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A Review of Toxoplasmosis in Humans and Animals in Libya

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ABSTRACT

Toxoplasmosis is a widely distributed zoonotic infection, caused by an obligate intracellular protozoan parasite *Toxoplasma gondii*in both humans and animals. The review summarizes published data on mode of infections, prevalence, life cycle, clinical aspects diagnosis, and risk factors of *T. gondii* in Libya. There is no adequate information exists on the mode of *T. gondii* transmission in Libya. Presence of stray cats and rodents in the houses and farms in different Libyan cities, probably play an important role in the maintaining the life cycle of *T. gondii* in the region. Libyan people might be also getting infection of *T. gondii* either by ingesting raw and undercooked grilled meat of lamb on festive occasions and sacrifice feasts and very often in restaurants on road side or by handling contaminated meat. Handling of infected meat by abraded hands at home might be transmitting toxoplasmosis to some extent through blood from broken skin especially among women in Libya. Diagnosis of *T. gondii* infection in Libya is based on serological detection of specific anti- *Toxoplasma* immunoglobulin, using different serological tests which have varied sensitivity and specificity in place to place. Various serological tests showed that toxoplasmosis is prevalent in eastern and western regions compared to southern parts of different Libyan localities from past few decades without any health education and control programmed. Prevalence of anti-ToxoplasmaIgG was more than anti-*Toxoplasma* IgM among pregnant women and patients. Variations in seroprevalence of *T. gondii* in Libya seem to correlate to lifestyle of cats (stray vs. pet), serological test utilized, climatic conditions, category of patients the with eating and hygiene habits of a population and other undefined factors. Little is known on the seroprevalence of toxoplasmosis in livestock. The sheep showed high seroprevalence and are suitable host for *T. gondii* in Libya.

مراجعة لداء المقوسات في الإنسان والحيوان في ليبيا

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الكلمات المفتاحية:
داء التكسوبلازما
القطط
تكسوبلازما جوندي
ليبيا

الملخص

تقدم هذه الورقة ملخصًا لمراجعة حول التوكسوبلازما جوندي في ليبيا، بما في ذلك معلومات عن عوامل الخطر، وأنماط العدوى، انتشارها، ودورات الحياة. يُعد داء المُقَوَّسَات، الذي يصيب البشر والحيوانات على حدٍ سواء، مشكلة كبيرة في عدة أجزاء من ليبيا. وعلى مدى العقود القليلة الماضية، ظهرت هذه العدوى في ليبيا، ولكن للأسف، لم يكن هناك قدر كبير من التثقيف الصحي أو برامج التحكم. لقد لوحظ أن النساء الحوامل والمرضى الآخرين لديهم معدل انتشار أعلى لمضادات التوكسوبلازما من نوع IgG مقارنة بنوع IgM. من المحتمل أن يكون وجود القطط والقوارض الضالة في المساكن والمزارع في مختلف المدن الليبية أمرًا حيويًا يساعد على اكمال دورة حياة التوكسوبلازما gondii *T.* في المنطقة. وبالتالي، قد تكون القطط هي المصدر الرئيسي لانتقال العدوى إلى الإنسان والحيوانات الأليفة الأخرى. في ليبيا، من غير المألوف أن تنقل الأطعمة غير المطهية التوكسوبلازما *T. gondii*ومع ذلك، قد يصاب الأفراد بالتوكسوبلازما جوندي عن طريق تناول لحم الخراف غير المطبوخ الذي تم شويه في الاحتفالات وأعياد التضحية، وكذلك في المطاعم على جانب الطريق. بالإضافة إلى ذلك، قد يؤدي التعامل مع اللحوم أو الأطعمة أو المشروبات الملوثة بالبويضات المتساقطة عن طريق السلالات إلى انتقال المرض. قد يؤدي التعامل مع اللحوم الملوثة بالأيادي، خاصة بين النساء في ليبيا، إلى انتشار داء المقوسات إلى حد ما عن طريق الدم من الجلد المجروح. بالإضافة إلى ذلك، فإن المزارع التي بها قطط أكثر عرضة للإصابة بداء المقوسات في مواشيها.

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يتم تشخيص عدوى T. gondii في ليبيا باستخدام نوع من الغلوبولين المناعي المضاد للتوكسوبلازما، والذي يعتمد على الموقع لحساسيته ونوعية.

1. Introduction

Toxoplasma gondii infects a wide range of mammals and birds. It is one of world's most common zoonotic parasitic infections (Dubey, 2010 and Younis *et al*, 2015). It is capable of infecting almost any cell type within an exceptionally broad host range - across humans, livestock, birds, companion animals and wildlife, making it one of the most 'successful' protozoan parasites on earth. Toxoplasmosis is an important health problem worldwide. It has been estimated that one third of the world population has been exposed to this parasite (Hill *et al*, 2005, Hill and Dubey, 2013, Dubey *et al*, 2014 and Rouatbi *et al*, 2019).

T. gondii has a complex life cycle (Dubey,2009). The felines, can host both sexual and asexual reproduction of *T. gondii*. Essentially, domestic cats are considered as definitive host of *T. gondii* and are the natural reservoir host of this parasite. Cats of the family Felidae are the key animal species in the life cycle of this parasite by excreting the environmentally resistant oocysts. In intermediate hosts, where asexual reproduction occurs are consist of all warm-blooded animals, including more than 30 species of birds and 300 species of mammals, with *T. gondii* being most common in sheep (Dubey, 2010).There are three different infective stages of *T. gondii*, which are (i) a rapidly dividing invasive tachyzoites, present during the acute or early infection in intermediate hosts as pseudocysts, (ii) a slowly dividing bradyzoites, present during the chronic or late stage of the disease in intermediate hosts persist as tissue cysts for protracted periods, and (iii) sporulated oocysts containing porozoites, shed as non-sporulated oocysts by the final hosts with feces. Sporulation occurs outside of the body to form sporulated oocyst containing four sporozoites. These oocysts are environmentally robust, and can retain infectivity in a cool damp environment for months (Dubey, 2010 and Subasinghe *et al*, 2011).

T. gondii has three dominant clonal classes of strains named as Type I, II and III. These genotypes are clonal in their structural features (Dubey, 2010). Different strains of the parasite induce different cytokine responses, triggering development of various clinical and biochemical disturbances in the host (Araujo and Slifer, 2003). Different genotypes of the parasite show great diversity in pathogenicity and drug sensitivity. Type I causes infection in rodents. Type II established as the infectious agent in small ruminants while Type III has yet not been proved as infectious strain. Recently, a genotype (Type IV) has also been reported mostly in wildlife (Ahmed and Tasawar, 2015). So far in Libya, Ali *et al* (2018) reported evidence of Type I strain of *T. gondii* in the city of Benghazi among patients clinically suspected of ocular toxoplasmosis.

The aim of our review is to describe actual knowledge on the prevalence of *T. gondii* in humans and animals in different Libyan cities. It also discusses aspects of transmission, life cycle, clinical manifestations, and diagnosis and on potential risk factors favoring infections of humans and livestock with *T. gondii*. Knowledge on potential risk factors is prerequisite to implement effective biosecurity measures in farms to prevent *T. gondii* infections.

2. Transmission of *T. gondii*

Different modes transmissions of *T. gondii* are shown in Figure1.The cats are the primary source of infection to human beings for toxoplasmosis. Human infection is acquired by consuming food or drink contaminated with oocysts of *T. gondii* shed by cats, or by accidentally ingesting oocysts from the environment or handling infected cats. Ingestion of tissue cysts containing bradyzoites or pseudocysts containing tachyzoites from raw or undercooked meat (Macra *et al*, 1996 and Dubey and Jones, 2008).Congenital transmission could result in the invasion of the placenta by tachyzoites which may cross the placenta and enter fetal tissues or the bloodstream (Pardini *et al*, 2018).*T. gondii* infection can also rarely be transmitted by tissue or organ transplants (Robert-Gangneux, and Darde, 2012). Transmission of the parasite can also occur by blood transfusion (Yazar *et al*, 2006 and Alshibani, 2017),bone marrow transplantation (Edvinsson*et al*, 2008) all ogeneic stem cell transplantation (Fricker-Hidalgo *et al*,2009) sputum (Laibe *et al* 2006) and breast feeding milk (Hiramoto *et al*, 2001 and Camossi *et al*, 2011).Animals get infection by the ingestion of oocysts contaminated in grasses, feed and water or by transmission from mother to fetus. Therefore toxoplasmosis in animals is significantly associated with presence of cats in the farms (Dubey, 2010). The definitive host cats, acquired infection of toxoplasmosis by eating infected meat of warm-blooded animals (cattle, buffaloes, sheep, goats, camels, rodents, pigs and birds) containing tissue cysts or pseudocysts or both. Handling of meat at home from infected animals, increases the possibility of contact with tissue cysts, particularly if no protective equipment, such as gloves, is worn. Additionally, tissue cysts may be ingested during hand-to-mouth contact after handling undercooked meat (Markell *et al*,1992). It can also be transmitted by containers, knives or other utensils, cutting boards or other preparation surfaces contaminated with raw meat. Prevalence of*T. gondii* infection is high in Libya but the main reason yet unclear as no adequate studies regarding availability of modes of transmission (Alkateb *et al*, 2007).In Libya, there are plenty of stray cats (so called domestic cats)which are roaming freely indoor and outdoor would be increasing more risk of *T. gondii* infection to both humans and domestic livestock (Mahmoud *et al*, 2019 and Rouatbi *et al*, 2019). Soil contaminated with cat's faeces may play role in transmitting infection through consumption of contamination of raw vegetables or water or fruits and poor hand hygiene are important risk factors in transmission of *Toxoplasma* infection(El-sayed and Almannoni, 2016. Alshaibani, 2017 and Mahmoud *et al*, 2019). Moreover, domestic cats usually defecate in open areas and contaminate the soil nearby houses and exposure of children playing in sandpits and geophagia resulting infection of *T. gondii*(Flegr *et al*, 2014 and Rouatbi *et al*, 2019). Therefore, presence of cats in a region posing an important risk factor for toxoplasmosis. Sheep, goats and camels are the traditional source of meat in this region. Libyan peoples usually slaughter domestic livestock on festive occasions. Peoples may be acquiring infection of *T. gondii* by eating raw and undercooked meat of infected animals(Kassem and Morsy,1991., Al-Mabruk *et al*, 2013., Gashout *et al*, 2016., Mahmoud *et al*, 2019 and Elgodwi ,2020).Moreover, at homes in Libya, handling of infected meat of animals or chicken might be playing role in the transmission of toxoplasmosis as bradyzoites or tachyzoites or both of *T. gondii* may enter into blood stream through broken skin.Ali *et al* (2019) have identified some important risk-factors- contact with farm animals, unfiltered water-sources are supposed to be risk-factors of toxoplasmosis in Asabieh city.

3. Life cycle of *T. gondii*

T. gondii is a coccidian parasite and has both asexual (schizogony) and sexual (sporogony) cycles in the same host that is felids (Figure.1). Since sporogony of parasite does not occur in any host and therefore, cats are considered as definitive host of *T. gondii*. In cats, non-sporulated oocysts are developed in gut and passed out in feces which get matured (sporulated) in the soil and are infective stage to both humans and herbivores. Intermediate hosts are a variety of livestock, and birds. In human beings asexual or schizogony cycle of parasite completed. At some frequency within the host, especially in immunodeficient patients (HIV/AIDS) there is apparently a low rate of spontaneous reactivation (reactivation of latent infection of *T. gondii*) whereby bradyzoites differentiate back to tachyzoites. Normally, the immune response efficiently prevents the dissemination of these tachyzoites. However, in immunocompromised hosts, reactivation may be unchecked and/or more frequent, leading to the provocative suggestion that the parasites might actively detect a lowered immunity against them (Gazzinelli *et al*, 1993 and Gross and Pohl, 1996). The result, in either case, can be a massive and potentially fatal recrudescence.

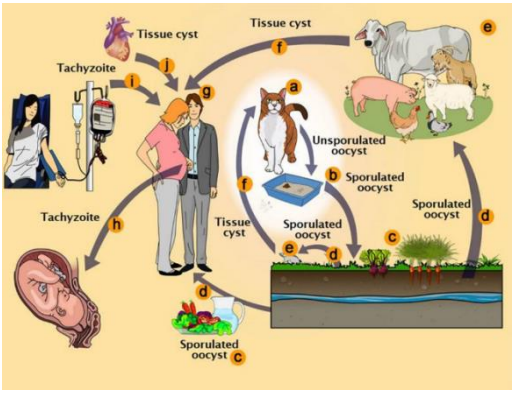

Fig. 1: Transmission pathways of *T. gondii* (Attias *et al*,2020)

Life cycle of *T. gondii* is not known in Libya. The population of small rodents in Libya is high and they may play a significant role as intermediate hosts for the final host, and play role in the spreading of the *Toxoplasma* infection (El- Gomati *et al*, 2010). Mahmoud *et al* (2019) found that presence of cats at home was significantly associated with seroprevalence of toxoplasmosis among pregnant women in Sebha and Tripoli city respectively. In Libya atmospheric conditions in various cities are probably favorable for the survival and spreading of oocysts shed by the definitive hosts, leading to higher contamination rates of intermediate hosts(El-Gomati *et al*, 2010 and Al-Mabruk *et al*, 2013). In such areas, the number of different herbivore species is also high creating further favorable conditions for *T. gondii* transmission in the region (Kassem and Morsy, 1991.Gashoutet *al*, 2016 and Rouatbi *et al*, 2019).

4. Clinical features of Toxoplasmosis

The primary infections of *T. gondii* are usually subclinical and the vast majority of significant morbidity and mortality in certain groups. This includes encephalitis, chorioretinitis, congenital infection and neonatal mortality (Weiss and Dubey, 2009).

4.1. Acquired Toxoplasmosis

Acquired infections are common and approximately 80% to 90% remain asymptomatic. In acute toxoplasmosis, patients may develop hepatomegaly, splenomegaly, fever, lymphadenopathy, meningoencephalitis and usually unilateral retinochoroiditis, blurred vision and rarely may turned to blindness (Murat and Michael,2019). In chronic toxoplasmosis patients remains asymptomatic or there is low grade fever, lymphadenopathy, unilateral retinochoroiditis, myocarditis, myalgia and arthralgia (Murat and Michael,2019).

4.2. Congenital Toxoplasmosis

Congenital infection results from a primary infection of the mother during pregnancy. Primary infection during pregnancy poses a risk of abortion or severe birth defects or miscarriage of the fetus .This vertical or congenital transmission could result in the invasion of the placenta by tachyzoites which may cross the placenta and enter fetal tissues or the bloodstream (Mahmoud *et al,* 2015 and Pardini *et al*, 2018). Congenital toxoplasmosis may cause abortion, neonatal death, or stillbirth and fetal congenital abnormalities develop mainly in the neuromuscular system and eyes (Remington *et al*, 1995 and Hayde and Pollak, 2000).This is most severe when maternal infection occurs early in pregnancy. Approximately 15-55% of congenitally infected children do not have detectable *T. gondii* –specific IgM antibodies at birth or early infancy. Approximately 67% of patients have no signs or symptoms of infection (Murat and Michael,2019). Usually in congenital infections there is bilateral retinochoroiditis occurs in about 15% of patients, which may persist to bilateral blindness and intracranial calcifications develop in about 10%. Cerebrospinal fluid (CSF) pleocytosis and elevated protein values are present in 20% of patients. Infected newborns developed anemia, thrombocytopenia, and jaundice at birth. Microcephaly has been reported. Affected survivors may have mental retardation, seizures, visual defects, spasticity, hearing loss or other severe neurologic sequelae.

T. gondii has emerged as one of the most common opportunistic infections in patients with AIDS. Toxoplasmosis in AIDS patients is considered to be a result of reactivation of latent infection, but the mechanism of reactivation is unknown. The clinical features of toxoplasmosis in immunocompromised patients, such as HIV patients are not specific and may likely mimic other signs that can lead to an erroneous outcome. The usual signs are fever with neurological imbalance (Nimir *et al*, 2013). In immunosuppressed (HIV, organ transplant or cancer) patients, the infection can lead to life-threatening cerebral toxoplasmosis (Akanmu *et al*, 2010 and Addebbous *et al*, 2012).

In pregnant animals, primary infection can lead to abortion, hence causing high economic losses. In ewes, if the infection occurs between 50 and 120 days of pregnancy, it induces abortion, expulsion of mummified fetuses, or the birth of stillborn and weak lambs (Buxton *et al*, 1991and Al-Mabruk *et al*, 2013). Most of the acquired infections of *T. gondii* in herbivores (sheep, goat, cattle, camel and equine) are subclinical. However, fever, ataxia and retinal degeneration and encephalomyelitis may develop. Severity of toxoplasmosis in ovine is associated with the stage of pregnancy (Kadle, 2014 and Younis *et al*, 2018). The most deva sting outcome of toxoplasmosis is miscarriage or abortion which is particularly important in both humans and domestic livestock. Additionally, it can cause a wide variety of neurological disease especially when transmitted congenitally (Weiss and Dubey, 2009).

5. Diagnosis of *T. gondii*

Diagnosis of toxoplasmosis in humans is performed using different techniques including serological testing, histological identification, and isolation in tissue culture as well as, molecular methods using the Polymerase Chain Reaction (PCR). Acute and latent *T. gondii* infections are mostly diagnosed by serological tests including increased antibody levels such as IgG, IgM, IgA and IgE. Various serological techniques have been established to determine recent and previous exposures to *T. gondii* infection: namely Sabin-Feldman dye test (SFDT) (Sabin and Feldman, 1948), Latex agglutination tests (LAT) (Dubey, 1997., Dubey and Jones, 2008., Robert-Gangneux and Dardé, 2012 and Liu et al., 2015), indirect fluorescent assay (IFA) (Rorman *et al*, 2006 and Saraei *et al*, 2010), and enzyme-linked immunosorbents assays (ELISA)(Dubey, 2010., Ben Abdallah *et al*, 2013., Liu *et al*, 2015., Gashout *et al*, 2016., Pardini *et al*,2018 and Elammari *et al*, 2021), or a combination of these methods (Rorman *et al*, 2006.,Dubey and Jones, 2008 and Robert-Gangneux and Dardé, 2012). ELISA is still considered as one of the most common techniques with high sensitivity and specificity in the quantitative detection of antibodies and all antigenically active molecules (Doskaya *et al*, 2014and Liu *et al*, 2015).

Worldwide, prevalence of the toxoplasmosis is measured by detection of specific anti-*Toxoplasma* IgG antibodies varies between 1% and 100 depending on different factors such as serological tests used for diagnosis, types of anti-*Toxoplasma* antibodies geographical location, age, habit of eating raw meat or unwashed fruit and vegetables, sociocultural and nutritional habits, general level of hygiene and contact with domestic cats (Al-Nahari and Al-Tamimi, 2010., Al-Jebouri *et al*, 2013 and Iddawela *et al*., 2017).

In Libya, both qualitative (Latex Agglutination Test) and quantitative (Indirect Hemagglutination Test, and Enzyme Linked Immunosorbent Assay) have been used for the serodiagnosis of toxoplasmosis (Khadre and El-Nageh 1987., Kassem and Morsy, 1991., Azwai*et al* 1993.,Alzaidy, 2007., El-Gomati *et al* 2008.,Al-Mabruk *et al*, 2013., Gashout *et al*, 2016.,Younis and Elamami, 2018 and Elammari *et al*, 2021).Gashout *et al* (2016) for the first time in Libya described establishment, optimization, and application of diagnostic PCR assay to amplify SAG2gene of *T. gondii* infection from Libyan HIV patients, women who have had spontaneous abortions, leukemia, and ocular infection patients who were sero-positive for specific *Toxoplasma* antibodies. They also found PCR has ability to diagnose active toxoplasmosis in immunocompromised and congenital toxoplasmosis when serological techniques fail to diagnosed the disease. Moreover, Haq *et al* (2016) applied PCR for high frequency detection of *T. gondii* DNA in human neonatal tissue indicating a high level of congenital toxoplasmosis in the city of Misurata from Libya.

6. Infection of *T. gondii* in Libya

T. gondii is prevalent among humans (10.4 to 69.4%) as well as animals (7.5 to 75.1%) in North Africa (Rouatbi *et al*, 2019). Worldwide, prevalence of the toxoplasmosis is mostly measured by detection of specificity-*Toxoplasma* IgG antibodies using ELISA. IgG seropositivity determined the chronic stage of disease, which is also

the latent toxoplasmosis and reflects previous exposure to the infection. Secondly, the immunoglobulin M (IgM) level determines the acute stage of the *T. gondii* infection and may indicate recent exposure to the disease. The majority of the studies have focused on the seroprevalence in pregnant women followed by patients with disorders frequently using serological tests were the ELISA, latex agglutination test (LAT), and IFAT (Elsaid *et al*, 2014., Gashout *et al*, 2016., Alshaibani, 2017 and Rouatbi *et al*, 2019).

Table1: Seroprevalence of Toxoplasmosis among pregnant women in different Libyan cities/ localities

City	Technique	Prevalence (%)	Reference
Benghazi	LAT	45.6	Legnain and Prawecka (1983)
Benghazi	IHA	47.4	Kassem and Morsy (1991)
El Beida	ELISA	44.0	Magrhi *et al* (2003)
Aljabal-El Akhder	LAT	25.6	Alzaidy (2007)
Tripoli	ELISA	45.0	Gashout *et al* (2008)
Zawia	ELISA	74.0	Aljabali(2008)
Surman	ELISA	68.8	Aljabali (2008)
Sabrata	ELISA	58.1	Aljabali (2008)
Benghazi	ELISA	44.8	Mousa *et al* (2011)
Fezzan	ELISA	23.6	Ebrahim (2013)
Benjawad	ELISA	37.1	Salima and Kassem (2015)
Aljabal- El Akhder	ELISA	30.7	Boshapor and Kassem (2015)
Misurata	Elecsys-Cobas e analyzer	26.7	Salem *et al* (2015)
Sebha	ELISA	25.8	Ramadan (2015)
Al Khoms	ELISA	39.3	Gamal and Jaroud (2015)
Sebha	ELISA	36.8	El-Sayed and Almannoni (2016)
Msallata	LAT	41.0	Zeglam and Shugi (2017)
Tarhuna	ELISA	33.0	Elyadi *et al* (2017)
Tripoli	Immunoassy system	41.0	Elgodwi (2020)
Sebha	Immunoassy system	36.0	Elgodwi (2020)
El Beida	ELISA	26.8	Elammari *et al* (2021)

The first serological study of *T. gondii* on human infections in Libya was done by Legnain and Prawecka (1983)in Benghazi among pregnant women. Four years later, Khadre and El Nageh (1987) carried out seroprevalence of toxoplasmosis on women in childbearing age pregnant women and non-pregnant, adult males and schoolchildren. Several seroprevalence studies have been conducted in pregnant women in different Libyan cities and results showed differences from region to other(Table 1). Most of studied seropositivity data presented in Table 1, were based on detection of anti-*Toxoplasma* IgG using ELISA, which varies from 23.6 to 74.0% among pregnant women (Aljabali, 2008 and Ebrahim, 2013). However, IgM seropositivity was low, and varies from 0.0 to 17.6% in different cities among the pregnant women using ELISA. Recently, Haq *et al* (2016) used PCR for the diagnosis of congenital toxoplasmosis and detected *T. gondii* DNA in 9.8% of the umbilical cord of neonates, indicating a high level of congenital toxoplasmosis in Misurata city.

Table2: Seroprevalence of Toxoplasmosis among general population and patients in different cities of Libya.

City	Category of patients	Assay	Prev. (%)	Ref.
Tripoli	Adult Males	LTA	51.6	Khadre and Nageh(1987)
	Adult Females		43.3	
	School Children		45.7	
Tripoli	Psychiatric Patients	ELISA	50.3	Elsaid *et al* (2014)
		LTA	61.7	
	Patients with Leukemia and Lymphoma	ELISA	66.7	
Tripoli	Infants with Ocular Infection	ELISA	50.0	Gashout *et al* (2016)
	HIV Patients	ELISA	88.5	
Zawia	Children with ocular infection	ELISA	50.0	
Sabrata	Patients with Leukemia and Lymphoma	ELISA	66.7	Gashout *et al* (2016)
Tripoli	Patients with Epilepsy	ELISA	29.4	Alshaibani (2017)
Benghazi	Patients clinically suspected of Ocular toxoplasmosis	ELISA	55.8	Ali *et al* (2018)
Benghaz	Type-2 Diabetic Patients	ELISA	41.5	Younis and Elamami (2018)
Asabieh	Patients attending Hospital	ELIFA	78.6	Ali *et al* (2019)
Tripoli	Patients attending Aljalla Maternity and Gynecology Hospital	ELISA	50.8	Mahmoud *et al* (2019)
Sirte	Patients attending Hospital	LAT	45.5	Hana *et al* (2021)

In Libya, results of several studies showed high prevalence of toxoplasmosis in the eastern and western regions compared to the southern region of the country. This can be attributed to the difference environmental conditions, such as the high rainfall, and high humidity, making it an environment suitable for the sporulation and surviving of oocysts. However, hot and dry environment as such in the southern regions of the country could be unfavoring the development and surviving of the parasite which may explain the moderate to low incidence of *T. gondii* in the southern regions (Boshapor and Kassem, 2015).

Seroprevalence of toxoplasmosis among non-pregnant women, psychological patients, school children, immunocompromised patients(leukemia, lymphoma and patients with HIV/AIDS), children with ocular infection, diabetic patients, patients with epilepsy and patients attending hospital is shown in Table 2.Higherseroprevalence of61.7% and 88.5% of *T. gondii* was estimated among psychiatric and HIV/AIDS patients respectively in Tripoli. The authors explain this as a causal relationship between toxoplasmosis infection and psychiatric diseases (Elsaid *et al*, 2014).Moreover, most of the time, psychiatric patients have a high risk of exposure to *T. gondii* infection due to lack of good personal hygiene, self-care skills, and a tendency to pica (Achaw *et al*, 2019).These habits frequently expose people to infections.

Livestock (sheep, goats, cattle, buffaloes, camels, and poultry) play an important role in food security, which provides a source of nutrients to other animals and humans in the region. Some animals may carry the bradyzoite cyst within tissues of their body and the parasite can subsequently be transmitted to other respective hosts through consumption of raw or undercooked portion of this infected tissue (Polley and Thompson, 2009). So far, there are only few studies in Libya related to seroprevalence data on *T. gondii* infection in animal species. Seropositivity in livestock is shown in Table 3.Indirect hemagglutination testing (IHAT) was used to serologically determine the prevalence of the infection in cattle, sheep, goats and horses sampled from different parts of Libya by Azawi *et al* (1993).El-Gomati *et al* (2010) used Toxocell latex test for the detection of *Toxoplasma* antibodies and found 35% positivity. A higher seroprevalence (71%) was reported in sheep from the western region to the central region using latex agglutination testing (Al-Mabruk *et al*, 2013). They consider sheep are suitable host for *T. gondii* in Libya. Research on the rodent intermediate host is scarce in Libya, and only a single report was documented (El-Gomati *et al*, 2010).

Table 3: Animal seroprevalence Toxoplasmosis in Libyan city

City	Animal	Assay	Prevalence (%)	Reference
Tripoli	Sheep	LTA	13.5	Gusbi (1986)
	Sheep		26.1	
	Goats		50.0	Azawi *et al* (1993)
Tripoli	Cattle	IHA	11.0	
	Horse		4.8	
Tripoli	Sheep	LAT	40.7	El-Gomati *et al* (2008)
Tripoli	Mice	MiceToxocell Latex Test	35.0	El-Gomati *et al* (2010)
Tripoli	Sheep	LAT	71.0	Al-Mabruk *et al* (2013)

7. Risk factors associated with *T. gondii*

Prevalence of the toxoplasmosis is measured by detection of specificanti-*Toxoplasma* IgG antibodies depending on different factors such as geographic allocation, age, habit of eating raw and undercooked meat or unwashed fruit and vegetables, sociocultural and nutritional habits, general level of hygiene and contact with domestic cats(KravetzandFederman,2005.,Al-Nahari and Al-Tamimi, 2010.,Al-Jebouri*etal,* 2013 and Iddawela *et al*, 2017).Farm management is also a risk factor. For example, in Algeria, sheep are reared in extensive systems and fed on fresh bulk feed or pasture, which is a greater risk as sources of contamination (Dahmani *et al*, 2018). Alghanaei and Abdulsalam (2019) summarized data on possible risk factors related to *T. gondii* infection in Libya. Risk factors could be:

(i) A higher seroprevalence of *T. gondii* is associated with geographical location such as humid areas, which are suitable for sporulation of oocysts. Humidity and sufficient rainfall conditions increased viability of oocysts and can survive for more than one year (Jimenez-Coello *et al*, 2012 and El-sayed and Almannoni, 2016). Results of studies in Libya showed higher prevalence of toxoplasmosis in eastern and western regions compare to southern parts of country, where incidence of *T. gondii* is moderate to low (Boshapor and Kassem , 2015).

(ii)Meat of warm-blooded animals and birds has beenconsidered a major source of *Toxoplasma* infectionespecially in countries that consumed raw or undercooked meat. Besides the consumption of *T. gondii* tissue cysts contained in meat, meat-derivedproducts, or offal can be an important source of infection in humans (Jiménez-Coello *et al*, 2012 and El-sayed and Almannoni,2016). Consumption of undercooked meat is significantly associated with *T. gondii* infection (Tenter *et al*, 2000,Dubey, 2010, Mousa *et al*, 2011, and Alshaibani, 2017). *T. gondii* cysts may persist in the tissues of the host for years (Dubey, 2010). Meat is predominantly consumed cooked in sauce, but undercooked grilled lamb is consumed during the Muslims' sacrifice feast, and very often in restaurants at the side of the road (Uhl, 2001). Therefore tissue bradyzoites consumed from infected meat precipitates infection of *T. gondii* in humans. Livestock (cattle, buffaloes, camels, sheep, goats, and poultry)play an important role in food security, nutrition, and the economies of North African countries by supporting rural livelihoods and employment, and ensuring access to animal source foods(FAO, 2016). Gamal and Jaroud (2015) reported significantly higher seropositivity rate (70.0%) among women consuming sheep meat compared to those (54.0%)consuming cow meat in Al Khoms city. Transmission of *T. gondii* infection through uncooked meat in Libya isuncommon because most people preferred to eat well cooked meat (Swalem and Feturi, 1994., Bader, 2002 and El-sayed and Almannoni, 2016).Generally, thorough cooking is always preferred in Libya, and therefore the most possible way of transmission is probably through handling of raw contaminated meat, during food preparation. Local meat, sheep, goat or camel might become contaminated with oocysts due to poor hygiene during handling of meat fromslaughter house to kitchen. In addition, in Libya, consumption of lamb is greater than that of beef. These trends may have increased exposure to toxoplasma because lamb has a higher risk of infection than beef or poultry (Mousa*et al*, 2011). As meat from infected animals' increases the possibility of contact with tissue cysts, particularly if no protective equipment, such as gloves, is worn. Additionally, tissue cysts may be ingested during hand-to-mouth contact after handling undercooked meat, or from using knives, utensils, or cutting boards contaminated by raw meat. Moreover, Al-Mabruk *et al* (2013) considered that sheep are the suitable host *T. gondii*. In a study in Sebha city of Libya conducted by El-sayed and Almannoni (2016), the roasted mutton or processed meat as hamburger, minced meat and Sharma which may be insufficiently cooked (Gamal and Jaroud, 2015 and El-sayed and Almannoni, 2016).Ramadan (2015) found that consumption undercooked was significantly associated with *T. gondii* infection among pregnant women in Sebha city. The higher prevalence is linked to the consumption of uncooked meat and vegetables or water which contaminated by the infectious stages of *T. gondii i*n the city of Tarhuna (Elyadi *et al*, 2017).Moreover, Mahmoud *et al* (2019) reported the seroprevalence of *T. gondii* (82.5%) among women consumed under cooked meat was higher than that (40.3%) reported in women consumed well-cooked meat in Tripoli. However, on the other hand, transmission of *T. gondii* infection through uncooked meat in Libya is uncommon because most people preferred to eat well cooked meat(Swalem and Feturi,1994.,Abu Setta and Yamani, 2008 and El-sayed and Almannoni, 2016).Ali *et al* (2019) reported that way of meat cooking was a significant risk factor associated with *T. gondii* infection as 80% of the population ate well-cooked meet where 20% of them ate undercooked meat in the city of Asabieh.

Women are at high risk of contracting *Toxoplasma* infection (Yue *et al*, 2010 and Pinto *et al*,2017). Hana *et al* (2021) reported that *Toxoplasma* infection was higher in female (55.6%) than male patients (35.9%) in city of Sirte. This can be explained by the fact that women are much more exposed to several of the risk factors and as a result of a longer exposure period (frequently having contact with cats as pet at homes, spend more time for cooking and handling of raw meat). Therefore, women have more frequency of infection than males.

(iii) Contact with domestic cats is primary source of infection in humans and major risk factor for toxoplasmosis (Dubey and Jones,2008., Jones *et al*, 2009 and Hatam-Nahavandi *et al*, 2021). Cats are essential in the life-cycle of *T. gondii* because they are the only hosts that can excrete the environmentally resistant oocysts in nature. Felids can shed millions of oocysts that can spread the infection to environmental conditions and contaminating flours of houses, soil nearby homes and residential areas, water, fruits and vegetables in farm houses in the region. Several studies conducted in Libya, showed association between the *Toxoplasma* infection and contact with cats (Kassem and Morsy, 1991., Abu Setta and Yamani, 2008., Ramadan, 2015., Gamal and Jaroud, 2015., Bohsapor and Kassem, 2015.,Younis and Elamami, 2018 and Mahmoud *et al*, 2019).On the contrary, other studies found no association between seroprevalence of toxoplasmosis and contact with cats.(Magrhi *et al*, 2003., AlKhunfas, 2008.,Mousa*et al*, 2011., Elsaid *et al*, 2014., El-sayed and Almannoni 2016). However, the acquisition of cats as pets is not common practice in Libya. Stray cats are found in farms, gardens or may enter houses from time to another to obtain their food from remains of raw meat thrown in the garbage (Alghanaei and Abdulsalam, 2019). This could increase the chance of infection especially for children living in houses with soil floor or playing in farms during picnics (Mousa*et al*, 2011 and El-sayed and Almannoni 2016). Moreover, the population of small rodents in Libya is high and they may play a significant role as intermediate hosts for the final host (cat), and plays role in the spreading of the *Toxoplasma* infection (El-Gomati *et al*, 2010).

Several risk factors for toxoplasmosis in Asabieh city were identified, direct contact with farm animals were at increased risk compared with those who did not have regular contact with them. Consumption of unfiltered water was also identified as a risk factor for toxoplasmosis in Libyan city of Asabieh (Ali *et al*, 2019).

In addition, contact with dogs showed significant associated with infection; therefore dogs might be an important route of *T. gondii* transmission (Elsaid *et al*, 2014 and Hatam-Nahavandi *et al*, 2021).

8 Conclusion

In this review we concluded, that anti–*Toxoplasma gondii* IgG antibodies were significantly more prevalent than anti-*Toxoplasma gondii* IgM antibodies among pregnant women in Libya, but little is known on clinical congenital toxoplasmosis. In addition, little is known on the seroprevalence of toxoplasmosis in livestock, particularly sheep destined for human consumption in this region. The

disease is wide spread in all parts of country with variable prevalence rates. Presence of cats in houses and farms playing significant role in the epidemiology of toxoplasmosis in different localities of Libya. Higher *Toxoplasma* antibodies (IgG and IgM) were found among pregnant women and immunocompromised/immunosuppressive patient in different Libyan cities. Obstetricians appear to provide more appropriate counseling of pregnant women about risk factors, such as avoid contact with cats, having a pet cat at home or in living area, eating raw or undercooked meat and eat properly washed vegetables and fruits may reduce the risk of congenital toxoplasmosis. Veterinary data of toxoplasmosis show that this can be achieved by controlling rodent pests and keeping cats out of sheds of animal or farm houses. Moreover, the population of small rodents in Libya is high and they may play a significant role as intermediate hosts for the final host. High IgM seropositivity among pregnant women necessitates systematic measures to prevent acute toxoplasmosis infection during pregnancy in Libya.

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