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**Study of some epidemiological, Haematological
and immunological Aspects in women with
chronic Toxoplasmosis**

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

﴿ قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ ﴾

بِسْمِ اللَّهِ
الرَّحْمَنِ الرَّحِيمِ

سورة البقرة
الآية (٣٢)

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DEDICATIONS

It is with genuine gratitude and warm regard that I'd like to dedicate this
work:

To my family (husband and son), most supportive

To my parents and sisters

To my friends

Tiba

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In the name of Allah, the Most Gracious and the Most Merciful Alhamdulillah, all praises to **Allah** for the strengths and his blessing in completing this thesis. Special appreciation goes to my supervisor, **Prof. Dr. Kassim Abdulla Hamza Al-Morshidy**, for his supervision and constant support, his invaluable help of constructive comments and suggestions throughout the experimental and thesis works have contributed to the success of this research. I would like to extend my sincere thanks to **Prof. Dr. Alaa Tareq Shakir** in Biology Department / College of Science / University of Babylon, for his technical support on my study.

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Researcher

SUMMARY

The results showed that 72% of the infected women had IgG antibody titer level less than 100. The current study aimed to investigate the chronic infection of toxoplasmosis in women in Babylon province and the relationship of that infection with some epidemiological, hematological and immunological parameter. 255 serum samples from women attending Gynecology & Children Babylon Hospital in Hilla city were examined using VIDAS technique in the period from October 2020 until the end of March 2021. A questionnaire was organized for each patient, which included the necessary information in the research, such as date, age, area of residence, educational level, pregnancy month, titer, abortions number, and blood group. 50 women were diagnosed with toxoplasmosis, while 40 samples were randomly selected to be the control group.

The results of the current study showed that the total percentage of chronic toxoplasmosis among women in the Babylon province was 19.6%. It was found that the percentage of infection in the age group of older than 30 years is the highest 34.1% compared with the infection percentages in other age groups (less than 20 years and 20-30 years), with a significant difference in infection percentages. The results of the current study found a significant increase in the incidence of chronic toxoplasmosis in urban areas 27.3% compared to rural areas 15.6%. It was noted that the incidence of chronic toxoplasmosis in women with university education level was higher 29.3% compared to infection rates in women with secondary and primary educational attainment and uneducated women with no significant differences in infection percentage. The results showed that the highest incidence of chronic toxoplasmosis was in women during the first trimester of pregnancy, which amounted to 21.9% compared with women in the second and third trimester of pregnancy with no significant difference in infection percentages. It was found that 33.33% of the infected women had

more than three abortion, and 31.9% of the women with chronic toxoplasmosis had blood group B.

The results showed that chronic toxoplasmosis infection has an effect on some hematological parameters, as a significant increase in the total number of white blood cells 8.24 and white blood lymphocytes 2.83 and a decrease in hemoglobin concentration 11.63 in infected women compared with non-infected women 7.49, 2.41, 12.35 respectively.

The results of the immunological study showed that the concentration of the immunological parameters Leukotrienes (LT-D4), Kininogenase, and Platelet Activation Factor (PAF) in sera of women with chronic toxoplasmosis were significantly higher (3.176 ng/ml, 27,752 ng/ml, and 4.594 ng/ml, respectively) than their concentrations in sera of non-infected women (2.874 ng/ml, 23.981 ng/ml, and 4.202 ng/ml, respectively). The results also showed that the highest concentrations of the immunological parameters were in infected women at the age of 20 to 30 years compared to other ages. We conclude from the results of the current study that toxoplasmosis infection has an effect on the immunological and hematological parameters, and this reflects the relationship between the pathogenic effect of the parasite and the host's immune responses to it.

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List of Abbreviations

Abbreviations	Meaning
Ab	Antibody
Ag	Antigen
ANOVA	Analysis of Variance
AST	Aspartate aminotransferase
CBC	Complete blood count
CD4	Cluster of differentiation 4
CD8	Cluster of differentiation 8
CNS	Center Nervous System
CVD	cardiovascular diseases
DC	Dendritic cells
DVT	deep vein thrombosis
EDTA	Ethilin diamine tetra acetic acid
ELIZA	Enzyme Linked immunosorbent assay
Hb	Hemoglobin
HK	High-molecular-weight-kininogen
HMW	high molecular weight
IgA	Immunoglobulin Class A
IgE	Immunoglobulin Class E
IgG	Immunoglobulin type G
IgM	Immunoglobulin type M
IU/l	international units / Liters
IU/ml	International unit in ml
IL-12	interleukin 12
IFN-γ	Interferon-gamma
KNG	kininogen
LAT	Latex agglutination test
LK	Low-molecular-weight-kininogen
LTs	Leukotrienes

ml	milliliter
µl	Microliter
NK cells	Natural killer cells
Ng/ml	Nanograms / milliliter
NO	nitrogen monoxide
PAF	platelet-activating factor
PCR	Polymerase chain reaction
PLT	Platelet
PAF-R	PAF-receptor
PAFLL	PAF-like lipids
PGE2	Prostaglandin E2
RBC	Red blood cell
sPD-1	soluble programmed death- 1
sPD-L1	soluble programmed death-ligand 1
SPSS	Statistical Program for Social Sciences
T. gondii	Toxoplasma gondii
T2DM	Type 2 diabetes mellitus
T- cells	Lymphocyte that differentiate in the thymus
T.cruzi	Trypanosoma cruzi
TK	T-kininogen
VIDAS	Vitek immuno diagnostic assay system
WBC	White blood cell
X2	Chi-Square

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CHAPTER ONE
INTRODUCTION

1-1: Introduction

Toxoplasmosis is a zoonotic disease caused by a protozoan parasite called *Toxoplasma gondii* (*T.gondii*) which infects all mammals and birds species throughout the world (Ghoneim *et al.*, 2009). Farther, toxoplasmosis disease is one of the most common parasitic infections affecting a third of the world's population (Akyar, 2011).

Asymptomatic infection is in the host with high immune efficiency (Bessières *et al.*, 2001). The host's immune system can stop parasite multiplication and tissue cysts formation in most body tissues, which are highly concentrated in the central nervous system, as well as skeletal muscles and cardiac muscles without symptoms in most cases (Miller *et al.*, 1999).

It appears to be very dangerous in people with immunodeficiency or immunosuppressive diseases and in pregnant women, where the infection can be transmitted from mother to fetus and lead to abortion or congenital malformations in the fetus (Villena *et al.*, 2010).

The infection is transmitted to humans by eating food contaminated with oocytes from infected cats eating poorly cooked meat containing tissue cysts, drinking unpasteurized milk, contaminated water, contaminated fruits and vegetables, and passing from mother to fetus during phase tachyzoite across the placenta and rarely through blood transfusion or transfusion of infected organs (Dubey, 2016).

When the women infected in pregnancy and transmission to the fetus by the placenta causes a danger to the fetus is the occurrence of abortion or death within the uterus, and the placenta is a key cause of facilitating the passage to the fetus and increase transmission of the disease from mother to fetus as the progressing age of Pregnancy (Zhou *et al.*, 2011; Dubey, 2016).

Over a hundred years ago, *T.gondii* has been discovered and intensively studied with the host's immune response against toxoplasmosis, the intensive study led to developing a practical model of immunity to *T.gondii*. the organism examination help researchers to identify a huge number of resistance requirements to pathogens intracellular, and they characterized several regulatory factors that control processes of inflammatory. However, for the next hundred years of immunobiology to *T.gondii*, an opportunity will be available for the researchers to give answers to the longstanding questions in this area using new reagents and techniques. These future studies will have a major role in building and developing a more comprehensive model of immunity against toxoplasmosis and increasing our comprehension of immunoregulation, especially in humans. Finally, the main challenge is to developing new treatments and vaccines by using this information to control patients infection (Tait and Hunter, 2009).

Many studies were based to evaluate seroprevalence and the importance of various risk factors for *Toxoplasma* infection like age, residential area, pregnancy trimester, abortion number, education level, and blood groups as mention in the studies that investigate a prospective cross-sectional survey was conducted among people (Al-Masoudi *et al.*, 2018; Shaker *et al.*, 2018; Mohammed and Al-Janabi, 2019).

Parasite infection can be associated with an increase in inflammatory mediators, such as cytokines, chemokines, and phospholipids (Machado *et al.*, 2012). There is also an increase in platelet aggregation and myonecrosis in both acute and chronic stages of the disease (Mukherjee *et al.*, 2011). The study of role platelet-activating factor (PAF) in experimental *Leishmania* (*Leishmania amazonensis*) infection indicates that endogenously produced PAF regulates macrophage ability to control *Leishmania* infection and found that PAF is essential for the control of *Leishmania* infection (Lonardoni *et al.*, 2000).

Also, Leukotrienes (LTs) are increasingly recognized to exert broad proinflammatory effects, their role in innate immune responses. These molecules are indeed synthesized by resident and recruited leukocytes during parasite infection. LTs indicate as key host-derived mediators of antiparasite and antimicrobial defense (Peters-Golden *et al.*, 2005).

For a long time, the kinin system has been considered to play a role in the pathophysiology of trauma, particularly in blood pressure changes and in inflammatory effects like a parasite and microbial infection. However, kininogenesis formation in *Plasmodium* infection has been explored. Older reports suggested that kinins may be involved in malaria pathology (Haberland, 1978).

1-2: Aim of Study

The current study aimed to know the effect of chronic infection with *T.gondii* on some immunological parameters, which have an important role in hypersensitivity reactions, through:

1. Investigation of chronic infection with toxoplasmosis in pregnant women in Babylon province who suffer from abortion by using the VIDAS device and linking this infection with some epidemiological factors such as age, area of residence and level of education.
2. Using the hematological analysis device to detected the complete blood picture (CBC) of infected and non-infected women.
3. The use of ELISA technique to detect the concentration of hypersensitivity criteria (PAF, LT-D4, Kininogenase).
4. Analyzing the results statistically and trying to find the relationship between the chronic infection of toxoplasmosis and the criteria for hypersensitivity dealt with in this study.

CHAPTER TWO
LITERATURES REVIEW

2-1: Background of *Toxoplasma gondii* (*T.gondii*)

T.gondii was first discovered more than 100 years ago in 1908 by Nicolle and Manceaux, when he was looking for a reservoir of *Leishmania* in the rodent *Ctenodactylus gundi* at the Pasteur Institute in Tunis (Innes, 2009).

In the same year the parasite was discovered by Alfonso Splendore in Brazil in rabbit tissue, the name *T.gondii* is derived from the Latin language and consists of two sections: The first section Toxon, which means Arc and the second section Plasma and means form (Dubey, 2009).

The first human case was discovered in 1923 by the scientist Janku, who described the parasitic cysts in the retina of a newborn child with cerebral aneurysm (Frenkel, 2000). Machattie first discovered the disease in 1938 in Baghdad Iraq strag dog spleen (Dubey and Jones, 2008).

Wolf was able in 1939 to isolate the parasite from the central nervous system of a newborn child with encephalitis and in 1970 discovered the complete parasite life cycle. Several studies have been conducted to identify the genetic differences between the isolates of the *T. gondii* parasite from humans and animals during the period between 1980 and 1990 (Dubey, 2008).

T.gondii is an intracellular parasite that is capable of infecting all warm-blooded animals including humans (Dubey, 2009). In most cases, it could cause abortion, immunocompromised individuals, encephalitis, and death (Halonen and Weiss, 2013). Transmission in humans are usually occurs via the ingestion of undercooked or raw meat containing cysts or consumption of contaminated food or water with oocysts, in addition to congenitally when the mother got the infection for the first time during pregnancy, where *T.gondii* easily transported to maternal blood and then affected the fetus via the placenta (Tenter *et al.*, 2000). Spontaneous abortion is among the most gestational complications that occurred in responding to this parasitic infection (Lyu *et al.*, 2013). In the first trimester of pregnancies, more than 80% of spontaneous abortions could occur

(Cunningham *et al.*, 2014), and the risk of abortion is boosted with increasing pregnancy age (Juliano *et al.*, 2008).

2-2: Classification

T. gondii was classified according to (Laurin, 2010):

Kingdom: Protista

subkingdom: Protozoa

Phylum: Apicomplexa

Class: Sporozoasida

Order: Eucoccidiorida

Suborder: Eimeriorina

Family: Sarcocystidae

Genus: *Toxoplasma*

Species: *T.gondii*

2-3: Strains of *T.gondii*

The parasite has three types of strains, type I (Rh), which is more ferocious than type II (II), called ME49, and type III (C56). It is also the Fastest-growing of the second and third strains (Radke *et al.*, 2001). The type I, II, and type III are widely studied and characterized by the growth rate, frequency by differentiation to the bradyzoite stage, gliding motility, the potential to cross biological barriers, disruption of host cell signaling as well as pathology during acute and chronic infection in mice. The type II strains cause the majority of infections in humans, which reflects the abundance of these strains in livestock (Howe and Sibley, 1995). Rodents also natural hosts for *T.gondii* and mice are widely used as laboratory models. The type I strain is considered as a virulent strain with a lethal dose of one single parasite in mice, whereas type II and type

III considered intermediate or low virulence strains (Sibley and Boothroyd, 1992).

Human infections are the first type strains, which are responsible for serious obstetric and immunosuppressive patients 75%. Vilares and Angelo (2004) studied to identify parasite that causes Toxoplasmosis in women using PCR technique all cases are related to the type I strain (A'aiz, 2010).

2-4: Life cycle

2-4-1: Tachyzoite

The term Tachyzoite is derived from the Latin language by the world Frenkel in 1973. The Tachos section means fast speed relative to the speed of its propagation of parasite. Its crescent shape characterizes it. Its length reaches six microns and its width is two microns and is accompanied by acute infection (Dubey *et al.*, 1998).

The tachyzoite phase of the pellicle is surrounded by two membranes known as the outer membrane of the plasmalemma, consisting of a single layer, while the internal membrane is composed of two layers that are close together. The internal membrane is characterized as non-continuous as it opens in three first positions at the front end and the second at the rear end and the third in the side flanges (Morrissette and Sibley, 2002).

The tachyzoite phase is known in other terms as the feeding phase or endozoite, as well as the proliferative phase; the tachyzoite phase is multiplied by the endodyogeny. As shown in Figure (2-1, A), the nucleus of the parent channel is divided into two parts, followed by the formation of a new membrane, consisting of two young posts. The mother cell membrane is then ruptured by independent individuals, followed by the rupture of the host cell wall and the spread of parasites to infect new cells (Shaw *et al.*, 2000).

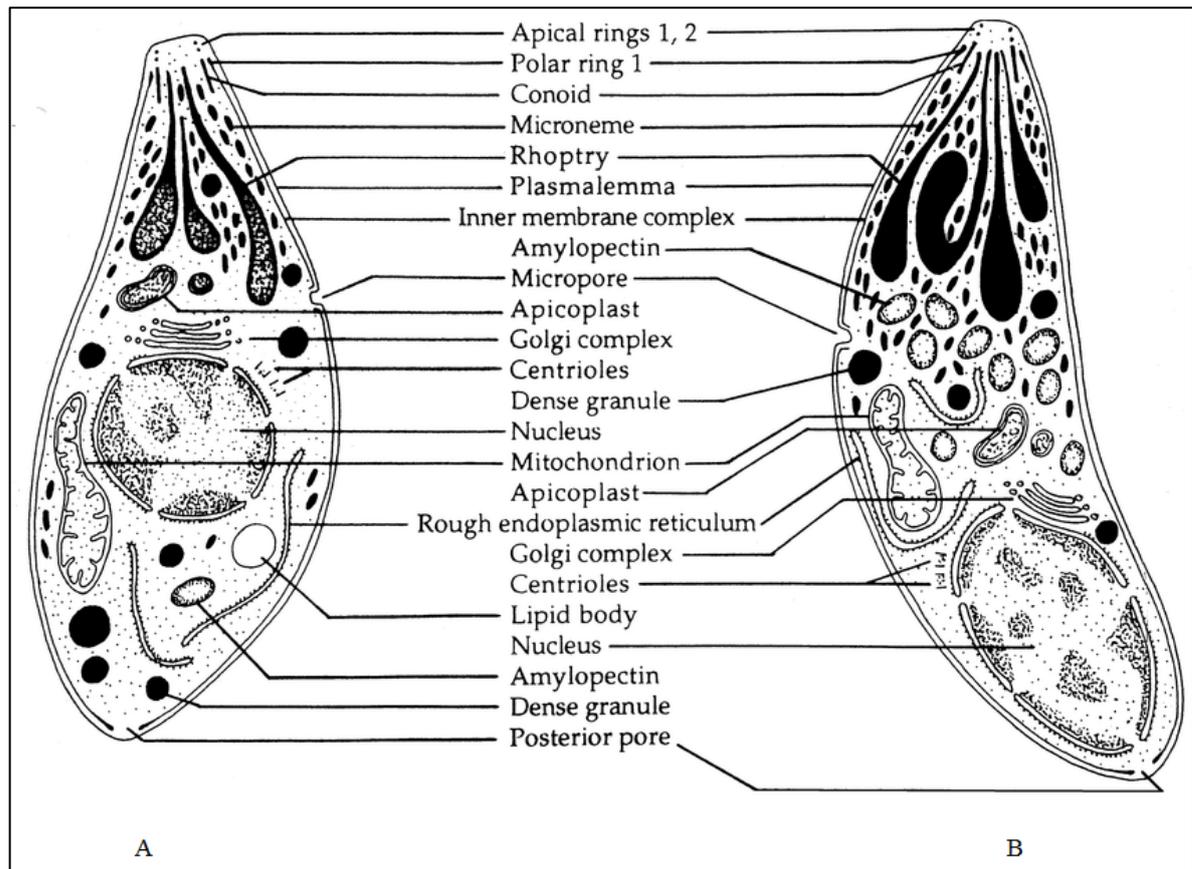


Fig (2-1): **A.** Tachyzoite, **B.** Bradyzoites (Dubey, 2016)

2-4-2: Bradyzoites

The term Bradyzoite was derived from the Latin language by the world Frenkel in 1973 since the Brady section means Slow because it slowly proliferates inside the cysts. Spherical or oval cysts are about 10-200 microns and are known as tissue cysts (Dubey *et al.*, 1998).

The cysts contain about 1000-2000 individuals in the shape of a crescent with a diameter of 1.5 microns and the size of the cyst depends on the number of individuals inside, see Figure (2-1, B). The slow-growing stage proliferates in an internal budding manner; the tissue wall dissolves in the stomach and releases the slow-growing phase that resists the effect of infectious juices (Weiss and Kim, 2000).

It reproduces slowly and becomes inside a gap surrounded by a thick real wall forming the wall of the cyst (Zhang *et al.*, 2010).

The slow stage of reproduction is mainly stabilized in the tissues of the nervous and muscular organs, which are present in the heart, brain, and retina. However, it may exist in the visceral organs such as the lungs, liver, and kidney. It lasts for a long period of several months or years or lasts a lifetime (Skariah *et al.*, 2012).

2-4-3: Oocysts

Double-layer membrane oocysts ranging in size from 10-12 microns (Tenter *et al.*, 2000). These oocytes are produced by the sexual reproduction within the epithelial cells of the host's intestines, where the immature oocysts exit with the feces into the external environment and then develop into two sporocysts, each containing four sporozoites, see Figure (2-3). These oocytes are highly resistant to environmental conditions, in wet soil or water for several months or several years (Possenti *et al.*, 2013).

The oocyst resist chemical treatments and ultraviolet radiation used to purify drinking water. oocyst phase and tissue cyst phase are the most dangerous stage in the transmission of infection to the middle and final hosts (Fritz *et al.*, 2012), Figure (2-2).

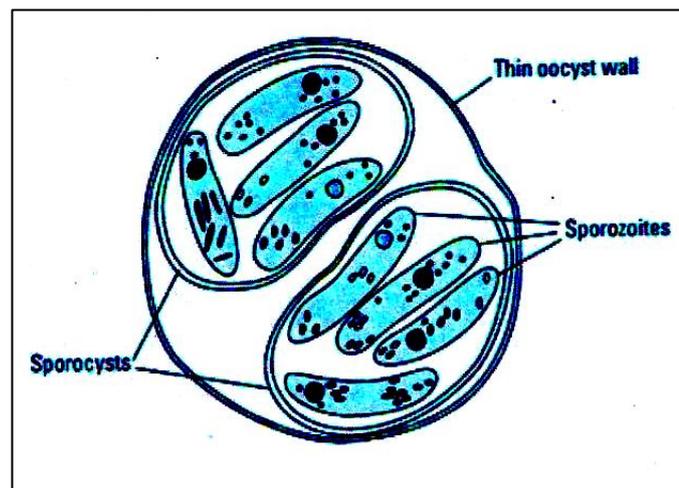


Fig (2-2) Oocysts of *T.gondii* (Dubey, 2016)

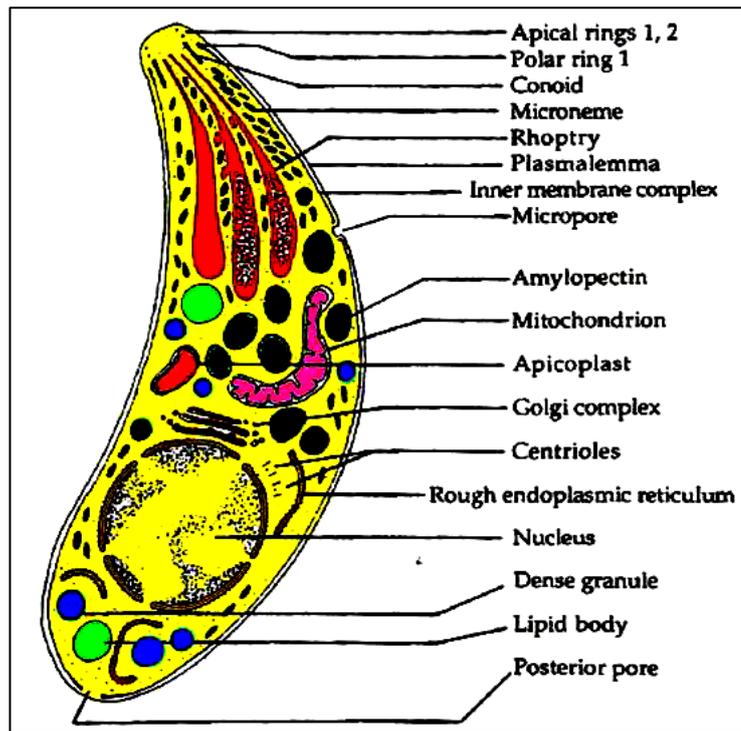


Fig (2-3) Sporozoites schematic diagram of *T. gondii* (Dubey, 2016)

2-5: Life Cycle

The stage of the life cycle of *T. gondii* is complex, consisting of two stages and each phase requiring a particular host; the first stage is the sexual cycle in the epithelial cells of the small intestine in the final host only (cats). The second stage is the asexual phase in the intermediate and final hosts (Van *et al.*, 2007). The intermediate host is infected when swallowing tissue cysts with uncooked raw meat or when ingesting oocysts with contaminated food and drink or with vegetables and fruits. The wall of tissue cyst and oocysts dissolves in the stomach with the influence of infectious juices, Figure (2-4).

The bradyzoites and spores are released respectively, penetrate the epithelial cells the lining of the small intestine, turn into the tachyzoite stage, and pass through the bloodstream (Lyons *et al.*, 2002). Which infect all the host cells as they penetrate the cells and have a gap to multiply in the manner of internal budding, after the number reaches 64-128 individual free after the destruction of the host cell, and excreted into the bloodstream (Black and Boothroyd, 2000).

The *T.gondii* parasite passes through the intermediate host in two stages of the first asexual reproduction: the multiplication of the tachyzoite stage in different types of host cells and the second begins with the conversion of the tachyzoites stage and the formation of the tissue cysts. This stage represents the end of the parasite's life cycle within the host (Andreoletti *et al.*, 2007).

The sexual stage of the parasite begins when swallowing tissue cyst by the final host with infected prey such as predators or swallowing oocysts. When the bradyzoites phase and the spores are released in the small intestine and then penetrate the epithelial cells of the intestines of the final host and divide for five generations of individuals and ends. The formation of the sex cells responsible for the production of male gametes (microgametocytes) and female gametes (microgametocyte). The fertilization process to form the zygote, which is surrounded by thick double and then develop to form the oocyst that is raised with cats feces (Ajioka *et al.*, 2001).

The unsporulated oocyst are kept out of cats for 3 to 18 days and, under appropriate environmental conditions, the sporulated oocyst is reduced to Meiosis and reproduce as eight sporozoites are produced in the single oocyst and become contagious within three weeks, which can infect the intermediate and final hosts of the non-sexual phase (Rorman *et al.*, 2006).

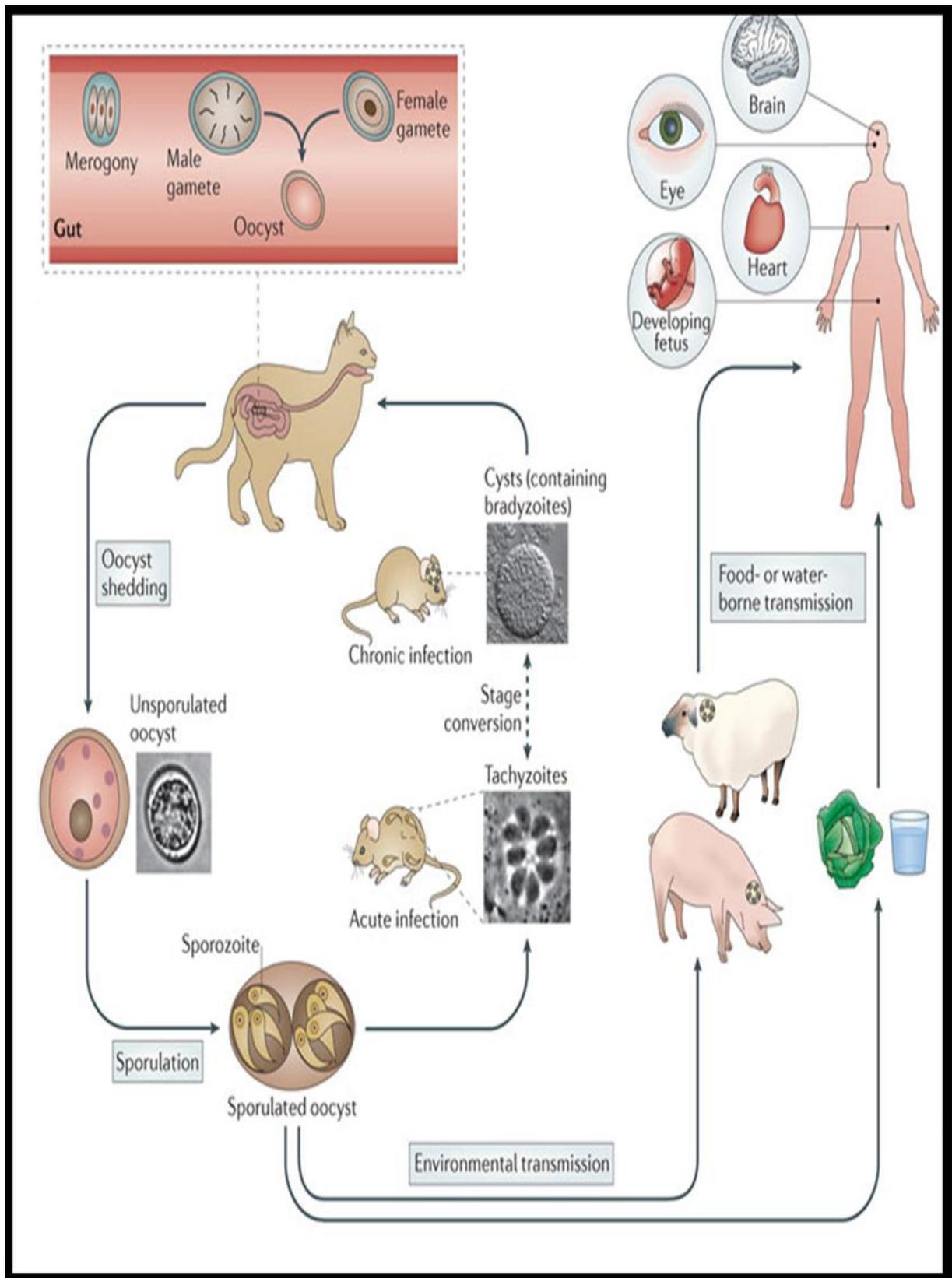


Fig (2-4): The life cycle of *T.gondii* (Hunter and Sibley, 2012)

2-6: Transmission modes

This parasite transmission in several ways:

1. Oral transmission: intermediate and final host of parasites are infected when eating infected meat containing tissue cysts. It affects humans when eating raw or poorly cooked meat, or when eating raw contact raw meat, as well as, contact with meat cutters from which would transfer tissue cysts from hand to mouth (Montoya and Liesenfeld, 2004).

Human and herbivorous animals may be infected with fecal contaminated fruits and vegetables in their oocysts with feces or when they contact contaminated soil and water (Jones and Dubey, 2012).

The tachyzoite may enter the host's body by penetrating the mucous tissue of the mouth and esophagus and then reach the circulatory system without entering the stomach.

This explains the infant's infection because of the tachyzoite of the mother's milk, causing the child to infect with the acquired toxoplasmosis. The tachyzoite in body fluids such as saliva, sputum, edema, tears, and semen (Tenter *et al.*, 2000). Drinking unpasteurized milk for infected animals is particularly important in rural areas as well as contaminated dairy products (Bayarri *et al.*, 2012).

Studies have shown the role of insects such as cockroach and flies in transporting oocysts from cat feces to foods (Frenkel *et al.*, 1995). Birds are a source of infection, some of them a source of food, such as chickens, ducks, and others, as birds are infected by eating earthworms or food contaminated with cat feces (Literák and Hejlíček, 1993).

2. Transition through the placenta: The stage of tachyzoite of the infected mother to the fetus through the placenta and often occurs in the transition to the initial infection of the mother with the parasite is transmitted because of the activation of chronic infection. The most dangerous

methods of infection due to the damage and birth defects of the fetus (Dalgıç, 2008).

3. The transition from one person to another: Occur in rare cases when transplants or blood transfusions from the infected person to another healthy or when acupuncture and sharp tools are contaminated for laboratory workers (Andreoletti *et al.*, 2007).

2-7: Epidemiology

2-7-1: Epidemiology of *T.gondii* around the world

Extensive studies have been conducted to investigate seroprevalence percentages in different parts of the world. The greatest importance comes from prevalence among women of childbearing age:

Pinlaor *et al.* (2000) recorded that the prevalence of toxoplasmosis in Costa Rica and the Guatemalan population was recorded at 94%. An epidemiological survey was conducted on the prevalence of Toxoplasmosis in the Netherlands among pregnant women in 2001; The study showed that 32% of pregnant women carry the specialized antibodies to toxoplasmosis by using the ELISA technique (Vlaspolder *et al.*, 2001).

The prevalence of the disease in the Kwazulu-Natal city of South Africa's was 39% among pregnant women and 43% among AIDS patients (Moonasar *et al.*, 2001).

Gilbert and Peckham (2002) report that the incidence of congenital toxoplasmosis in some European countries was 11% in Norway, 14% in Sweden, and up to 20% in Finland and 28% in Denmark, and the highest in the Netherlands 45%, Poland 54%, and France 59%.

Terazawa *et al.* (2003) found that the prevalence rates of toxoplasmosis in Southeast Asian countries was variable, as the prevalence in Indonesia was 70%, 2-75% in Bangladesh, while in Malaysia, Singapore, Thailand, Vietnam and

Japan was less than 20% and 30-60% in the Philippines. Amieva *et al.* (2005) recorded the acute incidence of neonatal deaths in Mexico and two cases per 1,000 new births using the ELISA-IgM technique.

Song *et al.* (2005) examined 5175 serum samples and 750 samples of chorionic fluid to investigate of chronic toxoplasmosis and found that the prevalence rate of chronic toxoplasmosis were 0.79% and 1.33% for both types of samples respectively in pregnant women in Korea. Alvarado-Esquivel *et al.* (2006) conduct a study on pregnant women in northern Mexico, where 343 serum samples were examined and that the prevalence of chronic toxoplasmosis was 6.1%. Francisco *et al.* (2006) reported that the incidence rate of *T.gondii* infection was in Brazil 40-80%. Toxoplasmosis is also common in African countries, with Nigeria registering 75% and Senegal with 40.2% Simpore *et al.* (2006).

Jones *et al.* (2007) report the incidence of toxoplasmosis infection in the United States of America among people aged 6-49 years 10.8%, in women aged 15-49 years 11% and 9% among Americans aged 12-49 years. In Turkey, Ocak *et al.* (2007) examined 1652 serum samples of pregnant women using the ELISA test to determent chronic and acute toxoplasmosis and found that the chronic was 52.1% and acute was 0.54%.

In South America, particularly in Cali, Colombia. Rosso *et al.* (2008) reported sero-prevalence rate in chronic and acute toxoplasmosis in pregnant women found that the percentage of infection was 45.8% and 2.8% respectively.

In the study of Abdi *et al.* (2008), 553 serum samples from Iranian women were tested, and found that the prevalence percentage of toxoplasmosis infection was 44.8%.

The incidence of toxoplasmosis infection varies widely in the world; showed that the study in Mexico by Alvarado-Esquivel *et al.* (2009), prevalence of chronic was 8.2% and acute was 2.3% among pregnant women by using the

ELISA technique. Jitender Prakask Dubey (2010) reviews the studies conducted to determine the toxoplasmosis in more than 80 countries (including Iraq), the results showed that the percentage of infection was 4% to 92%. Another study showed the prevalence of chronic toxoplasmosis in Thailand among pregnant women was 21.6% (Nissapatorn *et al.*, 2011). A study was conducted the acute toxoplasmosis in India by Pignanelli (2011) on 40 blood samples for women found that the incidence of IgM antibodies was 25% by using Real-Time qPCR. A study in Ethiopia by Zemene *et al.* (2012) included 201 blood samples of pregnant women by using the ELISA technique show the percentage of IgG was 83.6% and IgM was 2.5%.

The eating of unsweetened pork has been a major reason to contributor the spreading of toxoplasmosis infection in Taiwan, and the chronic and acute infection of toxoplasmosis were 9.3% and 0.28% respectively (Chiang *et al.*, 2012).

A study in Brazil found that the environment contaminated with oocysts of *T.gondii* is the decisive factor for the spread of infection among different age groups, and found the incidence rate was 50% among the age group 6-12 years and (50-80)% among women of childbearing age (Dubey *et al.*, 2012).

The incidence of infection among women of childbearing age in northern Portugal was high through a study by Lopes *et al.* (2012), which included 401 samples with prevalence percentage IgG was 93.9% and IgM was 2%, In India, a study by Malarvizhi *et al.* (2012) involved 232 blood samples of pregnant women by using ELISA to detect IgG and IgM, the results were 9.9% and 3.9%, respectively.

While in Aguascalientes City in Mexico, Alvarado-Esquivel *et al.* (2016) determined the *T.gondii* infection in pregnant women who attended prenatal care in 3 public health centers, results show 6.2% had IgG antibodies, and 4.8% of them was also positive for IgM antibodies.

2-7-2: Epidemiology of Toxoplasmosis in Arabic Countries

Many studies and research have been conducted in various Arab countries to determine the percentage of toxoplasmosis infection because this disease is of great importance in both health and economic terms, as it is one of the main causes of abortion in women and the other fatal complications it causes in humans and animals. The following is a review of the most important of those research and studies:

In Sudan, Elnahas *et al.* (2003) showed the percentages of chronic and severe acute toxoplasmosis among pregnant women were 65.9% and 14.3% respectively by using the ELISA technique.

Nimri *et al.* (2004) conducted a study on 148 Jordanian women with an abnormal previous pregnancy to determine chronic and acute toxoplasmosis and found that the percentages of infection were 45% and 2.7%, respectively. The results of Al-Harhi *et al.* (2006) study in Makkah by using the ELISA technique, found that the prevalence of chronic and acute toxoplasmosis among pregnant women (aged 17-45 years) were 29.4% and 5.6%, respectively.

In Kuwait, the results of the Iqbal and Khalid (2007) study on 224 pregnant women in the first four months of pregnancy showed that the prevalence of chronic and acute toxoplasmosis were 53.1% and 13.8%, respectively.

In Egypt, 51.49% of women were infected with toxoplasmosis in a study of Ibrahim *et al.* (2009), by using the ELISA technique.

The results of the study conducted in Qatar on 823 women of childbearing age found that the prevalence of IgG and IgM antibodies were 35.1% and 5.2% respectively (Abu-Madi *et al.*, 2010).

Elamin *et al.* (2012) conducted study in Sudan that showed that incidence percentage of toxoplasmosis infection was 39.4% by using the ELISA technique.

In another study conducted 224 Kuwaiti women in their first trimester were examined by VIDAS system to determine chronic and acute toxoplasmosis, the results of this study found 31(13.8 %) women were positive for IgM antibodies and 119(53.1%) women were positive for IgG antibodies (Iqbal and Khalid, 2007).

2-7-3: Epidemiology of Toxoplasmosis in Iraq

In Iraq, interest has increased recently in conducting research and studies of infection with the *T.gondii* parasite, because of this parasite of great health importance and the great danger it passes to the health of individuals, especially women. The following is a review of the most important of those research and studies:

Toxoplasmosis investigated and diagnosed by Shani (2004) in Basrah province, with 420 women who had been attend to the primary health care department in Basrah, with a prevalence percentage was 36.67%.

A study by Abdulmohaimen and Mezban (2010) in Baghdad among pregnant women between 20 and 50 years old and the incidence of toxoplasmosis by ELISA technique was 60%. In Muthanna, 44% of pregnant women diagnosed by LAT test was infected and highest incidence among women have 30-35 years old (Al-Seadawy, 2010).

The results of the study conducted by Kadir *et al.* (2011) in Kirkuk province show that cases of 319 patients with toxoplasmosis (36.6%) using latex, 54 positive by using ELISA (16.9%). The results of Al-Ramahi *et al.* (2005) in Diwaniyah province indicat that the infection percentage was 49.65%. The study of Al-Kalaby (2008) in the province of Najaf Al-Ashraf that the incidence percentage was 80% by using PCR technique, In Sulaimaniya, a study was conducted by AL-Taie (2009) showed the percentage of infection by using LAT and ELISA technique were 37.63% and 58.6%, respectively.

In Tikrit, Addory (2011) conducted a study to investigate the chronic and acute toxoplasmosis among pregnant women with miscarriage by ELISA technique and he found the total percentage of infection were 26.1% and 3.1%, respectively.

However, in Al-Hassnawi *et al.* (2015) study conducted Fifty-seven toxoplasmosis patients, and 102 subjects without toxoplasmosis as a control group. This study results showed a significant differences between toxoplasmosis patient group and the control group, where the level of *T.gondii* IgG in infected women with (26%) percentage was higher than in the control group with percentage (7%).

Abdullah and Mahmood (2017) make a study to determine the seroprevalence of the parasite antibodies in pregnant women attending to Maternity and Pediatric Hospital in Erbil city, they found two hundred sixty-three serum samples were tested, 92/263 (34.8%) of them had IgG antibodies and 34/263 (12.93%) were positive for IgM antibodies against *T.gondii*.

Mohammed and Al-Janabi (2019) conducted a comparative study in Babylon province to determinate the percentage of toxoplasmosis infection by more than one method, and they found the rate of infection by LAT test was 42.6%, while 4% and 22.6% by using the ELISA technique to detection IgG and IgM, respectively.

In another study, 500 pregnant women are attending to antenatal clinics at Teaching of AL-Hussain Hospital in Holy Karbala province were tested to determinate chronic and acute toxoplasmosis and that found the titer of infection of IgG has more than 0.9 and IgM has more than 0.8 (Lefta *et al.*, 2020).

Mohammed *et al.* (2020) investigated the sero-prevalence of anti-*T.gondii* IgG antibodies in Baghdad Iraq T2DM patients and the role of soluble programmed death-1 (sPD-1) and (sPD-L1) in Iraqi T2DM patients with chronic toxoplasmosis. The results showed that 117 (34%) samples of sera patients have

been founded T2DM with toxoplasmosis, 63(18%) samples have T2DM, 55(16%) cases have control toxoplasmosis (those patients were had toxoplasmosis but showing no symptoms) and 108 (32%) cases samples were considered as a control group without any infections.

2-8: Pathogenicity and Symptoms of *T. gondii*

The clinical manifestations of toxoplasmosis are the result of the tachyzoite propagation of the various cells of the body and multiplying within them, which cause the destruction and killing of the cells and spread the parasite to infect new cells causing inflammation, necrosis and tissue damage (Henriquez *et al.*, 2009). The damage caused by infection varies from symptomless in people with a healthy immune system (Demar *et al.*, 2007). To the death of the patient, especially those with immunodeficiency, and the infection of pregnant women and the damage to the fetus varies depending on the age of pregnancy in which the infection occurs (Leng *et al.*, 2009). Studies show that 90% of pregnant women who give birth to children with congenital toxoplasmosis do not have symptoms of the infection and if symptoms appear, they are similar to the flu symptoms of fever, malaise, lymph node disease, lymphadenopathy (Goldstein *et al.*, 2008). Toxoplasmosis can be divided into:

2-8-1: Congenital Toxoplasmosis

When a mother is first infected with the *T.gondii* parasite during pregnancy, the parasite can be transmitted to the fetus. The rate of transmission and the severity of the infection varies according to gestational age and the immune response to the mother (Aptouramani *et al.*, 2012). If the mother has sufficient immunity, she will be able to reduce transmission (Letscher-Bru *et al.*, 2003). The infection may causing congenital toxoplasmosis (Kravetz and Federman, 2005).

The severity of the disease in the fetus is inversely proportional to the age of pregnancy in which the infection occurred and the rate of transmission of the infection is directly proportional to the stage of pregnancy (Sáfadi *et al.*, 2003).

As the transition during the first trimester of pregnancy up to 15%, but the damage caused by, it is lead to severe causes of abortion or the birth of dead embryos or infected with congenital malformations. Increase the rate of transition during the second trimester of pregnancy to 25% lead to symptoms at birth, where the fetus is less likely to miscarry in this trimester of pregnancy, but it is prone to severe symptoms such as hydrocephalus (accumulation of water in the brain), calcifications of the brain, or inflammation of the retina of the eye. When the rate of transmission reaches 65% is not accompanied by symptoms at birth but develops with the child's age (Montoya and Liesenfeld, 2004).

A child may be born with problems such as a neurological, visual, and auditory disability at birth, and health problems may be so severe that the child dies a few days after birth (Freeman *et al.*, 2005). Congenital malformations include hydrocephalus, microcephaly, intracranial calcifications, mental retardation, chorioretinitis, delayed growth, hepatic and spleen enlargement (J. L. Jones *et al.*, 2003).

2-8-2: Acquired Toxoplasmosis

The *T.gondii* affects all age groups of both sexes and causes acquired toxoplasmosis, but it is rare in infants who have not reached their first year most of their infections are congenital (Freeman *et al.*, 2005). The incubation period ranges between 4-21 days (Rorman *et al.*, 2006).

The disease symptoms are similar to the symptoms of influenza, which are fever, headache, rashes, painful joints and muscles, weight loss and lymphatic colitis (Carme *et al.*, 2009). After three weeks of infection, the immune response to the body develops (Lekutis *et al.*, 2000).

The disease occurrence at any time after birth and may be localized in a particular organ of body. They infection often occurs in people with HIV, such as AIDS or cancer, as well as those who have been treated with cortisone for a long time. In many of these cases, the effect on the lymphatic system is emergence of hypertrophy in the lymph node (Beaman, 2001). The *T.gondii* is an opportunistic parasite is that exploits the weakness of the body's immune system to turn the chronic infection into an active one. The infection spread through the blood and tissue damage occurs. The most common clinical manifestations are encephalitis, neuropathy, high intracranial pressure, osteoporosis, hepatic hyperplasia liver and spleen, and nephropathy (Ajzenberg *et al.*, 2009).

2-8-3: Ocular Toxoplasmosis

Cases of this disease occur after the initial infection directly but most of the infection due to the activation of a previous infection caused by chronic rupture of tissue cyst and cause iris inflammation (Fekkar *et al.*, 2011). In addition to the choroidal network, inflammation and gray or white spots were found on the back of the retina, and necrosis occurs in the retina, accompanied by secretions and sometimes bleeding. Eye inflammation usually takes six weeks and then begins to decline, leaving behind a pigment and scar on the retina (Kaye, 2011). That can be cured in the eye can be treated but left untreated can lead to glaucoma, cataracts, and optic nerve atrophy (Bonfioli *et al.*, 2005).

2-9: Immunity against *T.gondii*

A complex immune response generated at the time of infection and includes a cellular immune response against the bradyzoites phase and humoral immune response against the tachyzoite in body fluids (Johnson and Sayles, 2002).

2-9-1: Cellular Immune Response

Cellular immunity includes the action of macrophages, T-lymphocytes, natural killer cells (NK), and Cytokines (Filisetti and Candolfi, 2004).

The macrophages are activated by IFN- γ to go to where the parasite is located to be swallowed and then surrounded by a phagosome glomerulus, The lysosomes are then carried out through the gap wall and parasite decomposition (Andrade *et al.*, 2006). Macrophages also use non-oxidizing mechanisms, such as the production of nitrogen monoxide (NO) to inhibit parasite proliferation (Schlüter *et al.*, 1999). The macrophages cell produces the enzyme Indoleamine 2,3 dioxygenase to inhibit tryptophan needed for parasite growth (Filisetti and Candolfi, 2004).

IFN- γ and cytokines are produced by T-lymphocyte (CD4, CD8) as produced by natural killer cells. IFN- γ activates the phagocytic cells for parasitic infection and kills them and stimulates this cells to produce important cytokines, including interleukin 12 (IL-12) and alpha-type necrosis factor (Cai *et al.*, 2000). Dendritic cells (DC) also acting on the production of interleukin 12, which activates natural killer cells to produce interferon Gama (IFN- γ) (Tait and Hunter, 2009).

2-9-2: Humoral Immune Response

The infection of the *T.gondii* parasite stimulates the immune system to generate IgG, IgM, IgA and IgE immunoglobulins and are effective in eliminating the tachyzoite phase (Filisetti and Candolfi, 2004).

The parasite leads to tissue penetration and the formation of tissue cysts (Sayles *et al.*, 2000). Antibodies have the ability to kill parasites outside the cells and not within it. Recent studies have shown the important and effective effect of the humoral immunity factors in the acquired resistance against the toxoplasmosis, Immunogenesis develops as the infection progresses, resulting in the antibodies . The first antibody formed is IgE, which appears very short and is

unstable at the stage of primary infection of toxoplasmosis (Dubey, 2008). IgA then begins to appear after parasitic permeation of the mucous immune system begins by secreting this antibody, which interferes with the parasitic ability of the parasites on adhering to the mucous surfaces, including the *T.gondii* parasites, thereby preventing systemic infection (Meek *et al.*, 2000).

Immune response to antibodies begins after the parasite enters the blood stream through the intestine and lymph. The IgM antibodies form within one to two weeks after primary infection, whereas IgG antibodies synthesis usually after four weeks from infection (Jawetz *et al.*, 2001). The IgG antibody is the second type of antibody that appears and contains four subtypes that differ in their ability to fix the complement. Three IgG1, IgG3 and IgG4 play a role in protecting the fetus because they have the ability to cross the placenta (Filisetti and Candolfi, 2004). IgM and IgA antibodies are the most common sign of obstetric infection because they do not cross the placenta and the newly born baby makes it (Pataki *et al.*, 2001). However, the IgA antibody test for *T.gondii* is recommended to diagnose obstetric infection because it is more sensitive than IgM antibodies (I. M. X. Rodrigues *et al.*, 2009).

2-10: Hematological parameters

2-10-1: The relationship between Toxoplasmosis infection with some blood components

T.gondii infection constitutes a complex immune response that includes both cellular immunity (macrophages, T lymphocytes, and natural killer cells), and humoral immunity (antibodies). Although antibodies represent the primary means of diagnosing toxoplasmosis in humans, while cellular immunity represents the main factor in responding to the host's immune response in the event of an attack by *T.gondii* (Filisetti and Candolfi, 2004). Granular leukocytes, especially neutrophils, are the most common leukocytes and have an important role in the host through their effective action in destroying the parasite

(Denkers *et al.*, 2011), it also plays a key role in the innate immune system and bone marrow responsible for producing neutrophils and rapidly accumulates at sites of invasion of microbial pathogens and in *T.gondii* infection. Neutrophils represent about 85% of circulating macrophages, more than 50% of the total circulating white blood cells, and large numbers of neutrophils arise in tissues, which would enable them to mobilize rapidly in response to inflammation or infection as the phagocytes invade the bacteria (Khanfer *et al.*, 2011). Phagocytosis has a role in toxoplasmosis infection, where high levels of macrophages reflect the effectiveness of immunity to infection, and we can reach the diagnosis of the infected patient by knowing the percentage of active neutrophils, which appear as deposits inside the plasma, and this percentage usually increases in bacterial infections (Kovalik *et al.*, 2011).

2-10-1-1: Hemoglobin (Hb)

Hb is the main component of oxygen transport in the blood, and it is necessary for the survival of living organisms, especially multicellular organisms, and hemoglobin works in the transport of other gases, as it contains about 10% of carbon dioxide through the union of carbon dioxide gas (with globin protein). Hb also carries a molecule of nitric oxide, which is one of the important regulatory molecules (Hsia, 1998), with one pair of alpha chains and one pair of beta chains (Voon and Vadolas, 2008), which is the main component of protein in red blood cells (92% of the dry weight). It is known that during pregnancy, many changes occur in the mother's blood circulation, where the blood rate increases by about 1.5 liters due to the increased need of the body and the expansion of blood vessels, and there is approximately one liter of blood around the uterine area and the placenta. In general, a clear increase in the average plasma volume of approximately 10-15% occurs during 6-12 weeks of pregnancy. On the other hand, the Hb concentration decreases, at a rate of grams/dL, and returns to relative stability in the last trimester of pregnancy (Yanamandra and Chandrahara, 2012). Another cause of anemia is that the

number of red blood cells is insufficient to meet the physiological demand of the body, or when the Hb is less than a certain limit (13% gm/dL for men and less than 12% gm/dL for women) (Penninx *et al.*, 2003). This varies according to gender, age, and pregnancy status, and also the low concentration of Hb in women with toxoplasmosis can be attributed to the multiplication of the parasite within the cells of the host body (Jones *et al.*, 1997). This may lead to the deterioration of red blood cells, which may cause anemia, and during pregnancy, the plasma experiences a relatively slight increase compared to red blood cells, which leads to a decrease in blood concentration, diluting the blood, which is called "physiological anemia" for pregnancy, and the ratio is also less than 11% gm/dL anemia blood in women with *T.gondii* infection (Yanamandra and Chandraharan, 2012).

2-10-1-2: White blood cells (WBC)

WBC names' comes from its appearance as a blood sample after being separated by centrifugation. White cells are found in a white nuclear cell layer of blood plasma and red blood cell sediment. WBCs in the immune system are involved in protecting the body against both external microbes and infectious diseases. All WBCs are produced from hematopoietic stem cells in the bone marrow, then WBCs are found throughout the body, including the blood and lymphatic system (Denburg and Bienenstock, 1979). Changes in the number of WBCs may indicate the presence of a disease, and the number of normal blood cells is about 4000-11000 cells per microliter of blood, which is approximately 1% of the total blood of a healthy individual. There are five different types of white blood cells in two groups (Hollowell *et al.*, 2005):

- The first group is called granulocytes (neutrophils, eosinophils, basophils)
- The second group is agranulocytic (monocytes and lymphocytes)

The number of WBCs increases above the normal limit and decreases below the normal limit in some cases. The increase means more serious

diseases, such as leukemia, myeloproliferative disorders, or injury caused by a bacterial, fungal, parasitic, or viral infection (Abramson and Melton, 2000).

2-11: Immunological Parameters

2-11-1: Platelet-Activating Factor (PAF)

The Platelet-Activating Factor (PAF) also known as PAF-acether or AGEPC (acetyl-glycerol-ether-phosphorylcholine) has been identified as a phosphoglycerylether lipid mediator involved in diverse physiological and pathophysiological processes. It seems apparent that PAF has different physiological roles in animals, plants, and unicellular organisms. It is considered the most potent lipid mediator known to date (Siafaka-Kapadai *et al.*, 1986; Demopoulos, 2000). Before the 1970s, lipid mediators were thought to be generally derived from phospholipids. However, PAF was the first intact phospholipid mediator to demonstrate messenger functions (Prescott *et al.*, 2000). The PAF structure is (I-O-alkyl-2 (R) acetyl-sn-glycerol-3-phosphocholine) (Koltai *et al.*, 1991), see Figure (2-5).

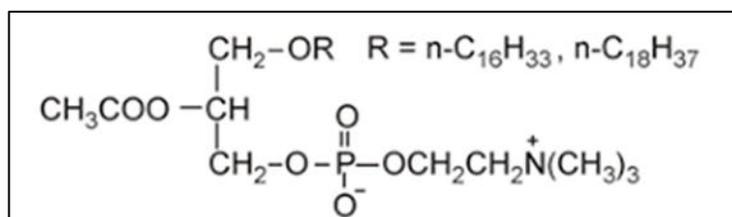


Fig (2-5): The chemical structure of PAF (Koltai *et al.*, 1991)

PAF was initially considered one molecule, which is commonly referred to as the classical PAF. Now it is understood that there are a large number of structurally related phospholipids or PAF analogues that are dissimilar in structure to PAF that interact with the PAF-receptor (PAF-R) and belong to the 'PAF family', collectively known as PAF-like lipids (PAFL). However, PAF refers to the classical structure reported in 1979, which is responsible for most of the known biological effects and is thought to be the most potent PAF molecule. PAF mediates a wide variety of cellular functions and cell-cell interactions.

Therefore, PAF is involved in several physiological processes including apoptosis, physiological inflammation, wound healing, reproduction, angiogenesis, long-term potentiation (MacLennan *et al.*, 1996; Birkl *et al.*, 2019).

Indeed, the study by Chap *et al.* (1981) provided the first evidence that platelets synthesize PAF, and they determined the subcellular localization of PAF biosynthesis in human neutrophils (Ribbes *et al.*, 1985). Studies began to discern that PAF was implicated in IgE anaphylaxis (Henson and Pinckard, 1977), and many of the properties of PAF released during IgE anaphylaxis began to be elucidated (Pinckard *et al.*, 1979). Furthermore, the role of PAF in platelet aggregation was beginning to be further understood by June 1979 (Chignard *et al.*, 1979).

Benveniste and others had determined several of the physical However, the parameter feature of PAF physiologically and in disease is that the biological effects of PAF can be modulated by diet, lifestyle, and environmental factors (Argyrou *et al.*, 2017; Tsoupras *et al.*, 2018; Travers, 2019). This means that PAF could be a potential therapeutic target for many chronic diseases (Demopoulos *et al.*, 2003; Tsoupras *et al.*, 2018; Lordan *et al.*, 2019).

PAF itself is synthesised constitutively or under appropriate stimuli by a variety of cells such as platelets, macrophages, monocytes, neutrophils, basophils, eosinophils, mast cells, and endothelial cells. PAF is synthesised by two markedly different pathways known as the *de novo* and remodelling pathways (Lordan *et al.*, 2017).

The signalling functions of PAF are mostly associated with acute and chronic inflammation in essentially all organs, which are well characterised in the literature (Prescott *et al.*, 2000; Yost *et al.*, 2010).

Apart from acute inflammation, PAF is involved in cell signalling mechanisms for a number of other physiological processes. For instance, PAF has several surprising roles in reproduction physiology. Indeed, PAF signalling

modulates female reproductive events including ovulation, fertilisation, preimplantation, implantation, and parturition. It is also thought that PAF plays a role in male reproduction due to the presence of PAF in spermatozoa, which may be involved in the induction of acrosome reaction and sperm motility (Kumar and Sharma, 2005; O'Neill, 2005; Lecewicz *et al.*, 2016; Sakellariou *et al.*, 2008). Phospholipids predominate in the brain and play several critical structural and physiological roles (Senanayake and Goodenowe, 2019). Therefore, it is unsurprising that PAF also seems to play a crucial role in cell signalling of the CNS. PAF is synthesised by neural cells spontaneously or following appropriate stimuli (Sogos *et al.*, 1990; Farooqui *et al.*, 2008). PAF is also a mediator of regular cardiovascular-related physiology as it involved in the mediation of blood pressure and normal inflammatory and haemostatic responses (Tselepis *et al.*, 1987; Evangelou, 1994; Montrucchio *et al.*, 2000).

The results of Lonardoni *et al.* (2000) study showed that the inhibition of parasite growth correlates better with the presence of PAF or absence of Prostaglandin E2 (PGE2) than with the levels of NO production. Also, show that after treatment of mice with PAF antagonists, the course of infection in a relatively resistant strain (C57BL/6) became similar to that of a more susceptible strain (BALB/c). These findings outline an essential role for PAF in the control of cutaneous leishmaniasis.

Another study found that *Trypanosoma cruzi* (*T.cruzi*) is the causative agent of the life-threatening Chagas disease, which causes increased platelet aggregation and myocarditis. Platelet-activating factor (PAF) is a powerful intercellular lipid mediator and second messenger that acts via a PAF-specific receptor (PAFR). Previous research from this group indicated that *T.cruzi* produces a phospholipid with PAF-like activity (Gazos-Lopes *et al.*, 2014).

2-11-2: Leukotriene (LT-D4)

Leukotrienes (LTs), formed by the 5-lipoxygenase-(5-LO-) catalyzed oxidation of arachidonic acid, are lipid mediators that have potent proinflammatory activities. Pharmacologic or genetic inhibition of 5-LO biosynthesis in animals is associated with increased mortality and impaired clearance of bacteria, fungi, and parasites. In addition, the decreased production of LTs in immunocompromised individuals might modulate the pathophysiology of helminth and protozoan infections (Rogerio and Anibal, 2012), see Figure (2-6).

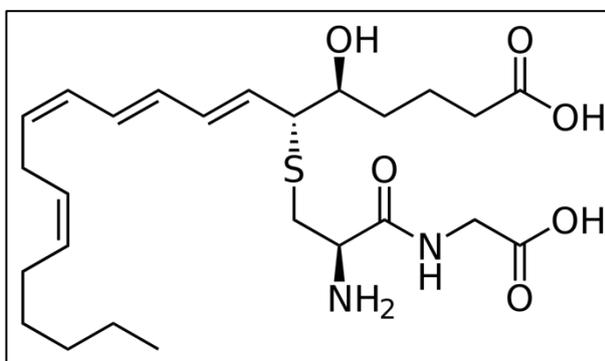


Fig (2-6): The chemical structure of Leukotrienes (D4) (Samuelsson *et al.*, 1987)

LTs play important roles in innate and adaptive immune responses and are involved in several inflammatory and infectious diseases (Peters-Golden *et al.*, 2005; Peters-Golden and Henderson Jr, 2007). For example, cysLTs increase vascular permeability and edema, and LTB₄ is involved in leukocyte chemotaxis, lysosomal enzyme secretion, neutrophil degranulation, adhesion molecule expression, defensins and nitric oxide (NO) production, phagocytosis, and other functions (Peters-Golden *et al.*, 2005).

LTs are produced during the interaction of phagocytes and microorganisms *in vitro* and experimental infections *in vivo* (Peters-Golden *et al.*, 2005). In addition, immunodeficient individuals, such as HIV patients, are characterized by low LT production (Sorgi *et al.*, 2009), which has been associated with

impaired immune responses and infection control. LTs play important roles in both Th1 and Th2 immune responses, which are involved in the defense against protozoan and helminth infections, respectively (Rogerio and Anibal, 2012).

The leukotrienes (LT) have been identified as potentially important inflammatory mediators of host defense. LTB₄ is a potent neutrophil chemoattractant and stimulus for aggregation, degranulation, and adherence to endothelium. The sulfidopeptide leukotrienes LTC₄, LTD₄, and LTE₄ (Lewis and Austen, 1984; Samuelsson, 1983).

LTs play a role in the controlling of helminth and protozoan infections by modulating the immune system and/or through direct cytotoxicity to parasites; however, LTs may also be associated with pathogenesis, as in cerebral malaria and schistosomal granuloma. Interestingly, some proteins from the saliva of insect vectors that transmit protozoans and secreted protein from helminth could bind LTs and may consequently modulate the course of infection or pathogenesis (Rogerio and Anibal, 2012).

Leukotrienes are important chemical mediators in a variety of inflammatory and allergic conditions, including those affecting the respiratory system. These signaling molecules can be divided into two groups: the pro-inflammatory leukotriene B₄ (LTB₄) and the spasmogenic leukotrienes C₄, D₄, and E₄, also termed cysteinyl-leukotrienes (Samuelsson, 1983). LTB₄ is one of the most powerful chemotactic agents known to date and acts via specific seven-transmembrane, G protein-coupled surface receptors on the target cells (Yokomizo, 1996). The profile of the biological properties of LTB₄ makes it a key component in the complex network of soluble and cell-bound factors that govern the development and maintenance of inflammation. Hence, LTB₄ has been proposed to play a role in a variety of acute and chronic inflammatory diseases such as arthritis, dermatoses, inflammatory bowel disease (IBD), and chronic obstructive pulmonary disease (COPD). In particular, LTB₄ seems to

play a role in the recruitment of inflammatory cells to the site of tissue injury (Haeggstrom, 2000).

The study of Haeggstrom (2000) gave us a brief overview of the biochemistry and molecular biology of LTA4 hydrolase, the enzyme catalyzing the final step in the biosynthesis of LTB₄.

Leukotrienes (LTs), both LTB₄ and Cysteinyl LTs (CysLTs) LTC₄, LTD₄, and LTE₄ are producing a wide variety of inflammation diseases. These are lipid mediators generated from Arachidonic acid via a multistep enzymatic process through which Arachidonic is produced from membrane phospholipids through the action of phospholipase A₂. LTB₄ is known as potent chemo kinetic and chemotactic agent whereas CysLTs are potent contracting agents of smooth muscle in airways and blood vessels. Leukotrienes play a major role in the pathogenesis of asthma and inflammatory disorder. The affinity of lipid bio-effectors is synthesized during the course of inflammatory reactions. Their pharmacological modulation can significantly attenuate the clinical manifestations associated with different inflammatory disorder. Selective leukotriene (LTs) inhibitors and receptor antagonists are currently under evaluation in the treatment of various inflammatory diseases (Nayak and Kumar, 2017).

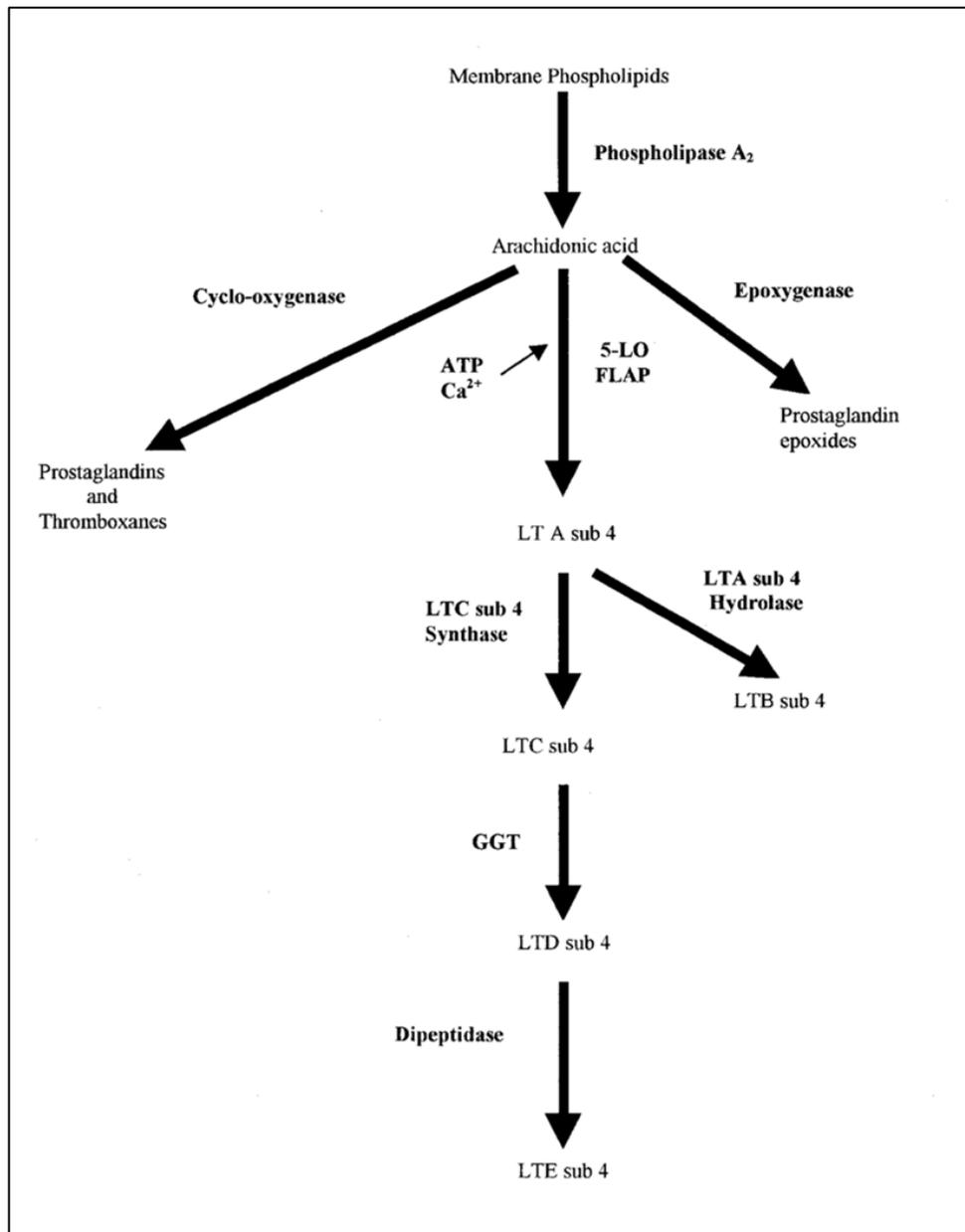


Fig (2-7): Leukotriene synthesis pathway (Nayak and Kumar, 2017).

2-11-3: Kininogenase

Kininogens are kinins precursor proteins, biologically active polypeptides take a part in blood clotting, inflammatory regulation, vasodilation, contraction of smooth muscle, and regulation of the renal system and cardiovascular. (Duchene and Ahluwalia, 2011).

kininogen (KNG) has two main kinds low- and high-molecular-weight kininogen, and a third one called T-kininogen found only in rats (Seth and Seth, 2009).

- 1- kininogen of high-molecular-weight (HK): is a non-enzymatic cofactor involved in the system of kinin-kallikrein, where it has a role in inflammation, blood pressure regulation, and blood clotting. It is synthesized in endothelial cells and a precursor protein for bradykinin, where it was produced generally by the liver (Haberland, 1978; Higashiyama *et al.*, 1986; Semba *et al.*, 2004).
- 2- kininogen of low-molecular-weight (LK): It is a precursor protein for kallidin. Whereas, it does not actively participate in blood coagulation, but its by-products can subsequently be converted and entered into the coagulation pathway (Haberland, 1978; Semba *et al.*, 2004).
- 3- T-kininogen (TK): it is only found in mice and a protein whose function is understudied. TK is believed to be a biomarker of aging in mice, which can be measured using the endothelial cell production level during the process of aging (Pérez *et al.*, 2006; Walter *et al.*, 1998).

HK consists of 644 residues of amino acid, where they separated into 6 various domain. The first three domains (1, 2, and 3) are called “heavy chain”, where domains 3 and 2 have an activity cysteine protease (Weisel *et al.*, 1994). the naming “light chain” is mentioned for the next two domains (5 and 6), and both bind certain molecules: The 5th domain binds zinc and heparin and binds selectively to anionic surfaces whereas the 6th domain binds prekallikrein, the protease precursor to kallikrein of plasma (Colman, 2001). The 4th domain connects the light and heavy chain together, its splitting at this site will releasing the bradykinin (Damasceno *et al.*, 2015). LK contains 427 residues of amino acid, and it also can cleavage into a “heavy chain” and a “light chain” (Takagaki *et al.*, 1985). However, T-kininogen contains 430 residues of amino acid (Takagaki *et al.*, 1985).

LK and HK are generated by the same kininogen (KNG) gene alternative splicing, which is located on chromosome 3q27 in humans (Veloso, 1998).

Kininogens are bind to cystatins through their comparable regions of glycosylated (Lalmanach *et al.*, 2010).

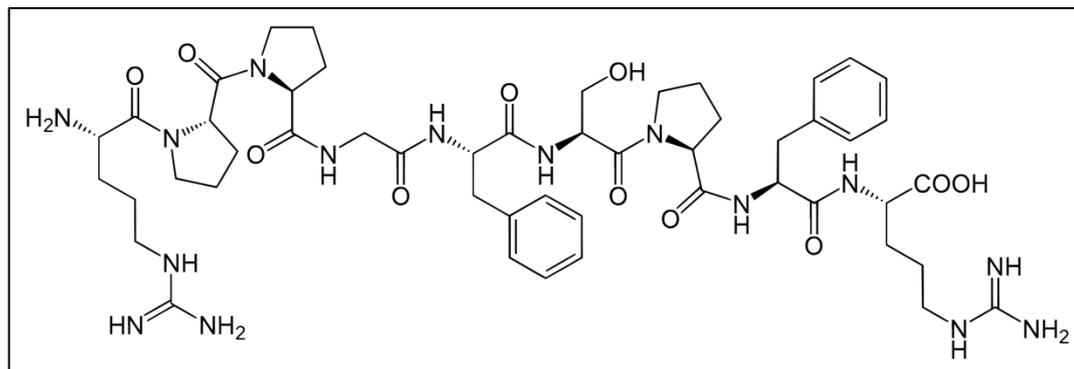


Fig (2-8): The chemical structure of Kininogenase (Lalmanach *et al.*, 2010)

Kininogen raised levels in the tissues and plasma are linked to diabetes, injury, myocardial infarction, and inflammation (Wong, 2016). In addition, kininogen role in the system of contact activation means that raised in levels of kininogen can participate in developing of hereditary angioedema (Moreno *et al.*, 2019), a disorder distinguished by periodic bouts of swelling.

A thought that KNG is playing a role in blood clots that block blood vessels, the formation of thromboembolism, and inflammation. KNG inhibition likely to be a selective strategy to combat stroke and deep venous thrombosis (DVT) (Langhauser *et al.*, 2012), and other vein thromboembolic diseases. It has been found that Kininogen-1 is an effective biomarker in detecting certain cancer types, such as colorectal cancer (Wang *et al.*, 2013).

The formation has been described in a variety of post-traumatic and related conditions, such as develop after multiple fractures, burns, anaphylaxis, endotoxin, pancreatitis, or severe hemorrhage (Gjinnnaess, 1972). In some of the earlier reports, kinin liberation was assumed basis on kininogen depletion rather than directly demonstrated. In addition, some of these older papers contain data only on total kininogen levels in plasma and do not differentiate between high molecular weight and low molecular weight kininogen. This differentiation, however, is important, because high molecular weight (HMW)

kininogen is the substrate for plasma kallikrein under physiological conditions (Cochrane *et al.*, 1973).

Plasma kallikrein, as well as plasmin and trypsin, release mainly bradykinin from HMW kininogen, while glandular and tissue kallikrein liberates mainly kallidin (lysylbradykinin) from LMW-kininogen. The changes of the various parameters of the kallikrein-kinin system in the disease states mentioned were interpreted primarily because of those pharmacological effects known at that time. Thus vasodilatation, reduction of blood pressure and increase in permeability producing edema have been of prime interest bringing into focus primarily the possible pathophysiological aspects of the activation of the kallikrein-kinin system (Hashimoto *et al.*, 1975).

Emphasize the physiological role which the kallikrein-kinin system may exert in the mammalian organism and on the cellular level. It is therefore necessary to reconsider the functions of this enzyme system in pathological conditions (Wuepper *et al.*, 1975).

CHAPTER THREE
MATERIALS & METHODS

3: Materials and Methods

3-1: Materials

3-1-1: Equipments and Instruments

The instruments and equipment used through this study are a listed in table (3-1).

Table (3-1): The instruments and equipments used in the present study

No.	Instruments	Company name	Origin
1	Centrifuge	Hettich	Germany
2	Cotton & Sterile alcohol	FA INC.	Korea
3	Deep freezor	National	Japan
4	Disposable syringes(5ml)	TED PELLA, INC.	USA
5	Disposable tip	Zhongfan Medical Technology	China
6	EDTA tubes	Sterilin	UK
7	ELISA Reader	Human	Germany
8	ELISA washer	Human	Germany
9	Eppendorf tubes	CAPP	China
10	Gel tubes	GE	China
11	Incubator	Memmert	Germany
12	Micropipette	DLAB	USA
13	Plain tube	AFCO	Jordan
14	Rack	Local	Iraq
15	Refrigerator	Concord	Lebanon
16	VIDAS	bioMerieux	France

3-2: List of Kits

The kits used throughout this study are listed in the Table (3-2).

Table (3-2): The used kits in the present study

No.	Kits	Company name	Origin
1	Platelet Activating Factor (PAF) ELISA Kit	BT LAB	China
2	Leukotrienes (D4) ELISA Kit	BT LAB	China
3	Kininogenase ELISA Kit	BT LAB	China

3-3: Information Collection

The present study is conducted on women who are suspected of chronic toxoplasmosis and have been referred by the specialist doctor at, Gynecology & Children Babylon Hospital and the Laboratories will conduct the necessary examinations to determine this infection. Furthermore, this study was conducted on 255 women, where 50 women were diagnosed with chronic toxoplasmosis, while 40 samples were randomly selected to be the control group. From the beginning of October 2020 to the end of March 2021, a questionnaire was organized for each patient that includes the data, age of the patient, the area of residence, blood type, educational level of the patient, month of pregnancy, does she have previous abortion, and the number of these abortion, see Appendix (1).

3-4: Samples collection

Collected 5ml blood samples from each enrolled woman. They were divided into two groups, the first was placed in EDTA tubes for performing CBC test. The other group was placed in tubes without EDTA for obtaining the serum. Separated the serum from blood using centrifugation for five minutes at 2000 R.P.M. Farther, it has been used the VIDAS technique to get patients' titer IgG in order to diagnose the patient's condition whether or not was infected with

chronic toxoplasmosis, after that, preserving the collected serum at -20°C until used (Abbas & Al-Hassnawi, 2020).

3-5: Experimental Design

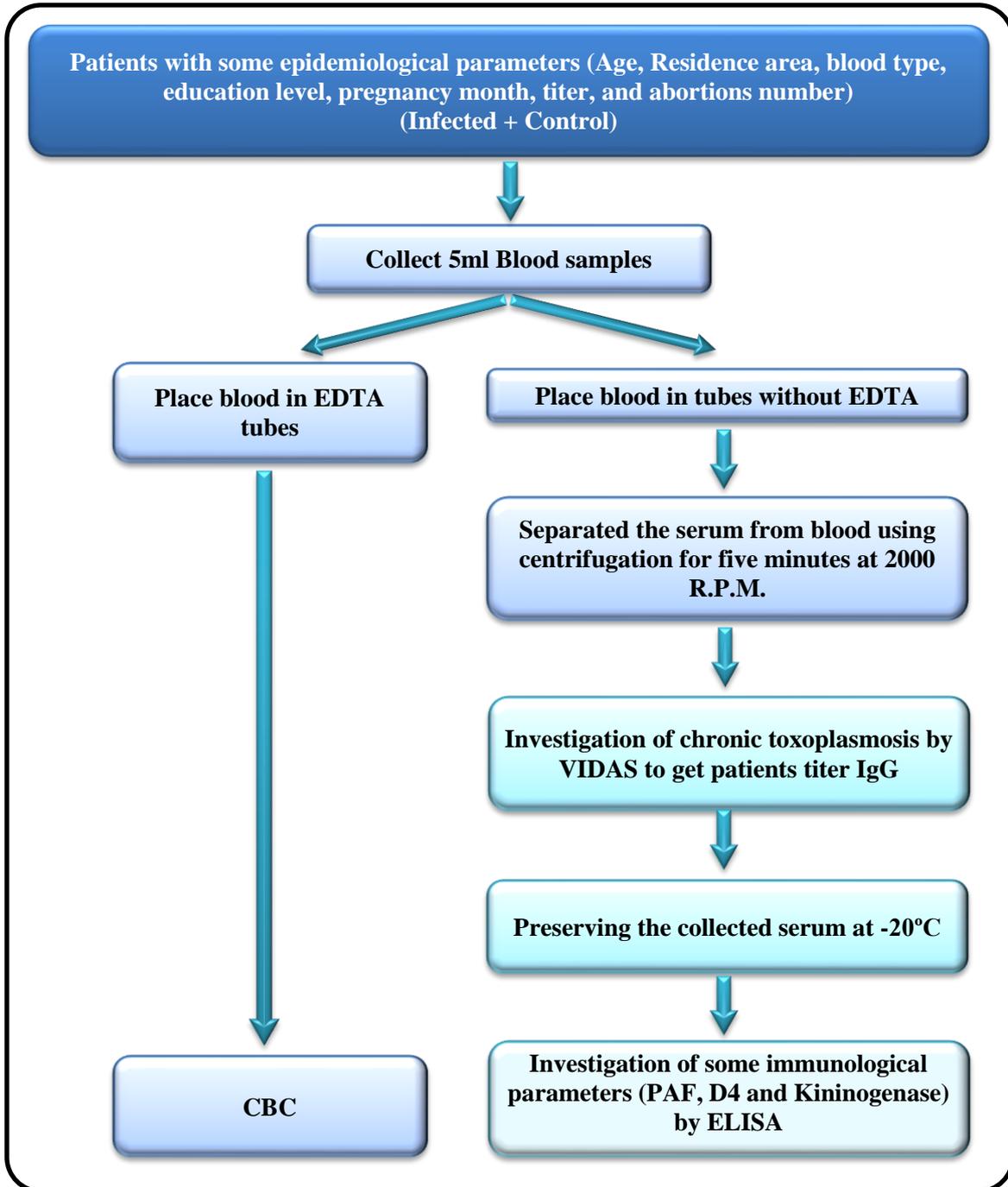


Fig (3-1): Experimental design of the present study

3-6: Ethics

The current study was conducted based on the Iraqi federalism, and policies of the local ethical committee, where all principles like beneficence, justice, risk, and persons respect were accounted for. The subjects and control were told about the importance, other specifics of the research, and explain the aim of this study and the protocol of ethics.

3-7: Method of VIDAS Toxo-IgG avidity measurement

Toxoplasmosis IgG aspiration measurement and interpretation were performed according to the manufacturer's directions (VIDAS Toxo-IgG avidity; bioMerieux / France) using the fully automated VIDAS machine. The test strip includes (6M) urea to remove low-strength IgG antibodies from their binding sites.

3-8: Immunological Tests

3-8-1: Measurement of PAF, LT-D4, and Kininogenase concentration

Table (3-3): Components of PAF kit used in this study (ELISA Kit / BT LAB / China)

No.	Components	Quantity
1	Standard Diluent	3ml×1
2	Plate Sealer	2 pics
3	Standard Solution (160ng/ml)	0.5ml×1
4	Zipper bag	1 pic
5	Stop Solution	6ml×1
6	Pre-coated ELISA Plate	12*8 well strips × 1
7	Substrate Solution A	6ml×1
8	User Instruction	1
9	Streptavidin-HRP	6ml×1
10	Substrate Solution B	6ml×1
11	Biotinylated human PAF Antibody	1ml×1
12	Wash Buffer Concentrate(25x)	20ml×1

Table (3-4): Components of LT-D4 kit used in this study (ELISA Kit / BT LAB / China)

No.	Components	Quantity
1	Standard Diluent	3ml×1
2	Plate Sealer	2 pics
3	Standard Solution (32ng/ml)	0.5ml×1
4	Zipper bag	1 pic
5	Stop Solution	6ml×1
6	Pre-coated ELISA Plate	12*8 well strips × 1
7	Substrate Solution A	6ml×1
8	User Instruction	1
9	Streptavidin-HRP	6ml×1
10	Substrate Solution B	6ml×1
11	Biotinylated human PAF Antibody	1ml×1
12	Wash Buffer Concentrate(25x)	20ml×1

Table (3-5): Components of Kininogenase kit used in this study (ELISA Kit / BT LAB / China)

No.	Components	Quantity
1	Standard Diluent	3ml×1
2	Plate Sealer	2 pics
3	Standard Solution (160ng/ml)	0.5ml×1
4	Zipper bag	1 pic
5	Stop Solution	6ml×1
6	Pre-coated ELISA Plate	12*8 well strips × 1
7	Substrate Solution A	6ml×1
8	User Instruction	1
9	Streptavidin-HRP	6ml×1
10	Substrate Solution B	6ml×1
11	Biotinylated human PAF Antibody	1ml×1
12	Wash Buffer Concentrate(25x)	20ml×1

3-8-2: Assay procedure of PAF, LT-D4, and Kininogenase kit (ELISA Kit / BT LAB / China)

1. All samples, standard solutions, and reagents were prepared according to the instructions, where all reagents were transported to the temperature of the room before they used. The examination was done in the temperature of the room.
2. The required strips number for the examination was located. Then, inserted the strips into the frames for using them, while unutilized strips are saved at 2°C to 8°C.
3. An amount of (50µl) was added standardized. Nevertheless, the antibody wasn't added to the standard well because the solution of standard includes Biotinylated-antibody.
4. An amount of (40µl) sample was added to sample wells, further a (10µl) anti-PAF, LT-D4, and Kininogenase antibody was added to sample wells. Further, an amount of 50µl streptavidin-HRP was added to sample wells (Not blank control well). The wells were mixed, then the plate was covered with a sealer with Incubate 60 minutes at 37°C.
5. the sealant was removed and the panel was washed five times with temporary washing solution. wells were soaked with 0.35ml wash buffer for 30 seconds to 1 minute for each wash buffer, overfilled wells with wash buffer. The plate was blotted onto paper towels.
6. Also, a (50µl) of substrate solution (A) has been added to all wells, and after that (50µl) of substrate solution (B) has been added to all wells. covered incubate plate with new stopper in dark at 37°C for 10 minutes.
7. Next step, added (50µl) of stop solution to all wells, the color changed immediately from blue to yellow.
8. The optical density (OD value) of all wells was determined using a microplate reader set to (450 nm) for ten minutes after the stop solution

added. The standard curve of parameters were shown in Appendix (6), Appendix (7), and Appendix (8).

3-10: Statistical Analysis

The experimental results were shown as descriptive statistics (mean, and \pm standard deviation). Besides, ANOVA one-way statistical analysis of variants was performed, followed by an independent samples Z-test to compare the means of two groups, and p-value ($p \leq 0.05$) was considered statistically significant, also value of Chi-square was measured statistically. Finally, with a homogeneity check using the variances homogeneity test, a univariate general linear model was carried out, to test the null hypothesis about other variables' effects on the single dependent variable means (Kim and Timm, 2006; Muller and Stewart, 2006).

CHAPTER FOUR
RESULTS AND DISCUSSION

4: Results and discussion

4-1: The Prevalence Study

Toxoplasma gondii (*T.gondii*) consider as one of the most common types of protozoan parasites in humans. In various territories, The *T.gondii* prevalence varies by 20% - 80% mostly (Tenter *et al.*, 2000). Basically, The consumption of undercooked or raw meat of an intermediate host (particularly sheep, rabbits, and pigs) considers an infection main source in humans, which contains tissue cysts, and also from water or food besmeared with soil containing the oocysts from cat feces (Beattie, 1982; Tenter *et al.*, 2000).

4-1-1: Distribution of chronic Toxoplasmosis

This study was conducted on 255 samples of women, where the examination results showed that 50(19.6%) sera out of 255 were positive for chronic toxoplasmosis, as shown in Table (4-1), and Appendix (2).

Table (4-1): Distribution of chronic Toxoplasmosis in Babylon province women

No. of examined	No. of infected	%	No. of non-infected	%
255	50	19.6	205	80.4

The number of infected samples taken for examination was equal to the number of infected sample taken by Al-Saeed *et al.* (2008) in Hilla city/Iraq, where 50 samples were infected out of 120 with an infection percentage (41.66%).

The current study result is compatible with those of the literature; a study by Al-kremy and Al-hassnawi (2020) conducted on 147 of Babylon' women and the percentage of infection was 19%. Also the results of study conducted by Kadir *et al.* (2011) in Kirkuk province included cases of 319 patients with toxoplasmosis and showed 54 positives by using ELISA technique (16.9%).

Another studies recorded higher percentage of infection with toxoplasmosis, where a study in Diyala province included 100 women and the results showed that the percentage was 44% of infection with toxoplasmosis (Shaker *et al.*, 2018). In the study of Abdi *et al.* (2008), 553 serum samples from Iranian women were tested, and found that the prevalence percentage of toxoplasmosis infection was 44.8%. The incidence of infection among northern Portugal women's was high through a study by Lopes *et al.* (2012), which included 401 samples with a percentage of infection was 93.9%. In India, a study by Malarvizhi *et al.* (2012) involved 232 blood serum samples of women by using the ELISA technique to detect chronic toxoplasmosis and the infection percentage was (9.9%). The different rates of infection with toxoplasmosis in various researches and in different cities all around the world, is a result of the difference in the method of nutrition, which has a major role in the variation in the infection incidence between different regions (AL-Awsi, 2020), as well as the lack of attention to health means increases the risk of contamination of water and food with oocysts, and eating them through the device digestive system (Lavine and Arrizabalaga, 2008).

4-1-2: Distribution of IgG antibody titer in women chronically infected with *T.gondii*

Through the results in Table (4-7), the taken IgG titer from the infected women in this study divided into three groups: Less than 100, between 100-200, and more than 300. Results were showed that the largest number 36(72%) of the cases are in the first group titer (Less than 100). While the remaining two groups (between 100-200 and more than 300) have an equal number of cases 7(14%).

Table (4-2): Distribution of IgG antibody titer in women with chronic toxoplasmosis

IgG titer	Number	%
Less than 100	36	72
Between 100 and 200	7	14
More than 200	7	14
Total	50	100

There are two different types of postnatal acquired *T.gondii*, depending on the immune competence and the infection stage of the host. Acute toxoplasmosis is one of its forms, and the presence of tachyzoites in the blood and some other tissues is one of its characterize. Acute infection can be detected by IgM antibodies, IgM antibodies appear after infection and disappear after recovery faster than IgG antibodies (Hill and Dubey, 2002). *Toxoplasma*-specific IgM antibodies can be detected for the first time about a week after the initial infection and decrease within 1-6 months (Jones *et al.*, 2014), and the severity of infection decreases to 25% in the seventh month of infection, while it may be possible to detect IgM months or years after infection throw the chronic phase (Montoya, 2002).

Acute toxoplasmosis is converted to the chronic stage (latent toxoplasmosis) in immunocompetent subjects. Chronic toxoplasmosis asymptomatic clinically, while it is a lifelong infection usually, with antibodies present in the blood serum, as well as the existence of bradyzoites parasites in tissue cysts of infected subjects (Kaňková *et al.*, 2007). IgG antibodies contain the highest rate, the IgG detection appear usually between one to two weeks. Moreover, the highest rate will reach in the period between six to eight weeks, and then decreased gradually within 1-2 years. while some other infected people will have high concentrations over years (Ambroise-Thomas and Petersen, 2013).

The antibody titer is a test that detects the presence and measures the amount of antibodies within a person blood (Bennett *et al.*, 2015). The antibodies are produced by the immune response to the parasites (Stewart, 2012). The high antibody titer of anti-*Toxoplasma* IgG is likely due to the large number of parasites entering the infected woman. Moreover, the level of antibodies significantly affects the infected host status. It may be the decrease in *T.gondii* titer IgG (less than 100) titer is one of the reasons for the weak immune response in infected women. The antiparasitic cellular immune response is the latent state protozoan and activated when the response of immune is weak (Da-Silva and Langoni, 2009). The delicate balance between escape and stimulating from the immune response is the basic formation to form chronic infection (Blader and Saeij, 2009). In immune response to *T.gondii*, the IgG antibodies remain the essential methods to diagnose chronic toxoplasmosis in humans (Filisetti and Candolfi, 2004).

4-1-3: Distribution of chronic Toxoplasmosis in women according to age

In this study, ages were divided into three groups, which are younger than 20 years, between 20-30 years, and older than 30 years. The results in Table (4-2) and Appendix (3), it were showed that the age group (older than 30 years) has the highest percentage of infection (34.1%). while the lowest percentage was (15.6%) for the (20-30 years) age group. The Chi-square statistical analysis test showed a significant association ($p < 0.05$) between age and chronic toxoplasmosis.

Table (4-3): Distribution of chronic toxoplasmosis infection in women according to age

Age	No. of examined	No. of infected	%
< 20 years	45	9	20
20 - 30 years	166	26	15.6
> 30 years	44	15	34.1*
Total	255	50	19.6

*. The mean difference is significant at the 0.05 level.
 Calculated $X^2=7.499$
 Tabular $X^2=5.99$
 df=2
 $p \leq 0.05$

The result was in agreement with Al-Harathi *et al.* (2006) results, where the highest percentage (48.8%) in the age group 35-45 years compare with other age groups. In contrast, other studies by Abbas and Al-hassnawi (2019) reported the highest percentage (68.75%) was in the age group 21-30. However, a study by Al-Masoudi *et al.* (2018) found that the age group 16-19 years has the highest infection rate. Generally, the suspected cause of the increase in toxoplasmosis between age groups may be for unequal degree of exposure to oocytes of *T.gondii* (Abdullah and Mahmood, 2017).

4-1-4: Distribution of chronic Toxoplasmosis in women according to residence area

Place of residence and geographical location is another form of disparity in the distribution of Toxoplasmosis rates. This study divided the residential area into two groups: rural and urban areas. The results showed that the majority of infected cases were from the urban area (27.3%), while the lowest cases were in the rural area (15.6%) (Table 4-3 and Appendix 4). The Chi-square statistical analysis showed a significant association ($p < 0.05$) between the residential area and chronic toxoplasmosis.

Table (4-4): Distribution of chronic Toxoplasmosis in women according to residence area

Residence area	No. of examined	No. of infected	%
Rural	167	26	15.6
Urban	88	24	27.3*
Total	255	50	19.6

*. The mean difference is significant at the 0.05 level.
 Calculated $X^2=5.008$
 Tabular $X^2=3.48$
 df=1
 $p \leq 0.05$

The results of the current study agreed with what was recorded by AL-Awsi (2020), which found a significant increase in the urban area (85.71%) than rural area (14.28%). With the fact that individuals in the city are more influential than the rural population and that the incidence of infection is greater in urban areas than in rural areas. Furthermore, the reason for the high rate of infection among infected women in urban compared to rural women may be due to the main risk factor among cats and the cysts of parasite oocytes they excrete with contaminated feces. In homes, in these areas, the concentration of *T.godii* oocytes is very high, and thus the risk of human infection increases, while the cats of rural areas have large areas to put cysts of parasite oocytes (Diaz-Suárez and Estevez, 2009). Also the results of this study were agreed with Sharifi *et al.* (2019) study in Mashhad / Iran, which found a significant increase in the urban area (89.7%) than rural area (10.3%).

However, other studies didn't found significant statistical differences among rural and urban areas (Flayyih Hasan, 2011; Hajsoleimani *et al.*, 2012; Sharbatkhori *et al.*, 2014), this result may be due to the lack of health awareness and the lack of awareness of the seriousness of toxoplasmosis, its transmission, prevention methods, and the convergence of infection rates between the rural and urban area is due to the similarity of dietary habits, as well as the presence

of sources of infection, whether in the countryside or the city, and this indicates that the infection is not confined to a particular area without another (AL-Taei, 2013).

Whereas, the results of other studies differed with this study results such as Al-Shikhly (2010) study in Baghdad Iraq, which found significant increase in rural area (59%) than urban area (41%). Another study by Abdullah and Mahmood (2017) in Erbil Iraq found that in rural dwellers (44.18%) where in urban area (30.5%), also another study in Babylon Iraq found that the highest infection of toxoplasmosis (25.3%) in the rural area compared with the urban area (12%) (Mohammed and Al-Janabi, 2019). Those results can be attributed due to the people who live in these places are more in contact with animals (cats) on farms or homes during work, and Toxoplasmosis can also be transmitted through poorly washed fruits and vegetables, also meat that is not thoroughly cooked. This may be referred to the education role among females in the urban area to lower infection incidence (AL-Obaedy, 2012; Mohamed *et al.*, 2013).

4-1-5: Distribution of chronic toxoplasmosis in women according to education level

In this study, the education level was divided into four groups, which were illiterate, primary, secondary, and university. The results in Table (4-4) showed that the university level has the highest percentages (29.3%) for the studied infected women, and all illiterate (15.8%), primary (14.9%), and secondary (20.4%) levels have close percentages.

Table (4-5): Distribution of chronic toxoplasmosis infection among women according to education level

Education level	No. of examined	No. of infected	%
Illiterate	76	12	15.8
Primary	67	10	14.9
Secondary	54	11	20.4
University	58	17	29.3
Total	255	50	19.6
Calculated $X^2=5.119$ Tabular $X^2=7.81$ df=3 p>0.05			

The Chi-square statistical analysis showed no significant differences ($p>0.05$) between the education levels and chronic toxoplasmosis. These results were identical to those obtained by many researchers over the world, where there are no significant differences of its results. Such as a study in Zanzan/Iran by Hajsoleimani *et al.* (2012), where the infection percentages were 40.6% and 43.8% for university graduated and elementary school respectively, while the lowest percentage were in Illiterate 34% and high school 30%. also, in Mashhad / Iran, a study showed that infection percentage of toxoplasmosis in the education level has varied by 44.8%, 38.9%, 11.1%, and 5.6% for diploma, ninth grade, bachelor, and illiterate, respectively (Sharifi *et al.*, 2019). As well as, Mohammed and Al-Janabi (2019) study reported that the highest infection percentage of toxoplasmosis was in elementary level (24%).

In contrast, other researchers conducted studies in other countries, and the results indicated that infection is more prevalent in illiterate or graduated from primary school women. Where a study in Aden city / Yemen, showed that there was a significant increase in the level of infection, where women of illiterate percentage (72.7%) were higher than education level women percentage

(47.8%) (Muqbil and Alqubatii, 2014). another study in Minia city in Egypt showed that primary education level is a significant risk factor with a percentage (53%) of toxoplasmosis infection (Kamal *et al.*, 2015). also, a study by Shaker *et al.* (2018) in Diyala / Iraq illustrates that the increase of Toxoplasmosis in women Because of the low level of education, where this study recorded a high percentage (40.9%) of infection with toxoplasmosis or women who are illiterate or have not completed primary school.

The result of no statistically differences between education level and the incidence of chronic toxoplasmosis does not indicate that this factor has no impact to reduce educated women infection (Aliwi *et al.*, 2010). The reason may be due to the small number of samples from the current study for each educational levels.

4-1-6: Distribution of chronic toxoplasmosis in women according to pregnancy trimester

This study divided the months of pregnancy into three groups: First, second, and third trimester, in addition to a group for not pregnant women. The results showed that the majority of studied cases (37) were in the first trimester of pregnancy for the infected (21.9%). While the lowest recorded cases were in the third trimester of pregnancy (0%). The Chi-square statistical analysis showed no statistical difference ($p>0.05$) between the pregnancy and chronic toxoplasmosis. In general, the highest infection percentage (23.5%) was in the not pregnant women with no statistical difference ($p>0.05$), Table (4-5).

Table (4-6): Distribution of chronic Toxoplasmosis in women according to pregnancy trimester

Pregnancy trimester	No. of examined	No. of infected	%
Not Pregnant	17	4	23.5
First trimester	169	37	21.9
Second trimester	60	9	15
Third trimester	9	0	0
Total	255	50	19.6
Calculated $X^2=3.729$ Tabular $X^2=7.81$ df=3 p>0.05			

These results give the understanding that all pregnancy trimesters have the same infection chance of toxoplasmosis. The result for infected pregnant women is in agreement with Malarvizhi *et al.* (2012) study in Tamil Nadu / India, where the highest infection percentage (15%) in the first trimester. In Iraq the study in Qadisiyah province, reported the highest percentage (52.7%) in the first trimester (Hadi *et al.*, 2016). Otherwise, The results of this study contradicted those observed by others, a study in Erbil City / Iraq found that the highest infection percentage (43.24%) was recorded in the second trimester with no significant differences (Abdullah and Mahmood, 2017). Another study in Basra province-Iraq showed that most infection number was in the second trimester of pregnancy with a percentage (75%) (Al-Tamemmi *et al.*, 2019).

4-1-7: Distribution of chronic toxoplasmosis infection among women according to abortions number

The result of Table (4-7) showed that aborted women with more than three abortion have higher significant percentage with chronic toxoplasmosis infection in comparison with other groups of abortion (none, one abortion, two abortions, and three abortion). Highest infected percentage has more than three abortion

(33.33%) followed by cases with three abortions (29.62%), none abortions (26.9%), two abortion (23.88%), and one abortions (13.17%). Although the highest percentages with more than three abortion were recorded. However, no significant differences ($p>0.05$) were recorded between abortions number chronic toxoplasmosis infection.

Table (4-7): Distribution of chronic toxoplasmosis infection among Babylon province women according to the abortions number

Abortions number	No. of examined	No. of infected	%
None	26	7	26.9
One abortion	129	17	13.17
Two abortions	67	16	23.88
Three abortions	27	8	29.62
More than three abortions	6	2	33.33
Total	255	50	19.6
Calculated $X^2=7.479$ Tabular $X^2=9.48$ df=4 p>0.05			

The current study agreed with the study presented by AL-Awsi (2020) where the highest percentage of aborted women was recorded (47.36%) for infected women with chronic toxoplasmosis who had have more or equal than three abortions. The decrease in immunity increases with the number of pregnancies and the number of recurrent abortions. The decrease in the body's immunity and the time of infection during pregnancy plays a big role in determining the fetus's fate (Al-Khashab, 2009). Also the result of this study agreed with Mohammed and Al-Janabi (2019) study, where this study did not found a significant analysis difference between the number of abortions and the percentage of infection.

While the results recorded by Al-Quraishi and Jawad (2020) study in Babylon/Iraq, it didn't compatible with the results of this study, as it was recorded that the highest abortion rate was one abortions with percentage of (34%). Another study in Diyala/Iraq showed that the women have had single abortion have the highest percentage with (46.15%) for non-pregnant women and (50%) for pregnant women (Shaker *et al.*, 2018). Also a study in Qadisiyah/Iraq presented the highest abortion number percentage was (43.6%) for women have hade single abortion (Hadi *et al.*, 2016).

4-1-8: Distribution of chronic Toxoplasmosis among women according to blood groups

Through the results in Table (4-8) and Appendix (5), and for the studied infected specimens, it showed that the largest number of samples 29(31.9%) in the blood group B from 50 infected women, while the blood groups A and O have somewhat equal percentage 10(14.1%) and 6(14.6%) respectively, and a percentage of 5(9.6%) for the AB blood group as a lowest percent for the infected specimens. The Chi-square statistical analysis showed a significant association differences ($p < 0.05$) between blood group and chronic toxoplasmosis infection in the blood group B. The current study documented that the highest incidence of Toxoplasmosis was for women of blood group B and the lowest incidence was for women of blood group AB.

Table (4-8): Distribution of chronic toxoplasmosis infection in women according to blood group

Blood type	No. of examined	No. of infected	%
A	71	10	14.1
B	91	29	31.9*
O	41	6	14.6
AB	52	5	9.6
Total	255	50	19.6
Calculated $X^2=13.989$ Tabular $X^2=7.81$ df=3 p≤0.05			

The current study is agreed with AL-Taei (2013) study in Thi-Qar province - Iraq, it reported that the highest percentage of infection was in women of blood group B, at a rate of 37.78%, where the number of positive cases was 34 cases out of 94 samples, and the lowest percentage of infection was from blood group AB, at a rate of 10.0%, which was the number of positive cases 9 cases out of 35 samples. It showed that there were significant differences between blood groups with an increase in blood group B.

Otherwise, the results of other studies did not match with this studies results, where blood group O recorded the highest percentage (41.07%) from 56 infected women with toxoplasmosis infection compared to the rest of the groups, and a statistical reference was discovered between *T.gondii* infection and blood groups(AL-Awsi, 2020; Shaker *et al.*, 2018). This is due to the fact that the molecules that determine the ABO system of blood groups consist of carbohydrates found in the structures of glycoproteins expressed in red blood cells and other tissues (Schenkel-Brunner, 2000). However, the mechanism of accession of microorganisms to the mucous membranes of hosts is not completely clear, and it is likely that the gluco-conjugat of the ABO system is

involved in this process (Henry, 2001). Studies have confirmed the existence of a relationship between the blood of parasite infection and blood groups, which suggests that there are possible receptors for *T.gondii* with blood group receptors (A. C. F. Rodrigues *et al.*, 2011).

There are studies showing the natural resistance to many infectious diseases and it depends on person blood group (Lell *et al.*, 1999). The blood groups are determined by the presence or absence of antigens (A, B) on the surface of red blood cells (Schenkel-Brunner, 2000). This determines the natural human resistance to many pathogens that carry on the surface of their cells antigens that are similar to those found in the different blood groups. there is a study that showed a correlation between infection of *T.gondii* and the blood group of B, AB type (Kolbekova *et al.*, 2007; Zhiburt *et al.*, 1997). Finally, the current study suggests that B antigen may be a receptor for the *T.gondii* parasite.

4-2: Hematological study

4-2-1: The variations in hematological parameters between women with chronic toxoplasmosis and non-infected

The result of the current study in (Table 4-9) showed the change in the levels of some parameters (Hb, WBCs, Neutrophils, Eosinophils, Basophils, Lymphocytes, and Monocytes) in women with chronic toxoplasmosis infection compared to those in non-infected women.

Table (4-9): The variations in hematological parameters between women with chronic toxoplasmosis and non-infected

Hematological parameters		Number	Mean	S.D.	Sig.
Hb (g/dl)	Infected	50	11.63*	1.18	0.003
	Control	40	12.35*	0.95	
Total WBC count (UL/Cells)	Infected	50	8.24*	1.43	0.019
	Control	40	7.49*	1.54	
Neutrophils (μL)	Infected	50	4.78	1.15	0.917
	Control	40	4.75	1.27	
Lymphocytes (μL)	Infected	50	2.83*	1.26	0.047
	Control	40	2.41*	0.49	
Monocytes (μL)	Infected	50	0.55	0.15	0.642
	Control	40	0.53	.14	
Eosinophils (μL)	Infected	50	0.18	0.06	0.542
	Control	40	0.17	0.07	
Basophils (μL)	Infected	50	0.02	0.03	0.667
	Control	40	0.02	0.03	

4-2-1-1: Hemoglobin (Hb)

The results in Table (4-9) showed that there was a significant decrease in the concentrations of hemoglobin (Hb) in the infected women with a mean of (11.63 g/dl) compared to the non-infected women by a mean of (12.35 g/dl) with the probability ($p < 0.05$). The significant decrease in hemoglobin concentration is the reason for a deficiency in the concentration of iron due to infection with this parasite, which leads to a decrease in the concentration of hemoglobin within the red cells, and this leads to anemia in the affected women (Javadi *et al.*, 2010). The results of current study agreed with AL-Awsi (2020) study in Mosul/Iraq, it presented that there was a significant decrease with average (12.66 g/dl) for Hb concentration in infected women with toxoplasmosis

compared with non-infected with average (13.12 g/dl), As they recorded a significant decrease in the level of hemoglobin in the women with toxoplasmosis compared with the healthy non-infected women (Shahzad *et al.*, 2006). This decrease in hemoglobin concentration may be attributed to the parasite proliferation in the host body (Al-Nasiri and Daoud, 2012).

The *T.gondii* penetration have been studied using murine erythroid cells in vitro by Tanabe *et al.* (1979), where *T.gondii* infiltrated erythrocytes and macroreticulocytes from mouse. Mature reticulocytes were less prone to penetration than immature cells, which indicates some change in their membrane properties during maturation.

The researchers confirmed that the infection with toxoplasmosis is accompanied by swelling in the lymph nodes, high body temperature, and anemia as a result of hepatitis, and its enlargement when the infection becomes chronic. The rapidly reproducing phases reach the brain, heart, and skeletal muscles, and sometimes accompanied by pulmonary complications (Hill and Dubey, 2002).

4-2-1-2: Total White Blood Cells (WBCs)

The total count of WBC (Table 4-9) was showed a significant increase ($p < 0.05$) in the infected women (8.24 UL/cells) comparison with non-infected women (7.49 UL/cells). White blood cells measured in order to assess the inflammatory response, infection, or immune system disorder in patients with toxoplasmosis infection, and the results of the current study agreed with Leka and Shrook (2012) study Babylon Province - Iraq, which showed that the number of WBCs has a higher value in infected women (12.80 UL/cells) compared to non-infected women (8.30 UL/cells). The increased number of white blood cells may be attributed to WBC ability to destroy the parasite as an immune response in the body, then cellular immunity will be activated as well as humoral immunity (Pier *et al.*, 2004). Further, this significant increase in the

level of WBCs represented a cellular defense method in the body (Bout *et al.*, 2002), the entry of *T.gondii* parasite into the human body faces a major immune response by infecting the body cells and tissues that attack it, which represents the direct cellular response that appears in mononuclear cells and macrophages (AL-Awsi, 2020).

The results of this study are identical to AL-Awsi (2020) study in Mosul/Iraq, which reported that there was a significant increase in the total count of WBCs in infected women (7.33 UL/cells) compared with non-infected women (6.19 UL/cells). White blood cells represent the main elements that control the autoimmune and acquired responses in the body's defenses against various viral, parasitic and bacterial infections. Knowing the number and differential count of white blood cells gives a clear idea and a detailed picture of the severity of the infection, which helps in timely treatment and preventing complications. Finally, the decrease or rise in the level of cells determines the extent of the activity of the immune system (Alberts *et al.*, 2005).

4-2-1-3: Lymphocytes

The recorded results in Table (4-9) showed a slight significant increase ($p < 0.05$) lymphocytes in the infected women with (2.83 μL) compare with non-infected women (2.41 μL). The increase in lymphocytes may be due to the presence of bacterial or parasitic infections (Al-Dabbag and Al-Dabbag, 2006). Furthermore, in acute infection it may reach 75% and then decrease and return to normal values within 4-6 weeks as it plays a fundamental role in the innate, unlimited immunity of the body (Roitt *et al.*, 2001). Its means the increase in lymphocytes are a type of active immunity, and these results agree with Ismail *et al.* (2013) that shows the activity of white blood cells and lymphocytes. On the other hand, the observed results of (Tonin *et al.*, 2013) study on rats serum that infected experimentally with *T.gondii*, and it showed a significant increase in lymphocytes in infected rats (4.572 μL) compares with control group (2.768 μL). Studies indicate that lymphocytes are an important regulator of mucosal

immunity against *T.gondii* infection acquired orally. Immunosuppressive lymphocytes may be directed at the site of microbial invasion, by monitoring by the systemic immune response. Protection against *T.gondii* depends on the ability of lymphocytes to pass into the intestine and other host organs (Shaw *et al.*, 1998).

The mucosal epithelial layer provides an interface between the external and internal environments of the gastrointestinal tract, where the gut-associated lymphoid tissue acts as an immune barrier against a wide range of infectious agents, including oral acquired parasites such as *T.gondii*, most notably the mucosa-associated lymphocytes of the small intestine. within the intestinal epithelium (Buzoni-Gatel *et al.*, 1999). Lymphocyte proliferation in primary and secondary lymphoid organs depends on the interactions between prolactin and growth hormone, with its activities and immunological effects against Toxoplasmosis spreading (Soares, 2004). The results of (AL-Awsi, 2020) study in Mosul city-Iraq, it was agreed with the current study results, which found a significant increase in the number of lymphocytes in women with *T.gondii* infection (7.74 μ L) in compare with control group (6.86 μ L).

4-2-1-4: Basophils

Basophils are one of the WBCs types, it was the least common granulocyte kind, which represents between (0.5% to 1%) of circulating WBCs. Generally, they are the granulocyte largest number, and they in charge of immune response with inflammatory reactions, also the formation of chronic and acute allergies, such as asthma, atopic dermatitis, hay fever, and anaphylaxis (Mukai and Galli, 2013). Basophils provide combinations that coordinating the immune responses like serotonin and histamine that induce inflammation (Khurana, 2009).

4-2-1-5: Neutrophils

They are also phagocytes, and have the ability to insert particles or microorganisms. To recognize the targets, they must be encapsulated in

opsonins (antibody opsonization) . Its known also as heterophils or neutrocytes. Neutrophils are the granulocytes most abundant type and make up about 40% to 70% from all of WBCs in humanbeans (Actor, 2012). they forme a primary part in the system of innate immune (Ermert *et al.*, 2013).

4-2-1-6: Monocytes

Monocytes performe three main functions in the immune system., these are cytokine production, antigen presentation, and phagocytosis. they were known also as the state of excess monocytes in the peripheral blood. an operations that raise a monocyte count such as stress response, immune-mediated disease,diabetes, atherosclerosis, sarcoidosis, chronic inflammation, necrosis, chronic myelomonocytic leukemia, cushing's syndrome, viral fever, red blood cell regeneration, granulomatous disease (Heidt *et al.*, 2014; Hoyer *et al.*, 2020). Monocytes make up 2% to 10% from all of WBCs in the human beings (Swirski *et al.*, 2009).

4-2-1-7: Eosinophils

Eosinophils are a diverse group of WBCs and a part of the immune system components, they responsible for certain infections in vertebrates and combating multicellular parasites, they make up (2 to 3%) of WBCs (Uhm *et al.*, 2012). Eosinophils involved in the viral infections fighting, where it's clear in the abundance of RNases inside their granules, removal of fibrin during inflammation. Eosinophils are substantial mediators of asthma pathogenesis and allergic responses. Besides, they were fight helminthes, the development of mammary gland puberty, allograft rejection, and oestrus cycling (Rothenberg and Hogan, 2006; Shi, 2004).

In fact, there were no significant differences ($p>0.05$) appeared for each of neutrophils, monocytes, eosinophils, and basophils. Where the recorded mean in infected women with chronic toxoplasmosis was 4.78 in Neutrophils, 0.55 in Monocytes, 0.18 in Eosinophils, and 0.02 in Basophils, while for the non-

infected women was 4.75 in Neutrophils, 0.17 in Monocytes, 0.53 in Eosinophils, and 0.02 in Basophils. The current study results are similar to those of AL-Taei (2013) study in Thi-Qar province – Iraq, where AL-Taei recorded no significant association for each of neutrophils (2.87 and 2.81), monocytes (0.51 and 0.59), eosinophils (0.13 and 0.13), and basophils (0.13 and 0.12) for infected and non-infected women, respectively.

4-3: Immunological study

4-3-1: The concentration of some immunological parameters (LT-D4, Kininogenase, and PAF) in infected women with chronic toxoplasmosis and not infected women

Table (4-10) shows the effect of chronic infection with *T.gondii* on the concentrations of some immunological parameters (LT-D4, Kininogenase, and PAF) in the sera of Babylon province women. The study found a significant increase ($p < 0.05$) in concentrations of these immunological parameters in sera of infected women compared with non-infected women with chronic toxoplasmosis.

Table (4-10): The concentrations of LT-D4, Kininogenase, and PAF among the control and the infected women with chronic toxoplasmosis

Immunological parameters	Infection	Number	Mean	S.D.	Sig.
LT-D4 ng/ml	Infected	50	3.176	0.571	0.002
	Control	40	2.874	0.475	
Kininogenase ng/ml	Infected	50	27.752	3.270	0.000
	Control	40	23.981	3.559	
PAF ng/ml	Infected	50	4.594	0.664	0.001
	Control	40	4.202	0.538	

Based on estimated marginal means
*.The mean difference is significant at the .05 level.

Leukotrienes (LTs) has a key role in controlling the protozoan and helminths infection by modifying the immune system via direct parasites cytotoxicity. It is worth mentioning that several proteins from the saliva of insect vectors that transport protein and a protozoans secreted from helminths can bind LTs, and thus may pathogenesis or modulate the course of infection (Rogerio and Anibal, 2012).

A significant differences increase ($p < 0.05$) has been observed in LT-D4 concentrations, where the concentration in infected women with chronic toxoplasmosis (3.124 ng/ml) is higher than control group (2.781 ng/ml), as shown in Table (4-10). This result shows that LT-D4 play a substantial role in the immune responses (Th1 and Th2) which are contributed in defense against helminth infections and protozoan (Peters-Golden and Henderson, 2007; Rogerio and Anibal, 2012).

The current study results match with results that indicate the increases of LTs concentrates, which associated with the control of protozoan diseases, such as cerebral malaria, and helminthic diseases through their ability to modulate inflammatory processes to promote direct cytotoxicity of protozoans, also can limit the growth of protozoan (Peters-Golden *et al.*, 2005).

kininogen (KNG) has two main type, high and low-molecular weight kininogen (Seth and Seth, 2009). where high-molecular-weight-kininogen (HK) participate in the system of kinin-kallikrein, which has a role in inflammation, blood pressure, and blood coagulation (Haberland, 1978; Higashiyama *et al.*, 1986; Semba *et al.*, 2004).

A significant differences increase ($p < 0.05$) in Kininogenase concentrations has been observed, where the concentration in infected women with chronic toxoplasmosis (27.320 ng/ml) is higher than control group (23.342 ng/ml), as shown in Table (4-10).. The increase in the proportions of this immune parameter indicates an increase in the immune response in the resistance of

parasites in terms of inhibiting the parasite and then eliminating it. Interestingly, the increasing levels of kininogen was related to infection and inflammations (Wong, 2016), where Kininogens has being involved in inflammatory regulation, blood coagulation, the regulation of the cardiovascular, renal systems, and vasodilation (Duchene and Ahluwalia, 2011).

The results of Del Nery *et al.* (1997) study, can demonstrate that the pathogenic parasite *T.cruzi* displays kinin-releasing activity as a response to the infection and that led to an increase and release of kininogenase.

In addition, another study match with the increases of kininogenase levels, where the total kininogen levels were very low in the control group, but increased by 75-fold during acute parasite infection (Griesbacher *et al.*, 2003).

PAF has several actions like decreased cardiac output, macrophages, monocytes, activation of platelets, stimulation of glycogenolysis in perfused liver, stimulation of uterine contraction, activation of polymorphonuclear leukocytes, hypotension, increased vascular permeability, and others. it look like PAF act in both normal physiological events and to mediate pathological responses, specially allergy and inflammation (Prescott *et al.*, 1990).

A significant differences increase ($p < 0.05$) in PAF concentrations has been observed, where the concentration in infected women with chronic toxoplasmosis (4.543 ng/ml) is higher than control group (4.116 ng/ml), as shown in Table (4-10). The increase in the proportions of this immune parameter indicates parasite growth inhibition has a better correlation with PAF existence (Lonardoni *et al.*, 2000). The present study finding illustrating that PAF has an essential role in controlling the infection of toxoplasmosis. Generally, PAF can be a possible curative target to various chronic diseases (Constantinos Demopoulos *et al.*, 2003; Tsoupras *et al.*, 2018; Lordan *et al.*, 2019).

The results of the current study agreed with other studies' results, where a study by Lonardonni et al. (2000) investigated the role of PAF in experimental *Leishmania* infection and the relationship between this mediator and nitric oxide (NO) production. The results of this study showed that the addition of PAF to C57BL/6 mouse macrophages significantly inhibited parasite growth and induced NO production for the infected mice with *leishmaniasis*.

Also, the present study results match with Aliberti *et al.* (1999) results, which suggests that PAF belongs to a group of mediators that coordinate the mechanisms of resistance to infections with intracellular parasites, which a group of mediators refer to mechanisms of PAF for induced NO secretion by *T.cruzi*-infected macrophages and the secreted NO inhibited intracellular parasite growth.

Finally, the results showed that the concentrations for immunological parameter LT-D4, Kininogenase, and PAF in the blood serum of women with chronic toxoplasmosis is higher than on the control group by 0.343ng/ml, 3.979ng/ml, and 0.427, respectively, and this confirms immunological parameter role in the immune response against the *T.gondii* parasite, as it works to resist and inhibit the parasite through many mechanisms and substances that stimulate it to kill the parasite (Fox *et al.*, 2004).

4-3-2: The relationship between the concentrations of some immunological parameters (LT-D4, Kininogenase, and PAF) with titer of IgG in infected women with chronic toxoplasmosis compare with non-infected women

The titers IgG were collected from the infected samples, its concentrations were divided into three groups (<100, between 100-200, and >300). The results in Table (4-11) showed a homogeneity ($p>0.05$) in the distribution of concentrations for each of LT-D4, Kininogenase, and PAF respectively in the homogeneity test. Besides, the one way ANOVA test presents no significant

differences at ($p>0.05$) for each of LT-D4, Kininogenase, and PAF between titer IgG and the concentrations of these immunological parameters, this may be because the higher titer concentrations were less than 100 with 36 titer IgG. Also, may be due to the means ratios of the immunological parameters are close to each other to the three titer groups.

Table (4-11): The relationship between concentrations of some immunological parameters LT-D4, Kininogenase, and PAF with titer of IgG

Immunological parameters	Titer (IgG)	Number	%	Mean	S.D.	Homogeneity Sig.	Sig.
LT-D4 ng/ml	<100	36	72	3.184	0.622	0.299	0.802
	101-200	7	14	3.055	0.553		
	>200	7	14	3.256	0.267		
	Total	50	100	3.176	0.571		
Kininogenase ng/ml	<100	36	72	27.686	3.390	0.769	0.193
	101-200	7	14	26.343	2.950		
	>200	7	14	29.499	2.391		
	Total	50	100	27.752	3.270		
PAF ng/ml	<100	36	72	4.592	0.714	0.230	0.723
	101-200	7	14	4.453	0.582		
	>200	7	14	4.744	0.494		
	Total	50	100	4.594	0.664		

The specified immunological response to parasites drives antibody production (Stewart, 2012). The high density of anti-*T.gondii* IgG antibody may be a response to a large number of parasites entering the host body. Moreover, the antibody number reflects infected host immune status, as well as the low concentrations of titer IgG (less than 100). The reason for low or high levels of IgG antibodies concentration in infected women is due to the extent of their

exposure to sources of pollution, as dietary habits have a role in the variation in the incidence of infection between different regions (Lavine and Arrizabalaga, 2008). Further, the low concentrations in the level of IgG antibodies may depend on the variance in the immune status of the women under study at the time of taking the sample. The role of the cellular and humoral immune response changes depending on the stage of infection and its location in the body (AL-Awsi, 2020).

One of the ways the parasite disappears from the host's immune system is its entry into cells, especially cells that have an immune role such as phagocytes and others, and this is what avoids the host's immunity, where the *T.gondii* parasite is an intracellular parasite. The parasite counteracting the cellular and humoral immune response remains the protozoan in a latent state and reactivated when the immune response is weakened (Silva and Langoni, 2009). The delicate balance between stimulation and escape from the immune response is key to create a chronic infection (Blader and Saeij, 2009). The *T.gondii* immune response of antibodies has a minor role but remains the primary method of personification toxoplasmosis in humans (Filisetti and Candolfi, 2004). A study results by Al-Sallami (2020) agreed with the present study results, it's recorded that the highest infection percentage was (75%) for infected women with toxoplasmosis titer of IgG (8-80), while toxoplasmosis infected women with titer IgG (≥ 300) got the lowest percentage of infection (6.25%).

4-3-3: The concentration of LT-D4, Kininogenase, and PAF in infected women with chronic toxoplasmosis and control women according to age group

The results in Table (4-12) presented that there were noticeable differences in the concentrations of immunological parameters between age groups. Basically, the age group (20-30 years) recorded the highest concentration than

other two age groups (older than 30 years) and (younger than 20 years), with a significant increase ($p < 0.05$).

Table (4-12): The concentration of LT-D4, Kininogenase, and PAF in infected women with chronic toxoplasmosis and control women according to age group

Immunological parameters	Infection	Age	N	Mean	Std. D	Sig
LT-D4 ng/ml	Infected	<20	9	2.876	0.3590	0.035
		20-30	26	3.473*	0.5812	
		>30	15	2.842	0.3510	
		Total	50	3.176	0.5711	
	Control	<20	6	2.987	0.4401	
		20-30	26	2.833	0.5048	
		>30	8	2.926	0.4388	
		Total	40	2.874	0.4758	
Kininogenase ng/ml	Infected	<20	9	26.337	2.3872	0.032
		20-30	26	29.181*	3.0786	
		>30	15	26.124	3.0568	
		Total	50	27.752	3.2708	
	Control	<20	6	21.691	5.5176	
		20-30	26	24.047	3.0313	
		>30	8	25.486	2.9888	
		Total	40	23.981	3.5596	
PAF ng/ml	Infected	<20	9	4.270	0.5138	0.245
		20-30	26	4.936	0.6180	
		>30	15	4.195	0.5095	
		Total	50	4.594	0.6649	
	Control	<20	6	4.291	0.6975	
		20-30	26	4.085	0.5108	
		>30	8	4.516	0.4086	
		Total	40	4.202	0.5386	

Based on estimated marginal means.

*. The mean difference is significant at the 0.05 level.

In the absence of previous literature dealing with the study of the high and low level of immunological parameters depending on tested samples' age, Table (4-12) showed that there were noticeable differences in the concentrations of immunological parameters between age groups. Basically, the age group (20-30 years) recorded the highest concentrations than the other two age groups (older than 30 years) and (younger than 20 years).

Interestingly, the increase in the proportions of this immunological parameter (LT-D4, Kininogenase, and PAF) for infected women with chronic toxoplasmosis and aged 20 to 30 years indicates that these immunological parameters have a better effect on *T.gondii* parasite, in terms of increasing the immune response to resistance parasites by inhibiting the parasite and then eliminating it (Al-Saeed *et al.*, 2008).

CONCLUSIONS
AND
RECOMMENDATIONS

CONCLUSIONS

We conclude from the results of the current study the following:

1. Chronic infection with toxoplasmosis is significant affected by some factors such as age groups, residential area, and the blood groups, while it is no significant affected by some other factors (education level, abortion number, and pregnancy trimester).
2. The majority of women infected with chronic toxoplasmosis have an IgG antibody titer less than 100.
3. Chronic toxoplasmosis affects some hematological parameters, such as the number of total white blood cells and lymphocytes increases, as well as a decrease in the level of hemoglobin, which leads to anemia that may cause abortion or other complications for the affected woman.
4. Chronic infection with toxoplasmosis affects the increase in the concentration of some immunological parameters (LT-D4, Kininogenase, and PAF), which have an important role in hypersensitivity reactions.
5. IgG antibody titer level does not affect the concentration of immune factors (LT-D4, Kininogenase, and PAF) important in hypersensitivity reactions in women with chronic toxoplasmosis.

RECOMMENDATIONS

1. Conducting a study on the relationship between the studied increased factors in the current study with the acute toxoplasmosis infection.
2. Study the other immunological factors that have a role in hypersensitivity reactions in acute and chronic toxoplasmosis.
3. Study the relationship between *T.gondii* parasite strains and the immunological parameters concentration that contribute to hypersensitivity reactions.

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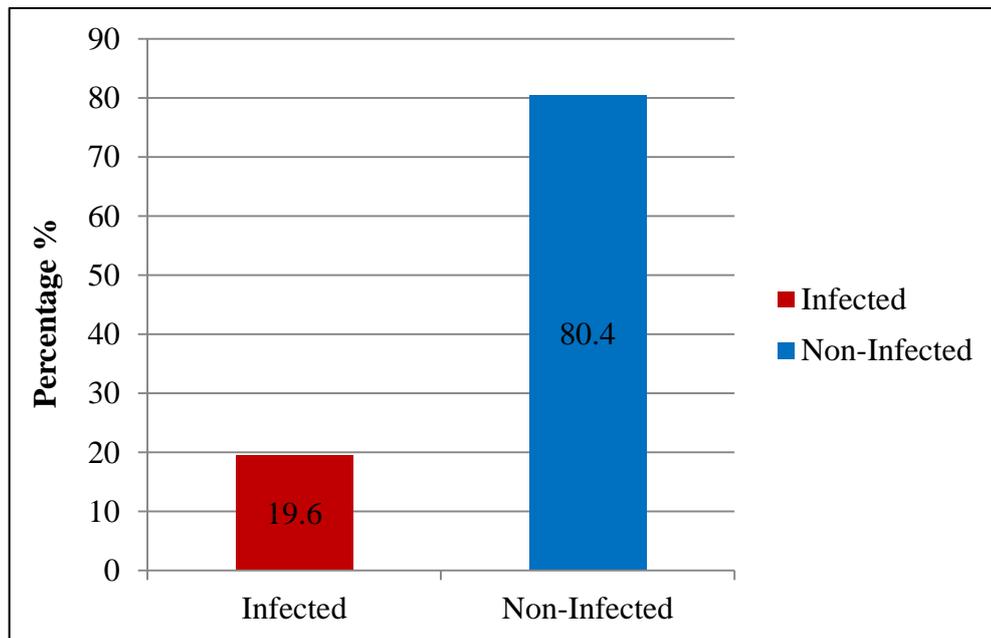
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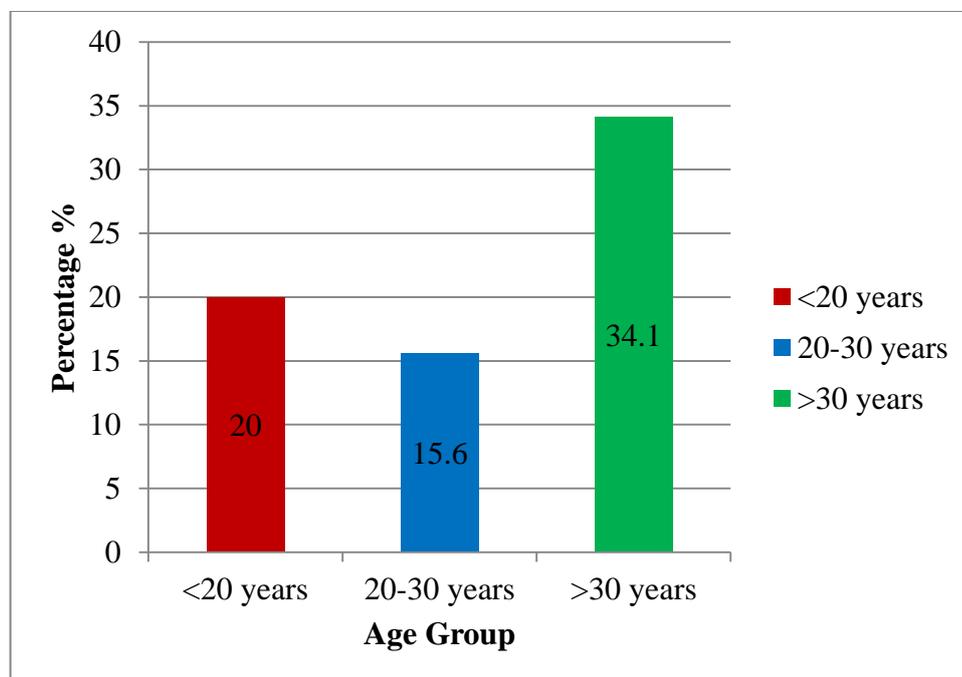
Appendix (1): Questionnaire

Sample number				
Full name				
Date				
Age				
Address	Rural		Urban	
Education level	Illiterate	Primary	Secondary	University
Pregnancy trimester	No	1 st	2 nd	3 rd
Abortions number				
Titer of IgG				
Blood group	A	B	O	AB

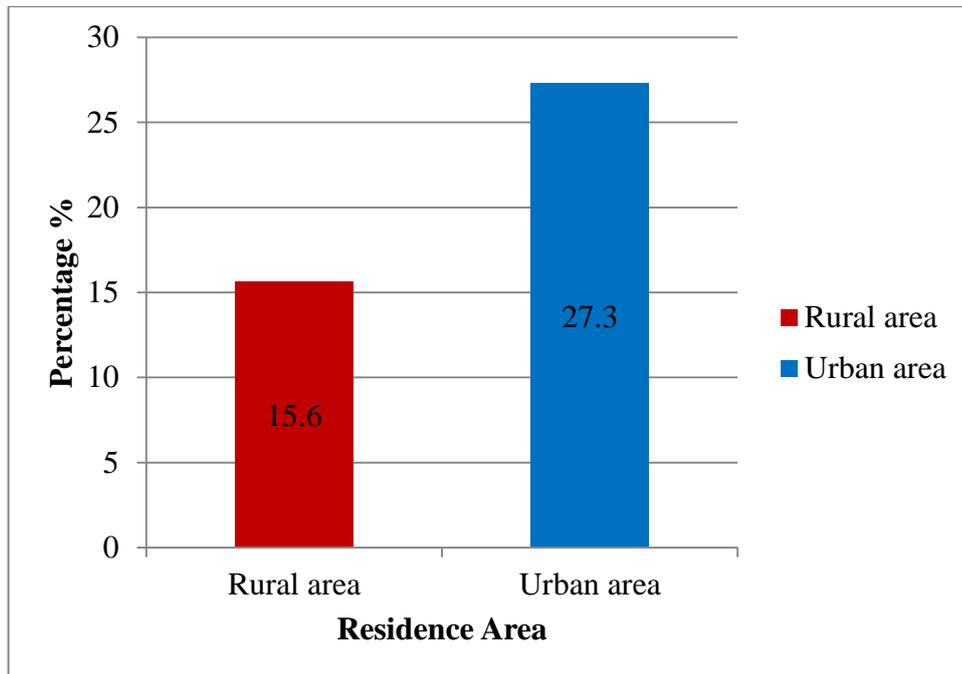
Appendix (2): Total percentage of infection with chronic toxoplasmosis in Babylon province women



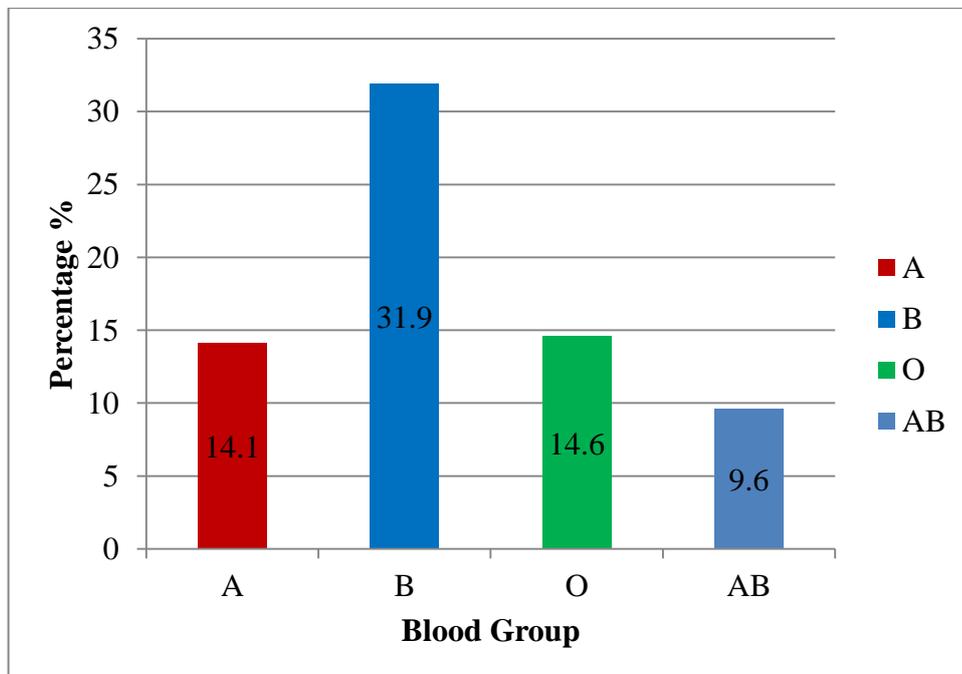
Appendix (3): Distribution of infection with chronic toxoplasmosis in Babylon province women according to age



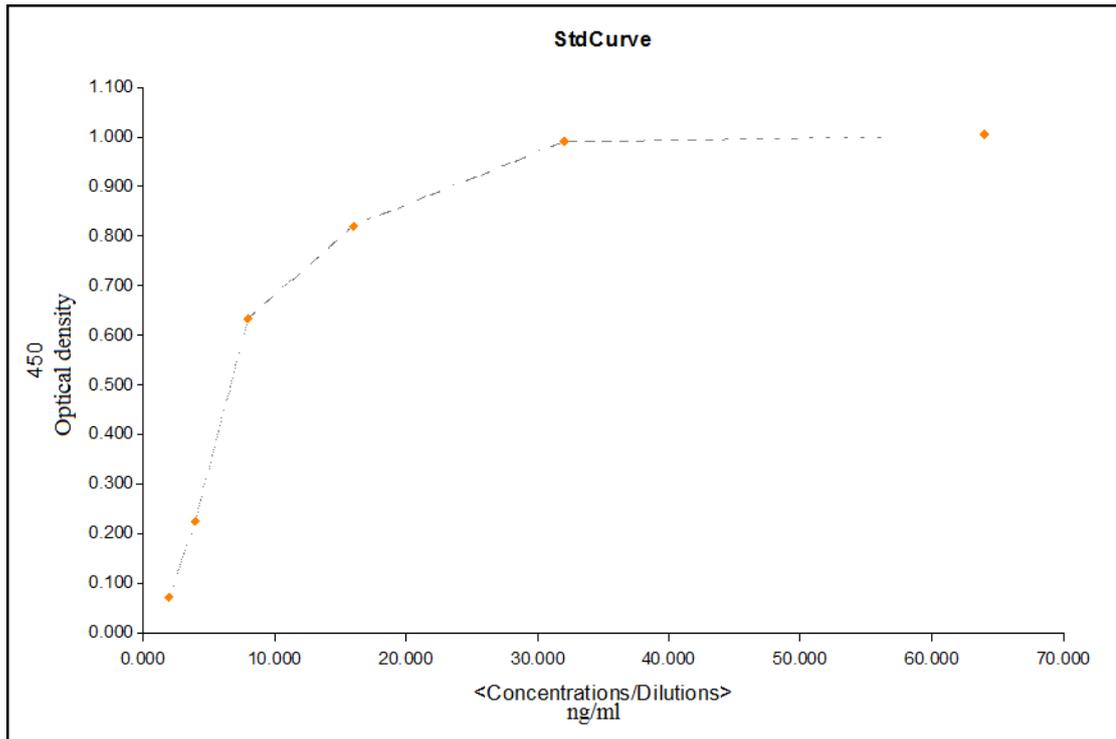
Appendix (4): Distribution of infection with chronic toxoplasmosis in Babylon province women according to residence area



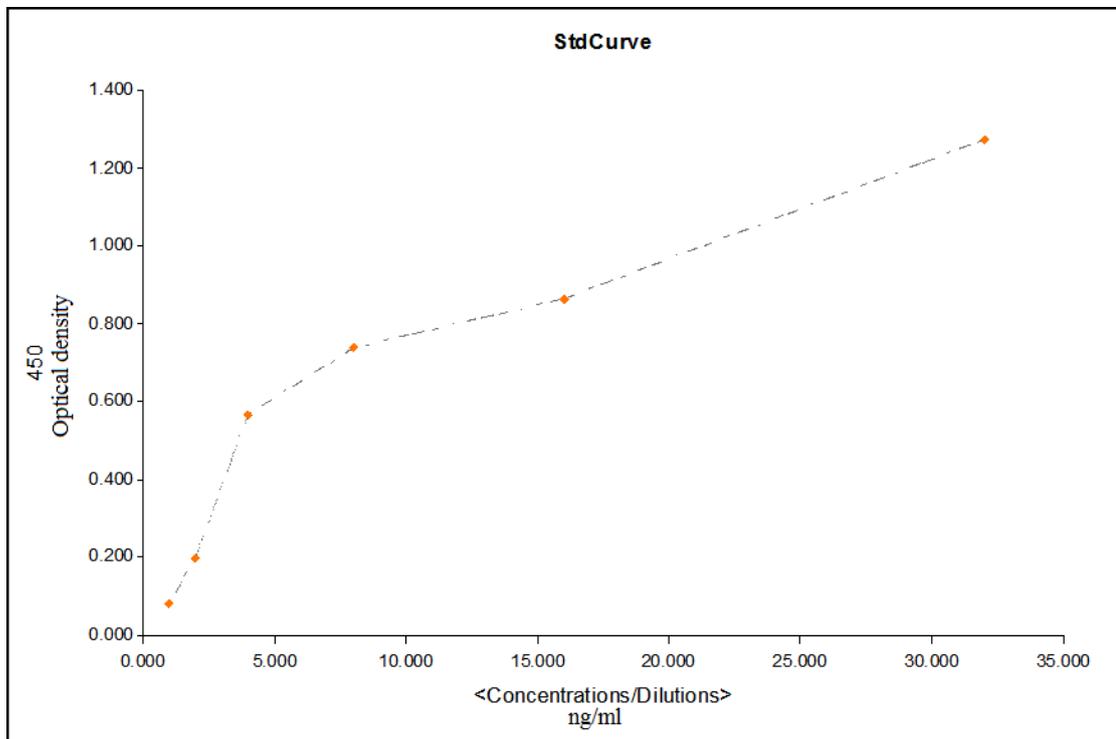
Appendix (5): Distribution of chronic toxoplasmosis in Babylon province women according to blood groups



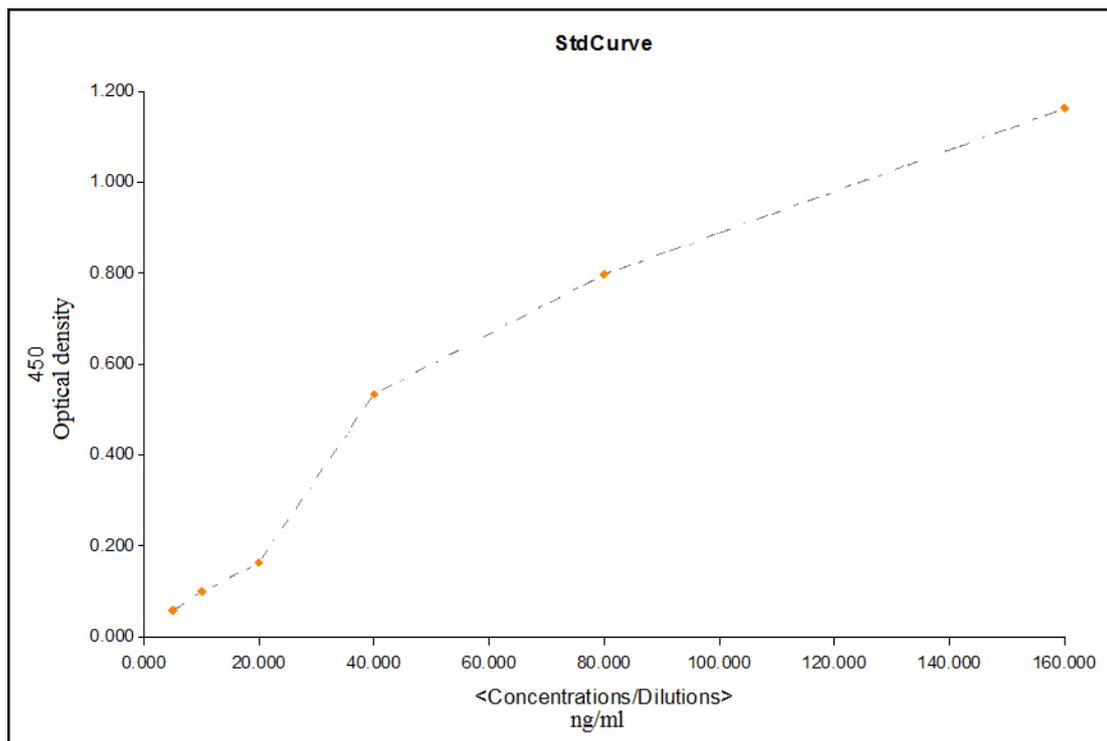
Appendix (6): The standard curve of PAF



Appendix (7): The standard curve of LT-D4



Appendix (8): The standard curve of Kininogenase



الخلاصة

بينت النتائج ان ٧٢% من النساء المصابات كان مستوى عيار الضد IgG في مصولهن اقل من ١٠٠. هدفت الدراسة الحالية الى التحري عن الاصابة المزمنة بداء المقوسات في نساء محافظة بابل وعلاقة تلك الاصابة ببعض المعايير الوبائية والدموية والمناعية. وتم خلال هذه الدراسة فحص ٢٥٥ عينة مصل من النساء المراجعات الى مستشفى بابل للنسائية والاطفال في مدينة الحلة بتقنية الفايدز VIDAS للمدة من بداية شهر تشرين الاول ٢٠٢٠ م ولغاية نهاية شهر اذار ٢٠٢١م. نظمت استمارة لكل مريضة تضمنت المعلومات الضرورية في البحث مثل التاريخ والعمر و منطقة الإقامة و المستوى التعليمي وشهر الحمل والعيار و عدد الاجهضات وفصيلة الدم. تم تشخيص إصابة ٥٠ امرأة بداء المقوسات ، بينما تم اختيار ٤٠ عينة عشوائياً لتكون مجموعة السيطرة.

بينت نتائج الدراسة الحالية ان نسبة الاصابة الكلية بداء المقوسات المزمّن في نساء محافظة بابل بلغت ١٩.٦%. ووجد ان نسبة الاصابة في الفئة العمرية اكبر من ٣٠ سنة هي الاعلى ٣٤.١% مقارنة مع نسب الاصابة في الفئات العمرية الاخرى (اقل من ٢٠ سنة ومن ٢٠-٣٠ سنة) مع وجود فرق معنوي بنسب الاصابة. وجدت نتائج الدراسة الحالية زيادة معنوية في نسب الاصابة بداء المقوسات المزمّن في المناطق الحضرية ٢٧.٣% مقارنة بالمناطق الريفية ١٥.٦%. لوحظ ان نسبة الاصابة بداء المقوسات الكوندية المزمّن في النساء ذوات المستوى التعليمي الجامعي كانت الاعلى ٢٩.٣% مقارنة بنسب الاصابة في النساء ذوات التحصيل التعليمي الثانوي والابتدائي والنساء غير المتعلّقات مع عدم وجود فروق معنوية بنسب الاصابة. اوضحت النتائج ان نسبة الاصابة الاعلى بداء المقوسات المزمّن كانت في النساء خلال الثلث الاول من الحمل حيث بلغت ٢١.٩% مقارنة مع النساء في الثلث الثاني والثلث الثالث من الحمل مع عدم وجود فرق معنوي بنسب الاصابة. وجد ان ٣٣.٣٣% من النساء المصابات قد عانت اكثر من ثلاث اجهضات، ووجد ايضا ان ٣١.٩% من النساء المصابات بداء المقوسات المزمّن كانت تحمل فصيلة دم من النوع B.

اوضحت النتائج ان الاصابة بداء المقوسات المزمّن لها تأثيرا على بعض المعايير الدموية، حيث لوحظ زيادة معنوية في العدد الكلي لخلايا الدم البيض ٨.٢٤ وخلايا الدم البيض اللمفية ٢.٨٣ وانخفاض في تركيز الهيموغلوبين ١١.٦٣ في النساء المصابات مقارنة مع النساء غير المصابات ٧.٤٩ و ٢.٤١ و ١٢.٣٥ على التوالي.

أظهرت نتائج الدراسة المناعية أن تركيز المعايير المناعية (D4) Leukotrienes و Kininogenase و Platelet Activation Factor (PAF) في مصول النساء المصابات بداء المقوسات المزمّن اعلى معنويا (٣.١٧٦ نانوغرام / مل، ٢٧.٧٥٢ نانوغرام / مل، و ٤.٥٩٤ نانوغرام / مل، على التوالي) من تراكيزها في مصول النساء غير المصابات (٢.٨٧٤ نانوغرام / مل، ٢٣.٩٨١ نانوغرام / مل، و ٤.٢٠٢ نانوغرام / مل، على التوالي). كما أظهرت النتائج ان أعلى تراكيز للمعايير المناعية في النساء المصابات في عمر ٢٠ الى ٣٠ سنة مقارنة بالاعمار الاخرى. نستنتج من نتائج الدراسة الحالية ان الاصابة بداء المقوسات الكوندية لها تأثيرا على المعايير المناعية والدموية وهذا ما يعكس العلاقة بين التأثير المرضي للطفيلي وما يبديه المضيف من استجابات مناعية اتجاهه.



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دراسة بعض المؤشرات الوبائية و الدمية والمناعية في النساء المصابات بداء المقوسات المزمّن

رسالة مقدمة إلى
مجلس كلية العلوم / جامعة بابل
وهي جزء من متطلبات نيل درجة الماجستير في العلوم
علوم الحياة / الحيوان

من قبل
طبيبة عبد الامير حسين الربيعي
بكالوريوس علوم حياة / ٢٠١٧
كلية العلوم – جامعة بابل

إشراف
أ.د. قاسم عبد الله حمزه المرشدي

تشرين الاول ٢٠٢١ م

١٤٤٢ هـ