

## Glasgow Outcome Scale Assessment in Patients with Cerebral Toxoplasmosis

Brigitta Berlianty,<sup>1</sup> Sofiati Dian,<sup>2</sup> Ahmad Rizal Ganiem<sup>2</sup>

<sup>1</sup>Faculty of Medicine Universitas Padjadjaran, Indonesia, <sup>2</sup>Department of Neurology, Faculty of Medicine Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital, Bandung, Indonesia

### Abstract

**Background:** Cerebral toxoplasmosis is a *Toxoplasma gondii* infection affecting the brain. Assessment of the functional outcome after treatment is needed as an evaluation for therapeutic management. One of the instruments used is the Glasgow Outcome Scale (GOS). This study aimed to assess the functional outcome of cerebral toxoplasmosis patients using GOS.

**Methods:** A Cross-sectional descriptive study with total sampling method was conducted. Medical records were retrieved from patients with cerebral toxoplasmosis registered at the Department of Neurology, Dr. Hasan Sadikin General Hospital, Bandung during year 2017–2019. Inclusion criteria were patients with cerebral toxoplasmosis aged >18 years and had a positive HIV serological test. The GOS was assessed and presented in frequency, using Microsoft Excel and SPSS software ver. 25.0.

**Results:** Of 87 patients, 68% had somnolent on admission to the hospital, 51% had hemiparesis/hemiplegia, and 76% had GOS 3, indicating severe disability. Almost one third (28%) of patients died during hospitalization with non-neurological complications as the most common cause of death (63%). On discharge from the hospital, 82% of the survivors were fully alert, 40% had hemiparesis/hemiplegia, and 33% had GOS 4 (mild disability).

**Conclusions:** Most of the cerebral toxoplasmosis patients come to the hospital with severe disability. During the treatment, one third of patients died, and those who survived had mild disability. GOS has improved after hospitalization, suggesting that GOS is useful for assessment of therapeutic management.

**Keywords:** Cerebral toxoplasmosis, Glasgow Outcome Scale, opportunistic infection, *Toxoplasma gondii*

### Introduction

Toxoplasmosis is an infection caused by *Toxoplasma gondii* (*T. gondii*).<sup>1</sup> This parasite has infected 30–50% of the human population in the world.<sup>2,3</sup> Cerebral toxoplasmosis is an infection of *T. gondii* that affects the brain with high mortality and morbidity rates, especially in low-to middle-income countries and tropical regions, including Indonesia.<sup>4,5</sup> Cerebral toxoplasmosis is an opportunistic infection that is often found in people living with human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) known as PLWHA.<sup>6–8</sup> As many as 30–70% of PLWHA infected with *T. gondii* have central nervous system disorders.<sup>9,10</sup>

Assessment of functional outcomes in cerebral toxoplasmosis patients is needed as

an evaluation tool regarding management. To assess the success of a patient's treatment, it should not only be assessed whether the patient is still alive or dead, but there is a need for a measuring instrument that can better explain the condition of nerve function when the patient survives. One of the measuring instruments proposed is the Glasgow Outcome Scale (GOS). The GOS is a scale originally used to assess the outcome of brain injury.<sup>11</sup> Recently, it is widely used to describe another neurological dysfunction. The GOS has a scale of five category ranging from GOS 1 whether patients has died to GOS 5 whether patients recover with good neurological function.<sup>12–14</sup>

There have been no studies related to functional outcomes assessment in cerebral toxoplasmosis patients using GOS in Indonesia. This study aimed to explore the

**Correspondence:** Brigitta Berlianty, Faculty of Medicine Universitas Padjadjaran, Jalan Raya Bandung-Sumedang Km. 21, Jatinangor, Sumedang, West Java- Indonesia, E-mail: brigittaberlian@gmail.com

functional outcome of patients with cerebral toxoplasmosis as assessed by GOS.

## Methods

The study was conducted using a cross-sectional descriptive method and a retrospective approach to cerebral toxoplasmosis patients at Dr. Hasan Sadikin General Hospital, Bandung from 2017 to

2019. Secondary data were obtained by total sampling through medical records at the Department of Neurology, Dr. Hasan Sadikin General Hospital Bandung, collected from August to November 2020.

The inclusion criteria in this study were patients with a diagnosis of cerebral toxoplasmosis aged >18 years and had a positive HIV serological test results. Exclusion criteria were patients who went home at their

**Table 1 Characteristics of Patients with Cerebral Toxoplasmosis from Dr. Hasan Sadikin General Hospital, year 2017–2019**

Characteristics	n (%)
Demography	
Age in years–median (IQR)	34 (26–41) <sup>a</sup>
Gender	
Male	66 (76)
Female	21 (24)
Chief complaint	
Decreased consciousness	57 (65)
Headache	12 (14)
Seizures	11 (13)
Motoric disorders	5 (6)
Visual disorders	1 (1)
Speech disorders	1 (1)
Supporting examination	
CT scan*	
Mass or lesion	84 (98)
No mass or lesion	2 (2)
IgG anti toxoplasma	
An examination was carried out	69 (79)
No examination statement	18 (21)
CD4** –median (IQR)	20.5 (9–56) <sup>a</sup>
Comorbidities	
Yes	45 (52)
No	42 (48)
Treatment	
Drug administration	
Pyrimethamine	3 (3)
Pyrimethamine + Clindamycin	58 (67)
High dose cotrimoxazole	26 (30)
Length of alive patient care –median (IQR)	15 (12–19) <sup>a</sup>
The patient died in treatment	24 (27.6)
Length of patient stay until death –median (IQR)	4 (3–7.75) <sup>a</sup>
Cause of death	
Neurological	7 (29.2)
Non-neurological	15 (62.5)
Unknown	2 (8.3)

Notes: All data were presented as n (%) unless stated otherwise was median (IQR)<sup>a</sup>, \* CT scan results were only available for 86 data, \*\*CD4 examination results were only available for 64 data

request thus they did not undergo complete treatment. This research received approval from the Research Ethics Committee of Universitas Padjadjaran no. 636/UN6.KEP/EC/2020 as well as a research permit by the Research and Development Committee and Ethics Committee of Dr. Hasan Sadikin General Hospital, Bandung. Data collected from the patient's medical records were analyzed and processed using Microsoft Excel and SPSS.

The data included in this study were age, gender, chief complaints, level of consciousness, motoric skills, comorbidities, drug administration, length of treatment, and results of supporting examinations such as CT scan, IgG anti-toxoplasma, CD4 count. When the patients died, the cause of death was recorded.

The diagnostic criteria for cerebral toxoplasmosis used were based on IgG anti toxoplasma examination and/or CT scan. Patient consciousness was determined based on clinical conditions, categorized into *compos mentis*, *somnolence*, *sopor*, and *coma*. Assessment of the GOS in determining the functional outcome of the patients was difficult to assess using retrospective data, however, the GOS assessment in this study was performed by considering the condition of consciousness, language disorders, and the motoric skills of the patients, and was defined as followed: GOS 1 was death, GOS 2 was coma, GOS 3 was *sopor/somnolence* or motoric strength 0-3 or language disorder, GOS 4 was *compos mentis* with motoric strength 4, and GOS 5 was *compos mentis* with motoric strength 5 or got

mild neurological sequelae. Furthermore, GOS 2 and 3 were categorized as bad outcomes while 4 and 5 as good outcomes.<sup>12-14</sup>

The causes of the death were categorized into neurological, non-neurological, and unknown causes. Neurological causes were designated as the abnormalities in the central nervous system, for example due to herniation and hydrocephalus; whereas non-neurological causes included respiratory failure, septic shock, and sudden cardiac arrest. Other causes were designated as unknown causes.

## Results

In total, 96 data from patients diagnosed with cerebral toxoplasmosis were retrieved. However, those with negative HIV serology results (n=1) and those who returned home at their request (n=8) were excluded from the study. Thus, 87 patient data were included.

The mean age of the patients was 34 years (interquartile range 26–41 years) with male was predominantly prevalent (76%) and most of them came with a chief complaint of decreased consciousness (65%) as shown in Table 1. The CT scan results showed that the mass or lesions was mostly in the brain (98%). Interestingly, patients who had no brain mass or lesions (n=69; 79%) had reactive anti-toxoplasma IgG results. The mean CD4 count was 20.5 cells/mm<sup>3</sup> (interquartile range 9–54.7). Most of the patients had more than one disease that was occurred simultaneously, with the majority were pulmonary infections and severe metabolic disorders (52%). Most

**Table 2 Level of Consciousness and Motoric Conditions**

Characteristics	Admission (n=87)	Discharge (n=63)
	n (%)	n (%)
Level of consciousness		
Compos mentis	21 (24)	52 (82)
Somnolence	59 (68)	10 (16)
Sopor	7 (8)	1 (2)
Coma	-	-
Language disorders		
Yes	-	-
No	25 (29)	38 (60)
Difficult to assess	62 (71)	25 (40)
Motoric disorders		
None	9 (10)	23 (36)
Hemiparesis/hemiplegia	44 (51)	25 (40)
Tetraparesis/tetraplegia	32 (37)	14 (22)
Can-not be assessed	29 (2)	1 (2)

**Table 3 Glasgow Outcome Scale**

Scale	Admission (n=87)	Discharge (n=87)
	n (%)	n (%)
1 : death	-	24 (28)
2 : persistent vegetative	-	-
3 : severe disability	66 (76)	12 (14)
4 : moderate disability	15 (17)	29 (33)
5 : good recovery	6 (7)	22 (25)

**Table 4 Distribution of the Glasgow Outcome Scale**

Admission (n)	Discharge (n)				
	GOS 5 (n=22)	GOS 4 (n=29)	GOS 3 (n=12)	GOS 2 (n=0)	GOS 1 (n=24)
GOS 5 (6)	6	-	-	-	-
GOS 4 (15)	6	8	1	-	-
GOS 3 (66)	10	21	11	-	24

of the treatments had used pyrimethamine and clindamycin (67%). During the treatment, 24 patients (28%) died. The mean length of stay for patients who survived was 15 days (interquartile range 12–19), whereas the length of stay for patients who died was 4 days (interquartile range 3–7.7). The most common causes of death were non-neurological causes (63%), namely respiratory failure, septic shock, and sudden cardiac arrest. Of neurological causes (n=7; 29%) 6 had herniations and 1 had hydrocephalus.

The level of consciousness and motoric skills of patients during admission and discharge showed that most of the patients had a high level of somnolence (68%) and had hemiparesis/hemiplegia (51%) as depicted in Table 2. At the time of discharge, most of them had a level of consciousness of *compos mentis* (82%), however, motoric conditions hemiparesis/hemiplegia were still about 40%.

At the time of admission to the hospital, the patients were mostly in GOS 3 (76%), while at the time of discharge 28% were on GOS 1 or had died or had better conditions in GOS 4 (33%) and GOS 5 (25%). Of the 66 patients who were initially on GOS 3 on the admission, 24 patients died, however, 10 patients improved to GOS 5, 21 patients to GOS 4, while the rest remained on GOS 3.

## Discussions

Opportunistic infections involving central nervous system in HIV-positive patients at Dr.

Hasan Sadikin General Hospital Bandung in 2017–2019 has shown that 58% are caused by *T. gondii* infection. Based on the results of the study, 72% of patients survived while 28% died. Patients who survived had a good outcome. The majority of patients with cerebral toxoplasmosis (68%) experienced somnolent during hospital admission, had hemiparesis/hemiplegia (51%), and had GOS 3 or severe disability (76%). Almost one third (28%) died during hospitalization with non-neurological complications as the most common cause of death (63%). On discharge from the hospital, 82% of the survivors were fully alert, 40% still had hemiparesis/hemiplegia, and 33% had GOS 4 or mild disability. Previous study has shown that the prevalence of toxoplasmosis in Indonesia was 44%, and 19% of patients with cerebral toxoplasmosis died.<sup>15–16</sup>

Assessment of functional outcomes using GOS is carried out when the patients have been admitted to the hospital and then discharged by considering the level of consciousness, language disorders, and motoric disorders. In our study, the level of consciousness shows an improvement, for example the somnolence state (68%) became *compos mentis* (82%). This is similar to other study, showing that the level of consciousness of cerebral toxoplasmosis patients at admission has a mean Glasgow Coma Scale of 13 or somnolence.<sup>17</sup> Language disorders are difficult to assess (71.3%) when the patients are admitted to the hospital, because the patients come in a somnolence and sopor state; whereas

on discharged from the hospital the patients reported no language disorder. Moreover, the percentage of motoric condition of the patients who are in hemiparesis/hemiplegia condition on admission decreased on discharge. The most prevalent GOS at admission is GOS 3 (76%), which is categorized as a bad outcome, indicating that many patients have severe disability.<sup>13</sup> After treatment, most patients have GOS 4 which is a mild disability or GOS 5 which is in good recovery,<sup>13</sup> similar to study showing that cerebral toxoplasmosis patients who survive would have a good functional outcome.<sup>16</sup>

The level of consciousness has a relationship with the patient's functional outcome because it can describe the condition of the disease and damage of the brain.<sup>18,19</sup> In this study, the majority of patients presented with somnolence condition and have a good outcome after treatment, conform the study showing that patients with coma and sopor would have poor outcomes of GOS, whereas somnolence and *compos mentis* have good outcomes.<sup>20</sup>

The demographic characteristics of cerebral toxoplasmosis patients have a mean age of 34 years and the majority are male (76%), and this is in accordance with several other studies.<sup>21,22</sup> Cerebral toxoplasmosis is a disease that causes clinical manifestations related to central nervous system disorders.<sup>4,23</sup> A decrease in consciousness is the most common complaint.<sup>16</sup>

The CT scan results showed that the majority of patients have mass or lesions in the brain. Moreover, anti-toxoplasma IgG has reactive results, and CD4 cells are low. The CT scan results may show several lesions, hypodensity, ring-shaped, accompanied by edema around the lesion in the basal ganglia and corticomedullary junction.<sup>24,25</sup> In general, anti-toxoplasma IgG patients have positive/reactive results and low CD4 count.<sup>26</sup> CD4 has an important role in suppressing the activation of *T. gondii*. More than 95% of cerebral toxoplasmosis is an activation of latent infection, especially in patients with CD4 levels <100 cells/mm<sup>3</sup>.<sup>17,27</sup>

Treatment also determines the patient's functional outcome. In our study, patients have been given a combination treatment of pyrimethamine and clindamycin. However, other combination of treatment may exist such as a combination of pyrimethamine and sulfadiazine, or a combination of pyrimethamine, clindamycin, and 1% cotrimoxazole.<sup>16,28</sup> Patients receiving

pyrimethamine and sulfadiazine as first-line treatment have a better treatment success rates.<sup>26,29</sup> Patients who are intolerant or allergic to sulfadiazine can be given clindamycin. Although it is known that the combination treatment of pyrimethamine and clindamycin has a lower effectiveness than the combination of pyrimethamine and sulfadiazine.<sup>16</sup> This combination is given because of the lack of sulfadiazine preparations in Indonesia.

The length of stay for surviving patients has a mean value of 15 days (interquartile range 12–19), and clinical improvement has been observed after 10 days of successful treatment.<sup>17</sup> In more severe levels, the duration of treatment may be longer.<sup>16</sup> Previous study has shown that the average of length of stay for living patients was 16.9 days in hospital and the median for patients who died was 15 days (interquartile range 3–61).<sup>30</sup>

Interestingly, the cause of death is not caused by neurological disorders and about 10% is not known for certain. However, the cause of death may be due to neurological disorders in other areas.<sup>16</sup> The difference is because most patients have other comorbidities such as pulmonary infections and severe metabolic disorders.

The limitation of this study is that the relationship between the level of patient improvement and the treatment carried out has not been explored further, therefore further study is needed.

To conclude, most of the patients with cerebral toxoplasmosis come to the hospital with severe disabilities. During the treatment, 27.6% patients died, and patients who are survived have mild disability. The Glasgow Outcome Score improved after hospitalization, suggesting that GOS can be used for reliable assessment.

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