

**EPIDEMIOLOGICAL RISK FACTORS OF CEREBRAL
TOXOPLASMOSIS IN HIV/AIDS PATIENTS (A study in Kariadi
Hospital, Semarang).**



Thesis
**Submitted in Partial Fulfilment of the Requirement for the Award
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ENDORSEMENT PAGE

THESIS

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- a. This thesis is original and has never been submitted to obtain an academic degree (Master's degree), either at Diponegoro University or in other tertiary institutions.
- b. This paper is purely of my own ideas, formulations and research, without the help of others, except the supervisor team and the resource persons.
- c. In this paper there are no works or opinions that have been written or published by others, unless clearly stated as a reference in the manuscript with the name of the author and the title of the original book included and included in the bibliography.
- d. I make this statement with truth and if later there are deviations in the truth in this statement, then I am willing to accept academic sanctions in the form of revocation of the degree that I have obtained and other sanctions in accordance with the norms prevailing at Diponegoro University in Semarang.

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Hassana

FOREWORD

All praise and gratitude belong only to Allah SWT who has given life to and has destined every step of His creatures, including we humans the most glorified creatures. The prophet S.A.W who brought the message and values of goodness to mankind, May the almighty be pleased with him. Alhamdulillah, I have completed this thesis as one of the requirements for the completion of a Masters in Epidemiology, at the School of Postgraduate Studies, Diponegoro University.

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**EPIDEMIOLOGICAL RISK FACTORS OF CEREBRAL TOXOPLASMOSIS IN
HIV/AIDS PATIENTS (A study in Kariadi Hospital, Semarang).**

ABSTRACT

Background: *Toxoplasma gondii*, an intracellular obligate coccidian protozoan is the causative agent of toxoplasmosis. The parasite develops in immune-compromised hosts which include HIV/AIDS patients, pregnant women, and children. Epidemiological information on the risk factors of cerebral toxoplasmosis has not been established and subsequently not available.

Objective: To explain the various epidemiological risk factors for the occurrence of cerebral toxoplasmosis in HIV/AIDS patients in RSUP Dr. Kariadi, Semarang.

Methods: A case-control design with a retrospective approach was used in this study, comprising of 64 subjects (32 cases and 32 controls). Samples were determined by positive test for toxoplasma IgG for all HIV patients included in the study. Chi-square test and Logistic Regression was used for data analysis.

Result: The result from the multivariate analysis found that treatment failure (OR = 4.392, 95% CI = 1.268 - 15.210) as the significant risk factor for cerebral toxoplasmosis in HIV/AIDS patients. Other variables were all proven not to be risk factors for the occurrence of cerebral toxoplasmosis in HIV/AIDS patients. Death was significantly higher in the case group than in the control group (71.4% vs. 31.2%, $p < 0.05$). Patients with cerebral toxoplasmosis had a significantly higher risk of mortality when compared to those without it.

Conclusion: Treatment failure was the only factor found to be a risk factor for the occurrence of cerebral toxoplasmosis in HIV/AIDS patients.

Keywords: HIV/AIDS, Cerebral Toxoplasmosis, CD4, RSUP Dr. Kariadi.

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ABSTRAK

LatarBelakang: *Toxoplasma gondii*, protozoa coccidian obligat intraseluler adalah agen penyebab toksoplasmosis. Parasit ini berkembang pada inang yang dikompromikan dengan kekebalan yang meliputi pasien HIV/AIDS, wanita hamil, dan anak-anak. Informasi epidemiologis tentang factor risiko toksoplasmosis serebral belum ditetapkan dan selanjutnya tidak tersedia.

Tujuan: Untuk menjelaskan berbagai factor risiko epidemiologis untuk terjadinya toksoplasmosis serebral pada pasien HIV/AIDS di RSUP Dr. Kariadi, Semarang.

Metode: Desain case-control dengan pendekatan retrospektif digunakan dalam penelitian ini, terdiri dari 64 subjek (32 kasus dan 32 kontrol). Sampel ditentukan engan tes positif untuk toksoplasma IgG untuk semua pasien HIV yang termasuk dalam penelitian. Uji Chi-square dan Regresi Logistik digunakan untuk analisis data.

Hasil: Hasil dari analisis multivariate menemukan bahwa kegagalan pengobatan (OR = 4,392, 95% CI =1.268 - 15.210) sebagai factor risiko signifikan untuk toksoplasmosis serebral pada pasien HIV/AIDS. Variabel lain semuanya terbukti tidak menjadi factor risiko untuk terjadinya toksoplasmosis serebral pada pasien HIV/AIDS. Kematian secara signifikan lebih tinggi pada kelompok kasus dibandingkan pada kelompok kontrol (71,4% vs 31.2%, $p < 0,05$). Pasien dengan toksoplasmosis serebral memiliki risiko kematian yang secara signifikan lebih tinggi bila dibandingkan dengan mereka yang tidak memilikinya.

Kesimpulan: Kegagalan pengobatan adalah satu-satunya faktor yang ditemukan menjadi faktor risiko untuk terjadinya toksoplasmosis serebral pada pasien HIV / AIDS.

Kata kunci: HIV / AIDS, Toxoplasmosis Serebral, CD4, RSUP Dr.Kariadi.

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LIST OF ABBREVIATIONS

AIDS	: Acquired Immune Deficiency syndrome
ART	: Antiretroviral treatment
BAL	: Bronchoalveolar Lavage
CNS	: Central nervous system
CSF	: Cerebrospinal fluid
CT	: Cerebral Toxoplasmosis
CD4	: Cluster of Differentiation
CT scan	: Computed Tomography
DNA	: Deoxyribonucleic acid
ELISA	: Enzyme linked immunosorbent assay
ESAs	: Excretory/Secretory antigen
FITC	: Fluorescein Isothiocyanate
GABA	: Gamma-amino butyric acid
HAART	: Highly Active Antiretroviral Therapy
HIV	: Human immunodeficiency virus
HLA-B8	: Human Leukocyte Antigen -B
HLA-DRB1	: Human Leukocyte Antigen –DRB1
IL-12	: Interleukin 12
IFN- γ	: Interferon gamma
IFA	: Indirect fluorescent antibody technique
IgG	: Immunoglobulin G
IgM	: Immunoglobulin M
IHA	: Indirect hemagglutination test
MHC	: Major histocompatibility complex
MAT	: Modified agglutination test
MRI	: Magnetic resonance imaging
NK cells	: Natural Killer cells

NO	: Nitric oxide
OIs	: Opportunistic infections
OT	: Ocular toxoplasmosis
PCR	: Polymerase chain reaction
PCR-RFLP	: PCR restriction fragment length polymorphism
qrtPCR	: Quantitative real-time PCR ()
RT-Qpcr	: Real time or quantitative polymerase chain reaction
SFDT	: Sabin Feldman dye test
SMX	: Sulfamethoxazole
TE	: Toxoplasmic encephalitis
TMP	: Trimethoprim
UNAIDS	: United Nations Program on HIV and AIDS
W.H.O	: World Health Organization

GLOSSARY

AIDS	: AIDS is a disease in which there is a severe loss of the body's cellular immunity, greatly lowering the resistance to infection and malignancy.
Acute Infection	: Is an infection that occurs at the early stage during of transmission. It is of short duration, rapidly progressive, and needs an urgent care.
Apicomplexa	: These are a large phylum of parasitic alveolates, where most of the members possess a unique form of organelle that comprises a type of plastid called an apicoplast, and an apical complex structure.
Asymptomatic	: This is a disease condition in which a patient is a carrier for a disease or infection but experiences no symptoms. In relation to toxoplasmosis, a person might be a carrier of the organism but shows no symptoms.
Bradyzoites	: A slowly multiplying encysted form of sporozoan parasite typical of chronic infection with <i>Toxoplasma gondii</i> .
Calcifications	: This is the hardening of tissue or other material by the deposition of or conversion into calcium carbonate or some other insoluble calcium compounds.
CD4	: Is a glycoprotein found on the surface of immune cells such as T helper cells, monocytes, macrophages, and dendritic cells. It is the part of the white blood cell that is used by HIV to replicate, and subsequently kill it. CD4 counts reflect the health of the immune system.
Chemotherapy	: It is the treatment of disease by the use of chemical substances, especially the treatment of cancer by cytotoxic and other drugs.
Chronic	: An illness that persists for a long time or constantly recurring.
Coccidian	: These are a subclass of microscopic, spore-forming, single-celled obligate intracellular parasites belonging to the apicomplexan family.
Co-infection	: A condition whereby a person is living with more than one infection at a time. HIV and Toxoplasmosis co-infection means that a person has both HIV and toxoplasmosis.
DNA	: A self-replicating material which is present in nearly all living organisms as the main constituent of chromosomes. It is the carrier of genetic information. It is the fundamental and distinctive characteristics or qualities of someone or something.
ELISA	: A laboratory test used to detect and measure the presence or absence of HIV and/or toxoplasma antibody in a patient's blood or other body samples.

Epidemics	: The rapid spread of infectious disease to a large number of people in a given population within a short period of time, usually two weeks or less.
GABA	: Gamma-amino butyric acid is a neurotransmitter that sends chemical messages through the brain and the nervous system, and is involved in regulating communication between brain cells. Its role is to inhibit or reduce the activity of the neurons or nerve cells.
HIV	:The Human Immunodeficiency Virus harms the immune system by destroying the white blood cells that fight infection and puts one at risk for serious infections and certain cancers.
Heteroxenous	:A process whereby an organism infests more than one kind of host, especially requiring at least two kinds of host to complete the life cycle
HLA-DRB1	: This gene provides instructions for making a protein that plays a critical role in the immune system. The HLA-DRB1 gene is part of a family of genes called the human leukocyte antigen (HLA) complex.
Immunodeficiency	:Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance. HIV patients with low CD4 count are susceptible to cerebral toxoplasmosis.
Immunocompetence	:The ability of the body to produce a normal immune response following exposure to an antigen. I
Interleukin-12	: (IL-12) is an interleukin that is naturally produced by dendritic cells, macrophages, neutrophils, and human B-lymphoblastoid cells (NC-37) in response to antigenic stimulation.
IFN- γ	: This is a type II interferon, is a cytokine that is critical for innate and adaptive immunity against viral, some bacterial and protozoal infections. IFN- γ is an important activator of macrophages and inducer of Class II major histocompatibility complex (MHC) molecule expression.
Latent infection	:An inactive or dormant infection which stays in the body for months or years and reoccurs again
Neutropenia	:The presence of abnormally few neutrophils in the blood, leading to increased susceptibility to infection.
Oocyst	: A hardy, thick-walled stage of the life cycle of coccidian parasites. It is the stage that is shed in the feces of people infected with parasites such as toxoplasma.
Opportunistic	:A microorganism or an infection which rarely affects patients except in unusual circumstances, typically when the immune system is depressed.

Pancytopenia	: A condition that occurs when a person has low counts for all three types of blood cells: red blood cells, white blood cells, and platelets. It is usually due to a problem with the bone marrow that produces the blood cells.
Parasite	: This is an organism that lives in or on an organism of another species (its host) and benefits by deriving nutrients at the other's expense.
PCR	: Is a laboratory technique used to make multiple copies of a segment of DNA. It is very precise and can be used to amplify, or copy, a specific DNA target from a mixture of DNA molecules.
PV	:A parasitophorous vacuole is formed during cell invasion, when an apicomplexan parasite uses part of the membrane of the host cell to form a parasitophorousvacuolar membrane (PVM).
Prognosis	:This is a prediction of the probable outcome of a disease or disorder.
Prophylaxis	:An action taken to prevent disease, especially by specified means or against a specified disease.
Proteolysis	:Proteolysis is the breakdown of proteins into smaller polypeptides or amino acids.
Reactivation	:The act or process of making something active again or becoming active again from a dormant state.
Serology	:The diagnostic examination of blood serum, especially with regard to the response of the immune system to pathogens or introduced substances.
Seroprevalence	:The number of persons in a population who test positive for a specific disease based on blood serum specimens. It is often presented as a percent of the total specimens tested or as a proportion per 100,000 persons tested.
Sporozoites	:A motile spore-like stage in the life cycle of some parasitic sporozoans (e.g. toxoplasma), that is typically the infective agent introduced into a host.
Tachyzoite	:A rapidly multiplying stage in the development of the tissue phase of <i>Toxoplasma gondii</i> development in acute infections of toxoplasmosis.
Trojan horse	: This is a tactic style toxoplasma uses to gain access to the brain through the blood brain barrier. It hides within a host cell, thereby bypassing mechanisms that the host cell employs to prevent the parasite from entering in its free form
TNF	: Tumor necrosis factor is a cell signalling protein (cytokine) involved in systemic inflammation and is one of the cytokines that make up the acute phase reaction.

Toxoplasmosis : An opportunistic infection caused by the apicomplexan protozoa *Toxoplasma gondii*. Transmitted mainly through undercooked meat, soil or cat faeces.

Zoonosis : A disease that can be transmitted from animals to people or, more specifically, a disease that normally exists in animals but that can infect humans.