

Original Article

Infectious diseases during pregnancy in Brazil: seroprevalence and risk factors

Galileu Barbosa Costa^{1,2 #}, Mário Cézar de Oliveira^{1,3 #}, Sandra Rocha Gadelha¹, George Rego Albuquerque⁴, Marcel Teixeira⁵, Mônica Regina da Silva Raiol¹, Sandra Mara Bispo Sousa^{1,6}, Lauro Juliano Marin¹

¹ Laboratório de Farmacogenômica e Epidemiologica Molecular, Departamento de Ciências Biológicas, Universidade Estadual de Santa Cruz, Ilhéus, Brazil

² Laboratório de Vírus, Departamento de Microbiologia, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

³ Laboratório de Imunopatologia, Instituto de Ciências Biomédicas, Universidade Federal de Uberlândia, Uberlândia, Brazil

⁴ Laboratório de Doenças Parasitárias, Departamento de Ciências Agrárias e Ambientais, Universidade Estadual de Santa Cruz, Ilhéus, Brazil

⁵ Laboratório de Parasitologia, Embrapa Caprinos e Ovinos, Brasília, Brazil

⁶ Departamento de Ciências Naturais, Universidade Estadual do Sudoeste da Bahia, Vitória da Conquista, Brazil

Authors contributed equally to this work.

Abstract

Introduction: Vertically transmitted infections are caused by a diversity of pathogenic microorganisms. Pregnant women are routinely screened to evaluate the risks and reduce the burden of disorders in their unborn children. We assessed the prevalence and possible risk factors for Cytomegalovirus (CMV), Rubella, Human T lymphotropic virus (HTLV), and *Toxoplasma gondii* in pregnant women from the South region of Bahia State, Brazil.

Methodology: Serum samples were obtained from 726 pregnant women aged between 13 and 44 years, with a median age of 24 years. ELISA assays were used to detect CMV, Rubella, HTLV and *T. gondii* IgG and IgM antibodies.

Results: The prevalence rates of IgG antibodies found were 95.2% for CMV, 97.0% for Rubella, and 72.3% for *T. gondii*. Furthermore, the prevalence of HTLV-1/2 was 1.2%. IgM antibodies were reactive only for CMV (0.8%) and *T. gondii* (3.7%). Variables independently associated with the detection of anti-*T. gondii* IgG antibodies were white self-reported race/ethnicity (Odds Ratio [OR] 2.26, 95% CI 1.26–4.06, P = 0.006), wage income (OR 0.55, 95% CI 0.35–0.88, P = 0.013), and history of previous pregnancy (OR 1.60, 95% CI 1.02–2.50, P = 0.038).

Conclusions: This study highlights the importance of monitoring for infectious diseases during pregnancy and initiation of early interventions to reduce the burden of fetal losses and other important infant sequelae attributable to congenital infections.

Key words: Cytomegalovirus; Rubella; Human T lymphotropic virus; Toxoplasma gondii; pregnant women; public health.

J Infect Dev Ctries 2018; 12(8):657-665. doi:10.3855/jidc.9492

(Received 08 June 2017 - Accepted 16 March 2018)

Copyright © 2018 Costa *et al.* This is an open-access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Infectious diseases are the major cause of maternal and fetal morbidity and mortality [1–3]. The increased susceptibility of such population is mainly due to changes in immune function during pregnancy [4–6]. Infections can be transmitted to the neonate vertically through the placenta, perinatally from vaginal secretions and blood and also postnatally, via breast milk and other sources [4]. The clinical manifestations of neonatal diseases vary depending on the infectious agent and gestational age at the time of exposure. The risk of infection is usually inversely related to gestational age at acquisition, with early acquisition sometimes resulting in congenital malformation syndrome [7]. Although some infections are asymptomatic, many have been associated with spontaneous abortion, fetal death, preterm birth, intrauterine growth restriction and a range of other birth defects [1,3,8]. Well documented infectious causes of these ailments include Cytomegalovirus (CMV), Rubella, and *Toxoplasma gondii*.

CMV infection often occurs during childhood and is one of the most frequently transmitted viruses during pregnancy [9,10]. After primary infection, CMV becomes latent, and can be reactivated in situations that compromise the immune system such as pregnancy. It has been reported that the risk of fetal damage is greater during primary infection, reactivation and reinfection during pregnancy [11–13]. Approximately 30–40% of primary maternal CMV infections result in transmission of virus to the fetus, which can result in symptomatic congenital disease [11–13].

Rubella is an important teratogenic virus and is a common childhood infection. Less severe cases may manifest as mild flu-like symptoms and rash. However, up to 90% of infants born from mothers who had the disease during the first 11 weeks of pregnancy develop Congenital Rubella Syndrome (CRS), presenting growth and mental retardation, cataracts, deafness, congenital organ defects, often affecting the heart [3,14].

Prevalence rates of *Toxoplasma gondii* infection in Brazilian pregnant women are very high in comparison with other parts of the world [15]. Infection with this protozoan parasite can cause severe illness when the organism is contracted congenitally or when it is reactivated in immune-suppressed individuals [15–19]. Approximately 35% of congenital toxoplasmosis is associated with neurological disease including hydrocephalus, microcephaly and mental retardation. Moreover, about 80% have ocular lesions and 40% of children have hearing loss [15].

Human T lymphotropic virus (HTLV-1/2) infection is transmitted during sexual intercourse, blood transfusion, sharing of contaminated needles and from mother to child especially through breastfeeding, although intrauterine and/or at the time of delivery contamination also occur [20,21]. Adult T cell (ATL), leukemia/lymphoma tropical spastic paraparesis or HTLV-1 associated myelopathy (TSP/HAM) and infective dermatitis have been linked to HTLV-1 infection [22,23]. Although several reports of neurological diseases TSP/HAM-like associated with HTLV-2 have been reported in the literature, HTLV-2 has not been definitively associated with any disease [24,25].

Although serological screening for the presence of or susceptibility to some of these infections is recommended, most women living in developing countries have no or limited access to healthcare services. In this scenario, it is important to investigate the prevalence and risks for pregnant women and their newborns for this at-risk group. Given the nature of the infectious agents mentioned above and the severity of the associated disorders, we aimed to investigate the seroprevalence and risk factors for these ailments in pregnant women from Southern Bahia, Brazil.

Methodology

Study area

A cross-sectional study was carried out during July 2009–2010 including a population of pregnant mothers who attended the women reference attention center (Maternidade Santa Helena) Ilhéus in citv (14°49'33.7"S, 39°02'03.7"W), South region of Bahia State, Brazil (Figure 1). Ilhéus has a total of 176,341 inhabitants distributed in an area of 1.584,693 km². The city is located in the Southern mesoregion of Bahia State, covered with Atlantic rainforest, has the most extensive coast of the State, and is characterized by a humid tropical climate [26].

Regarding the healthcare system, Ilhéus has a total of 122 healthcare stations of which 66 are public as part

Figure 1. Overview of South America and Brazil highlighted in yellow (left). On the right, a map of South Bahia State. The pink dot marks in Ilhéus city (the location where this study was performed), and the H marks the women reference attention center (Maternidade Santa Helena). The other colored dots highlights the neighboring cities also attended by Maternidade Santa Helena (Google Earth, 2017).



of Unified Health System (SUS). Two healthcare stations have services relating to emergency care in obstetrics, including Maternidade Santa Helena (Figure 1) [26]. This women reference attention center provides care not only to Ilhéus city but also to other cities in South Bahia State, surrounding the Ilhéus area. The average number of deliveries range from 9 to 12 deliveries per day, reaching up to 380 deliveries per month, and about 90% of births are performed by SUS [26].

Study design

Blood samples were collected from pregnant women between the ages of 13 and 44 years, who voluntarily agreed to participate in the study. Serum samples were sent to the State Central Laboratory of Public Health and subjected to duplicate ELISA testing for the presence of IgM and IgG antibodies against CMV, Rubella, *T. gondii* and HTLV. The HTLV positive samples were confirmed by Western Blot (HTLV BLOT 2.4 – Abbott, Silver Spring, USA) and polymerase chain reaction (PCR).

All volunteers completed a structured questionnaire to obtain demographic data (age, self-reported race/ethnicity, monthly income, educational level, and marital status) and practices considered risk factors (alcohol consumption whilst pregnant, smoking, tattoos/piercings, intravenous drug use, and history of pregnancies). Other risk factors specifically related to *T. gondii* such as contact with dogs and cats, raw meat and non-treated water consumption, land manipulation and miscarriage were also evaluated. These data were converted to variables and tested for correlation to the presence or absence of outcomes for each pathogen evaluated.

Statistical analysis

To identify risk factors associated with each pathogen, a bivariate analysis was carried out using Chi-square and Fisher's exact tests with a significance level of 5% using EPI-INFO software version 7.2 (www.cdc.gov/epiinfo). All variables with $p \le 0.2$ on bivariate analysis were subjected to collinearity

analysis determined by the Spearman's rank correlation test according to BioEstat 5.0. Subsequently, multivariate logistic regression analysis was performed using EPI-INFO.

Ethical considerations

Ethical clearance was obtained from the Ethics Committee on Human Research of Universidade Estadual de Santa Cruz under protocol number 194/2008. Prior to data collection, the objectives of the study were explained to all study participants. Informed written consent was obtained from all study participants. In the case of minors (age < 18 years old), consent was provided by the parents or legal guardians.

Results

A total of 726 pregnant women were enrolled in this survey. Most women attended Maternidade Santa Helena are from Ilhéus city (77%) however, other participants are from neighboring cities such as Canavieiras, Itacaré, Maraú, Serra Grande, Una, and Uruçuca were also included (Figure 1). The prevalence of specific antibodies against CMV, Rubella, HTLV, and Toxoplasma gondii are presented in Table 1. Rubella had the highest IgG seroprevalence (97.0%), followed by anti-CMV IgG (95.2%) and anti-T. gondii IgG (72,3%). Furthermore, the seroprevalence for HTLV-1/2 was similar to that observed in the general Brazilian population. In contrast, a low seroprevalence rate of IgM antibodies was observed for T. gondii (3.7%) and CMV (0.8%), when compared to the general population.

Table 2 summarizes demographic characteristics of study population. Approximately 20% of pregnant women were teenagers (with a lower limit of 13 years old; n = 3). The self-reported race/ethnicity of pregnant women enrolled was diverse, with brown predominating (53.9%), and the majority living on minimum wage (61%). Most women had medium/high levels of education, and analphabetism was observed only in five. Marital status was stratified into two groups: married or living with a spouse (83.7%), and single/divorced/widowed (15.4%). Self-reported

Table 1. Prevalence rates of IgG and IgM antibodies for Cytomegalovirus (CMV), Rubella, Human T lymphotropic virus (HTLV) and *Toxoplasma gondii* in pregnant women from Southern Bahia State, Brazil.

Pathogen	N of screened women	IgG (%)	CI 95%	IgM (%)	CI 95%
CMV	589	561 (95.2)	93.1 - 96.8	5 (0.8)	0.3 - 2.1
Rubella	508	493 (97.0)	95.1 - 98.3	0	
HTLV-1/2	511	6 (1.2)	0.5 - 2.7	Not tested	
T. gondii	463	335 (72.3)	68.2 - 76.5	17 (3.7)	2.2 - 5.9

race/ethnicity and income wage were significantly associated with the presence of anti-*T. gondii* IgG antibodies (Table 2).

Behavioral characteristics reported by few women include the presence of tattoos/piercings (23.1%), alcohol consumption whilst pregnant (13.1%), smoking (5.9%), previous blood transfusion (4.5%), and intravenous drug use (0.6%), and most had reported a history of previous pregnancy (53.3%). These variables had no correlation with CMV, HTLV-1/2 and Rubella seropositivity. However, more than one pregnancy was associated to the presence of IgG anti-*T. gondii* (p = 0.015) (Table 3).

Previously established risk factors specific to *T. gondii* seropositivity are shown in Table 4. However, none of these factors were significantly associated with anti-*T. gondii* IgG or IgM antibodies in this study. Other variables that showed a significant difference between those with positive and negative serology were

analyzed using the multivariate logistic regression model. Variables independently associated with the presence of IgG antibodies anti-T. gondii (p < 0.05) were self-reported race/ethnicity, history of previous pregnancy, and income (Table 5). Women who reported white self-reported race/ethnicity were 2.2 times more likely to possess anti-T. gondii IgG antibodies compared to other races (OR = 2.2; 95% CI = 1.26 – 4.06). Furthermore women who had a history of more than one pregnancy were 1.6 times more likely to possess anti-T. gondii IgG antibodies compared to those who reported their first pregnancy (OR = 1.6; 95% CI = 1.06 - 2.43). On the other hand, those pregnant women with an income > 1 minimum wage were less likely to possess anti-T. gondii IgG compared to those with an income < 1 minimum wage (OR = 0.55; 95%) CI = 0.34 - 0.88).

Table 2. Analysis of demographic characteristics for 796 pregnant women attended at reference attention service from Southern Bahia State, Brazil, 2009-2010, according to the seropositivity for Rubella, Cytomegalovirus (CMV), Human T lymphotropic virus (HTLV) and *Toxoplasma gondii* IgG antibodies.

Domographics		Rubella			CMV			HTLV			T. gondii		
Demographics	(n tested women = 508)†		(n teste	d women :	= 589)†	(n of tested women = 511) ⁺			(n of tested women = 463)†				
	Positive	Negativ	n valua	Positive	Negativ	n value	Positive	Negativ	n value	Positive	Negativ	n value	
	n (%)	e n (%)	p value	n (%)	e n (%)	p value	n (%)	e n (%)	p value	n (%)	e n (%)	p value	
Age (years)													
≤ 18	97 (19,1)	5 (0,9)	0.163	109 (18.5)	5 (0.8)	0.534	1 (0.2)	105 (20.5)	0.637	57 (12.3)	29 (6.2)	0.102	
> 19	396 (78,0)	10 (1,9)		452 (76.7)	23 (3.9)		5 (0.9)	400 (78.3)		276 (59.6)	98 (21.1)		
Self-reported race/ethni	icity												
White	72 (14,2)	1 (0,2)	0.924	83 (14.1)	2 (0.4)	0.547	0	78 (15.2)	0.860	33 (7.1)	28 (6.0)	0.015	
Black	124 (24,4)	4 (0,8)		138 (23.4)	10 (1.6)		2 (0.4)	123 (24.1)		87 (18.8)	29 (6.2)		
Brown	283 (55,7)	8 (1,6)		321 (54.5)	16 (2.7)		4 (0.8)	288 (56.3)		202 (43.6)	69 (14.9)		
Yellow	3 (0,6)	0		4 (0.8)	0		0	3 (0.6)		2 (0.4)	0		
Native	8 (1,6)	0		10 (1.6)	0		0	6 (1.2)		5(1.1)	1 (0.2)		
Income‡													
≤ minimum wage	287 (56,5)	9 (1,7)	0.272	329 (55.8)	18 (3.0)	0.560	4 (0.8)	312 (61.0)	0.545	212 (45.8)	68 (14.7)	0.004*	
> minimum wage	134 (23,8)	2 (0,4)		152 (25.8)	8 (1.3)		1 (0.2)	312 (61.0)		75 (16.2)	46 (9.9)		
Educational level+													
Have never gone to school	3 (0,6)	1 (0,2)	0.433	11 (1.8)	1 (0.1)	0.282	0	3 (0.6)	0.08	4 (0.8)	1 (0.2)	0.106	
Elementary school or less	234 (46,1)	5 (0,9)		266 (45.1)	11 (1.8)		5 (0.9)	230 (45.0)		154 (33.2)	51 (11.0)		
High school or more	249 (49,0)	7 (1,4)		284 (48.2)	6 (2.7)		1 (0.2)	261 (51.1)		170 (36.7)	75 (16.2)		
Marital status													
Married	70 (13,8)	1 (0,2)	0.434	480 (81.5)	24 (4.1)	0.223	0	77 (15.1)	0.370	60 (12.9)	21 (4.5)	0.396	
Single/divorced/widow	423 (83,3)	10 (2,0)	0.434	80 (13.6)	2 (0.3)	0.223	6 (1.2)	426 (83.4)	0.370	270 (58.3)	106 (22.9)		

 \dagger Counts might not equal to sample size due to missing data; \ddagger Minimum income value in Brazilian currency in 2009–2010 = R\$ 510,00 (US\$ 1,00 = R\$ 1,81 approximately); \ddagger Elementary school or less (\leq 8 years of study), High school or more (>8 years of study); \ast Odds Ratio: 1.91 (95% Confidence Interval: 1.17–3.02).

Table 3. Analysis of risk factors for 796 pregnant women attended at reference attention service from Southern Bahia State, Brazil, 2009–2010, according to the seropositivity for Rubella, Cytomegalovirus (CMV), Human T lymphotropic virus (HTLV) and *Toxoplasma gondii* IgG antibodies.

		Rubella CMV		HTLV			T. gondii						
Domographia	(n teste	(n tested women = 508)†		(n teste	(n tested women = 589)†			(n of tested women = 511) ⁺			(n of tested women = 463)*		
Demographics	Positive	Negative n	р	Positive	Negative n	р	Positive	Negative n	р	Positive	Negative n	n value	
	n (%)	(%)	value	n (%)	(%)	value	n (%)	(%)	value	n (%)	(%)	p varae	
Alcohol use													
Yes	72 (14.1)	2 (0.4)	0.589	80 (13.6)	4 (0.7)	0.586	1 (0.2)	61 (11.9)	0.544	43 (9.3)	13 (2.8)	0.262	
No	421 (82.8)	11 (2.1)		480 (81.5)	24 (4.0)		5 (0.9)	440 (86.1)		288 (62.2)	114 (24.6)		
Smoking													
Yes	31 (6.1)	0	0.435	33 (5.6)	1 (0.1)	0.508	2 (0.4)	34 (6.6)	0.061	18 (3.9)	3 (0.6)	0.119	
No	462 (90.9)	13 (2.5)		527 (89.4)	27 (4.6)		4 (0.8)	467 (91.4)		313 (67.6)	124 (26.8)		
Blood transfusion	history												
Yes	22 (4.3)	0	0.556	25 (4.2)	2 (0.3)	0373	1 (0.2)	22 (4.3)	0.244	11 (2.3)	7 (1.5)	0.205	
No	470 (92.5)	13 (2.5)		534 (90.6)	26 (4.4)		5 (0.9)	478 (93.5)		320 (69.1)	120 (25.9)		
Tattoo and/or pie	rcing												
Yes	117 (23.0)	1 (0.2)	0.153	132 (22.4)	4 (0.7)	0.183	2 (0.4)	116 (22.7)	0.425	73 (15.7)	31 (6.7)	0.336	
No	376 (76.0)	12 (2.3)		428 (72.6)	24 (4.0)		4 (0.8)	385 (75.3)		258 (55.7)	96 (20.7)		
Intravenous drug	use												
Yes	2 (0.4)	0	0.948	4 (0.7)	0	0.820	0	2 (0.4)	0.976	1 (0.2)	0	1.000	
No	487 (95.8)	13 (2.5)		551 (93.5)	28 (4.7)		6 (1.2)	493 (96.4)		326 (70.4)	125 (27.0)		
Pregnancies histo	ry												
1 st	265 (52.1)	8 (1.6)	0.395	251 (42.6)	14 (2.3)	0.364	5 (0.9)	263 (51.4)	0.138	182 (39.3)	55 (11.9)	0.015*	
> 1	228 (44.9)	5 (0.9)		309 (52.4)	14 (2.3)		1 (0.2)	237 (43.8)		148 (31.9)	72 (15.5)		

[†] Counts might not equal to sample size due to missing data; ^{*} Odds Ratio = 1.61 (95% Confidence Interval = 1.06–2.43).

Table 4. Analysis of specific risk factors for	Toxoplasma gondii for 352 [†]	pregnant women attended at	t reference attention service	e from Ilheus,
Southern of Bahia State, Brazil, 2009–2010,	according to the seropositivi	ty for IgG antibodies.		

Risk factors	N (%)	IgG positives (%)*	IgG negatives (%)**	Odds Ratio (CI95%)	P value
Contact with cats					
Yes	83 (23.6)	64 (77.1)	19 (22.9)	1.42 (0.80-2.53)	0.22
No	269 (76.4)	189 (70.2)	80 (29.8)		
Contact with dogs					
Yes	153 (43.4)	108 (70.6)	45 (29.4)	0.89 (0.56-1.42)	0.63
No	199 (56.6)	145 (72.8)	4 (27.2)		
Raw meat consumption					
Yes	24 (6.8)	14 (58.3)	10 (41.7)	0.52 (0.22-1.21)	0.20
No	328 (93.2)	239 (72.8)	89 (27.2)		
Non-treated water consumption					
Yes	61 (17.3)	48 (78.7)	13 (21.3)	1.56 (0.80-3.03)	0.21
No	289 (82.7)	203 (70.2)	86 (29.8)		
Land manipulation					
Yes	98 (27.8)	68 (69.4)	30 (30.6)	0.84 (0.50-1.42)	0.51
No	254 (78.2)	185 (72.8)	69 (27.2)		
Miscarriage history					
Yes	89 (25.3)	64 (71.9)	25 (28.1)	1.00 (0.58-1.71)	1.00
No	263 (74.7)	189 (71.8)	74 (28.2)		
Total	352 (100.0)	253 (71.9)	99 (28.1)		

† Counts were not equal to 463 sample size due to missing data; * Percent frequencies are shown by column; ** Percent frequencies are shown by row.

 Table 5. Multivariate logistic regression for 796 pregnant women attended at reference attention service from Southern Bahia State, Brazil, 2009-2010, according to the seropositivity for *Toxoplasma gondii* IgG antibodies.

Variables	Odds Ratio	CLS	95%	P value
White self-reported race/ethnicity	7			
Yes / No	2.2603	1.2577	4.0622	0.006
Wage				
$>$ minimum / \leq minimum	0.5542	0.3470	0.8852	0.013
Pregnancies history				
1 st / > 1	1.6031	1.0242	2.5091	0.038

Discussion

Infectious diseases are a common cause of morbidity and mortality in developing countries. Poverty, low education, lack of basic infrastructure, certain lifestyles and environmental conditions are known risk factors for a high incidence of infectious diseases among specific groups such as pregnant women [1,3,8,27-29]. In fact, most obstetrical and neonatal populations in Brazil have limited access to healthcare assistance and diagnostic examinations in the public health system, and so the prevalence of important infectious diseases is frequently underestimated. Screening and early diagnosis of these infections in high-risk pregnant women will facilitate the early detection and appropriate management of these infections.

CMV is a widespread and very well known cause of congenital disorders in vertically infected children [10-12,30]. The overall seroprevalence of anti-CMV IgG antibodies was very high in this study (95.2%) when compared to other studies conducted in Mato Grosso do Sul State (82% [31]) and in Sergipe State (76.6% [32]). Serra et al [33] analyzed 4620 pregnant women from several Brazilian regions and found a global IgG seroprevalence of 84%, although in Bahia State the prevalence rate was 78.1%. Regarding anti-CMV IgM antibodies, we found 0.8% seropositivity in pregnant women, which is also considered high. Although these results indicate a low seroprevalence, they suggest a recent or active CMV infection, with a great risks of vertical transmission. The presence of CMV infection can cause serious outcomes for the fetus, especially in the first trimester of pregnancy, while most infected women are asymptomatic. Hence, the developing baby could be at risk of vertical transmission and potentially resulting in a number of pathologies including growth retardation, microcephaly, chorioretinitis and hepatosplenomegaly [9-12,30]. However, the IgM seroprevalence reported here may not be a true reflection of the number of active infections because IgM antibodies can only be detected 1-3 months after the primary infection [9–13]. Although previous studies have reported correlations between a high prevalence of anti-CMV antibodies and social characteristics such as poverty, low education, and certain behaviours, there was no statistical association between serology and these variables in this study.

Rubella is an exanthematous illness that occurs worldwide with a seasonal distribution. This virus can act as a teratogen, inducing Congenital Rubella Syndrome (CRS) especially when transmitted from mother to fetus in the first trimester of pregnancy [3, 14]. The seroprevalence of IgG antibodies found here (Table 1) shows concordance with previous studies performed Brazil [31,32,34,35] which demonstrated in seroprevalence rates of 87.9%, 95%, 71.6% and 83.9%, respectively. In fact, the high levels of IgG antibodies detected are associated to the success of vaccination campaigns in women of fertile age. Although no IgM positive cases were found in this study, approximately 3% of pregnant women in this study were considered susceptible to infection (n = 15), which increases the risk of CRS in the subsequent pregnancies. Furthermore, it is possible that the immunization coverage is not complete in the studied region, so the prenatal screening is important to encourage vaccination postpartum in these specific cases.

In comparison to previous studies, the prevalence rate of HTLV-1/2 infection reported here (1.2%) is important [36–39]. Even though the prevalence in the city of Salvador is about 1.8% in the general population, others studies conducted with pregnant women showed a prevalence of between 0.84% and 0.88% in Salvador [40,41], and 0.98% in Cruz das Almas [42]. Vertical transmission is an important route of HTLV infection and children vertically infected can develop disorders such as infective dermatitis, ATL or HAM/TSP [43,44]. Moreover, the virus can also be transmitted during the breastfeeding process. Hence, the detection of HTLV infection through prenatal or neonatal screening would be a public health surveillance practice so that preventative measures could be introduced to reduce vertical transmission (e.g. avoidance of breastfeeding among mothers who are HTLV carriers).

The seroprevalence of *T. gondii* in the Brazilian population, in general, is considered variable but also is

one of the highest in the world [15]. The seroprevalence of anti-*T. gondii* IgG antibodies in the pregnant population studied here was higher compared to other epidemiological studies [15,45–48]. Conversely, the seroprevalence of IgM antibodies found here was similar to that observed in the other States of Brazil, such as Paraná (1.2%) and Minas Gerais (3.6%) [45, 47], although IgM can remain elevated for years, and a positive result does not always implicate a recently acquired infection, while a rise in IgM titer is evidence of acute infection [7].

Well established risk factors for *T. gondii* infection were not statistically relevant in this study (Table 5). Indeed, a number pregnancies > 1 (p = 0.038) were associated with a higher prevalence of infection due to the natural immunosuppression that occurs during pregnancy, as reported previously in Brazil [45, 49–51]. Also, income (p = 0.013) and ethnicity (p = 0.006) were related to a greater risk of anti-*T. gondii* IgG seropositivity. The positive correlation between social and economic variables with the risk of toxoplasmosis has also been reported in previous studies [16].

Serological screening for vertically transmissible pathgens such as CMV, Rubella, HTLV, and T. gondii is important to prevent birth defects and other negative neonatal outcomes. The results of this study emphasize the importance of follow-up for pregnant women that are seropositive for the pathogens investigated in this study. Although pregnant mothers may not have any suggestive signs or symptoms, we highlight the importance of Pre- and Neonatal programs that facilitate detection and management of these diseases to improve outcomes for neonates by reducing or eliminating the associated sequelae. Furthermore, our findings are a useful guide for perinatologists, public health specialists and health policy makers and will facilitate the development of improved prevention and control strategies in the future.

Conclusions

The results of this study emphasize the importance of monitoring the incidence to assess the risk of infectious diseases in pregnancy at all population levels, especially in groups of higher risk who depend on the public health system in the developing world. These data also support the need for improving regulations in the public health system in order to implement effective preventive programs that will reduce the risk of vertically acquired infections.

Acknowledgements

We thank all the staff from Maternidade Santa Helena, the Women Reference Attention Service in Ilhéus, for their excellent technical support. We are also thankful to all the volunteers for taking part of this study.

Author's contribution

Conception or design of the work: SRG and LJM; Data and samples collection: GBC, MCO, and MRSR; Data analysis and interpretation: GBC, MCO, SRG, GRA, MT, MRSR, SMBS, and LJM; Drafting the article: GBC and MCO; Critical revision of the article: GBC, MCO, SRG, GRA, MT, MRSR, SMBS, and LJM; Final approval of the version to be published: GBC, MCO, SRG, GRA, MT, MRSR, SMBS, and LJM.

Financial Support

This research was supported by Universidade Estadual de Santa Cruz (UESC). GBC and MCO had received fellowships from Fundação de Amparo à Pesquisa do Estado da Bahia (FAPESB) during the period of the study.

References

- 1. Jamieson DJ, Theiler RN, Rasmussen SA (2006) Emerging infections and pregnancy. Emerg Infect Dis 12: 1638-1643.
- Kourtis AP, Read JS, Jamieson DJ (2014) Pregnancy and infection. New Engl J Med 370: 2211-2218.
- Waldorf KMA, McAdams RM (2013) Influence of infection during pregnancy on fetal development. Reproduction 146: 151-162.
- Arora N, Sadovsky Y, Dermody TS, Coyne CB (2017) Microbial vertical transmission during human pregnancy. Cell Host Microbe 21: 561-567.
- PrabhuDas M, Bonney E, Caron K, Dey S, Erlebacher A, Fazleabas A, Fisher S, Golos T, Matzuk M, McCune MJ, Mor G, Schulz L, Soares M, Spencer T, Strominger J, Way SS, Yoshinaga K (2015) Immune mechanisms at the maternal-fetal interface: perspectives and challenges. Nat Immunol 16: 328-334.
- Racicot K, Kwon JY, Aldo P, Silasi M, Mor G (2014) Understanding the complexity of the immune system during pregnancy. Am J Reprod Immunol 72: 107-116.
- 7. Montoya JG, Remington JS (2008) Management of *Toxoplasma* gondii infection during pregnancy. Clin Infect Dis 47: 554-566.
- Seidman D, Hemmerling A, Smith-McCune K (2016) Emerging technologies to prevent pregnancy and sexually transmitted infections in women. Semin Reprod Med 34: 159-167.
- Kenneson A, Cannon MJ (2007) Review and meta-analysis of the epidemiology of congenital cytomegalovirus (CMV) infection. Rev Med Virol 17: 253-276.
- Walker SP, Palma-Dias R, Wood EM, Shekleton P, Giles ML (2013) Cytomegalovirus in pregnancy: to screen or not screen? BMC Pregnancy Childbirth 13: 96.
- 11. Nyholm JL, Schleiss MR (2010) Prevention of maternal cytomegalovirus infection: current status and future prospects. Int J Womens Health 2: 23-35.
- 12. Davis NL, King CC, Kourtis AP (2017) Cytomegalovirus infection in pregnancy. Birth Defects Res 109: 336-346.
- Bonalumi S, Trapanese A, Santamaria A, D'Emidio L, Mobili L (2011) Cytomegalovirus infection in pregnancy: review of the literature. J Prenat Med 5: 1-8.

- White SJ, Boldt KL, Holditch SJ, Poland GA, Jacobson RM (2012) Measles, mumps, and Rubella. Clin Obstet Gynecol 55: 550-559.
- 15. Dubey JP, Lago EG, Gennari SM, Su C, Jones JL (2012) Toxoplasmosis in humans and animals in Brazil: high prevalence, high burden of disease, and epidemiology. Parasitology 139: 1375-1424.
- Jones JL, Kruszon-Moran D, Wilson M, McQuillan G, Navin T, McAuley JB (2001) *Toxoplasma gondii* infection in the United States: seroprevalence and risk factors. Am J Epidemiol 154: 357-365.
- 17. Gilbert RE, Freeman K, Lago EG, Bahia-Oliveira LMG, Tan HK, Wallon M, Buffolano W, Stanford MR, Petersen E, for the European Multicentre Study of Congenital Toxoplasmosis (EMSCOT) (2008) Ocular sequelae of congenital toxoplasmosis in Brazil compared with Europe. PLoS Negl Trop Dis 2: e277.
- Pappas G, Russos N, Falagas ME (2009) Toxoplasmosis snapshots: Global status of *Toxoplasma gondii* seroprevalence and implications for pregnancy and congenital toxoplasmosis. Int J Parasitol 39: 1385-1394.
- 19. Silva ACAL, Rodrigues BSC, Micheletti AMR, Tostes Jr S, Meneses ACO, Silva-Vergara ML, Adad SJ (2012) Neuropathology of AIDS: An autopsy review of 284 cases from Brazil comparing the findings pre- and post-HAART (Highly Active Antiretroviral Therapy) and pre- and postmortem correlation. AIDS Res Treat 2012: 186850.
- 20. Mylonas I, Brüning A, Kainer F, Friese K (2010) HTLV infection and its implication in gynaecology and obstetrics. Arch Gynecol Obstet 282: 493-501.
- 21. Watanabe T (2011) Current status of HTLV-1 infection. Int J Hematol 94: 430-434.
- Bangham CR, Ratner L (2015) How does HTLV-1 cause adult T-cell leukaemia/lymphoma (ATL)? Curr Opin Virol 14: 93-100.
- Khan MY, Khan IN, Farman M, Al Karim S, Qadri I, Kamal MA, Al Ghamdi K, Harakeh S (2016) HTLV-1 Associated Neurological Disorders. Curr Top Med Chem 17: 1320-1330.
- 24. Murphy EL, Fridey J, Smith JW, Engstrom J, Sacher RA, Miller K, Gibble J, Stevens J, Thomson R, Hansma D, Kaplan J, Khabbaz R, Nemo G (1997) HTLV-associated myelopathy in a cohort of HTLV-I and HTLV-II-infected blood donors. Neurology 48: 315-320.
- 25. Oliveira PD, de Carvalho RF, Bittencourt AL (2017) Adult Tcell leukemia/lymphoma in South and Central America and the Caribbean: systematic search and review. Int J STD AIDS 28: 217-228.
- Instituto Brasileiro de Geografia e Estatística IBGE (2017) Population Estimates 2017, Cities – Ilhéus, Bahia, Brazil. Available: http://www.ibge.gov.br Acessed: 1 November 2017. [Article in Portuguese]
- Haberland N, Rogow D (2015) Sexuality education: emerging trends in evidence and practice. J Adolesc Health 56 Suppl 2: 15-21.
- Suárez-Varela MM, Nohr EA, Llopis-González A, Andersen AMN, Olsen J (2009) Socio-occupational status and congenital anomalies. Eur J Public Health 19: 161-167.
- 29. Suárez-Varela MM, Kaerlev L, Zhu JL, Lopís-González A, Gimeno-Clemente N, Nohr EA, Bonde JP, Olsen J (2010) Risk of infection and adverse outcomes among pregnant working women in selected occupational groups: A study in the Danish National Birth Cohort. Environ Health 9:70.

- Ornoy A, Diav-Citrin O (2006) Fetal effects of primary and secondary cytomegalovirus infection in pregnancy. Reprod Toxicol 21: 399-409.
- 31. Figueiró-Filho EA, Senefonte FRA, Lopes AHA, Morais OO, Souza Júnior VG, Maia TL, Duarte G (2007) Frequency of HIV-1, rubella, syphilis, toxoplasmosis, cytomegalovirus, simple herpes vírus, hepatitis B, hepatitis C, Chagas' disease and HTLV I/II infection in pregnant women of State of Mato Grosso do Sul. Rev Soc Bras Med Trop 40: 181-187.
- 32. Inagaki ADM, de Oliveira LAR, de Oliveira MFB, Santos RCS, Araújo RM, Alves JAB (2009) Seroprevalence of antibodies for toxoplasmosis, rubella, cytomegalovirus, syphilis and HIV among pregnant women in Sergipe. Rev Soc Bras Med Trop 42: 532-536.
- 33. Serra FC, Machado J, Nicola MH, Jorge MCAS, da Cruz LE, Giordano MV, Silva RO (2009) Seroprevalence of cytomegalovirus infection in pregnant women of socioeconomically advantaged class from Brazil. Braz J Sex Transm Dis 21: 12-15.
- 34. Steibel G, Milan C, Steibel JAP, Cunha Filho EV, Torrens MC, Stucky JM (2007) Prevalence of rubella IgG antibodies in pregnant women of São Lucas Hospital of PUCRS, Porto Alegre, Brazil. Scientia Medica 17: 115-118.
- 35. Artimos de Oliveira S, Bastos Camacho LA, Uzeda Barreto MC, Coca Velarde LG, Siqueira MM (2011) Serologic status of women in an urban population in Brazil before and after rubella immunization campaign using routine screening data. J Infect Dis 204 Suppl 2: 664-668.
- 36. Ribeiro MA, Proietti FA, Martins ML, Januário JN, Ladeira RV, Oliveira M de F, Carneiro-Proietti AB (2010) Geographic distribution of human T-lymphotropic virus types 1 and 2 among mothers of newborns tested during neonatal screening, Minas Gerais, Brazil. Rev Panam Salud Publica 27: 330-337.
- 37. Guimarães de Souza V, Lobato Martins M, Carneiro-Proietti AB, Januário JN, Ladeira RV, Silva CM, Pires C, Gomes SC, Martins CS, Mochel EG (2012) High prevalence of HTLV-1 and 2 viruses in pregnant women in São Luis, state of Maranhão, Brazil. Rev Soc Bras Med Trop 45: 159-162.
- 38. Dal Fabbro MM, Cunha RV, Bóia MN, Portela P, Botelho CA, Freitas GM, Soares J, Ferri J, Lupion J (2008) HTLV 1/2 infection: prenatal performance as a disease control strategy in State of Mato Grosso do Sul. Rev Soc Bras Med Trop 41: 148-518.
- 39. Olbrich Neto J, Meira DA (2004) Soroprevalence of HTLV-I/II, HIV, syphilis and toxoplasmosis among pregnant women seen at Botucatu - São Paulo - Brazil: risk factors for HTLV-I/II infection. Rev Soc Bras Med Trop 37: 28-32.
- Bittencourt AL, Dourado I, Filho PB, Santos M, Valadão E, Alcantara LC, Galvão-Castro B (2001) Human T-cell lymphotropic virus type 1 infection among pregnant women in northeastern Brazil. J Acquir Immune Defic Syndr 26: 490-494.
- 41. Dos Santos JI, Lopes MA, Deliège-Vasconcelos E, Couto-Fernandez JC, Patel BN, Barreto ML, Ferreira Junior OC, Galvão-Castro B (1995) Seroprevalence of HIV, HTLV-I/II and other perinatally-transmitted pathogens in Salvador, Bahia. Rev Inst Med Trop Sao Paulo 37: 343-348.
- 42. Magalhães T, Mota-Miranda AC, Alcantara LCJ, Olavarria V, Galvão-Castro B, Rios-Grassi MF (2008) Phylogenitic and molecular analysis of HTLV-1 isolates from a medium sized town in Northern of Brazil: Tracing a common origin of the virus from the most endemic city in the country. J Med Virol 80: 2040-2045.

- 43. Carneiro-Proietti AB, Catalan-Soares BC, Castro-Costa CM, Murphy EL, Sabino EC, Hisada M, Galvão-Castro B, Alcantara LC, Remondegui C, Verdonck K Proietti FA (2006) HTLV in the Americas: challenges and perspectives. Rev Panam Salud Publica 19: 44-53.
- 44. Proietti FA, Carneiro-Proietti AB, Catalan-Soares BC, Murphy EL (2005) Global epidemiology of HTLV-I infection and associated diseases. Oncogene 24: 6058-6068.
- 45. Lopes FMR, Mitsuka-Breganó R, Gonçalves DD, Freire RL, Karigyo CJT, Wedy GF, Matsuo T, Reiche EM, Morimoto HK, Capobiango JD, Inoue IT, Garcia JL, Navarro IT (2009) Factors associated with seropositivity for anti-*Toxoplasma* gondii antibodies in pregnant women of Londrina, Paraná, Brazil. Mem Inst Oswaldo Cruz 104: 378-382.
- 46. Rebouças EC, Dos Santos EL, Do Carmo ML, Cavalcante Z, Favali C (2011) Seroprevalence of Toxoplasma infection among pregnant women in Bahia, Brazil. Trans R Soc Trop Med Hyg 105: 670-671.
- 47. Fonseca AL, Silva RA, Fux B, Madureira AP, Sousa FF, Margonari C (2012) Epidemiologic aspects of toxoplasmosis and evaluation of its seroprevalence in pregnant women. Rev Soc Bras Med Trop 45: 357-364.
- 48. Moura FL, Amendoeira MR, Bastos OM, Mattos DP, Fonseca AB, Nicolau JL, das Neves LB, Millar PR (2013) Prevalence and risk factors for *Toxoplasma gondii* infection among pregnant and postpartum women attended at public healthcare

facilities in the City of Niterói, State of Rio de Janeiro, Brazil. Rev Soc Bras Med Trop 46: 200-207.

- 49. Dias RCF, Lopes-Mori FMR, Mitsuka-Breganó R, Dias RAF, Tokano DV, Reiche EMV, Freire RL, Navarro IT (2011) Factors associated to infection by *Toxoplasma gondii* in pregnant women attended in basic health units in the city of Rolândia, Paraná, Brazil. Rev Inst Med Trop Sao Paulo 53: 185-191.
- Avelino MM, Campos D Jr, Parada JB, Castro AM (2004) Risk factors for *Toxoplasma gondii* infection in women of childbearing age. Braz J Infect Dis 8: 164-174.
- Birgisdóttir A, Asbjörnsdottir H, Cook E, Gislason D, Jansson C, Olafsson I, Gislason T, Jori R, Thjodleifsson B (2006) Seroprevalence of *Toxoplasma gondii* in Sweden, Estonia and Iceland. Scand J Infect Dis 38: 625-631.

Corresponding author

Galileu Barbosa Costa, PhD Departmento de Microbiologia, Universidade Federal de Minas Gerais, Av. Presidente Antonio Carlos, 6627, Belo Horizonte, Brazil, 31270301. Phone: +553134092747 Fax: +553134092733 Email: galileuk1@gmail.com

Conflict of interests: No conflict of interests is declared.