Parasitology

cambridge.org/par

Toxoplasmosis in pregnancy: a neglected bane but a serious threat in Nigeria

Oyetunde T. Oyeyemi[1,2], Ifeoluwa T. Oyeyemi[1], Isaac A. Adesina[1], Adebisi M. Tiamiyu[1], Yinka D. Oluwafemi[1], Roseangela I. Nwuba[1] and Rafaella F. Q. Grenfell[2]

[1]Department of Biological Sciences, University of Medical Sciences, Ondo, Ondo State, Nigeria and [2]Diagnosis and Therapy of Infectious Diseases and Cancer Laboratory, René Rachou Institute, Fundação Oswaldo Cruz, Belo Horizonte, Minas Gerais, Brazil

Review

Cite this article: Oyeyemi OT, Oyeyemi IT, Adesina IA, Tiamiyu AM, Oluwafemi YD, Nwuba RI, Grenfell RF Q (2020). Toxoplasmosis in pregnancy: a neglected bane but a serious threat in Nigeria. *Parasitology* **147**, 127–134. https://doi.org/10.1017/S0031182019001525

Received: 10 August 2019
Revised: 19 September 2019
Accepted: 25 September 2019
First published online: 6 November 2019

Key words:
Adverse pregnancy outcome; Nigeria; pregnant women; toxoplasmosis.

Author for correspondence:
Oyetunde T. Oyeyemi,
E-mail: ooyeyemi@unimed.edu.ng

Abstract

Toxoplasmosis is a global health threat in which occurrence in pregnant women poses grave consequences to fetal wellbeing. Studies on prenatal *Toxoplasma gondii* infection are generally limited in sub-Saharan African countries, including Nigeria. The risk of transmission of toxoplasmosis is very high in Nigeria due to the favourable climatic conditions and prevailing behavioural and socio-economic factors that could aid transmission. Currently, there are no systematic and organized procedures for diagnosis and treatment of maternal toxoplasmosis in Nigeria. These conditions forecast possible unabated transmission in many areas and exponential impact on associated adverse events of the disease during pregnancy. This paper highlights the importance of early diagnosis and treatment during pregnancy which may forestall subsequent development of infection in children delivered by infected mothers. Inclusion of toxoplasmosis control policy in the routine antenatal care of pregnant women is therefore strongly recommended.

Introduction

Toxoplasmosis is a global health issue prevalent both in developed and developing countries. *Toxoplasma gondii*, the causal agent of toxoplasmosis, is present everywhere and can theoretically infect all warm-blooded vertebrates (Galal *et al.*, 2018). Since the first description in *Ctenodactylus gundi*, a species of rodent, in 1908 (Nicolle and Manceaux, 1908), the parasite has progressively been reported in a wide range of animals, making it one of the most wide spread zoonotic diseases (Robert-Gangneux and Dardé, 2012). In the 1960s, the sexual reproductive phase of the parasite was described in cat (Hutchison *et al.*, 1969; Dubey and Frenkel, 1972) and since then the cat has been known to play a central role in the transmission cycle of the parasite (Robert-Gangneux and Dardé, 2012). Toxoplasmosis has no restriction for boundary or race as significance of the disease has been reported in many countries of the world including the United States (11%), UK (9%), Singapore (17%), Chile (39%), China (11%), Brazil (50%), Nepal (55%) and Nigeria (78%) (Flegr *et al.*, 2014). Africa especially has become a focal point of transmission of *T. gondii* due to prevailing environmental factors and poor socioeconomic development.

While toxoplasmosis is a disease of all population strata, pregnant women and their newborns suffer most from the consequences of the disease (Bachmeyer *et al.*, 2006; Andrade *et al.*, 2009). The parasite *T. gondii* is haematogenously conveyed into the placenta to induce congenital infection in the growing foetus (Ander *et al.*, 2018). This infection can result in abortion or cause permanent disabilities or defects in surviving children (Millar *et al.*, 2014). In several cases, the outcomes of *in utero* infections by *T. gondii* include ocular disease and developmental delays (Olariu *et al.*, 2011).

This review reports the various epidemiological studies on maternal toxoplasmosis in Nigeria. Of importance is the disease contribution to maternal and fetal health and advocacy for inclusion of toxoplasmosis among prioritized diseases for routine screening during antenatal care in Nigeria and other sub-Saharan African countries.

The transmission cycle of *Toxoplasma gondii*: maternal-fetal route perspective

Hosts and vehicles

The life cycle of *T. gondii*, an obligate intracellular protozoan, is complex and involves essentially a feline definitive host e.g. domestic cats which harbour the sexual stage of the parasite, and numerous warm-blooded vertebrates as intermediate hosts for proliferation of asexual reproductive forms of the parasitic organism (Rouatbi *et al.*, 2019). Humans can become infected through ingestion of the parasite oocysts shed by felid definitive hosts, consumption of raw or undercooked meat containing tissue bradyzoites or vertically transmitted from infected pregnant woman across the placenta to the growing foetus (Tenter *et al.*, 2000; Mahmoud *et al.*, 2015).

CAMBRIDGE UNIVERSITY PRESS

Roles of placenta

In eutherian vertebrates, the primary function of the placenta is for gaseous, nutrient and waste exchange between maternal and fetal compartments. In addition, it restricts exposure of the foetus to infectious agents (Ander *et al.*, 2018). The specialized trophoblasts, syncytiotrophoblast and cytotrophoblast, which form the components of the placenta are known to form a primary barrier to the passage of pathogens that may infect the foetus by the haematogenous route (Ander *et al.*, 2018). Although these trophoblast layers play an important role in placental pathogen transmission restriction, the pathways of this restriction are still not well understood. The strategic location of trophoblasts which favours its close interaction with maternal and fetal blood has, however, inextricably favoured the parasite transmission to the foetus (Robbins *et al.*, 2012). The risk of transmission to the foetus may increase in pregnant women with the first experience of *T. gondii* infection (Tenter *et al.*, 2000). The transplacental invasion of tachyzoites and eventual penetration of fetal tissues or bloodstream may result in congenital infection (Pardini *et al.*, 2019). Common outcomes of congenital toxoplasmosis include fetal or neonatal death, defects mainly in the ocular region and neuromuscular system (Hayde and Pollak, 2000). In immunocompromised individuals, the common clinical signs are pneumonia, encephalitis and ophthalmologic disorders (Tenter *et al.*, 2000).

Epidemiology of toxoplasmosis during pregnancy

Sub-Saharan African countries perspective

Generally, more than one-third of the human population with *T. gondii* infection present an asymptomatic situation because of the roles played by the immune system (Flegr *et al.*, 2014). Toxoplasmosis could be latent when there is no overt clinical presentation of the disease but chronic infection oftentimes results in clinical symptoms (Flegr *et al.*, 2014). Several factors which include environmental and socioeconomic status are known to influence the seroprevalence of *T. gondii* which could vary from 4 to 80% in women (Lelong *et al.*, 1995; Dubey *et al.*, 2012; Lim *et al.*, 2012).

According to Uttah *et al.* (2013), 'toxoplasmosis is an epidemiological paradox; it is one of the most prevalent and most widespread parasitic infections, yet one of the most ignored of all human infections'. Lindstrom *et al.* (2006) had earlier noted that toxoplasmosis often remains undetected and untreated due to insufficient diagnostic procedures in sub-Saharan African countries. It has also been observed that toxoplasmosis is not routinely screened in pregnant women in most countries in sub-Saharan Africa (Linguissi *et al.*, 2012). Epidemiological studies available in different sub-Saharan African countries, however, suggest that seroprevalence of *T. gondii* infection in pregnant women varies greatly (Table 1).

The seroprevalence of *T. gondii* among pregnant women in sub-Saharan Africa ranges from 5.9 to 85.4%. A considerable variation in the incidence of *T. gondii* among pregnant women in sub-Saharan Africa may be ascribed to food (consumption of raw or undercooked meats or contaminated water) and environmental sources (exposure to soil or cat litter) (Elmore *et al.*, 2010; Walle *et al.*, 2013).

Unlike malaria and other infectious diseases, studies on maternal toxoplasmosis are relatively scarce in sub-Saharan African countries. The research neglect on this parasitic disease is detrimental considering its burden on pregnant women and their growing foetuses. All the regions of sub-Saharan Africa are at risk with the Central African countries showing the highest seroprevalence of maternal toxoplasmosis (Fig. 1). Data on Southern African countries are limited; therefore the seroprevalence presented in this review may significantly deviate from the true infection status in the region. The higher occurrence of toxoplasmosis in the Central and East Africa countries may be due to their geographical locations. Many of the countries in these regions are located along the equator and therefore receive maximum rainfall and sunshine. An increase in temperature and rainfall has been linked to an increase in transmission of *T. gondii* among pregnant women. A positive correlation has been reported between the prevalence of toxoplasmosis in pregnant women and the average annual temperature in the corresponding area (Ljungström *et al.*, 1995). Terrestrial animals such as rodents thrive in warmer temperature and an increase in their population makes them prone to predation by cats, dogs and pigs (Jiang *et al.*, 2012). Thus, higher temperatures may afford these hosts the opportunity to increase the transmission dynamics of *T. gondii* and extend its range of distribution (Gubler *et al.*, 2001). Rain, on the other hand, helps to create a moist environment for oocysts' survival and increase food supply to the rodent hosts (Gubler *et al.*, 2001; Afonso *et al.*, 2013). Increased incidence of *T. gondii* infection in felids has also been linked to increasing rainfall (Afonso *et al.*, 2010).

Ethiopia recorded the highest seroprevalence (85.5%) of maternal toxoplasmosis in the sub-Saharan Africa region (Gelaye *et al.*, 2015) and no study elsewhere in the world has recorded such high prevalence in the recent times among pregnant women. It is difficult to monitor transmission patterns or dynamics in pregnant women in sub-Saharan Africa because some countries experienced relatively stable transmission patterns while others showed a gradual increase or decrease from the 1990s to 2000s. In other instances, the transmission was rather sporadic. In Republic of Benin for example, a gradual decrease from 53.6 to 48.7% was recorded (Rodier *et al.*, 1995; Ogouyèmi-Hounto *et al.*, 2014) while the reverse situation was recorded in Burkina Faso i.e. an increase from 25.3% in 2006 to 31.1% in 2017 (Simpore *et al.*, 2006; Bamba *et al.*, 2017). In Cameroon, transmission dynamics among pregnant women showed no particular pattern while in Central Republic of Africa and Nigeria (after the 78% seroprevalence report by Onadeko *et al.*, 1992), transmission appeared to be stable (Morvan *et al.*, 1999; Akinbami *et al.*, 2010; Gamba *et al.*, 2013; Nasir *et al.*, 2015; Oboro *et al.*, 2016). The transmission trend observed in these countries is attributed to the peculiar features of each study area, behavioural attitudes and exposure to risk factors of transmission of *T. gondii*. Some countries such as Somalia and Togo where there are no records of maternal toxoplasmosis were found, however, to have recorded seroprevalence of toxoplasmosis in other population groups (Ahmed *et al.*, 1988; Tété-Bénissan *et al.*, 2018), thus suggesting a risk of transmission of *T. gondii* to pregnant women.

Toxoplasmosis in pregnancy: the Nigerian picture

It is certain that toxoplasmosis research and management priority is given relatively little attention compared to other parasitic diseases such as malaria. The little attention it has received is as a result of the risk toxoplasmosis poses in congenital infection. In Nigeria, the situation is worse as very few studies have addressed toxoplasmosis during pregnancy. Despite this obvious neglect, the Nigerian current situation on toxoplasmosis during pregnancy seems better than that of parasitic diseases such as schistosomiasis (Salawu and Odaibo, 2013, 2014). This is understandable as the status of the latter in congenital infection is yet to be fully ascertained. The diagnostic problem associated with toxoplasmosis could be responsible for the relative lack of data in Nigeria. Most of the studies employed the use of ELISA serological assay to determine anti-*T. gondii* immunoglobulin G (IgG) which involves some technicality and power supply.

https://doi.org/10.1017/S0031182019001525 Published online by Cambridge University Press

Table 1. Seroprevalence of toxoplasmosis in pregnant women in sub-Saharan Africa

Countries	Prevalence	Sample size	Reference
Angola	23.7	300	Lobo *et al.* (2017)
Benin	48.7	266	Ogouyèmi-Hounto *et al.* (2014)
Burkina Faso	31.1	316	Bamba *et al.* (2017)
Cameroon	29.5	200	Todjom *et al.* (2019)
Central African Republic	51.0	434	Gamba *et al.* (2013)
Côte d'Ivoire	60.0	1025	Adou-Bryn *et al.* (2004)
Democratic Republic of Congo	80.3	781	Doudou *et al.* (2014)
Ethiopia	32.5	360	Teweldemedhin *et al.* (2019)
Gabon	57.4	973	Moukandja *et al.* (2017)
Ghana	51.2	125	Ayi *et al.* (2016)
Kenya	22.0	NA	Kamau *et al.* (2012)
Madagascar	83.5	599	Lelong *et al.* (1995)
Mozambique	18.7	150	Sitoe *et al.* (2010)
Niger	15.1	218	Develoux *et al.* (1989)
Nigeria	42.4	288	Oboro *et al.* (2016)
Rwanda	9.6	384	Murebwayire *et al.* (2017)
Sao Tome and Principe	75.2	499	Hung *et al.* (2007)
Senegal	22.0	109	Ndiaye *et al.* (2007)
South Africa	22.3	2308	Capretti *et al.* (2014)
Sudan	20.1	163	Abdel-Raouff and Elbasheir (2014)
Tanzania	40.2	254	Paul *et al.* (2018)
Zambia	5.9	411	Frimpong *et al.* (2017)

Note: Seroprevalence is determined as a measure of chronic infection i.e. total serum anti-*Toxoplasma* IgG.

There are currently 17 reported studies on maternal toxoplasmosis in five geopolitical zones of Nigeria. From the first report in 1992 (Onadeko *et al.*, 1992) (Table 2), five other studies have been reported in the southwestern part of Nigeria. The south-south and the north-central regions have only reported two studies each on toxoplasmosis during pregnancy while three and four studies have been linked to the north-east and north-west regions of Nigeria respectively. Currently, there is no report on toxoplasmosis during pregnancy in the southeastern part of Nigeria. This is, however, not appropriate considering the demand for meat and probable environmental conditions of the region which could favour transmission of the causal agent of the disease.

Generally, the seroprevalence of maternal toxoplasmosis is higher in the southern than in the northern part of Nigeria (Fig. 2). This discrepancy in occurrence may be due to the differences in the meat consumption level in the regions. The southerners are known to consume more meat than the northerners and

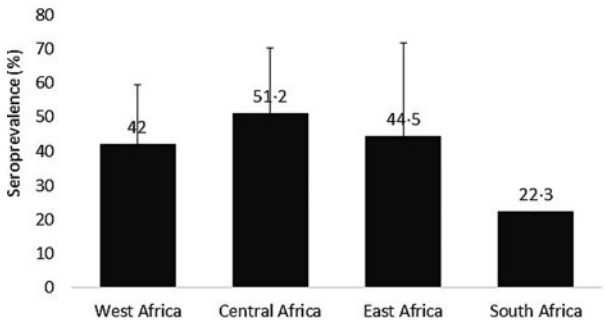

Fig. 1. Seroprevalence of maternal toxoplasmosis by sub-Saharan African regions. *Note*: Data computed from all available literature from 1980 to date.

they also relish some meat types such as pork and chicken which are natural hosts of *T. gondii* thus increasing their exposure to *T. gondii*. Another probable explanation is the environmental conditions that favour the development of unsporulated oocysts of the parasite. The extreme temperature and decrease relative humidity of the north (Eludoyin *et al.*, 2014) can make the unsporulated oocysts of *T. gondii* to be less environmentally resistant (Meerburg and Kijlstra, 2009) thereby decreasing its infectivity. The seroprevalence of *T. gondii* in Northern Nigeria is, however, high enough to merit adequate intervention in the region. The significant occurrence of toxoplasmosis in the region has been attributed to the people's love for pets, especially cats which are the definitive host of the parasite (Nasir *et al.*, 2015). A significant relationship between the transmission of toxoplasmosis and contact with domestic cats has been widely reported (Lin *et al.*, 2008; Zemene *et al.*, 2012).

There has been a decline in the incidence and prevalence of maternal toxoplasmosis in Nigeria since the early 1990s (Fig. 3). However, this decline is not *per se* as a result of a good alert system or management policy in pregnant women. It is more likely to be associated with the peculiarity of the locations and the study population.

Congenital toxoplasmosis and adverse pregnancy outcomes

The general overview

Congenital toxoplasmosis, with the global annual incidence of 190 100 cases (Torgerson and Mastroiacovo, 2013), is a major health problem resulting in severe burdens for those affected from foetus to adulthood (Carlier *et al.*, 2012). Maternal transmission is a rare occurrence if *T. gondii* infection occurs before pregnancy (Silveira *et al.*, 2003) but the risk becomes increased in immunocompromised women (Montoya and Remington, 2008). It is important to state that not all acute maternal infection will result in congenital disease (Carlier *et al.*, 2012). Other factors besides the mother's immunity that influence the likelihood of vertical transmission from mothers to their foetuses include the genotype of the mother, gestational age at the time of infection, the genetic make-up of the parasite and its virulence (Carlier *et al.*, 2012; Halonen and Weiss, 2013).

Congenital infection due to vertical transmission of toxoplasmosis is generally lower in the early gestational age i.e. first trimester (10–15%) compared to that found in the third trimester (60–90%). However, a more severe disease occurs during infection in the first trimester (Hernández-Cortazar *et al.*, 2015). The adverse pregnancy outcomes associated with *T. gondii* infection during the first trimester include abortion, stillbirth and premature birth (Chaudhry *et al.*, 2014). If the pregnancy is successfully maintained, neonatal deformation as a result of infection may cause a wide range of clinical morbidities such as blindness,

https://doi.org/10.1017/S0031182019001525 Published online by Cambridge University Press

Table 2. Seroprevalence studies on maternal toxoplasmosis in Nigeria

Year	Seroprevalence (%)	Sample size	Reference
1992	78.0	352	Onadeko *et al.* (1992)
1996	43.7	466	Olusi *et al.* (1996)
2009	29.1	374	Ishaku *et al.* (2009)
2010	40.8	179	Akinbami *et al.* (2010)
2011	32.6	276	Deji-Agboola *et al.* (2011)
2013	27.7	173	Alayande *et al.* (2013)
2014	26.8	179	Awobode and Olubi (2014)
2015	40.0	360	Nasir *et al.* (2015)
2016	65.6	288	Oboro *et al.* (2016)
2017	28.0	400	Ballah *et al.* (2017)
2018	30.44	391	Olusi *et al.* (2018)

heart and brain defects, neurological damage, chorioretinitis, mental retardation and death (Chaudhry *et al.*, 2014). Abortion is usually a rare occurrence if maternal infection occurs in the third trimester. Congenital infection in newborns infected in the last trimester usually goes unnoticed at birth but chorioretinitis develops in the child later in life (Carlier *et al.*, 2012).

As earlier mentioned, pre-pregnancy exposure to *T. gondii* poses little or no risk to the unborn child even in the case of re-infection during pregnancy, if the mother is infected with the same strain. However, few studies have reported possibilities of reactivation of the disease during pregnancy, sometimes from different and more strains, which could result in adverse pregnancy outcomes (Garweg *et al.*, 2005; Carlier *et al.*, 2012). This reactivation is often known to be initiated by the cystic form of the parasite (Borges *et al.*, 2019). In summary, the majority of available evidence suggests that previous maternal infection confers protection against vertical transmission of *T. gondii* but alteration in systemic immunity as a result of hormonal changes in some pregnancies can lead to toxoplasmosis activation which can result in transplacental transmission of the *T. gondii* to the growing foetus (Opsteegh *et al.*, 2015).

Congenital toxoplasmosis in Nigeria and adverse outcomes

Despite the growing body of evidence on potential adverse pregnancy outcomes associated with *T. gondii* maternal infection, available data on the subject are extremely scanty in Nigeria. A case report correlated an occurrence of cyst of *T. gondii* in the brain of a 17-month old child (found by using computed tomography scan) with *Toxoplasma* IgG (Amadi *et al.*, 2015). The mother's medical history during pregnancy revealed premature birth and the visible signs of toxoplasmosis in the child such as microcephaly and retarded growth indicated that the child might have acquired a congenital infection. A retrospective epidemiological study in the northern part of Nigeria also identified abortion (41.6%), stillbirth (61.5%) and neonatal death (62.5%) as common adverse events associated with maternal *T. gondii* infection (Alayande *et al.*, 2013). Oboro *et al.* (2016) reported 25% previous stillbirth or miscarriage occurrence in pregnant women positive to anti-*Toxoplasma* specific antibodies in Port Harcourt in the south-south region of Nigeria. In Lagos, a southwestern city, 23.8, 15.4 and 29.4% were reported for miscarriage, stillbirth

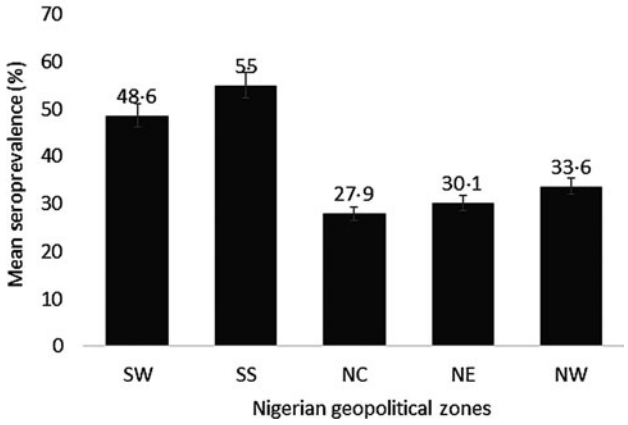

Fig. 2. Mean seroprevalence of toxoplasmosis during pregnancy in geopolitical zones of Nigeria.
Note: SW, south-west; SS, south-south; NC, north-central; NE, north-east; NW, north-west.

and ocular problem in pregnant women who were seropositive to *T. gondii* antibodies (Deji-Agboola *et al.*, 2011) respectively. In Gombe, another northern state, spontaneous abortion was as high as 60% in *T. gondii*-infected pregnant women while stillbirth and placental retentions were 6.8 and 10.4%, respectively (Ballah *et al.*, 2017). These studies suggest that although seroprevalence is higher in the south than in the north, adverse events associated with maternal infection seem to be more serious in the north than in the south. There might therefore be other factors that could be responsible for increased adverse events in the north in addition to maternal *T. gondii* infection during pregnancy. The influence of other reproductive health associated pathogens, low level of education and poor medical practices are suggested.

Toxoplasma gondii transmission and immune interplay during pregnancy

Trophoblast cells are the main barriers for preventing *T. gondii* infection of foetus during pregnancy. However, the mechanisms that underline successful fetal infection despite these effective barriers are still not fully understood. It has been hypothesized that the switch from T helper (Th)-1 which is the normal immune response pathway associated with *Toxoplasma* infection to the (Th)-2 pathway as a result of the richness of placental microenvironment in interleukin 10 (IL-10) could promote infection of placental tissue (Barbosa *et al.*, 2008). The role of interferon-γ (IFN-γ), which is the major cytokine for (Th)-1 immune response in *T. gondii* infection-associated immune effectors during pregnancy in congenital toxoplasmosis, has also been described (Pfaff *et al.*, 2007). For example in an experimental mouse model, IFN-γ production in response to *T. gondii* infection-induced abortion in pregnant mice but not in pregnant mice where IFN-γ producing gene was knocked out (Shiono *et al.*, 2007). Further to this, an *in vitro* study showed that IFN-γ upregulates the expression of certain molecule known as intercellular adhesion molecule (ICAM)-1 adhesin that lines the surface of trophoblasts, thus, enhancing the adhesion of infected monocytes (Pfaff *et al.*, 2007). Placental inflammation leads to overexpression of ICAM-1 (Juliano *et al.*, 2006) and eventual transepithelial transportation of the parasites (Barragan *et al.*, 2005).

The unique ability of placental cells to select human leucocyte antigen-G which may modulate the local maternal immune response to favour infection tolerance could compensate for the deleterious effect that *T. gondii* infection may induce during pregnancy (Hunt *et al.*, 2005).

https://doi.org/10.1017/S0031182019001525 Published online by Cambridge University Press

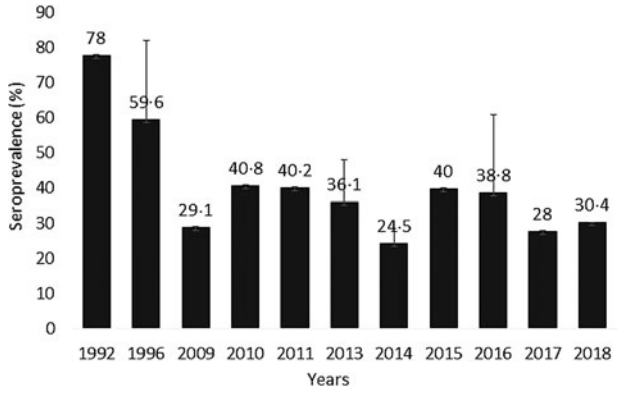

Fig. 3. Incidence of *T. gondii* maternal infection in Nigeria (1992–2018).

Diagnosis and treatment hurdles

Diagnostic options

Generally, early detection of infection during pregnancy and administration of appropriate treatment has been shown both to reduce risk of transplacental transmission of *T. gondii* to the foetus and to mitigate eventual sequelae after the intrauterine infection has already been established (Stray-Pedersen, 1992). It has always been challenging to diagnose congenital toxoplasmosis accurately because a combination of skills in epidemiological, clinical, laboratory and imaging analyses is required (Soares and Caldeira, 2019). Because toxoplasmosis is not a prioritized disease in sub-Saharan African countries including Nigeria, health care providers are yet to define a systematic approach and procedures for administering proper diagnosis of the disease. In Nigeria and other places in the world, the first line of diagnosis is the detection of anti-*Toxoplasma* specific antibodies IgG and IgM which are serological markers of infection. Differentiating acute from chronic infection is one of the greatest challenges in the diagnosis of toxoplasmosis (Chaudhry *et al.*, 2014). Although anti-*Toxoplasma* specific IgM antibodies clear out faster in the circulation than the IgG antibodies, they may remain detectable for years thus posing a difficulty in the diagnosis of congenital infection (Stray-Pedersen, 1993). The absence of these two antibodies before or in the first trimester of pregnancy depicts no previous infection and this is very useful in identifying women at risk of maternal infection during pregnancy (Hedman *et al.*, 1989). The presence of only anti-*Toxoplasma* specific IgG antibodies but without IgM antibodies signifies that a chronic infection is diagnosed (Chaudhry *et al.*, 2014). Interpretation of results, however, becomes difficult when serum tests positive for the two antibodies as the results might be due to either a low IgM titre from a previous infection or a recent infection (Jenum *et al.*, 1998).

Recently, attention has been paid to development of point-of-care (POC) tests to detect *Toxoplasma* infection. This testing method offers the advantage of being able to detect both *Toxoplasma*-specific IgG and IgM simultaneously. Lateral flow immunochromatography-based *Toxoplasma* ICT IgG–IgM test has been employed to diagnose *T. gondii* infection in both sera and whole blood samples with sensitivity and specificity ranging from 96 to 100% (Begeman *et al.*, 2017; Chapey *et al.*, 2017; Lykins *et al.*, 2018). The use of whole blood for POC diagnosis has especially been advocated in low-resource settings as it is less invasive and requires no sophisticated tools and electricity. POC testing can expand access to prenatal toxoplasmosis screening, and facilitate the screening of other congenital infections. This will improve the overall maternal and fetal health (Lykins *et al.*, 2018).

Serologic methods are not reliable for the diagnosis of toxoplasmosis in HIV/AIDS or immunosuppressed patients due to a decline in specific antibodies production. Thus, for toxoplasmosis-suspected immunocompromised patients, it is recommended that other diagnostic methods be used to confirm the true infection status. These methods can include the use of polymerase chain reaction (PCR) for amplification of the parasite DNA, parasite isolation from blood or body fluids, and histologic examination of available tissues with *T. gondii*-specific stains (Montoya, 2002). PCR has been reported to have a sensitivity and specificity of about 100% when used to confirm the detection of infection in amniotic fluid samples (Hohfeld *et al.*, 1994).

Treatment and associated hurdles

In previous decades, little was known about the effectiveness of available treatment options for congenital toxoplasmosis. This deficiency was partly due to the fact that maternal infection could only be identified by screening and studies on treatment efficacy could only be conducted in places where antenatal screening for toxoplasmosis is a routine practice (Gilbert, 2009). Also, the treatment efficacy of chemotherapy was linked to *T. gondii* short 'therapeutic window' when treatment can be effective on tachyzoites. According to Gilbert (2009), 'the window is limited by the duration of maternal parasitaemia, which probably ceases with the development of the maternal serological response'. Once in circulation, the therapeutic window of the parasite depends on how efficient the immune response of the foetus is able to potentiate the formation of cystic dormant bradyzoite which is resistant to antibiotics (Denkers and Gazzinelli, 1998). The maturation of fetal immunity is expected to be correlated with a shorter 'window' of tachyzoite replication and conversion to bradyzoite (Jamieson *et al.*, 2008). The implication of these in treatment is that early administration of chemotherapy after seroconversion might undermine treatment effectiveness (The SYROCOT Study Group, 2007). Although seroconversion in *T. gondii* plays an important role in treatment outcome depending on when it is administered, treatment failure could also be due to the invading parasite strain whether resistant or susceptible to drug treatment.

The correlation of window of therapy with lower treatment success by Gilbert (2009) has been largely underplayed giving more recent clinical evidence in different parts of the world. Several observational studies have confirmed that early maternal screening and treatment demonstrated significant impact in reducing *T. gondii* vertical transmission and prevented subsequent morbidities in babies and growing children (Li *et al.*, 2014). A significant reduction in maternal infection from 11 to 4% after amniotic fluid testing by PCR and subsequent treatment in France (Wallon *et al.*, 2013), and a 6-fold lower risk of vertical transmission in Austria after antepartum treatment (Prusa *et al.*, 2015) are important evidence to correlate prenatal treatment with lower risk of congenital infection. Unlike some developed countries that provide universal screening of pregnant women for congenital toxoplasmosis, such screening is uncommon in health service providers' centres in Nigeria.

It is important to note that only one clinical controlled drug trial study has been conducted so far for congenital toxoplasmosis. The study showed no significant difference in perinatal outcomes in spiramycin *vs* pyrimethamine + sulphadiazine groups (Mandelbrot *et al.*, 2018). The lack of power due to premature termination of study before reaching the expected sample size was the major limitation of the study. The reason there have been no trials (until the recent well-structured trial) is that the lack of equipoise would render most trials unethical. Presently, treatment recommendations from experienced experts are advocated. A combination of pyrimethamine, sulphadiazine and folinic acid is the recommended treatment regimen for pregnant

https://doi.org/10.1017/S0031182019001525 Published online by Cambridge University Press

women who are infected with *T. gondii* after 18 weeks of pregnancy. The same treatment is recommended for those with already established fetal infection confirmed by amniotic fluid PCR positive result or ultrasound result revealing consistent fetal deformities characteristics of congenital toxoplasmosis (Remington *et al.*, 2006). The basis for this recommended treatment strategy is particularly to eliminate fetal infection and prevent transmission in women especially in low resources countries where the diagnosis of amniotic fluid by PCR may not be feasible.

Conclusion

Considering the prevailing risk factors of toxoplasmosis in Nigeria, and the high prevalence level reported in many regions, it is evident that pregnant women are equally predisposed to the disease. However, the available reports in Nigeria on pregnant women showed that this disease is neglected. This is unsafe considering the deleterious impact of maternal toxoplasmosis on growing foetus. It is therefore important to gather more evidence on the prevalence of maternal toxoplasmosis in Nigeria, especially with the limited scopes of most of the currently available literature. Better designed baseline data of the disease occurrence in human, animals, food, soil and water are strongly recommended for an informed decision on control strategies.

Rational control of the disease requires a prompt and effective diagnosis, and early treatment during pregnancy. Prenatal treatment is likely to have a greater impact on the disease burden and its clinical manifestations than treatment after birth. A diagnostic option that will evade the common challenges in low resource countries such as Nigeria is recommended. Therefore, a POC diagnostic tool that will not require electricity and easy to perform can help for quick detection of *T. gondii* during pregnancy.

It is also important to state that owing to the significant burden of the disease on women and their foetuses, a comprehensive data-based information on maternal toxoplasmosis will facilitate the formation of a control plan that will subsequently be integrated into the public health policies of Nigeria.

References

Abdel-Raouff M and Elbasheir MM (2014) Sero-prevalence of *Toxoplasma gondii* infection among pregnant women attending antenatal clinics in Khartoum and Omdurman Maternity Hospitals, Sudan. *Journal of Coastal Life Medicine* **2**, 496–499.

Adou-Bryn KD, Ouhon J, Nemer J, Yapo CG and Assoumou A (2004) Serological survey of acquired toxoplasmosis in women of child-bearing age in Yopougon (Abidjan, Côte d'Ivoire). *Bulletin de la Société de Pathologie Exotique* **97**, 345–348.

Afonso E, Thulliez P and Gilot-Fromont E (2010) Local meteorological conditions, dynamics of seroconversion to *Toxoplasma gondii* in cats (*Felis catus*) and oocyst burden in a rural environment. *Epidemiology and Infection* **138**, 1105–1113.

Afonso E, Germain E, Poulle ML, Ruette S, Devillard S, Say L, Aubert D and Gilot-Fromont E (2013) Environmental determinants of spatial and temporal variations in the transmission of *Toxoplasma gondii* in its definitive hosts. *International Journal of Parasitology: Parasites and Wild Life* **2**, 278–285.

Ahmed HJ, Mohammed HH, Yusuf MW, Ahmed SF and Huldt G (1988) Human toxoplasmosis in Somalia. Prevalence of *Toxoplasma* antibodies in a village in the lower Scebelli region and in Mogadishu. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **82**, 330–332.

Akinbami A, Adewunmi AA, Rabiu KA, Wright KO, Dosunmu AO, Dada MO and Adeyemo TA (2010) Seroprevalence of *Toxoplasma gondii* antibodies amongst pregnant women at Lagos State University Teaching Hospital. *International Journal of Infectious Diseases* **14**, e288.

Alayande MO, Edungbola LD, Fabiyi JP and Awosan KJ (2013) Occurrence of antibody to *Toxoplasma* infection among pregnant women with obstetric histories and at different trimesters in Sokoto, Northwest Nigeria. *American Journal of Research Communication* **1**, 240–247.

Amadi OF, Ndu IK, Chinawa JM, Jean NC and Obidi NO (2015) Toxoplasmosis in a 17-month-old Nigerian: a case report. *Annals of Tropical Medicine and Public Health* **8**, 64–66.

Ander SE, Rudzki EN, Arora N, Sadovsky Y, Coyne CB and Boyle JP (2018) Human placental syncytiotrophoblasts restrict *Toxoplasma gondii* attachment and replication and respond to infection by producing immunomodulatory chemokines. *MBio* **9**, 1–14.

Andrade GM, Vasconcelos-Santos DV, Carellos EV, Romanelli RM, Vitor RW, Carneiro AC and Januario JN (2009) Congenital toxoplasmosis from a chronically infected woman with reactivation of retinochoroiditis during pregnancy – an underestimated event? *Jornal de Pediatria* **86**, 85–88.

Awobode HO and Olubi IC (2014) Prevalence of *Toxoplasma gondii* and HIV infection among pregnant women in Ibadan North Local Government, Oyo State. *African Journal of Medicine and Medical Sciences* **43**(suppl.), 39–45.

Ayi I, Sowah AO, Blay EA, Suzuki T, Ohta N and Ayeh-Kumi PF (2016) *Toxoplasma gondii* infections among pregnant women, children and HIV-seropositive persons in Accra, Ghana. *Tropical Medicine and Health* **44**, 1–8. doi:10.1186/s41182-016-0018-5.

Barbosa BF, Silva DA, Costa IN, Mineo JR and Ferro EA (2008) Bewo trophoblast cell susceptibility to *Toxoplasma gondii* is increased by interferon-gamma, interleukin-10 and transforming growth factor-beta1. *Clinical & Experimental Immunology* **151**, 536–545.

Bachmeyer C, Mouchnino G, Thulliez P and Blum L (2006) Congenital toxoplasmosis from an HIV-infected woman as a result of reactivation. *Journal of Infection* **52**, 55–57.

Ballah FM, Maikai BV, Magaji AA, Shuaibu AB, El-Nafaty AU, Sambo YT, Auwal AA, Faruk HU and Suleiman F (2017) Seroprevalence and risk of *Toxoplasma gondii* infection among pregnant women at Federal Teaching Hospital Gombe, Nigeria. *Asian Journal of Medicine and Health* **3**, 1–5.

Bamba S, Cissé M, Sangaré I, Zida A, Ouattara S and Guiguemdé RT (2017) Seroprevalence and risk factors of *Toxoplasma gondii* infection in pregnant women from Bobo Dioulasso, Burkina Faso. *BMC Infectious Diseases* **17**, 482.

Barragan A, Brossier F and Sibley LD (2005) Transepithelial migration of *Toxoplasma gondii* involves an interaction of intercellular adhesion molecule 1 (ICAM-1) with the parasite adhesin MIC2. *Cellular Microbiology* **7**, 561–568.

Begeman IJ, Lykins J, Zhou Y, Lai BS, Levigne P, El Bissati K, Boyer K, Withers S, Clouser F, Noble AG, Rabiah P, Swisher CN, Heydemann PT, Contopoulos-Ioannidis DG, Montoya JG, Maldonado Y, Ramirez R, Press C, Stillwaggon E, Peyron F and McLeod R (2017) Point-of-care testing for *Toxoplasma gondii* IgG/IgM using toxoplasma ICT IgG-IgM test with sera from the United States and implications for developing countries. *PLoS Neglected Tropical Diseases* **11**, e0005670. https://doi.org/10.1371/journal.pntd.0005670.

Borges M, Silva TM, Brito C, Teixeira N and Roberts CW (2019) How does toxoplasmosis affect the maternal-fetal immune interface and pregnancy? *Parasite Immunology* **41**, 1–11, e12606.

Capretti MG, De Angelis M, Tridapalli E, Orlandi A, Marangoni A, Moroni A, Guerra B, Arcuri S, Marsico C and Faldella G (2014) Toxoplasmosis in pregnancy in an area with low seroprevalence: is prenatal screening still worthwhile? *The Pediatric Infectious Disease Journal* **33**, 5–10.

Carlier Y, Truyens C, Deloron P and Peyron F (2012) Congenital parasitic infections: a review. *Acta Tropica* **121**, 55.

Chapey E, Wallon M and Peyron F (2017) Evaluation of the LDBIO point of care test for the combined detection of toxoplasmic IgG and IgM. *Clinica Chimica Acta* **464**, 200–201.

Chaudhry SA, Gad N and Koren G (2014) Toxoplasmosis and pregnancy. *Canadian Family Physician* **60**, 334–336.

Deji-Agboola AM, Busari OS, Osinupebi OA and Amoo AO (2011) Seroprevalence of *Toxoplasma gondii* antibodies among pregnant women attending Antenatal Clinic of Federal Medical Center, Lagos, Nigeria. *International Journal of Biological and Medical Research* **2**, 1135–1139.

Develoux M, Chandenierj J and Tinni A (1989) Toxoplasmosis in pregnant women in Niamey (Niger). *Bulletin de la Société de Pathologie Exotique* **82**, 406–409.

Doudou Y, Renaud P, Coralie L, Jacqueline F, Hypolite S, Hypolite M, Patrick M, Andreia Ida L, Van Sprundel M, Marleen B, Van Geertruyden JP and Pascal L (2014) Toxoplasmosis among pregnant

https://doi.org/10.1017/S0031182019001525 Published online by Cambridge University Press

women: high seroprevalence and risk factors in Kinshasa, Democratic Republic of Congo. *Asian Pacific Journal of Tropical Biomedicine* **4**, 69–74..

Denkers EY and Gazzinelli RT (1998) Regulation and function of T-cell mediated immunity during *Toxoplasma gondii* infection. *Clinical Microbiology Reviews* **11**, 569–588.

Dubey JP and Frenkel JK (1972) Cyst-induced toxoplasmosis in cats. *Journal of Protozoology* **19**, 155–177.

Dubey JP, Tiao N, Gebreyes WA and Jones JL (2012) A review of toxoplasmosis in humans and animals in Ethiopia. *Epidemiology and Infection* **140**, 1935–1938.

Elmore SA, Jones JL, Conrad PA, Patton S, Lindsay DS and Dubey JP (2010) *Toxoplasma gondii*: epidemiology, feline clinical aspects, and prevention. *Trends in Parasitology* **26**, 190–196.

Eludoyin OM, Adelekan IO, Webster R and Eludoyin AO (2014) Air temperature, relative humidity, climate regionalization and thermal comfort of Nigeria. *International Journal of Climatology* **34**, 2000–2018.

Frimpong C, Makasa M, Sitali L and Michelo C (2017) Seroprevalence and determinants of toxoplasmosis in pregnant women attending antenatal clinic at the university teaching hospital, Lusaka, Zambia. *BMC Infectious Disease* **17**, 1–8.

Flegr J, Prandota J, Sovičková M and Israili ZH (2014) Toxoplasmosis – a global threat. Correlation of latent toxoplasmosis with specific disease burden in a set of 88 countries. *PLoS ONE* **9**, 1–22.

Galal L, Ajzenberg D, Hamidović A, Durieux MF, Dardé ML and Mercier A (2018) *Toxoplasma* and Africa: one parasite, two opposite population structures. *Trends in Parasitology* **34**, 140–154. https://doi.org/10.1016/j.pt.2017.10.010.

Gamba EP, Nambei WS and Kamandji L (2013) Integrated screening for HIV, syphilis, and toxoplasmosis among pregnant women in the Central African Republic. *Médecine et Santé Tropicales* **23**, 421–426.

Garweg JG, Scherrer J, Wallon M, Kodjikian L and Peyron F (2005) Reactivation of ocular toxoplasmosis during pregnancy. *BJOG: An International Journal of Obstetrics & Gynaecology* **112**, 241–242.

Gelaye W, Kebede T and Hailu A (2015) High prevalence of anti-*Toxoplasma* antibodies and absence of *Toxoplasma gondii* infection risk factors among pregnant women attending routine antenatal care in two Hospitals of Addis Ababa, Ethiopia. *International Journal of Infectious Diseases* **34**, 41–45.

Gilbert R (2009) Treatment for congenital toxoplasmosis: finding out what works. *Memórias do Instituto Oswaldo Cruz* **104**, 305–311.

Gubler DJ, Reiter P, Ebi KL, Yap W, Nasci R and Patz JA (2001) Climate variability and change in the United States: potential impacts on vector- and rodent-borne diseases. *Environmental Health Perspectives* **109**, 223–233.

Halonen SK and Weiss LM (2013) Toxoplasmosis. *Handbook of Clinical Neurology* **114**, 125–145.

Hayde M and Pollak A (2000) Clinical picture. Neonatal signs and symptoms. Congenital toxoplasmosis. pp. 153–164.

Hedman K, Lappalainen M, Seppäiä I and Mäkelä O (1989) Recent primary *Toxoplasma* infection indicated by a low avidity of specific IgG. *Journal of Infectious Diseases* **159**, 736–740.

Hernández-Cortazar I, Acosta-Viana KY, Ortega-Pacheco A and Guzman-Marin ES (2015) Review. Toxoplasmosis in Mexico: epidemiological situation in humans and animals. *Revista do Instituto de Medicina Tropical de São Paulo* **57**, 93–103.

Hohfeld P, Daffos F, Costa J, Thulliez P, Forestier F and Vidaud M (1994) Prenatal diagnosis of congenital toxoplasmosis with a polymerase chain reaction test on amniotic fluid. *New England Journal of Medicine* **331**, 695–699.

Hung CC, Fan CK, Su KE, Sung FC, Chiou HY, Gil V, da Conceicao dos Reis Ferreira M, de Carvalho JM, Cruz C, Lin YK, Tseng LF, Sao KY, Chang WC, Lan HS and Chou SH (2007) Serological screening and toxoplasmosis exposure factors among pregnant women in the Democratic Republic of Sao Tome and Principe. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **101**, 134–139.

Hunt JS, Petroff MG, McIntire RH and Ober C (2005) HLA-G and immune tolerance in pregnancy. *FASEB Journal* **19**, 681–693.

Hutchison WM, Dunachie JF, Siim JC and Work K (1969) Life cycle of *Toxoplasma gondii*. *British Medical Journal* **4**, 806.

Ishaku BS, Ajogi I, Umoh JU, Lawal I and Randawa AJ (2009) Seroprevalence and risk factors for *Toxoplasma gondii* infection among antenatal women in Zaria, Nigeria. *Research Journal of Medical Sciences* **4**, 483–488.

Jamieson SE, de Roubaix LA, Cortina-Borja M, Tan HK, Mui EJ, Cordell HJ, *et al.* (2008) Genetic and epigenetic factors at COL2A1 and ABCA4 influence clinical outcome in congenital toxoplasmosis. *PLoS ONE* **3**, e2285.

Jenum PA, Stray-Pedersen B, Melby KK, Kapperud G, Whitelaw A, Eskild A and Enj J (1998) Incidence of *Toxoplasma gondii* infection in 35,940 pregnant women in Norway and pregnancy outcome for infected women. *Journal of Clinical Microbiology* **36**, 2900–2906.

Jiang W, Sullivan AM, Su C and Zhao X (2012) An agent-based model for the transmission dynamics of *Toxoplasma gondii*. *Journal of Theoretical Biology* **293**, 15–26.

Juliano PB, Blotta MH and Altemani AM (2006) ICAM-1 is overexpressed by villous trophoblasts in placentitis. *Placenta* **27**, 750–757.

Kamau P, Jaoko W and Gontier C (2012) Seroepidemiology of *Toxoplasma gondii* in ante-natal women attending Kenyatta National Hospital, Kenya. *International Journal of Infectious Diseases* **16**, e162.

Lelong B, Rahelimino B, Candolfi E, Ravelojaona BJ, Villard O and Kien T (1995) Prevalence of toxoplasmosis in a population of pregnant women in Antananarivo (Madagascar). *Bulletin de la Société de Pathologie Exotique* **88**, 46–49.

Li X-L, Wei H-X, Zhang H, Peng H-J and Lindsay DS (2014) A meta analysis on risks of adverse pregnancy outcomes in *Toxoplasma gondii* infection. *PLoS ONE* **9**, e97775.

Lim H, Lee SE, Jung BK, Kim MK, Lee MY, Nam HW, Shin J-G, Yun C-H, Cho H-I, Shin E-H and Chai J-Y (2012) Serologic survey of toxoplasmosis in Seoul and Jeju-do, and a brief review of its seroprevalence in Korea. *Korean Journal of Parasitology* **50**, 287–293.

Lin YL, Liao YS, Liao LR, Chen FN, Kuo HM and He S (2008) Seroprevalence and sources of *Toxoplasma* infection among indigenous and immigrant pregnant women in Taiwan. *Parasitology Research* **103**, 67–74.

Lindstrom I, Kaddu-Mulindwa DH, Kironde F and Lindh J (2006) Prevalence of latent and reactivated *Toxoplasma gondii* parasites in HIV-patients from Uganda. *Acta Tropica* **100**, 218–222.

Linguissi LSG, Nagalo BM, Bisseye C, Kagoné TS, Sanoud M, Tao I, Benao V, Simporé J and Koné B (2012) Seroprevalence of toxoplasmosis and rubella in pregnant women attending antenatal private clinic at Ouagadougou, Burkina Faso. *Asian Pacific Journal of Tropical Medicine* **5**, 810–813.

Ljungström I, Gille E, Nokes J, Linder E and Forsgren M (1995) Seroepidemiology of *Toxoplasma gondii* among pregnant women in different parts of Sweden. *European Journal of Epidemiology* **11**, 149–156.

Lobo ML, Patrocinio G, Sevivas T, De Sousa B and Matos O (2017) Portugal and Angola: similarities and differences in *Toxoplasma gondii* seroprevalence and risk factors in pregnant women. *Epidemiology and Infection* **145**, 30–40.

Lykins J, Li X, Levigne P, Zhou Y, El Bissati K, Clouser F, *et al.* (2018) Rapid, inexpensive, fingerstick, whole-blood, sensitive, specific, point-of-care test for anti-*Toxoplasma* antibodies. *PLoS Neglected Tropical Diseases* **12**, e0006536. https://doi.org/10.1371/journal.pntd.0006536.

Mahmoud H, Saedi Dezaki E, Soleimani S, Baneshi MR, Kheirandish F, Ezatpour B and Zia-Ali N (2015) Seroprevalence and risk factors of *Toxoplasma gondii* infection among healthy blood donors in south-east of Iran. *Parasite Immunology* **37**, 362–367.

Mandelbrot L, Kieffer F, Sitta R, Laurichesse-Delmas H, Winer N, Mesnard L, Berrebi A, Le Bouar G, Bory JP, Cordier AG, Ville Y, Perrotin F, Jouannic JM, Biquard F, d'Ercole C, Houfflin-Debarge V, Villena I, Thiébaut RL and TOXOGEST study Group (2018). Prenatal therapy with pyrimethamine + sulfadiazine vs spiramycin to reduce placental transmission of toxoplasmosis: a multicenter, randomized trial. *American Journal of Obstetrics and Gynecology* **219**, 386.e1–e9.

Meerburg BG and Kijlstra A (2009) Changing climate-changing pathogens: *Toxoplasma gondii* in North-Western Europe. *Parasitology Research* **105**, 17–24.

Millar PR, de Moura FL, Bastos OM, de Mattos DP, Fonseca AB, Sudré AP, Leles D and Amendoeira MRR (2014) Conhecimento sobre toxoplasmose entre gestantes e puérperas atendidas na rede pública de saúde do município de Niterói, Rio de Janeiro, Brasil. *Revista Do Instituto de Medicina Tropical de Sao Paulo* **56**, 433–438.

Montoya JG (2002) Laboratory diagnosis of *Toxoplasma gondii* infection and toxoplasmosis. Journal of Infectious Diseases **185**, S73–S82.

Montoya JG and Remington JS (2008) Management of *Toxoplasma gondii* infection during pregnancy. *Clinical Infectious Diseases* **47**, 554–566.

Morvan JM, Mambely R, Selekon B and Coumanzi-Malo MF (1999) Toxoplasmosis at the Pasteur Institute of Bangui, Central African

https://doi.org/10.1017/S0031182019001525 Published online by Cambridge University Press

Republic (1996–1998): serological data. *Bulletin de la Société de Pathologie Exotique* **92**, 157–160.

Moukandja IP, Ngoungou EB, Lemamy GJ, Bisvigou U, Gessain A, Toure Ndouo FS, Kazanji M and Lekana-Douki JB (2017) Non-malarial infectious diseases of antenatal care in pregnant women in Franceville, Gabon. *BMC Pregnancy and Childbirth* **17**, 185.

Murebwayire E, Njanaake K, Ngabonziza JC, Jaoko W and Njunwa KJ (2017) Seroprevalence and risk factors of *Toxoplasma gondii* infection among pregnant women attending antenatal care in Kigali, Rwanda. *Tanzania Journal of Health Research* **19**, 1–8.

Nasir IA, Aderinsayo AH, Mele HU and Aliyu MM (2015) Prevalence and associated risk factors of *Toxoplasma gondii* antibodies among pregnant women attending Maiduguri Teaching Hospital, Nigeria. *Journal of Medical Sciences* **15**, 147–154.

Ndiaye D, Ndiaye A, Sène PD, Ndiaye JL, Faye B and Ndir O (2007) Evaluation of serological tests of toxoplasmosis in pregnant women realized at the Laboratory of Parasitology and Mycology of Le Dantec Teaching Hospital in 2002. *Dakar Medical* **52**, 58–61.

Nicolle C and Manceaux LH (1908) Sur une infection a coyes de Leishman (ou organismes voisins) du gondi. *CR Hebdomad Seance Academic Scientijique* **147**, 763–766.

Oboro IL, Obunge OK and Wariso KT (2016) Sero-epidemiology of toxoplasmosis among pregnant women in the University of Port Harcourt Teaching Hospital, Nigeria. *Nigerian Health Journal* **16**, 1–12.

Ogouyèmi-Hounto A, Agbayahoun-Chokki F, Sissinto Savi de Tove Y, Biokou BB, Adinsi de Souza V, Assogba M, Kinde-Gazard D and Massougbodji A (2014) Evaluation of a rapid diagnostic test in the diagnosis of toxoplasmosis in pregnant women in Cotonou (Bénin). *Bulletin de la Société de Pathologie Exotique* **107**, 85–89.

Olariu TR, Remington JS, McLeod R, Alam A and Montoya JG (2011) Severe congenital toxoplasmosis in the United States: clinical and serologic findings in untreated infants. *Pediatric Infectious Disease Journal* **30**, 1056–1061.

Olusi T, Gross U and Ajayi J (1996) High incidence of toxoplasmosis during pregnancy in Nigeria. *Scandinavian Journal of Infectious Diseases* **28**, 645–646.

Olusi TA, Salawu SA and Oniya MO (2018) Seroepidemiology of toxoplasmosis among pregnant women in Osogbo, Southwestern, Nigeria. *Journal of Infectious Diseases and Immunity* **10**, 8–16.

Onadeko MO, Joynson DH and Payne RA (1992) The prevalence of *Toxoplasma* infection among pregnant women in Ibadan, Nigeria. *Journal of Tropical Medicine and Hygiene* **95**, 143–145.

Opsteegh M, Kortbeek TM, Havelaar AH and van der Giessen JW (2015) Intervention strategies to reduce human *Toxoplasma gondii* disease burden. *Clinical Infectious Diseases* **60**, 101–107.

Pardini L, Bernstein M, Carral LA, Kaufer FJ, Dellarupe A and Gos ML (2019) Congenital human toxoplasmosis caused by non-clonal *Toxoplasma gondii* genotypes in Argentina. *Parasitology International* **68**, 48–52.

Paul E, Kiwelu I, Mmbaga B, Nazareth R, Sabuni E, Maro A, Ndaro A, Halliday JOE and Chilongola J (2018) *Toxoplasma gondii* seroprevalence among pregnant women attending antenatal clinic in Northern Tanzania. *Tropical Medicine and Health* **46**, 39.

Pfaff AW, Abou-Bacar A, Letscher-Bru V, Villard O, Senegas A, Mousli M and Candolfi E (2007) Cellular and molecular physiopathology of congenital toxoplasmosis: the dual role of IFN-gamma. *Parasitology* **134**, 1895–1902.

Prusa AR, Kasper DC, Pollak A, Gleiss A, Waldhoer T and Hayde M (2015) The Austrian toxoplasmosis register, 1992–2008. *Clinical Infectious Diseases* **60**, e4–e10.

Remington JS, McLeod R, Thuilliez P and Desmonts G (2006) Toxoplasmosis. In Remington JS, Klein JO, Wilson CB and Baker C (eds), *Infectious Diseases of the Fetus and Newborn Infant*, 6th Edn. Philadelphia: Elsevier Saunders, pp. 947–1091.

Robbins JR, Zeldovich VB, Poukchanski A, Boothroyd JC and Bakardjiev AI (2012) Tissue barriers of the human placenta to infection with *Toxoplasma gondii*. *Infection and Immunology* **80**, 418–428.

Robert-Gangneux F and Dardé ML (2012) Epidemiology of and diagnostic strategies for toxoplasmosis. *Clinical Microbiology Reviews* **25**, 264–296.

Rodier MH, Berthonneau J, Bourgoin A, Giraudeau G, Agius G, Burucoa C, Hekpazo A and Jacquemin JL (1995) Seroprevalences of *Toxoplasma*, malaria, rubella, cytomegalovirus, HIV and treponemal infections among pregnant women in Cotonou, Republic of Benin. *Acta Tropica* **59**, 271–277.

Rouatbi M, Amairia S, Amdouni Y, Boussaadoun MA, Ayadi O, Al-Hosary AA, Rekik M, Ben Abdallah R, Aoun K, Darghouth MA, Wieland B and Gharbi M (2019) *Toxoplasma gondii* infection and toxoplasmosis in North Africa: a review. *Parasite* **26**, 6.

Salawu OT and Odaibo AB (2013) Schistosomiasis among pregnant women in rural communities in Nigeria. *International Journal of Gynaecology and Obstetrics* **122**, 1–4.

Salawu OT and Odaibo AB (2014) Maternal schistosomiasis; a growing concern in sub-Saharan Africa. *Pathogen and Global Health* **108**, 263–270.

Shiono Y, Mun HS, He N, Nakazaki Y, Fang H, Furuya M, Aosai F and Yano A (2007) Maternal-fetal transmission of *Toxoplasma gondii* in interferon-gamma deficient pregnant mice. *Parasitology International* **56**, 141–148.

Silveira C, Ferreira R, Muccioli C, Nussenblatt R and Belfort R Jr (2003) Toxoplasmosis transmitted to a newborn from the mother infected 20 years earlier. *American Journal of Ophthalmology* **136**, 370–371.

Simpore J, Savadogo A, Ilboudo D, Nadambega MC, Esposito M, Yara J, Pignatelli S, Pietra V and Musumeci S (2006) *Toxoplasma gondii*, HCV, and HBV seroprevalence and co-infection among HIV-positive and -negative pregnant women in Burkina Faso. *Journal of Medical Virology* **78**, 730–733.

Sitoe SP, Rafael B, Meireles LR, Andrade Jr HF and Thompson R. (2010) Preliminary report of HIV and *Toxoplasma gondii* occurrence in pregnant women from Mozambique. *Revista Do Instituto de Medicina Tropical de São Paulo* **52**, 291–295.

Soares JA and Caldeira AP (2019) Congenital toxoplasmosis: the challenge of early diagnosis of a complex and neglected disease. *Revista da Sociedade Brasileira de Medicina Tropical* **52**, e20180228.

Stray-Pedersen B (1992) Treatment of toxoplasmosis in the pregnant mother and newborn child. *Scandinavian Journal of Infectious Diseases* **84**, 23–31.

Stray-Pedersen B (1993) Toxoplasmosis in pregnancy. *Baillière's Clinical Obstetrics and Gynaecology* **7**, 107–137.

Tenter AM, Heckeroth AR and Weiss LM (2000) *Toxoplasma gondii*: from animals to humans. *International Journal of Parasitology* **30**, 1217–1258.

Tété-Bénissan A, Doctorant HM, Banla AK, Balogou A, Aklikokou K and Gbeassor M (2018) Seroprevalence and risk factors of toxoplasmosis in Togo. *European Scientific Journal* **14**, 56–69.

Teweldemedhin M, Gebremichael A, Geberkirstos G, Hadush H, Gebrewahid T, Asgedom SW, Gidey B, Asres N and Gebreyesus H (2019) Seroprevalence and risk factors of *Toxoplasma gondii* among pregnant women in Adwa district, northern Ethiopia. *BMC Infectious Diseases* **19**, 327.

The SYROCOT Study Group, Thiebaut R, Leproust S, Chene G and Gilbert RE (2007) Effectiveness of prenatal treatment for congenital toxoplasmosis: a meta-analysis of individual patients' data. Lancet 369, 115–122.

Todjom FG, Tsapi EM, Gamago GA, Vignoles P, Pone JW and Teukeng FF (2019) Seroprevalence of toxoplasmosis and associated risk factors in pregnant women at the Protestant Hospital, Mbouo-Bandjoun, Cameroon. *African Journal of Clinical and Experimental Microbiology* **20**, 221–230.

Torgerson PR and Mastroiacovo P (2013) The global burden of congenital toxoplasmosis: a systematic review. *Bulletin of the World Health Organisation* **91**, 501–508.

Uttah E, Ogban E and Okonofua C (2013) Toxoplasmosis: a global infection, so widespread, so neglected. *International Journal of Scientific and Research Publications* **3**, 1–6.

Walle F, Kebede N, Tsegaye A and Kassa T (2013) Seroprevalence and risk factors for toxoplasmosis in HIV infected and non-infected individuals in Bahir Dar, Northwest Ethiopia. *Parasites & Vectors* **6**, 15.

Wallon M, Peyron F, Cornu C, Vinault S, Abrahamowicz M, Kopp CB and Binquet C (2013) Congenital *Toxoplasma* infection: monthly prenatal screening decreases transmission rate and improves clinical outcome at age 3 years. *Clinical Infectious Diseases* **56**, 1223–1231.

Zemene E, Yewhalaw D, Abera S, Belay T, Samuel A and Zeynudin A (2012) Seroprevalence of *Toxoplasma gondii* and associated risk factors among pregnant women in Jimma town, Southwestern Ethiopia. *BMC Infectious Diseases* **12**, 1–6.

https://doi.org/10.1017/S0031182019001525 Published online by Cambridge University Press