UNIVERSITI PUTRA MALAYSIA

COMPARISON OF SEROPREVALENCE OF Toxoplasma gondiiAND ENVIRONMENTALFACTORS BETWEEN SCHIZOPHRENICAND NON-PSYCHIATRICPATIENTS IN HOSPITAL KAJANG, MALAYSIA

LOVETTA YATTA JUANAH

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COMPARISON OF SEROPREVALENCE OF *Toxoplasma gondii* AND ENVIRONMENTAL FACTORS BETWEEN SCHIZOPHRENIC AND NON-PSYCHIATRIC PATIENTS IN HOSPITAL KAJANG, MALAYSIA

By

LOVETTA YATTA JUANAH

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in fulfillment of the Requirements for the Degree of Master of Science

September 2012

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DEDICATION

This Thesis is dedicated to my sons; Sahr Mohamed Egbenda Juanah and Tamba Egbenda Juanah for leaving them behind at their tender ages in-order to further my studies. This piece of work is for them.

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Abstract of Thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirement for the degree of Master of Science.

COMPARISON OF SEROPREVALENCE OF *Toxoplasma gondii* AND ENVIRONMENTAL FACTORS BETWEEN SCHIZOPHRENIC AND NON-PSYCHIATRIC PATIENTS IN HOSPITAL KAJANG, MALAYSIA

By

LOVETTA YATTA JUANAH

September 2012

Chair: Juliana Jalaludin, PhD

Faculty: Faculty of Medicine and Health Sciences

Studies suggest an association between *Toxoplasma gondii* infection and schizophrenia and a high seroprevalence of *T. gondii* has been detected in psychiatric patients especially schizophrenia cases. This matched case-control study aimed at investigating the seroprevalence of *T. gondii* and associated environmental risk factors in schizophrenia patients and non-psychiatric controls at Hospital Kajang. A total of eighty-eight (88) schizophrenia patients and eighty-eight (88) non-psychiatric patients were enrolled as cases and controls respectively for this study and matched 1:1 by age,

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gender and race.Socio-demographic background and environmental risk data of the respondents were obtained from a validated and pre-tested questionnaire adapted from epidemiological questionnaire of the International Agency for Research on Cancer (IARC). Blood sample collected from each individual was centrifuged and analyzed for anti-*Toxoplasma gondii* IgG and IgM antibodies using Enzyme linked immunosorbent assay (ELISA). Mc-nemar chi-square analysis was used to measure the association between the characteristics of the subjects and *T.gondii* infectionand logistics regression analyses was applied to determine the level of risk involved. From the results, *T. gondii* antibodies were found in 45 (51%) of the 88 schizophrenia patients and in 27 (30.7%) of the 88 controls. The difference in the seroprevalences was statistically significant among the groups(OR= 2.41; 95% CI:2.16-3.01; p=0.023). The mean (SD) age of schizophrenia patients and control was 39.42 ±11.49 years (range: 18-60 years). For IgM antibodies to *T. gondii*, both cases and controls had the same level of seropositivity (1.1%). The socio-demographic characteristics among both groups had no significant relationship with *T. gondii* seroprevalence, (p>0.05). From the Chi- square analysis of environmental factors in both groups, *T.gondii* infection was significantly associated with several variables among the case and control groups; beef consumption (p= 0.003), pork consumption (p<0.001) and risky cat contact p=0.041).Further logistics regression analysis of these factors showed a significant association with *T.gondii*; beef consumption (OR=3.852, 95%CI 1.550 - 9.569; p=0.004), pork consumption (OR= 13.089, 95%CI= 4.730 – 36.219;p<0.001) and risky cat contact (OR=4.061, 95%CI=1.985 – 16.745; p<0.047). Hence, it can be explained that beef consumption; pork consumption and cat contact are environmental factors prone to the infection with *Toxoplasma gondii* parasites.In our study,elements toconfirmthe association of *T. gondii* infection and schizophrenia are

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demonstrated. It also lent further weights to the hypothesis that exposure to *T. gondii* may be a risk factor for schizophrenia.

Key words: Toxoplasma gondii, schizophrenia, seroprevalence, cat contact, pork consumption, meat consumption. Environmental factors, socio-demographic factors

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Abstrak tesis yang dikemukakan kepada senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

SEROPREVALENCE *Toxoplasmagondii*DANPERSATUANDENGANFAKTORRISIKOALAMKALANGANPESAKITSKIZOFRENICDANBUKANSKIZOFRENICDI HOSPITALKAJANG, MALAYSIA

Oleh

LOVETTA YATTA JUANAH

September 2012

Pengerusi: Juliana Jalaludin, PhD

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Kajian mencadangkan perkaitan antara jangkitan *Toxoplasma gondii* dan skizofrenia dan seroprevalens *T. gondii* yang tinggi telah dikesan pada pesakit psikiatri terutamanya dalam kes skizofrenia.Kajian kes-kawalan padanan ini dijalankan bertujuan untuk mengkaji seroprevalens *T. gondii* dan faktor-faktor risiko persekitaran yang berkaitan pada pesakit skizofrenia, dan kumpulan kawalan iaitu pesakit selain psikiatri di Hospital Kajang. Seramai 88 orang pesakit skizofrenia telah dipilih sebagai kumpulan kes dan 88 pesakit selain psikiatri dipilih sebagai kumpulan kawalan dan dipadankan dengan nisbah 1:1 mengikut umur, jantina dan bangsa. Latar belakang sosio-demografi dan maklumat risiko persekitaran responden telah diperolehi menggunakan borang soal selidik yang

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telah disahkan dan telah melalui pra-uji, adaptasi daripada soal selidik epidemiologi "International Agency for Research on Cancer" (IARC). Sampel darah setiap individu diemparkan dan dianalisa menggunakan "Enzyme linked immunosorbent assay" (ELISA) bagi mendapatkan antibodi IgG dan IgM anti-*Toxoplasma gondii*. Analisa "Chi-square" telah digunakan untuk menentukan perkaitan antara ciri-ciri subjek dengan jangkitan *T. gondii* manakala regresi logistik digunakan bagi menentukan paras risiko yang terlibat. Keputusan menunjukkan antibodi *T. gondii* telah ditemui pada 45 (51%) daripada 88 pesakit skizofrenia dan 27 (30.7%) daripada 88 kumpulan kawalan. Perbezaan seroprevalens adalah signifikan secara statistik (OR= 2.41, 95%CI= 2.16-3.01; p=0.023). Purata (Sisihan Piawai) umur bagi pesakit skizofrenia dan kumpulan kawalan adalah 39.42±11.49 tahun (julat: 18-60 tahun). Bagi antibodi IgM terhadap *T. gondii*, kedua-dua kumpulan kes dan kawalan mempunyai paras seropositif yang sama (1.1%). Ciri-ciri sosio-demografi bagi kumpulan kes dan kawalan tidak mempunyai hubungan yang signifikan dengan seroprevalens *T. gondii*, (p>0.05). Analisa bivariat bagi faktor-faktor risiko persekitaran menunjukkan, jangkitan *T. gondii* mempunyai perkaitan yang signifikan dengan beberapa pembolehubah; pengambilan daging lembu (p= 0.003), pengambilan daging khinzir (p<0.001) dan sentuhan kucing berisiko (p=0.041). Seterusnya, analisa regresi logistik yang dijalankan bagi faktor-faktor ini menunjukkan perkaitan yang signifikan dengan *T. gondii*; pengambilan daging lembu (OR=3.852, 95%CI 1.550 – 9.569; p=0.004), pengambilan daging khinzir (OR= 13.089, 95%CI= 4.730 – 36.219;p<0.001) dan sentuhan kucing berisiko (OR=4.061, 1.985 – 16.745; p<0.047). Maka, dapat ditunjukkan bahawa pengambilan daging lembu, pengambilan daging khinzir dan sentuhan kucing adalah faktor-faktor persekitaran yang mempengaruhi jangkitan oleh parasit *T. gondii*. Kajian ini memberikan komponen-

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komponen yang akan dapat memastikan perkaitan antara jangkitan *T. gondii* dan skizofrenia. Kajian ini juga menguatkan hipotesis bahawa pendedahan kepada *T. gondii* adalah salah satu faktor penyebabskizofrenia.

Kata kunci: Toxoplasma gondii, skizofrenia, seroprevalence,hubungan kucing, penggunaan daging babi,penggunaan daging, faktor persekitaran, faktor sosio-demogafi

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I certify that a Thesis Examination Committee has met on 20th September, 2012to conduct the final examination **of** Lovetta Yatta Juanah on her thesis entitled "Comparison of Seroprevalence of *Toxoplasma gondii* and Environmental Factors between Schizophrenic and Non-Psychiatric Patients in Hospital Kajang, Malaysia" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the **Master of Science**.

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfillment of the requirement for the degree of **Master of Science**. The members of the Supervisory Committee were as follows:

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Date:

DECLARATION

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I declare that the thesis is my original work except forquotations and citations which have been duly acknowledged. I alsodeclare that it has not been previously, and is not concurrently,submitted for any other degree at Universiti Putra Malaysia or atany other institution.

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LOVETTA YATTA JUANAH

Date: 20 September 2012

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LIST OF ABBREVIATIONS

WHOWorld Health Organization

*et al*and others

CI Confidence Interval

OR Odds Ratio

SD Standard Deviation

N Total number of sample

% Percentage

e.g.For example

^{o}Degree

ELISA Enzyme Linked Immunosorbent Assay

IgG Immunoglobulin G

IgMImmunoglobulin M

NmNanometre

DSM-IV Diagnostic and Statistical Manual of Mental Disorders- Fourth Edition

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CONJ Enzyme Conjugate

CAL Calibrators

H_2SO_4 Sulphuric acid

NEG Negative Control

POSPositive Control

CO Cut-off control

NaN_3Sodium azide

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CHAPTER 1

INTRODUCTION

1.1 Introduction

Toxoplasma gondii is an obligate intracellular protozoan parasite belonging to the phylum Apicomplexa and order Coccidia. *T. gondii* infections are prevalent in humans and warm-blooded animals worldwide. It was found in the spleen of the North African rodent *(Ctenodactylus gundi)*in 1908. More than 60 years after its finding, the life cycle of*T. gondii* was not completely understood. Undercooked meat has been suggested as a source of infection, this hypothesis was sustained by the identification of the tissue cyst stage of its life cycle.The capability of cat faeces to transmit disease, the explanation of the sexual stages and subsequent oocyst stage were defined in 1969 and provided the explanation of how herbivores became infected. The disease it causes is referred to as toxoplasmosis.*T. gondii* was first recognized as causing disease in humans in 1923 when congenital infection was identified as the source of ocular disease in a Czechoslovakian infant(Hofhuis *et al*., 2011). Congenital transmission and ocular disease were then established in independent studies. *T. gondii* is now known to be transmitted by tissue cysts in undercooked meat or oocysts released in infected cat faeces(Dubey, 2007).

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Felids are the only known definitive host and are the key animal species in the life cycle of this parasite because they excrete the environmentally-resistant stage known as the oocysts. Infection with *T. gondii* occurs pre- natally or post-natally. After birth, humans are generally infected with *T. gondii* after the ingestion of oocysts in contaminated soil or water, usually with cat faeces. Infection also occurs by the ingestion of tissue cysts in undercooked meat (Dubey *et al*., 2008). Congenital infection can be very fatal to the fetus(Edelhofer & Prossinger, 2010). The oocysts are the main factor in water resources infection. Unfiltered and surface water had been the main source of community-wide outbreak of toxoplasmosis (Jones & Dubey 2010). Transmission also results from blood transfusion or organ transplantation from an infected person. In humans, individuals at risk of toxoplasmosis include fetuses, new-borns and immunologically impaired patients. Toxoplasmosis however can be life threatening in immunocompromised or immunodeficient individuals especially those with defects of T-cell-mediated immunity, such as those with hematologic malignancies, bone marrow, solid organ transplants or AIDS(Chan *et al*., 2008).

In marginal population of healthy persons infected with *T. gondii* after birth, symptoms with usually mild fever and other manifestations like malaise, and lymphadenopathy can develop. However, there are rare cases where previously healthy humans have developed rigorous and even fatal diseases that include multivisceral and pulmon*ary* diseases, assumed to develop from more virulent types of the organism (Sroka *et al.*, 2010).

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Coccidians in general have complex life cycles. Although most are host-specific, and only transmitted by a fecal-oral route,*T. gondii* can also be transmitted congenitally and by carnivorism among cats. When ingested by cats, the wall of the tissue cyst is assimilated by the proteolytic enzymes in the stomach and small intestine and bradyzoites are released. Some penetrate the lamina propria of the intestine and multiply as tachyzoites. Within a few hours, *T. gondii* may disseminate to extra-intestinal tissues. Microgametocytes and macrogametocytes develop from bradyzoites and fuse to form zygotes. The zygotes then become encapsulated within a rigid wall and are shed as oocysts. Oocysts of *T. gondii* are formed only in cats, including both domestic and wild felids. Oocysts in newly passed faeces are unsporulated (non-infective) and sub-spherical to spherical in shape and 10 mm – 12 mm in diameter. The oocysts are very strong and may remain infectious for more than one year in warm humid environments. Sporulation occurs in the environment within 1–5 days, depending upon exposure to air and temperature(Kijlstra & Jongert, 2008).

After ingestion, bradyzoites released from tissue cysts or sporozoites from oocysts penetrate intestinal tissues, converted to tachyzoites, multiply, and are distributed in the body via blood or lymph. *T. gondii* enters the host cell by active dissemination of the cell membrane and becomes surrounded by a parasitophorous vacuole that protects it from host defence devices. The tachyzoite multiplies asexually by repetitive binary divisions until the host cell splits. After an unknown numbers of divisions, *T. gondii* tachyzoites give rise to another stage referred to as a tissue cyst found in the muscle and brain tissues. Tissue cysts grow and remain intracellular. After a few multiplication

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cycles, tachyzoites give rise to bradyzoites in a variety of tissues(Fig. 1.1). This stage is referred to as the chronic stage.

Latent toxoplasmosis results when bradyzoites or cyst forms inhabit the brain and muscular tissue of the body in a life-long manner. It is often asymtomatic in immunocompetent individuals, however, it is postulated that the presence of the parasite's cysts in the brain induces an increase risk to schizophrenia. *T. gondii*is considered one of the infectious agents that might trigger psychotic disorder (Pearce *et al*., 2012).

Schizophrenia, also called split personality disorder is a persistent, neuropsychiatric disease that affects populations across the world; it is found to be diagnosed in more than 2 million people in the United States alone. Genetic factors plays a role in its aetiology however, environmental factors are also important. Individuals with this disorder may have disorganized speech and behavior, physically rigid or lax behavior, significantly decreased feelings as well as delusions (Harrison *et al*., 2006). Epidemiologic studies propose infections like rubella, polio, herpes simplex as risk factors for the disease developing in later life. Many recent studies have also confirmed the hypotheses that *T. gondii* infection in humans and other mammals is a main contender and a possible cause of schizophrenia. Other related findings have indicated that *T. gondii* might be an etiological agent in some cases of mental illnesses (Hall *et al.*, 2009).

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Recent studies have shown that individuals with latent toxoplasmosis have significantly impaired psychomotor performance when compared with *Toxoplasma*-negative subjects. It is also proven that subjects with latent toxoplasmosis express specific changes in some personality factors. Both psychomotor performance and personality factors increase with duration of the infection (Flegr *et al*., 2003). Animal studies highlighted behavioural modifications in *Toxoplasma*-positive rodents. It was discovered that infected mice had impaired motor performance coupled with difficulties in learning capacity and memory. Infected rats have lower neophobia, reduced learning capability and reduced predator avoidance skills (Joanne, 2001).

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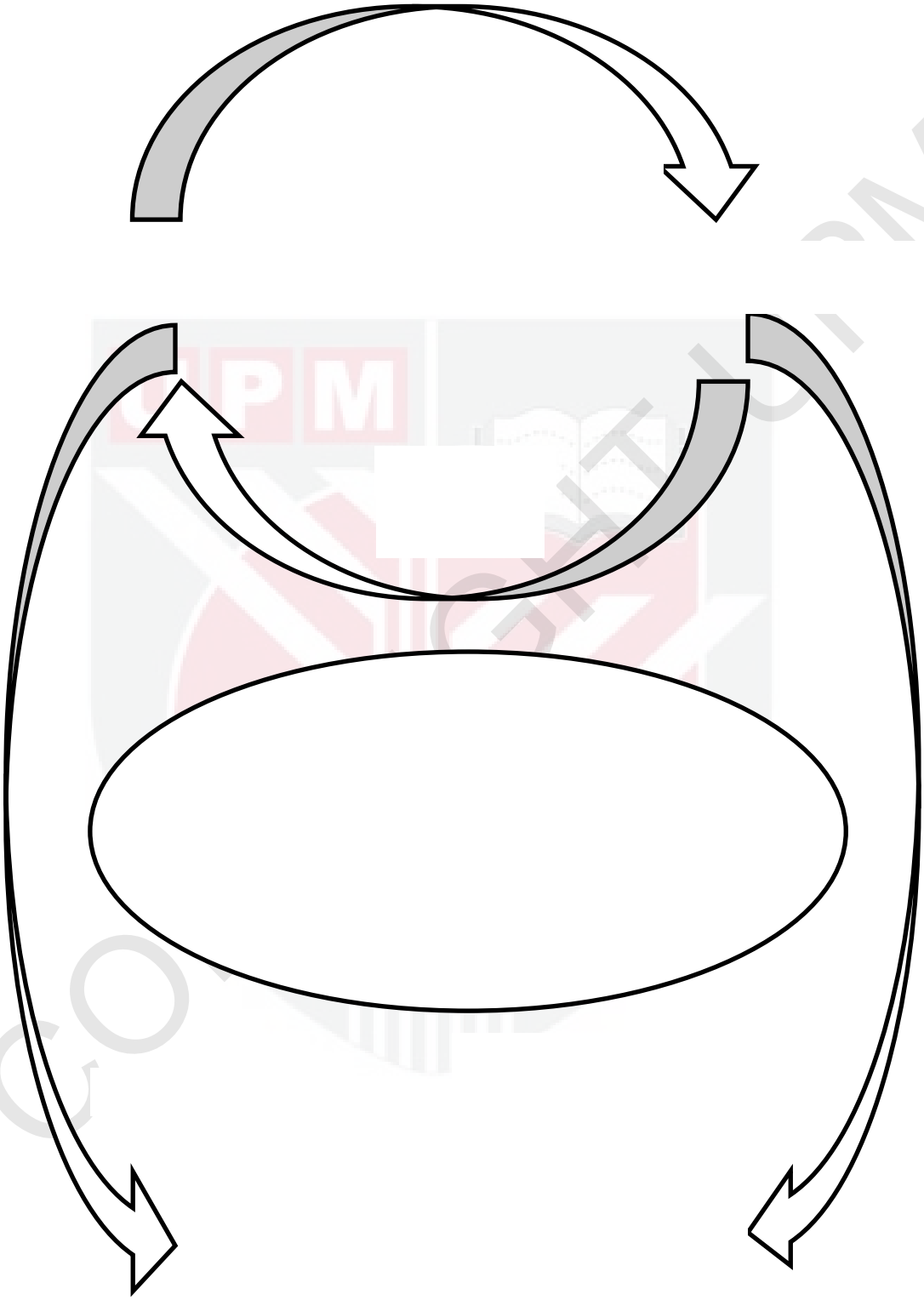

Figure 1.1 Life Cycle of *Toxoplasma gondii*

Source: (Dubey, 2007)

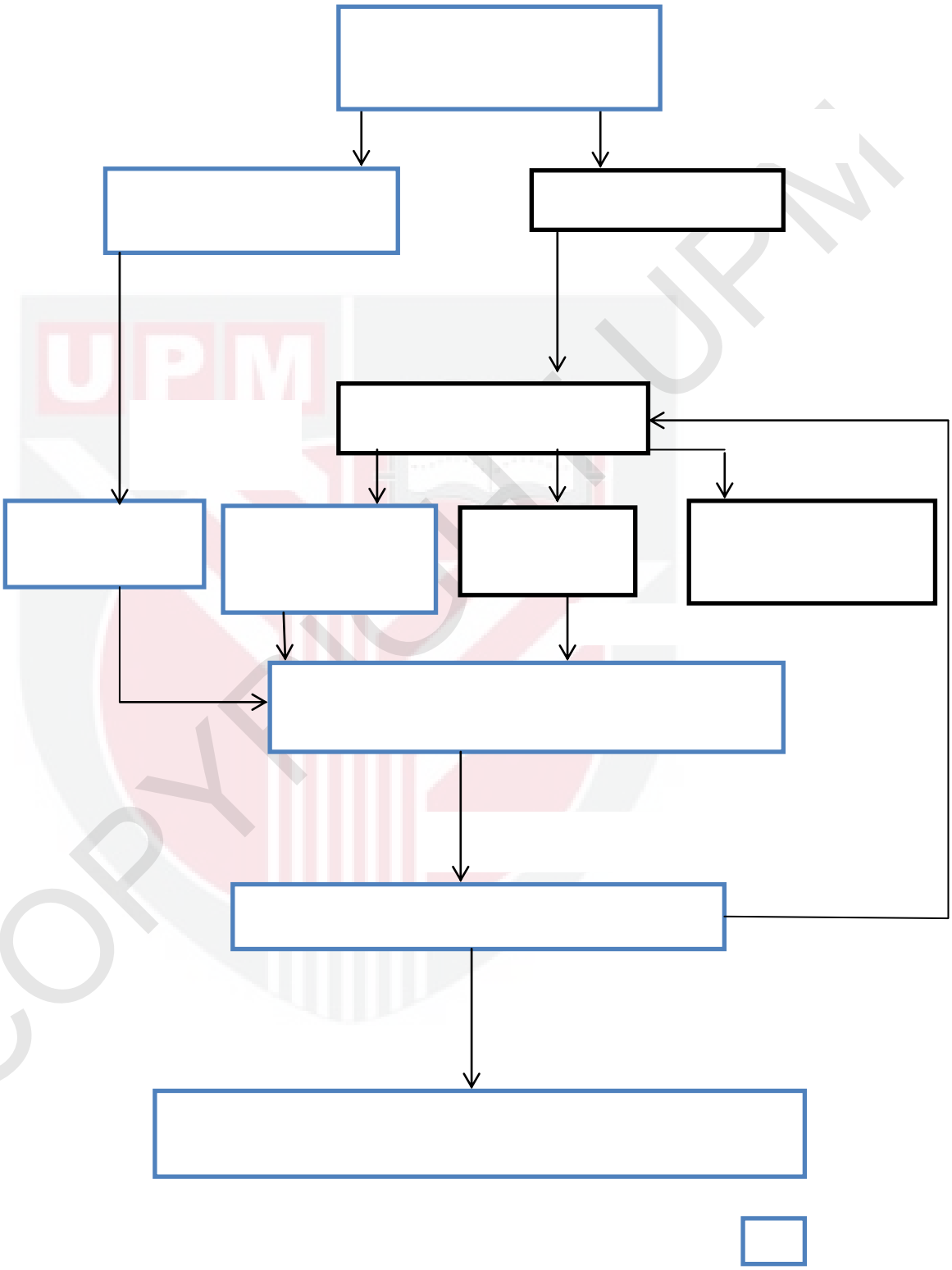

Figure 1.2 Conceptual frame work

1.2 Problem Statement

The central nervous system (CNS) is the most frequently affected site of the latent toxoplasmosis(Arias *et al.*, 2012). This infection may apply to a certain level, impact on the progress of mental disorders. Individuals with latent toxoplasmosis present specific changes in psychomotor performance. Their capacity of learning and memory declines rapidly, leading to prolonged significant response to simple reactions(Carruthers & Suzuki, 2007). Studies done byZhu (2009)concluded individuals infected with latent toxoplasmosis had lower I.Q ($p=0.003$) and lower chances of achieving high education ($p<0.001$). (This lower I.Q was seen in children aged3 to 13 years who had subclinical congenital toxoplasmosis. These clinical confirmations indicate that *T. gondii* infection in the CNS might cause mental damage).

Mental and behavioral disorders have key public health impact worldwide. They occur usually, affecting 10–16% of the world's population (Wang *et al*., 2006).These mental and behavioral disorders are also associated with high level of individual distress, disability and premature mortality. The cost in terms of lost productivity and use of health services is considerable and these disorders contribute to 12% of the global disease burdenwhich is greater than that caused by cardiovascular conditions or malignant neoplasms (World Health Organization, 2004). The treatment for mental and behavioral disorders is mostly symptomatic because their aetiology is still vague. The current consensus is that behavioral disorders have multiple etiological factors, including genetic tendency and environmental mediation (Cheraghipour *et al*., 2010).

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Toxoplasma gondii is a neurotropic protozoan parasite that was considered in the 20th century and later associated with a series of congenital sensory and neurological situations(Yolken & Torrey, 2006). *T. gondii* infection is extensive based on the fact that its infection is implicated by everyday hygiene and lifestyle and is reported to have an effect on up to a third of the world's population (Montoya & Liesenfeld, 2004). Obvious and severe disease from toxoplasmosis occurs in immune-compromised hosts which lead to cervical lymphadenopathy and ocular disease in some patients, and in most immune-competent individuals, infection is subclinical. *T. gondii* uses a multifaceted mechanism to gain access to the brain. When it gains access, it attacks various brain cells, including astrocytes and neurons, where it forms cysts(Lélu *et al*., 2010). When in the brain, the parasitecan then institute an unremitting infection within the central nervous system (CNS), manipulate intermediate host and can cause neurological and psychiatric symptoms in some infected individuals(Brown & Derkits, 2010).

Schizophrenia is a complex chronic neuropsychiatric disease of the central nervous system, believed to have multiple etiologies. Accrued evidence from many studies has shown that genetic factors play a role in its etiopathogenesis, and specific predisposing genes have been acknowledged. Environmental contact, including life style, socio-demographic, stress and life time events have also been identified as growing risk factors for the disease, as seen in figure 1.2. Epidemiological studies have established that winter-spring birth, urban birth, and perinatal and postnatal infection are all risk factors for the disease developing in later life (Brown, 2011). From a recent case-control study of 98 schizophrenia patients and 96 controls carried out by Hamidinejat *et*

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al.(2010)in Iran, it was concluded that *T.gondii* plays a role in the etiology of schizophrenia. This conclusion was based on their Bradford hill criteria analysis. This clearly shows that chronic toxoplasmosis has notable and plausible epidemiologic and symptomatic similarities to schizophrenia.

A study of 199 patients with bipolar disorder reported to have increased seroprevalence of *Toxoplasma gondii* compared to controls(Torrey *et al*., 2007). Correspondingly, a study of 42 patients with persistent-compulsive disorder also reported an increased prevalence of anti-*Toxoplasma* IgG antibodies in contrast with controls.Studies word-wide have found a higher seroprevalence of *T. gondii* among schizophrenia patients than non-psychiatric controls (Alvarado-Esquivel *et al*, 2011), (Haminedijat *et al*, 2011), (Chan *et al*., 2010), Dugruman-Al *et al*., 2009), (Emelia *etal*., 2012). This research serves a preliminary study for Malaysia

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1.3 Study Justification

Several studies have established that schizophrenic patients have an increased prevalence of *T. gondii* infection compared with control individuals. Importantly, arecent meta-analysis of 23 studies found an increased prevalence of *T. gondii* antibodies in patients with schizophrenia. Whilst the odds ratio of 2.73 is modest, it exceeds that of other environmental and genetic factors measured to date. This suggests that *T. gondii* infection is associated with a large number of cases of schizophrenia. The reasons why only a fraction of characters that have been infected with *T. gondii* develop schizophrenia are unclear. Possibilities include differences in genetic vulnerability, method of infection (tissue or oocytes), and/ or time of infection (in the womb, childhood or adulthood). Otherwise, it has been proposed that behavioral traits linked with schizophrenia could result in increased infection with the parasite. For example, the transmission of the parasite could be associated with lack of personal hygiene, which is a characteristic of schizophrenic patients. Nonetheless, this is improbable to explain all cases, and since *T. gondii* encysts in the brain, there is a clear possibility to affect neuronal function directly.

Research conducted by(Flegr, 2007)suggests that *T. gondii* infection leads to the stimulation of astrocytes, hence increase in kynuric acid (KYNA) formation in the brain. This outcome becomes amplified in individuals with elevated brain tryptophan dioxygenase (TDO) activity (Individulas with genetic predisposition for schizophrenia). The increase in KYNA levels contributes to the undue inhibition of glutamatergic and

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nicotinergic neurotransmitter, dopamine, which is believed to play a vital role in the cognitive impairments experiences in schizophrenics

Evidence is accruing for immune-mediated monoaminergic and glutamatergic interactions that could contribute to psychiatric disorders including schizophrenia. Dysregulation of these neurotransmitter structures is longknown to be important in behavioral shortfalls connected to schizophrenia. In addition, Henriquez *et al* (2009)report an unfamiliar immune response to *T. gondii* in patients with schizophrenia, which could contribute to the increased vulnerability of this group.

In mice, *T. gondii* has been confirmed to mainly infect nerve cells. Accordingly, infection could directly affect neuronal function and thus explain neuropsychological shortfalls. Neurochemical changes have been demonstrated in mice with *T. gondii* infection. During acute infection, there is a 40% rise in homovanillic acid levels and a reductionin noradrenaline levels as compared with controls. Dopamine levels are unaffected during acute infection but were increased in the mice with chronic or secondary *T. gondii* infections(Flegr *et al.*, 2011).

Cysts are presumed to be present in the brain for the life of infected humans, though reported at routine post-mortem scrutiny. As encephalitis is the normal disease manifested during reactivation of *T. gondii* infection in immunocompromisedindividuals, substantial numbers of cysts are expected to be

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present in this tissue. Studies in at least certain strains of mice indicate that cyst number can drop with time, suggesting that individual cysts have a limited lifespan(Joanne, 2001).

There is growing interest in the role of microbial agents in the initiation and subsequent development of psychiatric disorders especially neuropsychiatric disorders. This is based on the hypothesis that infectious agents such as *T. gondii*, herpes simplex virus cytomegalovirus and influenza virus may play an etiological role in some mental and behavioral disorders(Conejero-Goldberg *et al.*, 2003). Many extensive works have been done and are on–going, in order to investigate the association between schizophrenia and *T. gondii,* and a special issue dedicated recently in Schizophrenia Bulletin (Eskild, 2007).

Toxoplasmosis is a common infection and has a high seroprevalence rate among Malaysians(Nissapatorn & Abdullah, 2004). Nonetheless, little or no studies have been done among schizophrenia patients and controls.

Previous studies have reported to investigate that either toxoplasmosis may be more frequent as serofrequency and more intense as serointensity in patients with schizophrenia or major depression compared with psychiatrically healthy controls(Emelia *et al*., 2012). The measurement were associated with clinical course and from there, Hinze-Selch *et al.* (2007) did a cross-sectional and prospective investigations

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of individuals with schizophrenia and major depression admitted to the hospital ward and healthy controls.The groups were adjusted for age and geographic home region while serofrequency was comparable between the groups. They found out that serointensity was significantly higher in the patients than controls.

Results from studies done by Hamidinejat *et al.* (2010), who studied *T. gondii* infections in schizophrenic patients showed that individuals with schizophrenia had significantly increased level of serum IgG antibodies to *T. gondii* (57%) as compared to controls (29.2%) ($p<0.05$) at 95% CI (1.65-5.41).

Brain disorders and associated deformities are growing at its fast rate in both developing and developed countries (World Health Organization, 2004). The brain is a highly functional and key organ in the human body and thus brain disorders of any kind could lead to a high fatal potential factor in mortality and morbidity(Flegr *et al*., 2011). A study that aims to bridge these two infections has all its rewards connected to increase in community education programmes and enhances prevention and control measures.

Studies have shown that infection with *T.gondii* in animals can lead to distorted behavior and changes in levels of numerous neurotransmitters that are implicated in the pathogenesis of schizophrenia(Flegr *et al.,* 2003). This study therefore aims at investigating the potential association between toxoplasmosis and schizophrenia and

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environmental risk factors. This research will contribute to the novel findings on toxoplasmosis, as a risk factor for the onset of schizophrenia or bipolar disorders.

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1.4 Objectives

1.4.1 General Objectives

To study the seroprevalence of *Toxoplasma gondii*and associated environmental risk factors in schizophrenia patients and non-psychiatric controls.

1.4.2 Specific Objectives

i. To compare the seroprevalence of *Toxoplasma gondii* infection among schizophrenia patients and non-psychiatric controls.

ii. To compare the seroprevalence of anti-*Toxoplasma* IgM and anti-*Toxoplasma* IgG antibodies among schizophrenia patients and non-psychiatric controls.

iii. To determine the socio-demographic factors associated with *Toxoplasma gondii* infection among schizophrenia patients and non-psychiatric controls.

iv. To determine the environmental risk factors associated with *Toxoplasma gondii* infection among schizophrenia patients and non-psychiatric controls.

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1.5 Hypotheses

i. There is a significantly higher seroprevalence of *Toxoplasma gondii* infection in schizophrenia patients than in non-psychiatric controls.

ii. The seroprevalence of anti-*Toxoplasma* IgG antibodies is significantly higherthan anti-IgM antibodies in schizophrenia patients than non-psychiatric controls.

iii. Socio-demographic risk factors are significantly associated with *Toxoplasma gondii* infection among schizophrenia patients than non-psychiatric controls.

iv. Environmental risk factors are significantly associated with *Toxoplasma gondii* infection among schizophrenia patients than non -psychiatric controls.

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1.6 Definition of variables

1.6.1 Conceptual Definitions

i. Environmental Risk factors

Environmental risk factors are those factors that play an important role in shaping developments from new-born period to adolescence. Those characteristics in a person's surroundings that increases the risk of diseases (Brown, 2011).

ii. Sociodemographic risk factors

Socio-demographic characteristics of a population include age, sex, education, level of income, marital status, occupation, religion etc.

iii. Psychosocial risk factors

It involves both the social and psychological characteristic of a patient's life. It combines psychiatric history taking with essentials of problem solving in psychiatric therapy, often used in patients who have been existing with intentional self-harm.

iv. Seropositivity of *Toxoplasma gondii*

Seropositivity means showing a positive reaction to a test on blood serum for a particular disease that exhibits seroconversion. *Toxoplasma gondii* seropositivity refers

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to the presence of specific antibodies of *T. gondii* (i.e IgM and IgG and IgA antibodies) in a blood serum or plasma after analysis (Barbosa *et al*., 2009).

v. Schizophrenia

This is a severe mental disorder characterized by delusions, hallucinations, incoherence and physical agitation; it is classified as a "thought" disorder while bipolar disorder is a "mood" disorder(Hamidinejat *et al*., 2010)

1.6.2 Operational Definitions

i. Environmental Risk factors

These includedbehavioral risk factors, such as risky contact with cats, undercooked beef consumption, drinking untreated water, gardening/agriculture, eating unwashed fruits, smoking cigarettes and pork consumption. These all have been found to increase the risk of *T.gondii.*(Barbosa *et al.*, 2009)

ii. Lifestyle risk factors

Lifestyle risk factors included: contact with cat and its feaces, contact with soil; diet; eating raw or undercooked meat especially pork and drinking untreated water. Contact

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with cat has been a significant contributing factor to toxoplasmosis infection and hence schizophrenia (Gunnell *et al*., 2005).

iii. Socio-demographic Risk Factors

Socio-demographic factors in this study included; age, gender, race, income, marital status, education level and occupation. The above risk factors have been found to affect *T.gondii* seroprevalence.Schizophrenia cases are found to increase in individuals with little or no education and those with stress at work (Alvarado-Esquivel *et al.,* 2011).

iv. Psychosocial Risk Factors

Psychosocial risk factors in this study were those social and psychological factors that affect an individual's sense of thought and leads to stress, which is a hazard in its own right. Psychosocial risk factors can lead to musculoskeletal disorders. For example, there can be stress-related changes in the body (such as increased muscle tension) that can make people more susceptible to mental diseases (Carneiro *et al.*, 2009).

v. Seropositivity of *Toxoplasma gondii*

Immunoglobulin M (IgM) antibodies are predominantly involved in secondary immune response while immunoglobulin G (IgG) antibodies are mainly involved in primary

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response. The presence of these anti- *Toxoplasma gondii* antibodies in a serum of an individual indicated seropositivity of toxoplasmosis.(Eskild, 2007).

vi. Schizophrenia

Schizophrenia is also called split personality disorder. It is a chronic, severe, debilitating illness that affects populations across the world. It ischaracterized by disintegration of thought processes and of emotional responsiveness and is associated with delusions and hallucinations (Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, DSM-IV)

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