testing. Factors associated with the acquisition of these pathogens and the production of IgG antibodies were: urban area of residence, contact with soil, consumption of raw or undercooked meat, contact with domestic animals, the last two trimesters of pregnancy, and blood transfusion. This study contributed to a better understanding of the prevalence and risk factors of TORCH infections in pregnant women in Yaoundé.

Keywords: TORCH infections, IgM, IgG, Cytomegalovirus, Herpes simplex virus, Rubella virus, *Toxoplasma gondii*, Seropositivity.

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Introduction

Pregnant women are more susceptible to a variety of infections. Maternal infection in pregnancy occur at any time during gestation and the severity depends upon virulence of agents, susceptibility of mother, gestational age of fetus and route of infection (Agrawal et al., 2016). TORCH infections (Toxoplasmosis, Rubella, Cytomegalovirus, Herpes simplex) can be transmitted from mother to child during pregnancy. Often asymptomatic or moderate in pregnant women, they can cause serious consequences in the fetus: jaundice, meningitis, rash, anemia, thrombocytopenia, hydrocephalus, intracranial calcification, microcephaly, low birth weight, prematurity, stillbirth, chorioretinitis, developmental delay, etc. (Lynn et al., 2023). The acronym TORCH refers to a group of infections that can be transmitted from mother to baby during pregnancy, childbirth, or shortly thereafter. These are infections of the following microorganisms: *Toxoplasma gondii*, rubella virus, cytomegalovirus (CMV) and herpes simplex viruses (HSV) (De Vries, 2019). The parasite *Toxoplasma gondii*, a protozoan with intracellular development, can cause congenital infection in the event of primary acquisition during pregnancy (Robert-Gangneux and Dion, 2020). The rubella virus belongs to the family *Togaviridae* and the genus *Rubivirus*, which has a positive single-stranded RNA. It is frequently associated with severe malformations, known as congenital rubella syndrome (CRS), when its infection occurs during the first trimester of pregnancy (Eno et al., 2018). The human herpes virus 5, also known as cytomegalovirus (CMV), a double-stranded genome of wrapped DNA, belongs to the *Herpesviridae* family. During pregnancy, primary maternal infection, reinfection, or reactivation of the latent virus may lead to infection and reproduction of Cytomegalovirus in the placenta. Infection of the placenta can cause fetal damage by modulating the immune system, disrupting placental development, and impairing its functioning (Hamilton et al., 2020). The herpes simplex virus is a member of the *Herpesviridae* family that features a double-stranded genome of wrapped DNA. During pregnancy, the immune system's ability to fight infection decreases,

increasing the likelihood of recurrence of infection in women previously infected with Herpes simplex virus. The risk of the mother developing disseminated HSV infection during pregnancy, particularly in the second and third trimester, is less well understood (Hammad & Konje, 2021). Maternal exposure to factors such as: contact with aerosols from infected people, non-immunization, contact with host animals, consumption of raw or undercooked food, sexual contact, body contact, blood transfusion, and organ transplantation increases the risk of contracting these infections (Baghel & Inamdar, 2021). Several diagnostic methods are used and serological testing allows the search for the immune response to pathogens (IgM and IgG) (Batra et al., 2020). In Cameroon, despite relatively routine screening for toxoplasmosis and rubella, women continue to carry fetuses with congenital damage and give birth to newborns with neonatal problems. This situation could be due to the combined action of TORCH complex infections. The aim of our study was to determine the seroprevalence of IgM and IgG against complex infections and to highlight the various risk factors associated with pregnant women in two hospitals in the city of Yaoundé.

Materials and methods

A cross-sectional study was conducted for four months, from August to November 2023, in the Microbiology Laboratory of the Faculty of Science of the University of Yaoundé I, on plasmas stored in cryotubes of the laboratory's serum repository. These plasmas came from blood taken from pregnant women who came for prenatal consultations in 02 hospitals in the city: The Yaoundé Gynaeco-Obstetric and Pediatric Hospital and the Yaoundé General Hospital. During the collection of these blood samples, a technical sheet was duly completed for each participant and provided information on the sociodemographic and clinical information of these parturient women. From this accompanying sheet, parameters were extracted for our study: age, area of residence, occupation, marital status, level of education, religion, consumption of undercooked meat, permanent contact with the ground, contact with domestic animals (cats among others), gestational age and history of miscarriage.

In the serum bank, 83 samples were selected on the basis of the available data sheets and the appropriate plasma volumes. Each sample was tested for IgG and IgM antibodies specific to the microorganisms of interest, using *One Step TORCH IgM/IgG rapid diagnostic tests (TOX IgM/IgG, RV IgM/IgG, CMV IgM/IgG, HSV-I/2IgM/IgG (Bioneavan co.LTD., NO.18 Ke YuanLu, GongYeKaiFaQu, Huang Cun Zhen AaXing County, Beijing)*. According to the manufacturer's instructions, the kits and samples to be tested were first brought to room temperature (18-24°C) in order to avoid moisture condensation on the membrane, then the cassette was removed from its packaging and placed on a dry horizontal work surface, and then 30µl of plasma from the already homogenized sample on a vortex was added to it. When sample migration was found difficult, 20µl of sample dilution solution was added immediately, and an additional 50µl of the same solution 5 minutes later. 15 to 20 minutes after the addition of plasma, the different results were observed. The appearance on the cassette of a red band at the level of the control area and another at the level of the test area indicated a positive result. The single appearance of a red band at the control area indicated a negative result (Njiki et al., 2022).

Statistical analysis: Data were entered into an Excel 2016 spreadsheet, double-checked for accuracy and cleaning, then closed for data analysis. The cleaned dataset was then transferred into the Statistical Package for Social Sciences (SPSS) version 22.0 was used for statistical analyses. Categorical variables and their comparison were done using a X^2 test or Fisher exact test wherever applicable, Odds ratio was used to highlight the strength of an association between microorganism's presence and the infection's risk factors. *p*-value <0.05 was considered as statistically significant.

Ethics approval: An authorization for the use of the samples from the serum library has been obtained from the Microbiology Laboratory of the Faculty of Sciences of the University of Yaoundé 1 and an ethical clearance from the Joint Institutional Board for Animals and Human Bioethics (JIRB) of the University of Yaoundé 1 (Ref N° BTC-JIRB2023-146).

Results

With the data sheets that accompanied the preserved samples, it was noted that the average age of the women whose samples were worked on was 27.6±5.5 years, in a range ranging from 14 to 40 years. The majority of women were between 19 and 33 years old, i.e. 85.6% (n=71/83) of the participants. The majority of these women had a university degree (55.4%, n=46/83), came mainly from the urban areas of the city of Yaoundé (91.6%, n=76/83), and were Christian (96.4%, n=80/83). Regarding exposure to the different risk factors, we found that only 13.2% (n=11/83) were in contact with domestic animals (cats and dogs), 31.3% (n=26/83) consumed raw food, 67.5% (n=56/83) consumed undercooked meat, and 73.5% (n=61/83) were in contact with soil (Table 1). Gestational age showed a significant high frequency in the second and third trimesters, with 38/83 (45.8%) and 30/83 (36.1%) of women, respectively. The number of miscarriages had a history of miscarriage in 34.9% (n=29/83) of women (Table 2).

Table 1: Sociodemographic characteristics of the study population

Variables	Terms	Frequency (n)	Percentage (%)	*p*-value
Age group	14-18	3	3.6	< 0.0001
	19-23	17	20.5	
	24-28	22	26.5	
	29-33	32	38.6	
	34-39	7	8.4	

	40 and over	2	2.4	
Level of education	Primary	6	7.2	< 0.0001
	Secondary	31	37.3	
	Upper	46	55.4	
Profession	Employee	40	48.2	0.8
	Unemployed	43	51.8	
Residence	Rural	7	8.4	< 0.0001
	Urban	76	91.6	
Religion	Christian	80	96.4	< 0.0001
	Muslim	3	3.6	
Pets	None	70	84.3	< 0.0001
	Cat	7	8.4	
	Hens	1	1.2	
	Goats	1	1.2	
	Dog	4	4.8	
Raw food consumption	No	57	68.7	0,001
	Yes	26	31.3	
Consumption of undercooked meat	No	27	32.5	0,002
	Yes	56	67.5	
Contact with the ground	No	22	26.5	< 0.0001
	Yes	61	73.5	

Table 2: Gestational parameters of the study population

Variables	**Terms**	**Frequency (n)**	**Percentage (%)**	**P value**
Gestational age	1st trimester	15	18.1	< 0.0001
	2nd trimester	30	36.1	
	3rd trimester	38	45.8	
History of miscarriage	Any	54	65.1	< 0.0001
	01	19	22.9	
	≥ 2	10	12.0	

A seropositivity of 1.2% at IgM (n=1) was observed only for herpes simplex virus type 1. The search for these antibodies against the various infectious agents of the TORCH complex was negative (Table 3).

Testing for the presence of specific IgG in these plasmas revealed 34.9% (n=29) seropositivity for *T. gondii,* 30.1% (n=25) for HSV-1, and 28.9% (n=24) for both rubella virus and cytomegalovirus. This result is still negative for HSV-2 (Table 3).

Table 3: IgM and IgG Sample Seropositivity

	IgM positive (n, %)	IgG positive (n, %)	P value
TOXO	0	29 (34.9%)	< 0.0001
RUB	0	24 (28.9%)	
CMV	0	24 (28.9%)	
HSV-1	1 (1.2%)	25 (30.1%)	
HSV-2	0	0	

The search for risk factors for the production of IgG directed against the various infectious agents of the TORCH complex showed:

An association between *T. gondii* infection and contact with soil (OR of 3,4). And so, women with permanent contact with soil had a 3.4 percent higher risk of contracting *T. gondii* and producing specific IgG, but this was not statistically significant.

An association between rubella virus infection and the third trimester of pregnancy (OR 2.9), the second trimester of pregnancy (OR 2.2) and contact with soil (OR 2.7).

Hence, women in the second and third trimesters of pregnancy had a 2.2- and 2.9-times higher risk of contracting the rubella virus and producing specific IgG, respectively, as well as those with permanent contact with the soil (2.7 times higher), but this was not statistically significant.

An association between cytomegalovirus infection and the third trimester of pregnancy (OR 8.4). Therefore, women who were in the third trimester of pregnancy had an 8.4-fold higher risk of contracting cytomegalovirus and producing specific IgG, but this was not statistically significant.

An association between herpes simplex virus type 1 infection and: blood transfusion (OR 3.5), absence of occupation (OR 3.1), urban residence (OR 2.3), and second and third trimesters of pregnancy (OR 2.8 and 2.3, respectively). Thus, women who had a history of blood transfusion had a 3.5-fold higher risk of contracting HSV-1 and producing specific IgG, and this was statistically significant.

Table 4: Risk factors for the production of IgG by the different infectious agents of the TORCH complex

Characteristics	TOXO (IgG) OR [IC 95%]	RUB (IgG) OR [IC 95%]	CMV (IgG) OR [IC 95%]	HSV-1 (IgG) OR [IC 95%]
Occupation (unemployed)	1.50 [0.5-3.9]	1.7 [0.6-3.8]	1.7 [0.6-4.8]	3.1 [1.03-948]
Area of residence (urban)	1.38 [0.2-8.0]	0.2 [0.6-1.43]	2.1 [0.2-19.2]	2.3 [0.2-21.3]
Religion (Muslim)	0.91 [0.6-12.3]	1.1 [0.8-5.3]	1.04 [0.07-14.7]	//
Raw food consumption (yes)	1.15 [0.4-3.1]	0.5 [0.1-1.8]	0.9 [0.3-2.9]	//
Consumption of raw meat (yes)	1.08 [0.3-2.9]	1.1 [0.3-3.5]	0.3 [0.1-0.9]	//
Ground Contact (Yes)	3.41 [0.9-11.6]	2.7 [0.7-4.8]	1.2 [0.3-3.9]	//
Pets (Cat)	//	//	//	//
Miscarriage	//	//	1.9 [0.6-5.5]	//
Blood transfusion	//	//	0.5 [0.05-23.7]	3.5 [0.5-22.9]
2nd trimester of pregnancy	//	2.2 [0.8-6.4]	1.6 [0.2-5.5]	2.8 [0.1-1.1]
3rd trimester of pregnancy	//	2.9 [0.6-7.9]	8.4 [0.7-10.4]	2.3 [0.3-2.9]

Discussion

The main objective of this study was to determine the seroprevalence of TORCH infections in pregnant women in two hospitals in the city of Yaoundé, on a total number of 83 plasma samples taken from the serum bank of the Microbiology Laboratory of the University of Yaoundé I.

Our Yaoundé cohort had an average age of 27 years with a high number of participants in the 19-33 age group (85.6%), so the maximum number of women achieve fertility between 20-24 years old, thus, the population is mostly young, sexually active and likely to become pregnant. The university level was in the majority in our study (54.4%), and almost all women (91.6%) lived in urban areas. The social behavior and eating habits of the pregnant woman found that 13.2% had at least one pet (cats and dogs) and 73.5% were in contact with the ground, with 67.5% consuming undercooked meat. These high frequencies could be justified by taking into account the quality of the practice of personal and food hygiene, the quality of cooking of the meat. Good hygiene in habits and good food hygiene could prevent the occurrence of infection. The majority of women were in the 2nd or 3rd trimester of pregnancy. The age of pregnancy plays a very important role in the frequency of vertical transmission of these microorganisms to the fetus. It is rare in the 1st trimester, increases in the 2nd trimester and is frequent in the 3rd trimester (Kremp, 2007). As a result, the majority of these ages of pregnancy demonstrates the preparation for childbirth of the latter and the acquisition of the relative modalities.

A history of miscarriage was present in the cohort at 34.9%. TORCH microorganisms usually cause miscarriages. Indeed, most miscarriages due to TORCH infection are caused by *T. gondii* and the rubella virus which can reach the placenta and cause primary infections, leading to spontaneous abortion. There is no established link between CMV and HSV infections and miscarriage yet (Kakayi et al., 2021).

IgM seropositivity, although low, was observed. The presence of anti-HSV IgM is usually associated with primary infection. Levels of these antibodies often decrease over time. This means that a positive herpes IgM result is most often associated with a new infection. However, there are people with a reactivation of herpes infections who may also have positive herpes IgM blood results (Cole, 2020). IgG seropositivity was 34.9% for *T. gondii*, 30.1% for HSV1 and 28.9% for rubella virus and CMV. The presence of IgG without IgM in women undergoing their first screening in the third trimester raises doubts, as it may be the result of a previous infection occurring at any time in life prior to pregnancy. However, statistical data have confirmed that the possibility of an infection occurring in the first trimester with the subsequent loss of IgM cannot be excluded. The variation in seroprevalence is also due to differences in the geographical distribution of these microorganisms, socio-economic practices, the level of awareness and information, personal hygiene and eating habits of the study participants (Paquet & Yudin, 2018; Winter & Moss, 2022; Leruez-Ville & Ville, 2019; Hammad &Konje, 2021).

The risk factors found in our study population were: urban area of residence – contact with the soil – consumption of raw or undercooked meat – contact with pets – last trimesters of pregnancy, blood transfusion.

In Ghana, no relationship has been documented between the consumption of undercooked meat, contact with the soil and Toxoplasmosis (Singh et al., 2021). On the other hand, another study conducted in Cameroon shows a contradiction concerning the 1st and ^{2nd} trimester of pregnancy as a risk factor for the acquisition of the infection (Taku et al., 2019). Population density in urban areas could explain the high circulation of these microorganisms.

The statistical insignificance of these results could be due to the small sample size or the protective effect of other factors.

Conclusion

Our results indicate the presence of infectious agents of the TORCH complex in Cameroon.

The evidence of IgG seropositivity at a level of 28.9% against rubella highlights a low level of immunization of these pregnant women before or during pregnancy.

Good hygiene in habits and good food hygiene could also prevent the occurrence of infection.

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