TURKISH REPUBLIC OF NORTH CYPRUS
NEAR EAST UNIVERSITY
HEALTH SCIENCE INSTITUTE

EVALUATION OF PROGESTERONE, ESTROGEN AND PROLACTIN LEVELS IN PREGNANT WOMEN WITH TOXOPLASMOSIS IN ERBIL CITY / IRAQ

MOHAMMED QASIM BURHAW

MEDICAL MICROBILOLOGY AND CLINICAL MICROBIOLOGY MASTER PROGRAM

DEPARTMENT OF MEDICAL MICROBILOGY AND CLINICAL MICROBILOGY

ADVISOR
ASSISTANT PROFESSOR DR. ESREF CELIK
CO-ADVISOR
ASSISTANT PROFESSOR DR. SAMIR JAWDAT BILAL

NICOSIA 2021

EVALUATION OF PROGESTERONE, ESTROGEN AND PROLACTIN LEVELS IN PREGNANT WOMEN WITH TOXOPLASMOSIS IN ERBIL CITY / IRAQ

MOHAMMED QASIM BURHAW

MASTER'S THESIS

MEDICAL MICROBILOLOGY AND CLINICAL MICROBIOLOGY MASTER PROGRAM

DEPARTMENT OF MEDICAL MICROBILOGY AND CLINICAL MICROBILOGY

ADVISOR

ASSISTANT PROFESSOR DR. ESREF CELIK

CO-ADVISOR

ASSISTANT PROFESSOR DR. SAMIR JAWDAT BILAL

NICOSIA 2021

NICOSIA 2021

APPROVAL

The Directorate of Health Sciences Institute

This study has been accepted by the Thesis Committee in Medical Microbiology and Clinical Microbiology Programme as Master Thesis.

Thesis committee:

Chair of the committee :		Assist. Prof. Dr. Eşref Çelik Near East University
Member	:	Assist. Prof. Dr. Ayşe Sarioğlu Near East University
Member	:	Assist. Prof. Dr. Emine Evren Girne University

Approval:

According to the relevant articles of the Near East University Postgraduate Study – Education and Examination Regulations, this thesis has been approved by the above mentioned members of the thesis committee and the decision of the Board of Directors of the institute.

Prof. Dr. K. Hüsnü Can Başer
Director of the Institute of Health Sciences
Near East University

DECLARATION

Hereby, I declare that this thesis study is my own study, I had no unethical behaviors in all stages from planning of the thesis until writing there for, I obtained all the information in this thesis in academic and ethical rules, I provided reference to all of the information and comments which could not be obtained by this thesis study and took these references into the reference list; and, had no behavior of breeching patent rights and copyright infringement during the study and writing of this thesis

Date:

Signature

Mohammed Qasim Burhaw BURHAW

DEDICATION

I dedicate my thesis to my beloved parents

ACKNOWLEDGEMENTS

In the name of Allah, as an authors I would like to express the appreciation to my supervisor, Assistant Professor Dr.Esref Celik and Co-supervisor Assistant Professor Dr. Samir Jawdat Bilal for his guidance and assistances throughout the study. Without them assistances this thesis could not be done successfully

There are far to many that deserve acknowledgement and it is unfair to single out individuals but authors would like to mention the decision-makers who participated in this research. Without their willingness to share their thoughts and knowledge with us, this research would not have been possible. Last but not least, deepest thanks to the authors'' family, parents and friends for their encouragements, (Bio) lab members and full moral supports throughout the advancement of this study

ÖZET

Toxoplasma gondii, dünya nüfusunun üçte birinin enfekte olduğu toksoplazmoz hastalığının etkenidir. Hamile kadınlarda, çeşitli sorunlara neden olabilir, bu sorundan biri hormonal değişikliklerdir. Gebelik sırasında toksoplazmoz prevalansı artar. Çalışmamızın amacı, gebelik sırasında Toxoplasma gondii ile enfekte olan kadılardaki bu hormonların oranını değerlendirmektir. Bu amaçla , anti-T.gondii antikor değerleri (IgG ve IgM) bir grup Iraklı-Erbil gebe kadında izlendi. Progesteron, prolaktin ve östrojen hormonlarının düzeyleri cobas 6000a alet kullanılarak ölçüldü. Farklı trimesterde gebe olan kadınlarından toplam 75 örnek toplandı ve kontrol grubu olarak 30 negatif örnek alındı. Toksoplazmoz örneği pozitif 45 olgu saptandı. Çalışma popülasyonu katılımcı karakteristik Yaş (17-43) arasında idi. Ayrıca, tüm farklı trimesterde (birinci 9, ikinci 17, üçüncü19), toksoplazmoz pozitif olan gebe kadınların kan örneklerinde progesteron , östrojen ve prolaktin hormon değerlerine bakıldı. Yapılan hormonal test sonuçlarına göre, toksoplazmoz veri analizi ve sonuç gözlemi ile toksoplazma IgM'de istatistiksel olarak anlamlı olmadığını göstermiştir. Ancak toksoplazma IgG negatif ve pozitif sonuçlara göre anlamlı fark saptandı. Araştırmamıza göre pozitif ve negatif toksoplazmozlu gebelerin hormonal düzeyleri karşılaştırıldığında prolaktin düzeyinde anlamlı farklılık bulunurken, progesteron ve östrojen düzeylerinde istatistiksel olarak fark bulunmadı.

Anahtar Kelimeler: Progesteron, Östrojen, Prolaktin, Hamile Kadınlar, Toksoplazma.

ABSTRACT

Toxoplasma gondii is the causative agent of toxoplasmosis in which a third of the world's population is infected. In pregnant women, it can cause a variety of problems, one of this is hormonal changes. The prevalence of toxoplasmosis increases during pregnancy. The aim of our study is to evaluate the proportion of these hormones in women infected with Toxoplasma gondii during pregnancy. For this purpose, anti-T.gondii antibody values (IgG and IgM) were monitored in a group of Iraqi-Erbil pregnant women. Levels of progesterone, prolactin and estrogen hormones were measured using the cobas 6000a instrument. A total of 75 samples were collected from pregnant women in different trimesters and 30 negative samples were taken as a control group. 45 cases with positive toxoplasmosis samples were detected. The study population was between the characteristic age of the participant (17-43), progesterone, estrogen and prolactin hormone values were measured in the blood samples of pregnant women with toxoplasmosis positive at all different trimesters (first 9, second 17, third 19). According to the hormonal test results, toxoplasmosis data analysis and result observation showed that toxoplasma is not statistically significant in IgM. However, a significant difference was found according to toxoplasma IgG negative and positive results. According to the negative and positive results of toxoplasmosis, there was a significant difference in prolactin, whereas no statistically significant difference was found in progesterone and estrogen levels. In conclusion to our sudy, when compared the hormonal levels of pregnant women with positive and negative toxoplasmosis, significant difference was found in prolactin level, in opposition there was no statistical difference was found in progesterone and estrogen levels .

Keywords: Progesterone, Estrogen, Prolactin, Pregnant Women, Toxoplasma.

Table of Contents

DECLARATION ..... **I**

DEDICATION ..... **II**

ACKNOWLEDGEMENTS ..... **III**

ÖZET ..... **IV**

ABSTRACT ..... **V**

TABLE OF CONTENTS ..... **VI**

LIST OF FIGURES ..... **IX**

LIST OF TABLES ..... **IX**

LIST OF ABBREVIATIONS ..... **X**

CHAPTER 1: INTRODUCTION **1**

1.1. Scope of the study **1**

1.2. Aim of the Study **1**

2. General information **2**

2.1. Bacground of Toxoplamosis **2**

2.2. *Toxoplasma gondii* **4**

2.3. Etiology **6**

2.4. Cellular stages **7**

2.4.1 Oocysts……..……..7
2.4.2 Tachyzoites……..……...8
2.4.3 Bradyzoites…….……8
2.4.4. Merozoites……..……9
2.5. Evolution between form…….……..9
2.6. Transmission of T. gondii……..……..……...10
2.7. Morphology of T. gondii……..……..……11
2.8. Life cycle of T. gondii……..……..……..12
2.9. Pathogenesis of toxoplasmosis…….……..13

2.10. Attachment to host cell ……..14
2.11. Host Ligand……15
2.12. Survival Mechanisms of T. gondii…….……..16
2.13 Immunology……....16
2.14. Types of antibodies/Immunoglobulin……..17
2.14.1. IgG:…… 17
2.14.2. IgM: ……17
2.14.3. IgA: ……..18
2.14.4. IgD: ……..18
2.14.5. IgE: ……..18
2.15. Epidemiology of T. gondii……18
2.16. Clinical manifestations of toxoplasmosis……19
2.17. Toxoplasmosis in Meat animals……...20
2.18. Global Seroprevalence of toxoplasmosis……20
2.19. Diagnosis of toxoplasmosis……...21
2.20. Serological Detection of T. gondii……21
2.21. Histologic Detection of T. gondii……..22
2.22. Molecular detection of T. gondii……..22

2.23. Treatment of toxoplasmosis…….22
2.24. Prevention…….23

CHAPTER TOW: MATERIALS AND METHODS 25
2.1. Samples……25
2.2. Nature of the Study…….....25
2.3 Study Population……..26
2.4. Blood sample collection……...26
2.5. Analysis of Samples……26
2.6. Toxo Ab immunoassay in Cobas 6000……..……..27
2.7. The determination of Toxoplasma gondii IgG&IgM ……..……27

2.8. Cobas e 601 module ……28
2.9. The cobas product… ……..28
2.10. Test principle……..30
2.11. Assay…….....30
2.12. Calculation…….31
2.13. Interpretation of the Results…….31
2.14. Material……..32
2.15. Data Analysis……..32
2.16. Ethical Consideration…….32

CHAPTER THREE: MATERIALS AND METHODS……..33
3.1. Results……..33
3.1. General characteristics of study participants……...33

CHAPTER FOUR: DISCUSSION……..…….36
4.1. Discussion…….36

CHAPTER FIVE: CONCLUSION AND RECOMMENDATIONS…….……40

5.1. Conclusion……40
5.2. Recommendations……...41

REFERENCES……...42

CURRICULUM VITAE……53

ETHICAL COMMITTEE……54

PLAGIARISM RESULT……...……55

LIST OF FIGURES

Figure: 1. 1. Ultrastructure of Toxoplasma gondii as seen under the electron microscope.....11

Figure: 1. 2. Life cycle of T. gondii…….…..12

LIST OF TABLES

Table 1. Significant differences in Toxoplasmosis IgM and IgG according to the negative and positive result…….……...…….....34

Table 2. Significant differences in Hormones according to the negative and positive result……...……...……34

LIST OF ABBREVIATIONS

T. gondii	Toxoplasma gondii
HIV	Human Immunodeficiency Virus
AIDS	Acquired Immunodeficiency Syndrome
IgM	Immunoglobulin M
IgD	Immunoglobulin D
IgE	Immunoglobulin E
IgA	Immunoglobulin A
Ab	Antibody
Ag	Antigen
T	Toxoplasmosis
GPI	Glycosyl-phosphatidy-linositol
CHO	Chinese hamster ovary
IFA	Indirect Fluorescent antibody assay
ELISA	Enzyme-Linked Immunosorbent assay
IAAT	Immunosorbent agglutination assay test
PCR	Polymerase Chain Reaction
ECL	Electro-chemi-luminescence
LLD	Liquid level detection
PTH	Parathyroid hormone
hCG	Human chorionic gonadotropin
SPSS	Scientific Program for Social Sciences

CHAPTER ONE: INTRODUCTION

1.1. Scope of the study

The toxoplasma gondii, a member of the Apicomplexa phylum, is the etiologic agent of toxoplasmosis, a widespread infection of humans and other warm-blooded animals. This parasite is a pathogen of medical, veterinary and economic importance

Toxoplasmosis gondii can cause major complication to pregnant women for example miscarriage and congenital problem. The controlling of the disease bay early diagnosis and treatment cause bay certain parasite are very important in order to decrease risk on pregnant women and it is fetus. The present revision pointed in order to recognize pregnant women with the infection caused by *T. gondii* and it is major affectivity on hormones that responsible in pregnancy, and evaluation the activity of parasite in decreasing pregnant rate in women in Erbil city of Iraq

This study design in order to documentation of the T. *gondii* infection in pregnant women and it is major affectivity on hormones, the isolated sample will be achieved from different private clinic in Erbil city, gynecologist department, the blood samples were taken from pregnant women, then transferring to laboratory in order to evaluate the affectivity of patient with toxoplasmosis, then screening of hormone (Progesterone, Estrogen , Prolactin) are tested in order to evaluation the level of hormonal disturbance.

1.2. Aim of the Study

The study aimed to screen and study the female hormone during the pregnancy, and evaluation the rate of these hormones among toxoplasma gondii.

The importance of the present study can be summarize as:

1- Finding of the prevalence of toxoplasmosis in pregnant women in Iraq/Erbil City.
2- Screening of pregnant hormonal level and it is efficacy that caused by toxoplasma gondii.

2. General information

2.1. Bacground of Toxoplamosis

Toxoplasmosis is an infection caused by a parasite with the protozoan Toxoplasma gondii. The infection results in different types of proven syndromes in humans, environmental mammals, and many bird classes (Rayan & Ray, 2004). There has been progress throughout time about toxoplasmosis and they have been mentioned below in sequential order. T. gondii was first detected in North African from a rodent (Nicolle & Manceaux, 1909). Castellani, in 1914, is believed to be the first to define T. gondii organisms in human blood via a 14 year Ceylon child who passed away due to illness characterized by strong anemia, splenomegaly and fever (Weiss & Dubey, 2009) The first human case of ocular toxoplasmosis testified by Janku in Prague, in 1923, the case was noticed in an infant of 11 months of age. Later on intrauterine spread was described in a new born baby by Wolf and Cowen in 1937. One species (T. gondii) is responsible for the infection in animals, reported by A. B. Sabin in 1939. Toxoplasmosis can be deadly in adults found by Pinkerton and Weinmann in 1940. Asymptomatic persons were also part of the detection of T. gondii cysts in 1945 by Kean and Grocott. Hogan, in 1951, established the first medical descriptions of ocular toxoplasmosis. Beverley and Beattie, in 1958, confirmed the above findings in 39 reported cases (Weiss &

Dubey, 2009) Later on in 1959, Beverly found regular inherited transmission in mice. Jacobs, Remington and Melton, in 1960, stated that meat of infected animals might be the source of contamination. Georges Desmonts, in 1960, started examining transformation of T. gondii to women's fetus in Paris. Moreover prophylactic method of treatment was practiced on pregnant women with developed seroconversion. Years later, Frankel and his fellow experts showed that the experiences in the past were on felines not on humans, as Vietzke clarified the case as an infectious driver among individuals in 1968. It's important to mention that toxoplasmosis was first detected in 1950 in Turkey by Akcay and the first human case was identified by Unat in 1953 (Onul, 1980). Two of the main forms of the main parasite are tissue cyst and oocysts which play important role in the transmission. A study by Jones in 2003 shows that hot areas with low altitudes and moist environment helps to increase the infection of T. gondii. Human Infection can arise via: (i) Tissue absorption cysts in un-cooked meat. (ii) Food absorption or polluted water with mature oocysts fecal-orally. (iii) Mother to fetus transmission called Transplacental or vertical transmission. (iv) Donors can also rarely transmit the infection via needle stick wounds, blood transfusion or orange transplantation. Approximately one in three people in the world may get infected by Toxoplasmosis (Ayeh-Kumi, et al., 2010) (Monotoya & Liesenfeld, Toxoplasmosis, 2004). Ayeh-Kumi (2010) claims that between 30% and 65% of people are already infected by toxoplasmosis. Toxoplasmosis is transmitted to humans by oral ingestion of cysts in infected animal tissues or sporocysts in their extracts, produced by Toxoplasma gondii protozoa. Reticuloendothelial system, muscle, eye and brain tissue, especially in the formation of cysts in many tissues or manifests with acute infection, it is an infectious disease that can transplacental pass from infected pregnant to fetus resulting in congenital infection, anomalies and abortion (Desmonts, Gouvreur, & Congenital, 1974).

Infections transmitted by the congenital tract can cause chorioretinitis, blindness, strabismus, hydrocephalus, microcephalus and cerebral calcifications in stillbirths of infants. It is thought that the transmission of infection from mother to fetus will almost

always be possible if the mother is infected during pregnancy, but it is rarely thought that an immunocompromised woman with acute infection 6–8 weeks prior to pregnancy may also transmit the infection to the fetus. Therefore, it is important to diagnose acute infections using appropriate diagnostic methods and to investigate the fetus when necessary (Garcia, Navarro, Ogawa, De-Oliverra, & Kobilika, 1999) , (Montoya & Remington, 2000).

Until 1970 only asexual stages (tachyzoites or trophozoites, bradyzoites or cystzoites) of Toxoplasma gondii were known. Its sexual cycle and the environmentally resistant stage, the oocyst, were discovered in 1970. During the past 40 years, I had the fortune of being associated with many aspects of the discovery of the life cycle of this parasite. I will attempt to review these events of the finding of the sexual phase of the parasite and its impact on disease and control. Toxoplasma gondii was found by scientists working with Leishmania or viruses. Transmission of the parasite was a mystery ever since its discovery in the rodent Ctenodactylus gundi. Chatton and Blanc in 1917 found that gundis were not infected naturally, but acquired infection in captivity. Gundis live in the foothills and mountains of southern Tunisia. They were used in research on leishmaniasis at the Pasteur Institute in Tunis. Chatton and Blanc (1917) suspected that T. gondii was transmitted by arthropods because it was found in the blood of the host. Chatton and Blanc (1917) in Tunis and Woke et al. (1953) and others in the USA investigated possible transmission by several species of arthropods with essentially unsuccessful results (Dubey, J. P. 2009).

2.2. *Toxoplasma gondii*

It is belong to parasitology, the *T. gondii* is a eukaryotean protozoan (specially an apicomplexan) with obligate intracellular that causes the infectious disease toxoplasmosis. Found worldwide, *T. gondii* is capable of infecting virtually all warm-blooded animals, but felids, such as domestic cats, are the only known definitive hosts in which the parasite may undergo sexual reproduction. In

humans, *T. gondii* is one of the most common parasites in developed countries; serological studies estimate that 30–50% of the global population has been exposed to and may be chronically infected with *T. gondii*, although infection rates differ significantly from country to country. For example, estimates have shown the highest prevalence of persons infected to be in France, at 84%, as at 2000. Although mild, flu-like symptoms occasionally occur during the first few weeks following exposure, infection with T. gondii produces no readily observable symptoms in healthy human adults. This asymptomatic state of infection is referred to as a latent infection and has recently been associated with numerous subtle adverse or pathological behavioral alterations in humans, though it has been shown recently that the association between behavioural changes and infection with T. gondii is weak. In infants, HIV/AIDS patients and others with weakened immunity, infection may cause a serious and occasionally fatal illness, toxoplasmosis (Bouchut, A., et al, 2015; Cook, T. B., et al, 2015; Flegr, J., et al, 2011; Sugden, K., et al, 2016).

It has been shown that T gondii modifies the behaviour of infected rodents in ways that increase the chances of rodents being preyed upon by felids. Evidence for this "manipulation hypothesis" comes from experiments that show that infected rats with T gondii have a reduced aversion to cat urine. Since cats are the only hosts through which T gondii will sexually reproduce to complete and begin its life cycle, it is suspected that such behavioral manipulations are evolutionary adaptations that increase the reproductive success of the parasite. The rats would not shy away from places where cats live and should a cat attempt to prey on them, they would also be less likely to flee. The key T gondii mechanisms which It is now established that induced behavioral changes in rodents occur via epigenetic remodeling in neurons that control the associated behaviors; for instance, it modifies epigenetic methylation to trigger hypomethylation in the medial amygdala of arginine vasopressin-related genes to greatly reduce predator aversion. Another tends to be widespread histone-lysine acetylation in cortical astrocytes the epigenetic system that T gondii employs. There are variations between non-infected and infected humans in aversion to cat urine, and

sex differences between these groups were clear., and it is one of the parasite that have an obligate protozoan feature of all warm-blooded animals for example humans which the infection has been accompanying to schizophrenia, the infection with *T gondii* most probability occur by contact with the feces (primary source of infection) of animals who have infected previously with parasite, especially domestic cats, and the definitive host of *T gondii* protozoan completes life cycle. Moreover, the sources parasitic infection result in ingestion of infected meat, and contact with the contamination material such as exposure soil and water with oocytes, and maternal-fetal transmission. Whatever, the infection with *T gondii* are asymptomatic because it was long thought that latent *T gondii* infection but it can produce pathological symptoms such as meningoencephalitis, myocarditis and retinochoroiditis, some time lead to death (Bouchut, A., et al, 2015; Cook, T. B., et al, 2015; Flegr, J., et al, 2011; Sugden, K., et al, 2016).

2.3 Etiology

The seroprevalence reports of toxoplasmosis in various countries and continents differ significantly. Some variations are found when the genotypes of the parasite isolated from human and animal. Type I strain are often linked with inherited diseases in humans according to genotypical characteristics. In clinical cases, type II was largely excluded from instances of toxoplasmosis and is often correlated with recurring disease reactivation and in 65 percent of AIDS patient's cases, this type is removed. When it comes to type III, they are often separated from the case of humans. The variation is thought to be due to factors such as the host's geographical, socioeconomic and environmental conditions. Parasite genotype, parasite load and parasite growth phase are among other considerations. Such parasites are essential intracellular parasites, they are developed in-vitro media and need a living structure of organisms, for instance laboratory mice, embryonic eggs or culture of tissue. According to the sort of host and therefore the duration of infection, toxoplasma gondii is outlined in 3 totally different forms. These forms within the life cycle of the

parasite are referred to as oocysts, tachyzoites and bradyzoites. (Montoya JG. 2000; Furtado, Winthrop, Butler, & Smith, 2013).

2.4. Cellular stages

The toxoplasma gondii have various characterized of stages during life cycle, in each stages the parasite will change in to specific cellular stages which have different morphology. Moreover, the toxoplasma gondii have the tachyzoites, merozoites, bradyzoites and sporozoites stages.

2.4.1. Oocysts

This parasite is originated in felines with the shape of an oval, thick and resistant wall and a measurement of 10x12 μm. 10 million oocysts may be replaced with fecal per day by a cat that bears toxoplasma oocysts (Dubey, Ferreira, Martins, & Jones, 2011). In the midst of sufficient heat and humid, oocysts that are not yet contagious as cat feces appear are infectious. The time of sporulation relies on atmospheric temperature and oxygen. Sporulation was not shown to be less than 4 ° C and higher than 37 ° C (Kuman, 2002). The oocyst comprises 2 sporocysts, each of which produces 4 sporozoites. In moist soil, mature oocysts can last for 18 months. The type of the oocytes of the parasite is contagious and spreads sporozoites to the infection. Tissue cyst (bradyzoite) and parasite taken oocysts, invasion of the cat bowel epithelial cells, and first asexual reproductive behavior by splitting it into two merozoites (schizogony), which evolved at the end of this period. Zygote formed by microgamete and macrogamete immature oocyst fertilization is produced by feces. Every natural oocyst is transferred to all vertebral bodies, in particular herbivores, the oocysts enter the digestive tract and the released sporozoites first propagate in the intestinal epithelium and then disperse parasitemia to the entire body. Tissue cysts form and the parasite get

dormant after this period when acute toxoplasmosis develops. As cats consume tissue-cyst food (birds, rodents, and herbivores), the intestinal cysts and therefore the normal T. gondii cycle of life release (Torok, Moran, & Cooke, 2013) (Montoya & Remington, 2000) (Tore, 2001)

2.4.2. Tachyzoites

It is a rapidly growing, aggressive and somatic type of parasite, classified as trophozoites and endozoides and is present in the acute infection cycle. The type tachyzoites is oval or fluffy, 2-3 wide and 5-7 long and needs an intracell environment even if all eukaryotic organelles are required for reproduction. Acute as well as reactivated pathogens are possible with tachyzoites. In the cells of the infected vertebral tachyzoites, vacuoles can cause the infection of all types of cells and can form a rosette every 6 to 8 hours (Dubey, 1998; Dubey, 1998) (Radke, Striepen, & Guerini, 2001). The host cells then erupt into the environment, infecting new cells to create fake cysts or tissue cysts. The pathogens then blast. Giemsa and Wright stain are well colored. Microscopy of electron shows a highly developed organelle structure (Kuman, 2002). The blood, semen, genital and menstrual liquids and tears are separated. Trophozoites have been shown to survive 4–7 days in these fluids and 10 trophozoites are transmitted through the mucosa. Tissue cysts may be present in any organ but are most commonly seen in the brain, skeletonal muscles with heart glutes and are closely linked with the recurrent process of disease transmission. (Foch, Mcdaniel, & Chacko, 2000).

2.4.3. Bradyzoites

Upon colonization of the intended cell, tachyzoites produces a tissue cyst called a bradyzoite. Tachyzoites proliferate rapidly to shape the rosette at the same time, which contributes to cell disruptions. Bradyzoites, on the other hand, develop slowly growing, tissue cysts. Tissue cysts produced by goal tissue tachyzoites remain divided during development and the amount of tissue cysts grows slowly. The young and old tissue

cysts of 20-200 micron diameter, with more or less bradyzoite number, can be observed depending on the period of the infection. The acid vessel, Wright, Giemsa, Gomori's Methamine Silvering and Immunoperoxidase are very well colored tissue cysts with different dimensions. Throughout histological parts already done on the 8th day of infection, tissue cysts can be seen. When the tissue cyst is found in the brain, the tissue cyst is spherical and adapts to the shape of the heart's and skeletal muscles. Even if tissue cysts can be found in every organ, the chronic phase of infection is most common in the brain, the skeletal muscle, and heart muscle. It is somewhat immune to stomach acid and other natural factors, so the main source of infection is fresh or uncooked beef or other types of red meat. Infected meat tissue cysts are not likely to survive by heating up to 67 degrees, gamma irradiance (0.4 kGy), freezing and thawing at –20 degrees Celsius but are never dead from heating in a micro oven (Weiss, L. M., & Kim, K. 2011; Vanagas, L., et al, 2012).

2.4.4. Merozoites

The tachyzoites are recognized by very rapid division, as same as of the merozoites which are divide very fast and it has role before sexual reproduction in order to increase the number of the parasite inside the host (cat's) intestine. The bradyzoites later on become merozoites inside the intestinal epithelial cells when the feline definitive host eats a contamination tissue cyst with the bradyzoites. Later on and it is in the short-period of lived the parasitic population begins to progress in the intestinal epithelium very rapid, following the merozoites developed the sexual stages of the parasite become noninfectious and undergo sexual reproduction which later on causing in zygote-containing with oocysts (Weiss, L. M., & Kim, K. 2011; Vanagas, L., et al, 2012).

2.5 Evolution between form

The last host cat and every living thing that can be tainted with toxoplasma is present in trophozoites and bradyzoites of Gondi. The proliferation of the parasite sporogony

(sexual proliferation) takes place in Felidae (Felidae family) only. The main thing is the host animal. The cat may be infected with any form of toxo from the digestive tract. T gondii reach the small intestine epithelial cells through consuming rodent, mouse and worm. Scale of 10-16 merozoidal agents finishes schizogony (asexual proliferation) in the small intestinal epithelium. As a product of oocysts there is sporogony (sexual proliferation). Gametocytogenesis in 3–15 days is used to create macro-merocytes and microgametocytes by oocysts. Macrogametocytes and microgametocytes develop and evolve into macrogametes. Zygote is formed as a result of macrogamete fertilization by microgamete. Zygote is immature oocysts in 4 days on average and is excreted first in the digestive cavity, then excreted with the feces. In the first instance, oocysts are two sporoblasts, and in 1–5 days, sporty sporozoites of 4 haploids. In about three weeks when the cat is obtaining mature oocysts through the digestive tract, the excretion of immature oocysts takes 1-2 months. A contaminated cat can produce 107 – 109 oocysts each day in an intense phase. Sporozoites are contagious in other species and humans to mature oocysts, trophozoite animals and adult bradizoites. Infective oocysts live for 18 months in the soil (Weiss, L. M., & Kim, K. 2011; Vanagas, L., et al, 2012).

2.6. Transmission of T. gondii

T. Gondi is the global zoonosis, which can kill almost everyone and everything. It is l ocated more in hot and humid areas than in cold and dry places because of the life-cycle of the parasite. Cats, which are the definitive hosts of T. gondii, become infected by ingesting the sporulated oocysts or in some cases infected animals like rats or mice (Baron, 1996). The oocysts are highly contagious to most mammals, including humans and birds. Infection of T. gondii spread by various routes such as: (i) Raw red or undercooked meat, including the cysts. (ii) Drinking water and Consuming water or food that is infected with oocysts. (iii) Also from infected pregnant women . (v) Contaminated organ been transplanted and transferring blood from an infected person. Also there are some researches mention the transmission may due to insects, the insects can also be a source of transportation of the disease (flies, cockroaches, worms, and

slugs). Epidemiological scholars have shown that cats are mainly essential for the transmission of parasites in many parts of the world. Tissue cysts are highly prevalent in human-consuming food. Around 1% of cats have been identified in excreted oocysts in various parts of the world (Tore, 2001). (Montoya & Remington, 2000).

2.7. Morphology of T. gondii

Three major stages of infectious Toxoplasma gondii exist. Tachyzoites (in group), bradyzoites (in tissue cysts) and sporozoites (in oocysts). They are all highly infectious to humans. Sporozoites and tachyzoites. Sporozoites. Gondi are very similar in terms of their appearance, cell inclusions and organelles with the similar number of rhoptries, in all three forms (Baron, 1996). Bradyzoites differ in structure from tachyzoites according to studies by (Dubey, 1998). At the rear end is located the nucleus of bradyzoites, while at the central end of the nucleus is tachyzoite. In addition, rhoptry contents are labyrinthine in tachyzoites, while bradyzoites are often electron-dense (Kwofie, 2012).

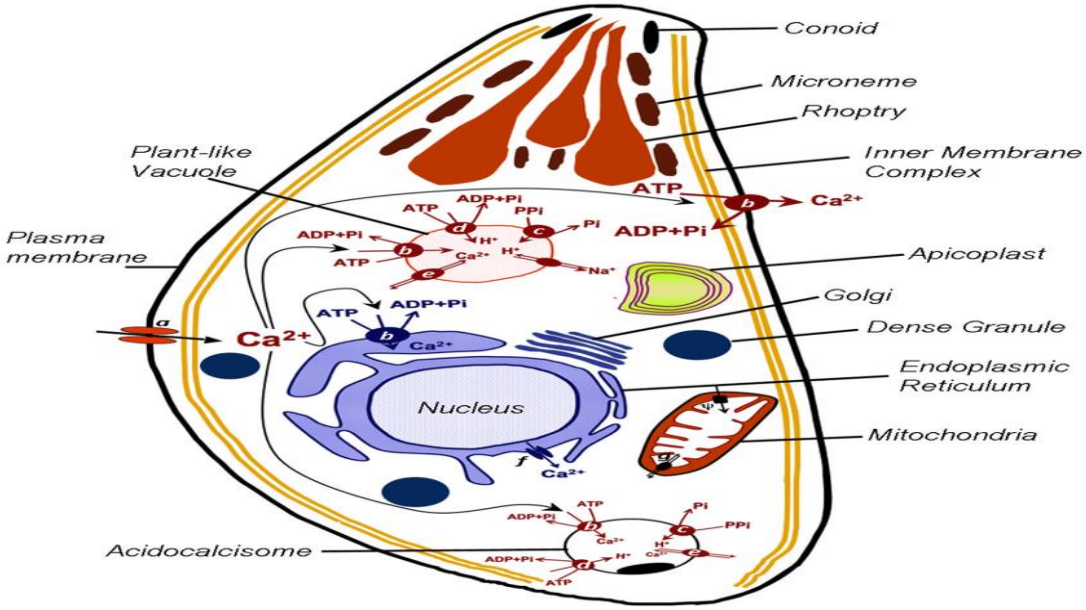


Figure: 1.1. Ultrastructure of Toxoplasma gondii as seen under the electron microscope
Source: Baum, J. et al.2006

2.8. Life cycle of T. gondii

The authoritative host, like domestic cats, has now been identified in T as representatives of the Felidae family. According to Baron (1996), gondii was enacted in 1970. Different hospitality is offered by other hot blood-blooded animals including humans and birds. T- gondii infection of domestic cats. Cyst-type gondii (Dubey, Ferreira, Martins, & Jones, 2011) the parasites persist and move into the stomach where they infect cats ' epithelial cells. The parasites then develop into sexual activity and replicate several oocytes. Cat's cell epithelia infected with oocysts that are dumped in the feces of cat Consumption of soil, water or plants infected by oocysts results in contaminating the host (Dubey, 1998).

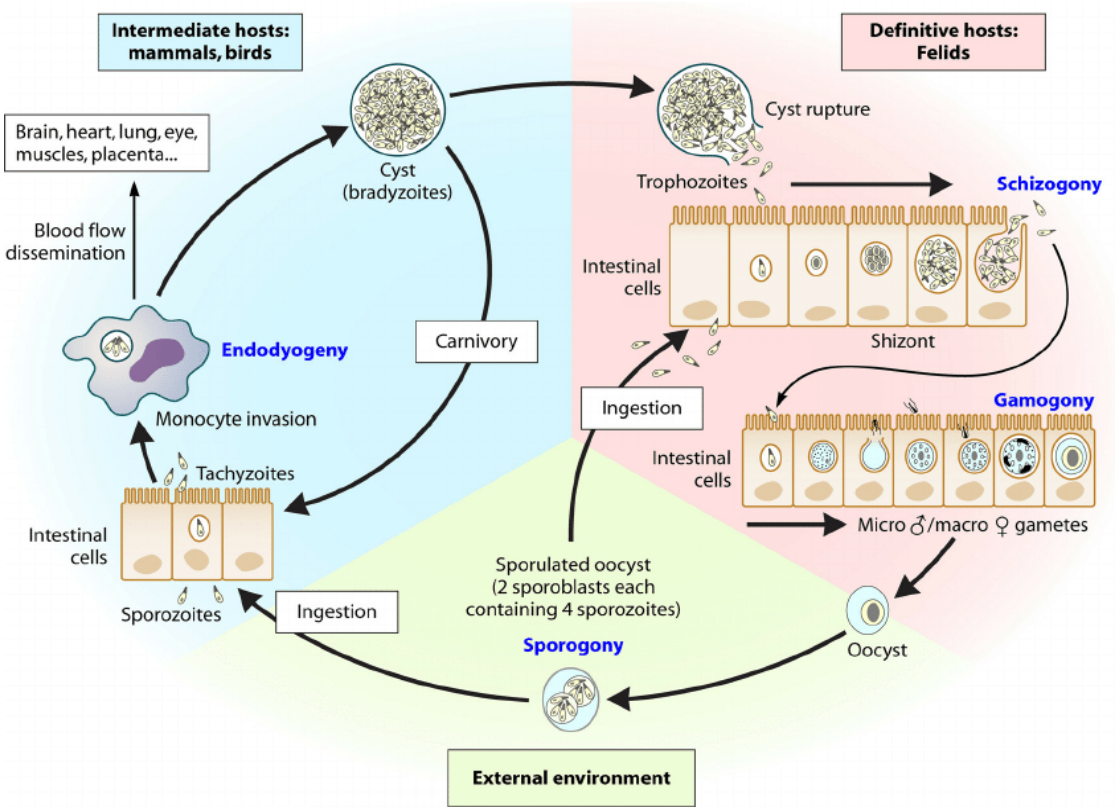


Figure: 1.2. Life cycle of T. gondii

Source: Baum, J. et al.2006

Human beings are contaminated with unclean vegetables or polluted water or litters. A while after ingestion, oocysts convert into tachyzoites. These tachyzoites localize in the neural and muscle tissue, and grow into a tissue cyst called bradyzoites, containing the cysts of the tissue. Ingest crude or poorly cooked meat that contains the tissue cyst results in human infection by the parasite (Baron, 1996)

2.9. Pathogenesis of toxoplasmosis

The peculiar genotypes for congenital toxoplasmosis are more extreme than that attributed to normal genotypes. Some infants suffering from a more severe congenital infection appear to experience a Toxoplasmas antigen, which may be important for their disease's pathogenesis. In congenitally infected infants, immunoglobulin G (IgG) monoclonal gammopathy has been described and IgM levels may increase in congenital toxoplasma newborns. Among congenitally infected people, glomerulonephritis was identified with deposits of IgM, fibrinogen, and Toxoplasma antigen. (Hokelek, 2019)

Toxoplasmosis development occurs after T. gondii infection. Gondi parasites congenital or intakes infected tissue cysts in food or water sporulated with cat's feces as reported by Baron (1996). Congenital parasites. Gondia parasites the host cell is engaged and finally destroyed during incubation from 5 to 18 days by active cell propagation. (Dubey, 1998) . Stray-Pedersen (1993) and Dunn et al. (1999) reported that a more severe form of congenital toxoplasmosis involves retinal infection and causes visual impairment chorioretinitis. In congenital toxoplasmosis, mainly in immunosuppressed patients, necrotic brain as noted by Stray-Pedersen may occur (Tenant-Flowers, M., et al, 1991; Luft, B. J., & Remington, J. S. 1992; Wong, S. Y., & Remington, J. S., 1993; Dunn, et al., 1999).

2.10. Attachment to host cell

For an intracellular pathogen to gain entrance into a cell, the surface of Toxoplasma must first make intimate contact with the cell's surface. Since the host and pathogen lipid membranes typically have a negative net charge, receptor-ligand interactions are needed to resolve this repulsive force and achieve the strong attachment needed for both motility and invasion. Among the known intracellular pathogens, T gondii is unique in being very promiscuous in its capacity to invade a large variety of host cells. This parasite is capable of invading almost every mammalian cell type and even insect and fish cell lines when cultivated in vitro. This large range of potential host cells will enable Toxoplasma to express a variety of ligands with multiple receptors or there are few receptors attached to the ligands shared to various type of cell (Boothroyd, J. C., et al, 1998; Manger, I. D., et al,, 1998; Black, M. W., & Boothroyd, J. C. 2000).

The surface of Toxoplasma has been thoroughly characterized to classify the components involved in this phase in order to distinguish between these two scenarios. This parasite's plasma membrane tends to consist mainly of a variety of proteins that are connected by a glycosylphosphatidylinositol (GPI) moiety to the membrane. It has been determined that much of the surface consists of a family of proteins similar to the surface antigen SAG upon the discovery of the genes for these proteins. SAG1 is the most abundant of these proteins on the surface and has been involved, at least in part, in the initial host membrane attachment events. This protein is evidently may not be the only parasite molecule involved in attachment because, even with altered properties, Sag1 mutants are still infectious: they bind less well, but take less time on average to reach a host cell: 1 h after introducing syringe-released tachyzoites to a new infected cells monolayer, about twice as many Sag1-mutants penetrated compared to wild type parasites. Using the neoglycoprotein bovine serum albumin glucosamide as a modest inhibitor, the association between SAG1 and the host cell can be partially blocked. There is also evidence presentation the parasites' ability to bind laminin to the extracellular matrix protein, and this can be used as a bridge to the host cell's ubiquitous

laminin receptors. Although anti-laminin antibodies blocked attachment at a level close to that seen with anti-SAG1 antibodies, the Toxoplasma laminin receptor has not been identified. (Boothroyd, J. C., et al,, 1998; Manger, I. D., et al,, 1998; Mineo, J. R., & Kasper, L. H., 1994; Mineo, J. R., et al, 1993; Kasper, L. H., & Mineo, J. R., 1994; Black, M. W., & Boothroyd, J. C. 2000).

2.11. Host Ligand

The host cell surface's contribution to attachment has been less well described. In at least some of the lines tested in vitro, the expression of the as yet unidentified attachment ligand(s) on the surface of the host cell appears to be cell cycle dependent. Parasite attachment increased threefold in synchronized populations of Chinese hamster ovary (CHO) and bovine kidney (MDBK) cells as the cells progressed from the G1 stage to the mid-S level and decreased back to baseline as the cells reached G2/M. This link between attachment and the cell cycle can explain the finding that there is an important, non-random variance in the number of vacuoles within individual host cells within a fibroblast population (although this cannot be the entire explanation because most of these host cells grown to near confluency would probably be in G0). Antibodies elevated against synchronized MDBK cells harvested at various points during the cell cycle showed that polyclonal serum elevated against mid-S phase cells was almost three times more successful at blocking attachment than serum elevated against G1 phase cells. His block was not unique to the MDBK cell line, because CHO cells as the host were used to have a similar effect. Such evidence would indicate that a common antigenic ligand is used in Toxoplasma attachment in both cell lines, although it does not preclude the possibility of a mutual, cell cycle-dependent epitope that blocks steric hindrance interaction. Studies that use polysaccharides as inhibitors and probes have given several hints to the existence of the host-parasite relationship. These experiments demonstrate that there is a form of sugar-lectin interaction involved in parasite attachment because, depending on the concentration of the polysaccharide used, some polysaccharides (heparin, fucoidan, and dextran sulfate) can promote or

block parasite attachment to host cells. Proteoglycan synthesis deficient cell lines often display a decreased capacity to bind the parasites, again suggesting a parasite lectin-like activity in the phenomenon of attachment. The existence of these lectins is not yet recognized (Ortega-Barria, E., & Boothroyd, J. C. 1999; Grimwood, J., et al, 1996; Black, M. W., & Boothroyd, J. C., 2000).

2.12. Survival Mechanisms of T. gondii

Toxoplasma gondii has shown to trigger the trophoblast cell apoptosis, a single-cell virus commonly found in animals, and ultimately inflict fetal harm and abortion. Dense granule protein 15 (GRA15) is a key ingredient in the innate immunity to T, however. Host-cell apoptosis appears unclarified in gondii infection and its pathogenesis. T. gondii experience other mechanisms to prevent damage from the host immune syst em following human disease and eventual intrusion. The use of plasmids to invade ho st cells involves these (Henrik, et al., 1999). This helps the immune system of the host to withstand injury. The application of the anti-apoptotic mechanism is a T mechanism. Host immune system to escape injury. (Hippe, et al., 2009) They also note that the pro-apoptosis effector proteins such as Bak and Bax are being affected. When these proteins are disrupted, toxo Pro-apoptosis effector proteins have changed shape and structure of T. gondii. This results in the inability of proteins to be moved to the host cells and apoptosis is initiated during this process. Another mechanism used by T is host cell autophagy. The escape damage gondii. This is because of T's ability. Autophagy to start gondii. This reduces host cell volumes, reducing the ability of the host immune system to kill T. gondii (Wang, Weiss, & Orlofsky, 2009)

2.13. Immunology

Antibodies are made of light chain and heavy chain proteins, which form a structure shaped like a Y. While the base of the y-form structure is retained and therefore similar to all antibodies, each antibody is distinguished by its tips in the forks of the Y-shaped

structure (Selamawit, 2004). The tips are antigen-based, while the preserved region is immune-based (Litman et al., 1993). In response to antigenic stimulation, antibodies are generally secreted and therefore represent approximately 20% of plasma protein. An antibody's primary aim is to defend the body by combining antigens to neutralize bacteria, toxins, viruses and other patenticides and aliens, such as T. Gondii (Switzerland, 2015; Selamawit, 2004).

2.14. Types of antibodies/Immunoglobulin

Five main types of antibodies in the body are developed, they are:

2.14.1 IgG:

According to Selamawit (2004) IgG is the most ample immunoglobulin that is unseen in the body and forms around 80% of the entire antibodies it spreads more easily in additional vascular areas in relation to other immunoglobulin and neutralized toxin while it binds to the extra-vascular areas of microorganisms. Thus, it is the only antibody that can pass the placenta in humans where it gives the fetus and newborn immunity (Pier et al., 2004). In the first 6-12 months of life the infant receives protection against immunity, while the baby's own immune system matures. IgG is capable of preventing systemic infection spread.

2.14.2 IgM:

It forms of about 10% of all blood serum immunoglobulins, according to Selamawit (2004). Plasma cells are synthesized in primary infections at an early stage to deter the spread of pathogens in the early stages of infection (Pier et al., 2004 and Geisberger et al., 2006).

2.14.3. IgA:

It constitutes nearly 20% of all blood vessels (Selamawit, 2004). Mostly in serum, tears, sweat, milk, colostrum, saliva, etc., it is found (Pier et al., 2004). IgA is summed up as dimmers fusing a short J chain (polypeptide). It enhances IgA's tolerance to protease action. In the early life stages of newborns, IgA throughout breasts avoids invasion of the gastrointestinal tract by invading pathogens (Selamawit 2004). And, for mammals, they cannot touch the placenta.

2.14.4. IgD:

This constitutes less than 1% of all immunoglobulins through monovalent immunoglobulin (Selamawit, 2004). The lymphocyte occurs on the surface of B-cells and joins monomeric IgM. It renders it antigen receptor for basophils and mast cells to generate antimicrobial factors, as stated by Geisberger et al. 2006.

2.14.5 IgE:

The monomer contains 0.004% of all serum immunoglobulins (Selamawit, 2004). It was reported that IgE molecules, particularly mast cells and basophils, bind to allergens and to tissue cells. IgE receptor reactions contribute to allergic reactions, for example asthma, hives, and hay fever.

2.15. Epidemiology of T. gondii

Toxoplasmosis is regarded as the third largest infectious disease that causes eat-borne deaths following the tradition of listeriosis and salmonellosis. (Jones, Lopez, & WilsonM, Congenital toxoplasmosis, 2003) (Dubey, Ferreira, Martins, & Jones, 2011). The variation is thought to be the result of geographical, socioeconomic, and environ mental matters such as the host age, genetic status, and host status. (Furtado, Winthrop,

Butler, & Smith, 2013). Transmission of mother-fetal T. gondii occurs within one to four months of placenta colonization by Dubey et al. (2009) and Stray-Pedersen (1993) as reported. This has a negative health effect on pregnancies and newborns (Garweg, Scherrer, Wallon, Kodjikian, & Peyron, 2005), (Liesenfeld, et al., 1997). Furtado et al. (2013) research stated that, as pregnancy progresses, the likelihood of mothers-to-children transmission rises. Infection with Toxoplasma gondii gained during early pregnancy is more likely to lead to clinical conditions. In addition, the risk of congenital acute toxoplasma -infection is estimated. (Jones, Lopez, & WilsonM, Congenital toxoplasmosis, 2003) (Stray-Pedersen, 1993) (Dunn, et al., 1999). Pregnancy gondii infection ranges from 20% to 50% if strict treatment systems do not adhere. Dunn et al. (1999), estimates in France, for the period 1987 to 1995, that the risk of mother-to-child transmission was 6% at the age of 13 weeks, 40% at 26 weeks and 72% at 36 weeks. In the case of fetuses and neonates, congenital toxoplasmosis can cause severe to fatal sequelae.

2.16. Clinical manifestations of toxoplasmosis

T. gondii contamination threatens fetuses and newborns in the time of pregnancy. Reactivation may take place in women who are pregnant with HIV who receive high doses of immunosuppressive treatment such as organ transplant, malignant and connective tissue disorders (Remington & Klein, 1995) (Mitchell, et al., 1990). T gondii that can be spread for disease to the fetus. According to a Montoya and Remington study (2010), this could cause severe encephalitis, myocarditis, hepatitis or pneumonitis. Congenital intracranial calcification, microcephalus, hydrocephalic convulsions and severe intrauterine growth restrictions also include clinical manifestations of congeal toxoplasmosis (Dubey, Ferreira, Martins, & Jones, 2011). Comprehensive studies in neonates conducted by Di Carlo et al. (2008) and Brown et al. (2009) have shown that delays in treatment of toxoplasmosis can lead to severe sequelae, including neurological and mental impairment.

2.17. Toxoplasmosis in Meat animals

The major economic importance of the disease for meat animals and for people as consumers is often considered to be an issue of medical importance and public health concern. In a study by Fayer (1981), however, Toxoplasmosis transmission was suggested. Tissue cysts were distributed between carnivores through gondii, Toxoplasma-type transmission. The Gondi is relatively higher for herbivorous and omnivorous meat. Studies by Arko-Mensah (1999) and Gilbert (2002) showed that, in ingestion of raw or poorly cooked food contaminated with cyst contamination, most adults are toxoplasmosis. Nowadays in Cyprus meat, such as sheep, goats, bovine animals, and lamb, is eaten daily and at higher rates.

2.18. Global Seroprevalence of toxoplasmosis

Garweg et al., 2005 and Liesenfield etc. (1997), respectively, have severe health consequences on pregnancies or newborns. Pregnancy gondii infection ranges from 20% to 50% if strict treatment regimens have not been adhered to as Jones et al.. (2003), Dunn et al. (1999) and Stray-Pedersen's (1993) have studied. Remington et al. (2001) and Dunn et al. (1999) recorded a low risk of congenital toxoplasma transmission of acute maternal infections (IgM) in the first trimester and strong (65%-90%) if the acute maternal infection was detected in the third Trimester and severe (65%-90%), respectively. Toxoplasmosis studies vary geographically in seroprevalence (Jacquire, 1995). It is estimated that nearly one third of the global population are affected by toxoplasmosis reported by Ayeh-Kumi et al. (2010) and Montoya and Liesenfeld (2004). Ayeh-Kumi et al. (2010) also reported that toxoplasmosis infects between 30% and 65% of the world population. It is estimated that global seroprevalence is 46.1% (Jacquire, 1995). A Jones et al. (1996) study found that HIV-infected individuals had geographical variations in their encephalitis toxoplasma. According to Partisani (1991) in Europe, Africa and Latin America the seroprevalence of latent toxoplasma infection is measured at 75% to 90%. The Seroprevalence of toxoplasma infection in El Salvador

was estimated by Montoya and Liesenfeld (2004). The fatality of toxoplasma in people with weak immunes, such as people with HIV / AIDS, and particularly pregnant women were also mentioned in a report by Dupont etc. (2012). A research was also reported in 1994. T seroprevalence now. Zemene et al. (2012) in southwestern Ethiopia and Gebremedhin et al. (2014) in central Ethiopia have registered gondii IgG antibodies of 81.1 million. Likewise, the seroprevalence of toxoplasma IgG antibodies was assessed by Akinbami et al. in Nigeria (2010) as 40.8%. CDC measured seroprevalence for Jones et al. between 1999 and 2004 at 10.8% of toxoplasmosis in the U.S. and seroprevalence for women of childbearing age (15-44 years) at 11.0 million (2007). The distribution of toxoplasmosis increased with age and the women of childbearing age. (Garcia, Navarro, Ogawa, De-Oliverra, & Kobilika, 1999).

2.19. Diagnosis of toxoplasmosis

Typically, serological tests are used to diagnose toxoplasmosis. A test to determine whether a person was infected is used to measure immunoglobulin G (IgG). If the duration of disease is expected to be measured, a procedure which will also be used in combination with other examinations, such as a greedy check, is of special significance for pregnant women. Direct observation of the parasite in stained tissue, cerebral fluid (CSF) or other biopsy material can also lead to the diagnosis. These techniques are less commonly used because these specimens are difficult to obtain. Blood or other body fluids (e.g. CSF) can also remove parasites, but that process can be difficult and time-consuming. Molecular techniques also can be used for detection DNA In case of possible mother-to-child (Inherited) transmission. Eye disease is diagnosed on the basis of eye damage, symptoms, disease histoy, and often serological tests (CDC, 2018).

2.20. Serological Detection of T. gondii

It includes the detection of T. In the serum of infected patients gondii antibodies. Key among the serological methods employed in diagnosing toxoplasmosis include the

Sabin-Feldman Dye test, the Indirect Hemagglutination assay, the Indirect Fluorescent antibody assay (IFA), the direct agglutination test (DAT), the Latex agglutination test (LAT), the Enzyme-Linked Immunosorbent assay (ELISA) and the Immunosorbent agglutination assay test (IAAT).The most efficient and preferred method, and consequently the gold standard in the diagnosis of toxoplasmosis, according to Hill and Dubey (2002) is the Sabin-Feldman Dye test. Due to its high sensitivity and toxoplasmosis specificity, this method is widely used. But, in contrast to ELISA as stated by Baron (1996), it is costly and highly dangerous for people living in this area.

2.21. Histologic Detection of T. gondii

The determination of T is involved here. Biopsy or necropsy of the host tissue .Baron (1996) has shown that histological detection is most effective in patients with immuno depression that may have delayed anticorpse synthesis and low anticorpore volume pr oduced.

2.22. Molecular detection of T. gondii

The identification of the genes (DNA) of biological samples is part of this procedure. The use of Polymerase Chain Reaction (PCR), for isolation and enhancements of DNA from organic samples as reported by Switaj and other (2005) requires molecular detection. PCR is best suited to immunodeficiency patients (Kwofie, 2012).

2.23. Treatment of toxoplasmosis

Spiramycin and Pyrimethamine are the main medicines of choice widely used for human toxoplasmosis. Spiramycin, the antibiotic macrolide, is used to prevent Toxoplasmosis-switching as a fetal prophylaxis (Montoya & Remington, 2000) Fetal gondii is used after maternal Toxoplasmosis disease. While the fetus is uninfected, gondii occurred. After fetal infection has occurred, pyrimethamine and sulfadiazine are

used. These medicines act as combined agents by blocking the path to the metabolism of the cell, including p-aminobenzoic acid (Sulphonamides) and folic-folic acid cycles (Pyrimethamine) (Caroline & Mark, 2013). However, because of the potential teratogenicity of pyrimethamine and sulphonamide therapy should not be administered in a first trimester of pregnancy (Montoya & Remington, 2000). A study by Baron 1996) reported that thrombocytopenia and/or leukopenia may sometimes develop through sulphonamide or pyrimethamine treatment. But thrombocytopenia is reduced by combination therapy with folic acid.

2.24. Prevention

Primary prevention. Educational materials that contain messages on how to prevent pregnant women from becoming infected have resulted in reduced rates of seroconversion. The educational methods must be in written for example (books, magazines, or simple handouts), and it is presented in various tongues, moreover it should be joined into the school program lessons and appointments, especially it is role of the physicians and health care policy in this fild in order to educate both of the pregnant and those women who have plane for make a children. The necessity to take these precautionary measures continually essential to be re-inforced all through pregnancy women for sero-negative and the measures that can be taken in an attempt to prevent the *Toxoplasma gondii* infection to the human. Moreover the despite of complexity of the mode of toxoplasmosis transmission, improved human and hygiene can be used to prevention. Toxoplasmosis prevention requires the prevention of envir onmental oocysts and tissue cysts (Lappalainen & Hedman, 2004). Institutionalization of education and public health programs can reduce toxoplasma infection, especially in pre-natal care (Fabiana et al., 2007). These programs include wearing gloves in litter changing, ridding feaces of cats and careful hand washing with soap after handling raw meat and cooking gear these programs (Hill & Dubey, 2002). Pregnant women and impaired patients are to prevent contact with soil, cats and the use of raw meat or products such as milk that is not pasteurized (Fabiana, Daniela, regina, Roberta, &

Italmar, 2007). Chewing up to 67 ° C or frozen to -20 ° C should be fresh meat and other products. While eating the berries and other raw vegetables (Hill & Dubey, 2002; Goldstein, E. J., et al, 2008)

CHAPTER TWO: MATERIALS AND METHODS

2.1. Samples

This study was prospective data collection. Demographic data of pregnant whom applied to obstetric and gynecologist outpatient clinic, Moreover, the sample was collected in Erbil-Iraq city, from gynecologist section in different clinical relate to this specialist, from (15 Jul 2020 to 1 Nov 2020). The total 75 sample of positive patients who have *Toxoplasmosis* with having pregnant in all different trimester was collected and there was 45 cases sample with 30 negative samples as a controls group was collected, The blood samples was collect in Erbil city, Hence, the samples transferred to the laboratory, following performing serological testes which based on Ag + Ab reaction, by resent instrument called cobas 6000 machine. Next, investigation for three female hormones was conduct like, Estrogen, Progestron, and prolactin, and study, the results of patients group will be compare with of controls group.

2.2. Nature of the Study

The study aimed to screen and study the female hormone during the pregnancy, and evaluation the rate of these hormones among toxoplasma gondii.

The importance of the present study can be summarize as:

3- Finding of the prevalence of toxoplasmosis in pregnant women in Iraq/Erbil City.
4- Screening of pregnant hormonal level and it is efficacy that caused by toxoplasma gondii.

The research design of this study is quantitative method

2.3. Study Population

The population contains pregnant women aged between 17 and 43 years as minimum and maximum rate who gained antenatal care at Erbil-Iraq city, from gynecologist section in different clinical relate to this specialist. Data was achieved through drawing blood samples from each enrolled pregnant woman.

2.4. Blood sample collection

Each participating pregnant woman venous blood samples was collected as an aseptically drawn, in order to separator blood component to serum tubes approximately 5ml of venous whole blood. The blood will then be isolated on numbered tubes and processed at-20Cºfor use at 900 rpm for ten minutes.

2.5. Analysis of Samples

The sample analysis in this study performed according to data collect (prospective study) which was diagnosis by cobas 6000 instrument, the test performing in (Bio lab) microbiology laboratory after that the investigations for both type of IgM and IgG was performed, in case of positive sample the hormonal (prolactin, estrogen, progesterone) test also performed. Nowadays *T gondii* acute and chronic infection can detected by using Cobas instrument with using Toxo IgG & IgM kit belonged to the Roche Diagnostics marketed. About the samples handling the serum of the patient should be stored nearly around the −20°C until running the test. The assay Toxo IgG and IgM are used for each patient serum sample and interpretation result (positive or negative) measured with Cobas 6000 Toxo IgG and IgM.

2.6. Toxo Ab immunoassay in Cobas 6000

In cobas 6000 the ten microliter sample, a biotinylated recombinant *T gondii* specific Ag and *T gondii*-specific recombinant Ag labeled with a ruthenium compound form a sandwich complex. Afterward the adding of streptavidin-coated micro-particles, followed by producing the solid phase which is result in interaction of biotin and streptavidin, after that in the measuring cell collect the mixture reaction where the micro-particles are attractively taken onto the superficial of the electrode. Later on the extra un-bound materials of each assay will be removed by the b ProCell. Presentation of the power into electrode which result in the promotion of the chemiluminescent emission that measure by photomultiplier. The IgG & IgM assay results expressed in an international units per milliliter. The explanation of the result based on on the producer's criteria which arranged like: (i) Less than 1.0 IU/mL mean negative. (ii) Between the ≥1.0 to <3.0 IU/mL mean equivocal result. (iii) More than 3.0 IU/mL mean positive for IgG & IgM antibodies.

2.7. The determination of Toxoplasma gondii IgG&IgM

The infection that caused by protozoan *Toxoplasma gondii* medically termed as a toxoplasmosis, in the healthy immune-competent people normally infection involve mild or no symptoms. But in case of the pregnancy women the infection with *Toxoplasma gondii* will result in various fetus complication, moreover, in the early trimester of the pregnant women the parasite have much more ability to produce several damage to the fetus, but in the late of the trimester the chance of the parasitic transmitting are increases. The management of pregnant women especially in early stage are very important for the treatment in acute infection in order to prevent or upgrade congenital damage. The diagnosis begin with the detection of the anti-Toxoplasma IgG & IgM Ab. The Ab produced in primary response have a lower avidity than the non-primary response, high avidity in early the gestation suggests that infection occure more than 4 months ago and rules out a recent primary acute infection.

2.8. Cobas e 601 module

The system of the module is completely work automated and the ECL equipment are sued in the analyzer (for immunoassay analysis). The instrument is designed recent method which involve both type of result quantitative and qualitative in vitro examination and resolves the broad range of various requests such as (i) Anemia; bone, cardiac and tumor markers. (ii) Critical care; fertility/hormones. (iii) Maternal care; and infectious diseases.

2.9. The cobas product

Testing capabilities

- Immunoassays with the (Electrochemiluminescence technology)

Throughput

- 170 examinations per hours

Samples

- In Cobas the serum, plasma and urine can be used

Integrity methods

- Cups & tips for carryover are disposable
- LLD can determine the clot, liquid level with reagents

Reagents

- Positions of the cassette involve up to 25 reagent

First class performance

- High quality such as (sensitivity, reliability, and reproducibility, with ECL technology
- 25 test can be run and throughput 170 tests/h

Smart sample work-flow

- Programmed sample reorganization
- Free pipetting of the samples with avoid pollution
- Ability to automatic re-run test

Single reagent conception

- Suitable & free management of the error packs
- Stabilities with great economic practice with suitable sizes of the kit

System dependability

- The functions is automated conservation
- Low maintenance period

Testing Time:

- per test 18 min

Test principle:

- Single phase sandwich test with dual Ag

Calibration:

2 point

Traceability:

- Third international (TOXM) Standard, UK, NIBSC.

On-board stability:

- 14 days

Sample volume:

- 10 µL **cobas e** 601

Sample: cobas e 601: Serum collected using standard sampling tubes or tubes containing separating gel. Li-heparin, K2-EDTA, K3-EDTA and Na-citrate plasma.

Interpretation: If result less than 1 IU/mL = Negative

Toxo IgG and IgM: 1 – 3.0 IU/mL = gray zone

Toxo IgG and IgM: ≥3.0 IU/mL = Positive

Source

1. Remington, J.S. et al. (2006). Infectious Diseases of the Fetus and Newborn Infant (Sixth Edition). Philadelphia: W.B. Saunders, 947-1091.
2. Elecsys Toxo IgG (#04618815190, #07028008190) method sheet 2020-07, V 14.0 and V 3.0.
3. Montoya, J.G. et. al. (2004). Lancet 363, 1965-1976.

2.10. Test principle:

µ-Capture test principle. Total duration of assay: 18 minutes.

1st incubation: 10 µL of sample are automatically pre-diluted 1:20 with Diluent Universal. T. gondii-specific recombinant antigen labeled with a ruthenium complexa) is added. Anti-Toxo IgM&IgG antibodies present in the sample react with the ruthenium-labeled T. gondii-specific recombinant antigen.

2nd incubation: Biotinylated monoclonal h-Ig-specific antibodies and streptavidin-coated micro-particles are added. The complex becomes bound to the solid phase via interaction of biotin and streptavidin.

The reaction mixture is aspirated into the measuring cell where the micro-particles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. Also the assay result are resolute automatically via the specific software program, in addition associating by the electrochemiluminescence indication found from the assay reaction product by the sample with signal of the cutoff of the calibration.

2.11. Sample Assay

Before performing sample assay the resuspension of the microparticles should be automatically takes place before any processing. Read in the test-specific parameters via the reagent barcode. In case of the incomparable state the barcode cannot be read correctly, manually the 15-digit sequence of numbers should be entered properly.

The reagent kit should be placed until the temperatures riches approximately to the 20 °C, following placing the necessary reagent in to instrument (reagent disk) of the analyzer, the reagent should be avoided from any foam formation, the cobas system are worked automatically therefor the instrument maintain the temperature constantly around 20 °C automatically with the opening/closing the lid of the reagent bottles. Residence the calibrator’s reagent in to the sample area.

After performing each calibration, the reagent of calibration should be stored between the 2-8 ℃ degree or remove (MODULAR ANALYTICS E170, cobas e 601). Moreover, the calibration information for each reagent kit assay are read automatically into the analyzer. Moreover, for optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

2.12. Calculation

The analyzer automatically calculates the cutoff based on the measurement of TOXIGM Cal1 and TOXIGM Cal2. The result of a sample is given either as reactive or non-reactive as well as in the form of a cutoff index (signal sample/cutoff).

2.13. Interpretation of the Results

Results obtained with the Elecsys Toxo IgM assay can be interpreted as follows: Non-reactive: < 1. COI
Equivocal: ≥ 0.3 - < 1.0 COI
Reactive: ≥ 3.0. COI
Samples with a cutoff index <1 are non-reactive in the Elecsys Toxo IgM assay. Samples with a cutoff index between ≥ 3 and <1.0 are considered equivocal. The sample should be retested. In case the result is still equivocal, a second sample should be tested. If measurement of the sample showed greatness than the amount of the cutoff, it dosent mean that the aggregate quantity of the antibody are contemporary available in percent sample.

2.14. Material

- Cobas 6000 machine
- TOXO IgM Kit
- TOXO IgM Kit
- Sample Cups
- Septum
-Yellow Tub
-Micro-Pipette
-Macro-Pipette
-Pipette Tip
- Caps

2.15. Data Analysis

In order to evaluate the answers from the completed survey, Microsoft Excel and the Scientific Program for Social Sciences (SPSS, version 13.0) program were used. The optional test was Mann-Whiney test. The significant rate to analysis correlation P value 0.05.

2.16. Ethical Consideration

RESEARCH ETHICS COMMITTEE APPROVAL SHEET

Title of the project: Evaluation of Progesterone, Estrogen and Prolactin Levels in Pregnant Women With Toxoplasmosis in Erbil City / Iraq.

Principle investigator: Assistant **.** Prof. Dr.Esref Celik

Assistant investigator: Mohammed Qasim Burhaw

CHAPTER THREE: RESULTS

4.1 RESULTS

4.1 General characteristics of study participants

This data of the study was collected in Erbil city from of pregnant whom applied to obstetric and gynecologist outpatient clinic. The duration of sample collection was between (15 Jul 2020 to 1 Nov 2020). The total 75 sample of pregnant women approached to the study, 45 as a cases group and 30 as a control group. As participant characteristic the population ages of the pregnant women was between (17 - 43). Moreover, the sample of positive patients who have *Toxoplasmosis* with having pregnant in all different trimester (firest 9, second 17, thierd19) was collected.

Table 1. **Significant differences in Toxoplasmosis IgM and IgG according to the negative and positive result**

TOXOPLASMOSIS (IgG)(IgM)	Infection	N.	Average Rank	P. Value
IgG	Negative	30 (40%)	18.37 [b]	<0.001
	Positive	45 (60%)	51.09 [a]	
Total		75 (100%)		
IgM	Negative	30 (40%)	40.37	0.443
	Positive	45 (60%)	36.42	
Total		75 (100%)		

There was no statistically significant difference in toxoplasma IgM results. But there was significant difference in toxoplasma IgG results was found (Table 1).

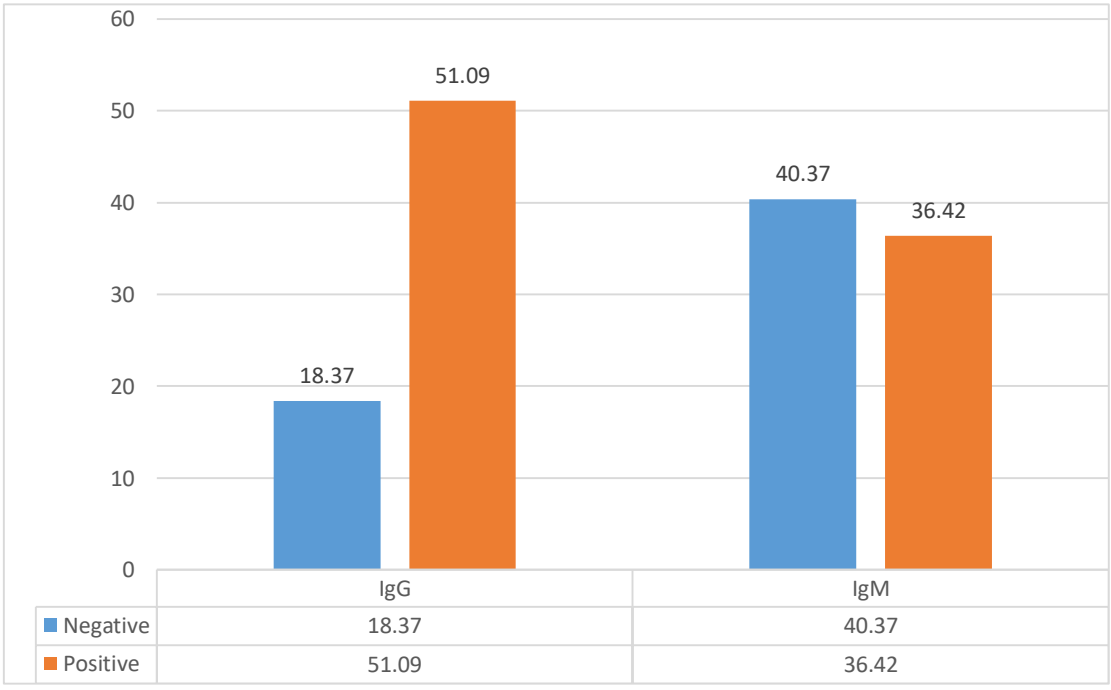
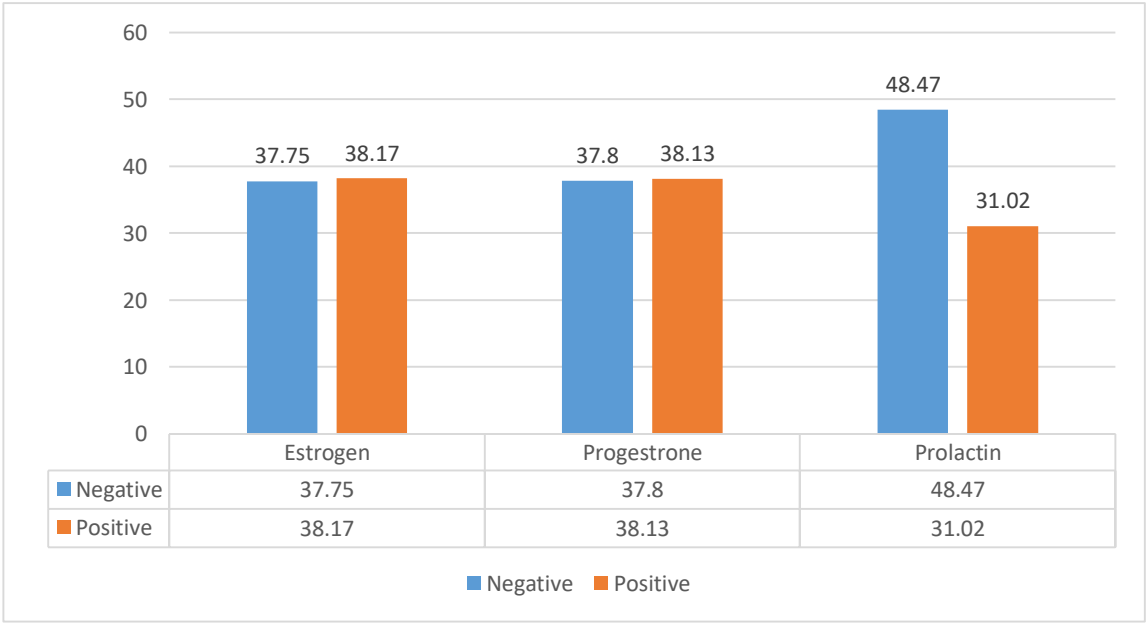


Table 2. **Significant differences in Hormones according to the negative and positive result**

TOXOPLASMOSIS (Hormones)	Infection	N.	Average Rank	P. Value
Progesterone	**Negative**	**30 (40%)**	**37.80**	**0.948**
	Positive	**45 (60%)**	**38.13**	
Total		**75 (100%)**		
Estrogen	**Negative**	**30 (40%)**	**37.75**	**0.935**
	Positive	**45 (60%)**	**38.17**	
Total		**75 (100%)**		
Prolactin	**Negative**	**30 (40%)**	**48.47** [a]	**0.001**
	Positive	**45 (60%)**	**31.02** [b]	
Total		**75 (100%)**		

There was no statistically significant difference in Progesterone and Estrogen, while there are significant found in Prolactin (Table 2).



CHAPTER FOUR: DISCUSSION

4.1. Discussion

The toxoplasmosis is a serious risk in pregnancy and therefore plays an important role in public health. Although the disease is generally asymptomatic in healthy individuals, the main groups that can be seen due to mortality and disease are immunosuppressive individuals. The prevalence of toxoplasma infection, which is common in the world, varies from country to country and from region to region. In the world, except for the Antarctic continent has been shown in all continents.

The aim of this study was to investigate the positivity rates of toxoplasma infection which may cause hormonal changes, and the effect of various risk factors of toxoplasmosis IgM and IgG values in pregnant women's hormonal balance.

The causative agent of the toxoplasmosis referred to the protozoan of the parasite wich termed as *Toxoplasma gondii* (*T. gondii*). Healthy individuals generally have mild or no symptoms, Moreover, the severity of parasite and it is resulting in damaging fetuses occur during pregnancy, especially in the primary infection during pregnancy because the risk is highest in early of the pregnancy infection, moreover, the transmitting will increases if infection in later of the pregnancy. The acute of infection of toxoplasmosis can be prevent by early detecting with early treatment, following, the detection of the parasitic infection with anti-Toxoplasma IgG and IgM are very necessary.

The sample analysis in this study performed according to data collect (prospective study) which was diagnosis by cobas 6000 instrument, the test performing in (Bio lab) microbiology laboratory after that the investigations for both type of IgM and IgG was performed, in case of positive sample the hormonal (prolactin, estrogen, progesterone) test also performed.

In this study, we have attempted to explain if there was an association between the level of the hormonal (Prolactin, estrogen, progesterone) and the frequency of *T gondii* infections in both type of IgM and IgG among the pregnancy women. Introductory data, comparing the prevalence of T. gondii infection in the population of pregnancy women with the hormonal level below and above the normal with the population of those having normal hormones level.

In the Al-Warid, H. & Al-Qadhi, B. 2012, the study results showed that there were no significant differences in progesterone levels between infected and non-infected women with *T.gondii*, although high progesterone level were noticed in non-infected women compared with low level in women infected with *T.gondii* (18.30 ± 9.84 ng/ml) and (11.19 ± 9.76 ng/ml) respectively, which agree with our analysis result that tell us also there was no significant differences in progesterone levels found (P.value = 0.948).

In our study, the result of the P.value of estrogen was 0.935, which is tell us there was no significant differences found. As the same idea the results of the Al-Warid, H. & Al-Qadhi, B. 2012, also showed no significant differences in estrogen levels between infected and non-infected women although high level of estrogen were noticed in infected women with *T.gondii* compared with non-infected women (88.19 ±101.10 ng/ml) and (53.61 ± 76.24 pg/ml) respectively.

In the Previous study Kadhim, R. A., & AL-awadi, H. M. 2013, mention the prolactin is one of the most important hormones involved in immunoregulation in host body. Exogenic prolactin can induce anti-parasitic activity in microglial cells as a reaction against the *T gondii* infection. In current study we observed significant decrease in levels of prolactin in all positive of anti-Toxoplasma antibody pregnant women groups (total pregnant, 1st, 2nd and 3rd trimesters of pregnancy) when compare with control groups. The high levels of prolactin hormones in seronegative groups (control) in opposition to seropositive groups (chronic infection) may be indicate to protective

action of prolactin in a host organism against Toxoplasma infection. In our study also we found the significant decrease in levels of prolactin, the P.value was (0.001).

Between 1986 and 1999, a study evaluating the seroprevalence of toxoplasma in fertile women in 53 countries was found to be 42%. According to this study, it is stated that approximately 2.5 billion people in the world are infected with T. gondii (Hill D., 2002).

Serological diagnostic methods are used routinely in the early diagnosis of toxoplasma infection during pregnancy. Toxoplasma infection in the first trimester of pregnancy causes congenital malformations in 90% of fetuses (Linguissi LSG, et.al.2012). Infection in the pre-pregnancy period does not cause sequelae in the baby (Liu Q. Et.al, 2009). In Turkey, most of the studies conducted retrospectively to determine seropositivity rates between 30% and 79% of IgG positivity of parasites were found (İnci M.,et,al.2009, Kuk S,et.al 2012, Sütçü A.,et.al 1998).

Toxoplasma IgG and IgM positivity were 82.6% and 1.8%, respectively, in Lebanese pregnant women (n: 2456). In this study, IgG seropositivity was found to be the highest among the 35-44 age group (87.81). this study, IgG seropositivity was found to be the highest among the 35-44 age group (87.81%), two abortions due to T. gondii infection were recorded during pregnancy and 64 cases had seroconversion (Hasan Nahouli,2017 Toxoplasma IgG positivity was higher in Lebanese pregnant women than in pregnant women of Cyprus.

Toxoplasma IgG seropositivity rate was found to be 67.5% among pregnant women in Egypt. In the last 20 years, the rate of toxoplasmosis has increased in the studies conducted in Egypt. This prevalence is higher than other global rates (Hala K.El Deeb, 2012).

In the Al-Warid, H. & Al-Qadhi, B. 2012, basis on ELISA test anti Toxoplasma antibodies (IgG and IgM) detected in sera, three types of toxoplasmosis were identified. These were acute (positive for IgM), sub-acute (positive for both IgG and IgM) and chronic (positive for IgG). This study demonstrated that there was high prevalence of chronic toxoplasmosis (31.70%) when it compared with acute and sub-acute types of toxoplasomsis which were (24.39%) and (21.95%) respectively, while the percentage of control group (subjects who had negative results for both IgG and IgM) was (21.95%). Moreover, the study from Iran also showed high percentages of chronic toxoplasmosis which was (82%) compared with (18%) for acute infection (Rahbari et al., 2012), while others showed that cases of acute infection were higher than cases of chronic infection.

In the last 35 years, researchers worldwide have made a great effort to advance in the field of knowledge on how the hormones are involved in *T. gondii* infection, however, a major number of studies and the use of modern molecular methods are required to define the mechanistic role of hormones in the regulation of toxoplasmosis.

CHAPTER FIVE: CONCLUSION AND RECOMMENDATIONS

5.1. Conclusion

Toxoplasma gondii, a member of the Apicomplexa phylum, is the etiologic agent of toxoplasmosis, a widespread infection of humans and other warm-blooded animals. Moreover, there are not only *T gongii* can affect host hormones responses to infection, but parasites can have pronounced effects on hormone signaling within the host. Additional studies suggest that protozoan parasites such as *T gondii* can alter hormone concentrations in their hosts. One of the most important problems of *T. gondii* infection in humans is congenital toxoplasmosis and pregnancy hormonal impregnation may play a role. In the current study we evaluated three important hormones like prolactin, progesterone and estrogen.

Congenital toxoplasmosis is one of the most significant burdens of *T. gondii* infection in humans. Both the maternal–fetal transmission and hormonal levels during pregnancy are poorly understood and yet, may play an important role during the course of the disease. In the current study and depending on the result observation on pregnant women we found, there are no statistically significant difference in toxoplasma IgM results. But there was significant difference in toxoplasma IgG results was found, inaddition, there was no statistically significant difference in Progesterone and Estrogen, while there are significant found in Prolactin

In a study conducted in Iraq-Erbil city, and it is according to the conclusion, the alterations in estrogen and progesterone hormones not found in the current study, while the possibly influence of prolactin found according to the statistical analysis, and it is among to the toxoplasmosis infection during pregnancy women.

5.2 Recommendations

1. Since the toxoplasmosis risk factors have not been assessed and discussed, a further study is recommended by recent method such us PCR, especially among pregnant women in Erbil-Iraq.

2. Toxoplasmosis affect the concentration of some hormones in female therefore its recommended to be periodically screened.

3. Moreover, in determining the risk factors for toxoplasmosis infections and it is relation with female hormonal balance. Politicians in healthcare provision are again advised that the diagnostic laboratory tests routinely carried out during gynecological care include the checking of pregnant women for toxoplasmosis and some sexual hormone.

4. Further studies are required to determine the mechanism of hormone action in the *T. gondii* infectious process.

References

Arko-Mensah, J. (1999). A serological survey of toxoplasmosis in pigs. *University of Ghana*, 67-84.

Al-Warid, H. S. & Al-Qadhi, B. N. (2012). Evaluation of progesterone and estrogen hormonal levels in pregnant women with toxoplasmosis. *Eur. J. Sci. Res*, *91*, 515-519.

Ayeh-Kumi, Opoku, A. G., Kwakye, N., Dayie, N., Asmah, R., Obeng, N., Kretchy, J. (2010). *Seroprevalence of toxoplasmosis among patients visiting the Korle-Bu Teaching Hospital.* Accra, Ghana: Revies in Infect.

Baron, S. (1996). *Medical Microbiology* (4 ed.). Galveston, Texas, USA: University of Texas Medical.

Bobic, B., Sibalic, D., & Djurkovic, D. (1991). High level of IgM antibodies spesific for Toxoplasma gondii in pregnancy 12 years after primary toxoplasma infection. *Gynecol Obstet Invest*, 182-184.

Bouchut, A., Chawla, A. R., Jeffers, V., Hudmon, A., & Sullivan Jr, W. J. (2015). Proteome-wide lysine acetylation in cortical astrocytes and alterations that occur during infection with brain parasite Toxoplasma gondii. *PloS one*, *10*(3), e0117966.

Black, M. W., & Boothroyd, J. C. (2000). Lytic cycle of Toxoplasma gondii. *Microbiology and molecular biology reviews*, *64*(3), 607-623.

Boothroyd, J. C., Hehl, A., Knoll, L. J., & Manger, I. D. (1998). The surface of Toxoplasma: more and less. *International journal for parasitology*, *28*(1), 3-9.

Brown, E., Chau, J., Atashband, S., Westerberg, B., & Kozak, F. (2009). *A systematic review of neonatal toxoplasmosis exposure and sensorineural hearing loss* (Vol. 5). Pediatr Otorhinolaryngol.

Calballero-Ortega , H., Urib-Salas, F., Conde-Glez , C., & Pelaez, C. (2012). *Seroprevalence and national distribution of human toxoplasmosis.* mexico: national health survey.

Cook, T. B., Brenner, L. A., Cloninger, C. R., Langenberg, P., Igbide, A., Giegling, I., ... & Groer, M. W. (2015). "Latent" infection with Toxoplasma gondii: association with trait aggression and impulsivity in healthy adults. *Journal of psychiatric research*, *60*, 87-94.

Caroline, P., & Mark, H. (2013). Toxoplasmosis in pregnanacy: Prevention, screening and treatment. *Obstet Gynaecol Can*, 35-37.

CDC. (2013, 03 13). Toxoplasmosis in pregnant women.

Desmonts, G., Gouvreur, J., & Congenital. (1974). *A Prospective Study of 378 Pregnancies* (Vol. 290). New England Journal of Medicine.

Di-Carlo, P., Romano, A., Schimmenti, M., Mazzola, A., & Titone, L. (2008). *Materno- fetal Toxoplasma gondii infection: critical review of available diagnostic methods.* Infez Med.

Dubey, J. (1995). *Duration of Immunity to shedding of Toxoplasma gondii oocysts by cats.* UK: Int J. Parasitol.

Dubey, J. (1998). Structures of Toxoplasma gondii tachyzoites, bradyzoites, and sporozoites and biology and development of tissue cysts.

Dubey, J. (2009). History of the discovery of the life cycle of Toxoplasma gondii. *39*(8), 877-882.

Dubey, J., & Jones, J. (2008). *Toxoplasma gondii infection in humans and animals in the United States* (Vol. 11). Inter. J. Parasitol.

Dubey, J., Ferreira, L., Martins, J., & Jones, J. (2011). *Sporulation and survival of Toxoplasma gondii oocysts in different types of commercial cat litter* (Vol. 5). UK: J. Parasitol.

Dunn, D., Wallon, M., Peyron, F., Petersen, E., Peckham, C., & Gilbert, R. (1999). *Mother-to-child transmission of toxoplasmosis: risk estimates for clinical counselling* (Vol. 353). Lancet.

Dubey, J. P. (2009). History of the discovery of the life cycle of Toxoplasma gondii. *International journal for parasitology*, *39*(8), 877-882.

E, C., & Lovin, D. (2002). *study on specific IgG avidity as a tool forrecent primary toxoplasma gondii infection diagnosis.* J Pre Med 56-62.

E, P., & Ve, A. (2002). Gebe kadinlarda Toxoplasma gondii IgM ve IgG antikorlarinin ELISA yontermi ile arasirilmasi. *Turkiye Parazitoloji Dergisi*, 350-351.

Fabiana, M., Daniela, D., regina, M., Roberta, L., & Italmar, T. (2007). *Toxoplasma gondii infection in Pregnancy* (Vol. 5). Brazilian Journal og Infect. Dis.

Faulon, W. (1992). Congenital toxoplasmosis: Is screening desirable? *Acand J. Infec Dis*, 11-17.

Fayer, R. (1981). Toxoplasmosis update and Public health Implications. *Canadian Veternary Journal, 22*, 344-352.

Foch, B., Mcdaniel, N., & Chacko, M. (2000). *Vaginal douching in adolescents attending a family planning clinic* (Vol. 13). J Pediatr Adolesc Gynecol.

Furtado, J., Winthrop, K., Butler, N., & Smith, J. (2013). *Ocular toxoplasmosis I: Parasitology, epidemiology and public health.* (Vol. 41). Clin Exp Ophthalmol.

Flegr, J., Lenochová, P., Hodný, Z., & Vondrová, M. (2011). Fatal attraction phenomenon in humans–cat odour attractiveness increased for Toxoplasma-infected men while decreased for infected women. *PLoS Negl Trop Dis*, *5*(11), e1389.

Garcia, J., Navarro, I., Ogawa, L., De-Oliverra, R., & Kobilika, E. (1999). *Seroprevalence of human toxoplasmosis in rural zone of Jaguapita* (Vol. 6). Brazil: Salud Publications.

Garweg, J., Scherrer, J., Wallon, M., Kodjikian, L., & Peyron, F. (2005). *Reactivation of ocular toxoplasmosis during pregnancy* (Vol. 2). International Journal Obstet Gynecol.

Gilbert, G. (2002). Infections in pregnant women. *Med J. Aust, 5*(176), 229-236.

Guler, E., Guvenir M, Arıkan A., & Süer K. (2018). *Toxoplasma IgG-IgM and IgG avidity test as a result* . near east university hospital in northcyprus: International XXXVIII . Turkish Microbiology Congress Abstract Book PS 196.

Grimwood, J., Mineo, J. R., & Kasper, L. H. (1996). Attachment of Toxoplasma gondii to host cells is host cell cycle dependent. *Infection and immunity*, *64*(10), 4099-4104.

Grimwood, J., Mineo, J. R., & Kasper, L. H. (1996). Attachment of Toxoplasma gondii to host cells is host cell cycle dependent. *Infection and immunity*, *64*(10), 4099-4104.

Goldstein, E. J., Montoya, J. G., & Remington, J. S. (2008). Management of Toxoplasma gondii infection during pregnancy. *Clinical Infectious Diseases*, *47*(4), 554-566.

Hedman, K., Lappalainen, M., Seppala, I., & Makela, O. (1989). Recent primary toxoplasma infection indicated by a low avidity of specific IgG. *Journal of Infect Dis.*

Henrik, V., Sanne, L., Lone, C., Seren, B., Anders, F., & Eskild, P. (1999). *Complete protection against lethal Toxoplasma gondii infection in mice immunized with plasmid encoding the SAG1 Gene* (Vol. 12). Infect Immun.

Hill, D., & Dubey, J. (2002). Toxoplasma gondii: Transmission, diagnosis and prevention. *Clinical Microbiology Infect.* , 634-640.

Hippe, D., Weber, A., Zhou, L., Chang, D., Hacker, G., & Luder, C. (2009). *Toxoplasma gondii infection confers resistance against BimS-induced apoptosis by preventing the activation and mitochondrial targeting of pro-apoptotic Bax* (Vol. 19). Journal of Cell Sci.

Hokelek, M. (2019). What is the pathogenesis of congenital toxoplasmosis? *American society for microbiology*.

Jacquire, P. (1995). Epidemiology of toxoplasmosis in Switzerland. *Schwez Med Wochenschr Suppl, 65*, 29-38.

Jones, J., Hanson, D., & Chu, S. (1996). *Toxoplasma encephalitis in HIV-infected persons: risk factors and trends. The adult/Adolescent spectrum of disease group* (Vol. 10).

Jones, J., Lopez, A., & WilsonM. (2003). *Congenital toxoplasmosis* (Vol. 67). Am Fam Physician.

K, H., Lappalainen , M., Seppaia, I., & Makiila, O. (1989). *Recent primary toxoplsmosis infection indicate bya low avididty of speific IgG.*

K, H., Lappalainen, M., sepayaa, I., & Makela, O. (J Infection Dis159 736-740). *Recent priamarytoxoplasma infection indicate by a low vidity of specific IgG.* 1989.

Kapperud, G., Jenum, P., Stray-Pedersen, B., Melby, K., Eskild, A., & Eng, J. (1996). *Risk factors for Toxoplasma gondii infection in pregnancy* (Vol. 4). Norway: Am J. Epidemiol.

Kadhim, R. A., & AL-awadi, H. M. (2013). Changes in testosterone, progesterone and prolactin levels in pregnant women with chronic toxoplasmosis. *Medical Journal of Babylon*, *10*(3), 699-708.

Kuman, A. (2002). *Toxoplasma gondii: Topçu AW, Söyletir G, Doğanay M. İnfeksiyon Hastalıkları ve Mikrobiyolojisi* (Vol. 2). Ankara: Nobel Tip Kitapevleri.

Kwofie, K. (2012). *Risk of mother-to-child transmission of Toxoplasma gondii infection among pregnant women in the Greater Accra region.* Kumasi, Ghana: Kwame Nkrumah University Of science and Technology.

Kasper, L. H., & Mineo, J. R. (1994). Attachment and invasion of host cells by Toxoplasma gondii. *Parasitology Today*, *10*(5), 184-188.

L, T.-3. (2001). yas kadinlarda Toksoplazmoz seropozitifligi. *Klinik Laboraturant Arastirma Derg*, 93-95.

Laboudi, M., & Abderrahman Sadak . (2017). *serodiagnosis of toxoplasmosis:Tthe effect of measurement of IgG avidity in pregnant women* . Rabat in Morroco: Acta Tropica.

Laboudy, M., & Abdurrahim, S. (2017). *serodiagnosis of toxoplasmosis :the efect of measurement of IgGavidity in pregnant women.* Rabat in Morroco: Acta Tropica.

Lappalainen, M., & Hedman, K. (2004). Serodiagnosis of toxoplasmosis. The impact of measurement of IgG avidity. *Ann Dell Istit sup Di san, 40*, 81-88.

Liesenfeld, O., Press, C., Montoya, J., Gill, R., Isaac-Renton, J., & Hedman, K. (1997). *False-postive results in immunoglobulin M (IgM) Toxoplasma*.

Linguissi, L., Nagalo, B., Bissee, C., & Kagon, T. (2012). *Seropervalance of toksopazmosis and rubella in pregnant women attending antenatal private clinic at ouagadougou* . Asian Pacific of Tropical medicine.

Luft, B. J., & Remington, J. S. (1992). Toxoplasmic encephalitis in AIDS. *Clinical infectious diseases*, *15*(2), 211-222.

M, A., & H.M., T. (2002). Gebe kadinlarda Toxoplasma gondii ve CMV antikorlari sikigi . *genel Tip Derg*, 9-13.

Mitchell, C., Erlich, S., Mastrucci, M., Hutto, S., Parks, W., & Scott, G. (1990). *Congenital toxoplasmosis occurring in infants Perinatally infected with Human Immunodeficiency Virus* (Vol. 9). Pediatr Infect Dis.

Moncada, P., & Montoya, J. (2007). *Toxoplasmosis in the fetus and newborn: an update on prevalence, diagnosis and treatment.*

Monotoya, J., & Liesenfeld, O. (2004). *Toxoplasmosis.* 1965-1976: Lancet.

Monotoya, J., & Remington, J. (2008). *Management of Toxoplasma gondii infection during pregnancy* (Vol. 47). Oxford Academic.

Montoya, J., & Remington, J. (2000). *Toxoplasma Gondii; Paractice of infectious diseases* (5 ed., Vol. 2). Churchill Livingstone.

Manger, I. D., Hehl, A. B., & Boothroyd, J. C. (1998). The surface of Toxoplasma tachyzoites is dominated by a family of glycosylphosphatidylinositol-anchored antigens related to SAG1. *Infection and immunity*, *66*(5), 2237-2244.

Mineo, J. R., & Kasper, L. H. (1994). Attachment of Toxoplasma gondii to host cells involves major surface protein, SAG-1 (P-30). *Experimental parasitology*, *79*(1), 11-20.

Mineo, J. R., McLeod, R., Mack, D., Smith, J., Khan, I. A., Ely, K. H., & Kasper, L. H. (1993). Antibodies to Toxoplasma gondii major surface protein (SAG-1, P30) inhibit infection of host cells and are produced in murine intestine after peroral infection. *The Journal of Immunology*, *150*(9), 3951-3964.

Mineo, J. R., McLeod, R., Mack, D., Smith, J., Khan, I. A., Ely, K. H., & Kasper, L. H. (1993). Antibodies to Toxoplasma gondii major surface protein (SAG-1, P30) inhibit infection of host cells and are produced in murine intestine after peroral infection. *The Journal of Immunology*, *150*(9), 3951-3964.

Nester, E., Anderson, D., Pearsall, N., & Nester, M. (2004). *Microbiology: a human perspective* (4 ed.). New York, USA: McGraw Hill.

Nicolle, & Manceaux. (1909). *Sur un protozoaire nouveau du gondi.* Paris, France: C R Soc Biol.

Onul. (1980). *Infeksiyon Hastaliklari.* Ankara: Ankara Universitesi Tip fakultesi .

Osman, E., Bekir, C., & Ibrahim, K. (2019). Seroprevalance of canine brucellosis and toxoplasmosis in female and male dogs and relationship to various factors as parity, abortion and pyometra. *Indian J. Anim*, 954-958.

Q, L., Wei, F., Gao, S., & Jiang, L. (2009). *Toxoplasma gondii infection in pregnant women* . china.

Ortega-Barria, E., & Boothroyd, J. C. (1999). A Toxoplasma lectin-like activity specific for sulfated polysaccharides is involved in host cell infection. *Journal of Biological Chemistry*, *274*(3), 1267-1276.

Radke, J., Striepen, B., & Guerini, M. (2001). *Defining the cell cycle for the tachyzoite stage of Toxoplasma gondii* (Vol. 115). Mol Biochem Parasitol.

Rayan, & Ray. (2004). *Sherris Medical Microbiology* (4 ed.). New York, USA: McGraw.

Rahbari, A.H., Keshavarz , H., Shojaee , S., Mohebali , M. and Rezaeian , M. 2012. “IgG Avidity ELISA Test for Diagnosis of Acute Toxoplasmosis in Human”. Korean Journal of Parasitology. 50(2), pp.99-102.

Remington, J., & Klein, J. (1995). *Infectious Diseases of the fetus and newborn Infant* (4 ed.). Philadelphia, USA: W. B. Saunders.

Remington, J., McLeod, R., Thuilliez, P., & Desmonts, G. (2001). *Toxoplasmosis.* W.B. Saunders.

Soyletir, G., Babacan, F., Soyoglu, U., & Ve, a. (1989). Dogurganlik Yas grubu kadinlarda toksoplazma antikorlarnin dagilimi. *Turk Mikrobiyoloji Cem Derg*, 378-383.

Stray-Pedersen, B. (1993). Toxoplasmosis in pregnancy. Baillieres Clin Obstet Gynaecol.

Stray-Pederson, (1992). Treatment of toxoplasmosis in the pregnant mother and newborn child. *Scand journal infect Dis. Suppl.*, 23-31.

Suer HK, Guler E, Arıkan A., & Guvenır M. (2012). Yakin Dogu hastanesine basvuran gebe kadinlarn Rubella ve Toksoplazma pevelansinin iki yillik degerlendirilmesi XXXV. *Turk Mikrobioloji Kongresi kongre kitabi* , 361.

Sugden, K., Moffitt, T. E., Pinto, L., Poulton, R., Williams, B. S., & Caspi, A. (2016). Is Toxoplasma gondii infection related to brain and behavior impairments in humans? Evidence from a population-representative birth cohort. *PLoS One*, *11*(2), e0148435.

Tenant-Flowers, M., Boyle, M. J., Carey, D., Marriott, D. J., Harkness, J. L., Penny, R., & Cooper, D. A. (1991). Sulphadiazine desensitization in patients with AIDS and cerebral toxoplasmosis. *AIDS (London, England)*, *5*(3), 311-315.

Thiebaut , R., Leproust, S., Chene, G., & Gilbert, R. (2007). Effectivness of prental treatment for congenital toxoplasmosis analysis of individual patients' data. *Lancet*, 369.

Tore, O. (2001). *Toxoplasma gondii: Topçu AW, Söyletir G, Doğanay M. İnfeksiyon Hastalıkları ve Mikrobiyolojisi,.* Ankara: Nobel Tip Kitapevleri.

Torok, E., Moran, E., & Cooke, F. (2013). *Oxford Handbook of Infectious Diseases and Microbiology.* USA: Oxford University Press.

Ustacelebi, S., Koksal, I., Canturk, H., Saify, J., Ersoz, D., & Sellioglu, B. (1986). Hamilelikte TORCH etkenlernie Karsi Antikorlarin saptanmasi. *Mikrobiyol Bult*, 20:1-8.

Vanagas, L., Jeffers, V., Bogado, S. S., Dalmasso, M. C., Sullivan Jr, W. J., & Angel, S. O. (2012). Toxoplasma histone acetylation remodelers as novel drug targets. *Expert review of anti-infective therapy*, *10*(10), 1189-1201.

Wang, Y., Weiss, L., & Orlofsky, A. (2009). *Host Cell autophagy is induced by Toxoplasma gondii and contributes to parasite growth* (Vol. 43). Biol Chem.

Weiss, & Dubey. (2009). Toxoplasmosis: a history of clinical observation. *Int J parasitol*.

Weiss, L. M., & Kim, K. (Eds.). (2011). *Toxoplasma gondii: the model apicomplexan. Perspectives and methods*. Elsevier.

Wong, S. Y., & Remington, J. S. (1993). Biology of Toxoplasma gondii. *Aids*, *7*(3), 299-316.

CURRICULUM VITAE

MOHAMED QASIM BURHAW

Biology Teacher

PERSONAL INFORMATION

Date of Birth : 20 \ 7 \ 1990

Place of Birth : Erbil

Nationality : Kurdish

Address : Iraq _ Kurdistan _ Erbil

OBJECTIVE

To enhance my knowledge and capabilities by working in a dynamic organization that prides itself in giving substantial responsibility to new talent.

CONTACT

PHONE:
+964 750 485 9635
+90 533 835 4439

Emil :
muhammedqasim630@gmail.com

EDUCATION

(Bachelor)
I have been Graduated from university of Salahaddin College of Science + Education _ Biology Department Iraq _ Erbil From **2012 _ 2013**

(Master)
Studies master in Medical Microbiology at Near East University (Turkey _Northern Cyprus) **2019 _ 2021**

WORK EXPERIENCE

(Kar Group Company)

- I worked for one year at khurmala oil field In Erbil from 2013 to 2014.

(Biology Teacher)

- I taught for six years at Dore typical high school In Barzan (Erbil) from 2014 to 2019.

SKILLS

- Laboratory
- Microsoft Word
- Microsoft PowerPoint

Meeting Code:
Paper Code:
Date:28/10/2020

HAWLER MEDICAL UNIVERSITY

COLLEGE OF MEDICINE

RESEARCH ETHICS COMMITTEE APPROVAL SHEET

Title of the project: Evaluation of Progesterone, Estrogen and Prolactin Levels in Pregnant Women With Toxoplasmosis in Erbil City / Iraq.

Principle investigator: Assist **.** Prof. Dr.Esref Celik
Assistant investigator: Mohammed Qasim Burhaw

Prof. Salah Abubaker Ali
Head of the Ethics Committee

Assist. Prof. Asmaa Ghanim Hussein
Member

Assist. Prof. Yousif Baha'addin Ahmed
Member

Assist. Prof. Ruqaya Muhammad Ghareeb
Member

Lecturer Dr. Shereen Ismail Hajee
Member

Evaluation of progesterone, Estrogen and Prolactin Levels in pregnant Women wiith Toxoplasmosis from Erbil City Iraq

ORIJINALLIK RAPORU

%18	%16	%13	%
BENZERLIK ENDEKSI	İNTERNET KAYNAKLARI	YAYINLAR	ÖĞRENCI ÖDEVLERI

BIRINCIL KAYNAKLAR

1	mmbr.highwire.org	
	İnternet Kaynağı	%4
2	ddr.nal.usda.gov	
3	İnternet Kaynağı	%2
	www.biodinamica-ltda.com.br	