Original Research

COGNITIVE, MOTOR, AND LANGUAGE ASSESSMENT IN CHILDREN WITH HUMAN IMMUNODEFICIENCY VIRUS

Putu Indah Budi Apsari[1], I Nyoman Supadma[2], Ketut Dewi Kumara Wati[3], I Wayan Dharma Artana[3]
[1]Department of Microbiology and Parasitology, Faculty of Medicine and Health Sciences, Universitas Warmadewa, Bali, Indonesia
[2]Famili Husada Hospital, Bali, Indonesia
[3]Department of Child Health, Universitas Udayana/ Sanglah Hospital, Bali, Indonesia

ABSTRACT

The cognitive, motor and language aspect of HIV-infected children is an important issue affecting their quality of life. The capute scale, divided into Cat and Clams scores, is commonly used to assess children's cognitive, motor, and language functions. This study assessed Cat and Clams' scores of HIV-infected children. We performed Cat and Clams assessment on 136 children consisting of 68 HIV-infected children and 68 normal children as control aged 0-36 months. The Capute scale examined both groups at the first meeting (first month), and for the rest six months, we evaluated the progress of cognitive, motor, and language development. In the first meeting, we found that HIV-infected children had significantly low capute scores than the control group. The sixth-month Capute score in HIV-infected children was also significantly lower than the control group. HIV-infected children had lower Capute scores than normal children.

***Keywords**: HIV; child; virus; CAT/CLAMS*

Correspondence: Putu Indah Budiapsari, Department of Microbiology and Parasitology, Faculty of Medicine and Health Sciences, Universitas Warmadewa, Bali, Indonesia. Email: putuindah51@yahoo.com

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Highlights:

1. HIV-infected children had lower capute scores than normal children.
2. HIV child age range 12-24 months almost suffer delayed speech, and were in suspect criteria was founded.

INTRODUCTION

According to World Health Organization (2022), children with HIV infection risk developmental and behavioral challenges. Worldwide, AIDS currently accounts for 3% of deaths in children under five years of age—and 6% of those in sub-Saharan Africa, where AIDS has become one of the major killers of young children. One in seven people dying of HIV-related illness worldwide is a child under 15 years old. Most of these children acquire HIV from their HIV-infected mothers during pregnancy, birth, or breastfeeding. With successful antiretroviral interventions, the risk of mother-to-child HIV transmission can be reduced to 2%. However, such interventions are still not widely accessible or available in most resource-limited countries, where the burden of HIV is highest. An estimated 1,500 children get newly infected with HIV every day. The number of children receiving ART increased from about 75,000 in 2005 to almost 200,000 in 2007.

HIV infection adversely affects growth, morbidity, mortality, and neuro-development (Wedderburn et al. 2019). The virus can enter the central nervous system (CNS) during pregnancy, resulting in neuronal injury in the developing brain (Rie et al. 2007). This neuronal injury causes progressive encephalopathy in children. Delays are seen in cognitive, language, and motor

functions (Rie et al. 2007). The prevalence of these delays may be as high as 60% (Baillieu & Potterton 2008, Rie et al. 2007). HIV-associated central nervous system (CNS) diseases are prevalent in countries with limited treatment resources. Notably, in these parts of the world, perinatally infected children and adolescents show significantly impaired neurocognitive performance compared to the uninfected population (Weber et al. 2017). Clinical features include loss or failure to achieve appropriate developmental milestones, impaired brain growth, and global or selective impairments in cognitive, language, motor, attention, behavior, and social skills that may affect day-to-day functioning (Walker et al. 2013).

Clinically and immunologically, stable HIV-infected children had more frequent behavioral problems and lowered developmental and cognitive scores than established childhood norms (Nozyce et al. 2006). Some degrees of cognitive decline may present even in the early and asymptomatic stages of HIV infection. The benefits of antiretroviral treatment for cognitive performance can be detected after only a few weeks of follow-up. Supadma et al. (2020) stated a positive correlation exists between CD4 and Capute score of HIV children.

Andrade et al. (2012) stated that HIV infection in children could cause brain damage in the form of neurocognitive disorders. Younger HIV+ children also have lower scores in various domains of development while still having the most significant potential for benefit from early intervention (McHenry et al. 2018). Untreated HIV infection in children was associated with the development of cognitive, motor, language, and psychological impairment. Early developmental delays in language and cognitive abilities can affect various daily life functions (Levy 2018). Early identification and intervention can prevent cognitive and language impairment.

A capute scale is a screening tool that is widely used to evaluate developmental milestones, such as cognitive, language, and visual-motor, first published by Capute and Biehl in 1973 and revised by Capute and Accardo in 1978. Capute scale consists of two examinations: the cognitive adaptive test (Cat) and the clinical linguistic and auditory milestone scale (Clams). Differential performance on the significant development streams (motor, language, problem-solving, and adaptive) can be used to formulate and confirm neurodevelopmental diagnoses.

The Capute Scales are composed of CAT and CLAMS, an easy and practical screening neurodevelopmental assessment test for HIV-infected children in an outpatient setting. With the ease of this test, we could incorporate it into routine practice and early detect children with delayed development who benefited from the early stimulation program (Vanprapar et al. 2005). This study assessed cognitive, motor, and language development in HIV-infected children compared to HIV-negative children using Capute scales.

MATERIALS AND METHODS

The study was conducted in Sanglah Hospital and Werdhi Kumara kindergarten in Bali, Indonesia, from December 2013 to May 2014. The prospective cohort analytical study recruited children aged 0-36 months as participants. The target populations were HIV–infected children and normal children. The status of HIV-infected children was assessed using medical records and confirmed diagnosis by several examinations that met the criteria of HIV infection. The control group was defined by no record of HIV infection and another comorbid disease. The inclusion criteria were children aged 0-36 months in stable clinical conditions whose parents or guardians were willing to participate by signing informed consent and filling out the questionnaires. Exclusion criteria were children with co-morbidities disease, loss to follow-up, or their parents refusing to participate. We targeted 68 subjects per group selected by consecutive sampling.

HIV subjects and normal subjects were tested by Cat and Clams score of HIV-infected children compared to normal children. The research sample was followed for six months to assess the probability differences between the first examination and the upcoming six months examination result.

CAT/ CLAMS is a 100-item scale administered in a standardized manner in two parts and is obtained through observation (CAT) and parenteral report (CLAMS). CAT consists of visual-motor problem-solving items that are performed directly with the child. CLAMS item consists of language acquisition. A score was derived for CAT and CLAMS separately. CAT/ CLAMS score is the numerical average of the two, converted to a developmental quotient (DQ) by dividing the total score by the chronological age in months and multiplying by 100. The DQ of 85 to 125 is normal, 70 to 85 is borderline, and under 70 is delayed. Cat and Clams score between HIV- infected group and the normal group was tested by independent

t-test. The Mann-Whitney U test tested Cat and Clams scores between the first and six months of examination. This study was approved by the Ethics Committee of the Research and Development Unit, Universitas Udayana/Sanglah Hospital, Bali, Indonesia.

RESULTS

A total of 136 subjects were selected, consisting of 68 samples in the HIV-infected group, and 68 samples were selected as the control group. Based on the characteristics of both sexes in HIV and control groups, it was found that 54.5% of the sexes in the HIV group were mostly male as many as 37 patients, while 55.9% of the control group was mostly female, with as many as 38 patients. The average age of both groups was 21 months old, while the age range in both groups was mostly 12-24 months old. There were 30 patients in the HIV group undernourished (44.1%) and three patients malnourished (4.4%), but the control group was almost in good nutrition. Besides, family income in the HIV group was lower than in the control group. In socioeconomic grouping, 25 patients had a low economic state (36.8%), and 39 had a medium economic state (57.4%). In the control group, the patients were predominantly of medium-high socioeconomic status. We found no difference in parents' educational levels between groups. There were 68 subjects with HIV. The characteristics of subjects in the infected group are shown in Table 2. HIV groups were mostly 31 males aged 12-24 months (48.4%). There were 39 patients in the asymptomatic stage (57.4), while 14 patients were in the mild stage (20.6%), 13 patients in the moderate stage (19.1%), and two patients in the severe stage (2.9%), but all patients were in stable condition as they were treated with antiretrovirals.

Table 1. Characteristics of subjects

Subject characteristics	HIV group n = 68	Control group n = 68
Gender, n (%)		
Male	37 (54,5)	30 (44.1)
Female	31 (45)	38 (55.9)
Age (Month), Mean (SD)	21.3 (8.9)	21.7(8.9)
Range of age (n%)		
0-12 Months	14 (20.6)	17 (25.0)
12-24 Months	31 (25.6)	33 (48.5)
24-36 Months	23 (33.8)	18 (26.5)
Nutritional state (n%)		
Normal	35 (51.5)	68 (100)
Undernourished	30 (44.1)	-
Malnourish	3 (4.4)	-
Family income (n %)		
< 1 Million IDR	28 (41.2)	0 (0)
1-2.5 Milion IDR	32 (47.1)	30 (44.1)
2.5-5 Milion IDR	8 (11.8)	38 (55.9)
Socio-economic state (n%)		
Low	25 (36.8)	0 (0)
Medium	39 (57.4)	34 (50)
High	4 (5.9)	34 (0)
Mother educational level		
Elementary School	1 (1.5)	1 (1.5)
Junior High School	20 (29.4)	20 (29.4)
Senior High School	41 (60.3)	41 (60.3)
Vocational Degree	4 (5.9)	4 (5.9)
Bachelor Degree	2 (2.9)	2 (2.9)
Father educational level		
Elementary School	3 (4.4)	3 (4.4)
Junior High School	21 (30.9)	21 (30.9)
Senior High School	40 (58.8)	40 (58.8)
Vocational Degree	3 (4.4)	3 (4.4)
Bachelor Degree	1 (1.5)	1 (1.5)

Table 2. Characteristic of HIV infected children

Characteristic	Frequency (%)
Gender	
Male	37 (54.5)
Female	31 (45.5)
Age	
0-12 month	14(20.5)
13-24 month	31(45.5)
25-36 month	23(33.8)
Stage of infection	
Asymptomatic	39 (57.4)
Mild	14 (20.6)
Moderate	13(19.1)
Severe	2 (2.9)
Developmental state (6 months examination)	
Mental retardation	1 (1.5)
Delayed speech	2 (2.29)
Normal	40 (58.8)
Suspect	25 (36.8)
Clinical manifestation	
Gastro-Intestinal Tract (diarrhea)	2 (2.9)
Gastro-Intestinal Tract (vomiting)	1 (1.5)
Upper Respiratory Infection	17 (25)
Skin Hyperpigmentation	1 (1.5)
No Complaint	42 (61.8)
Wasting syndrome	5 (7.4)

Table 3. The result of the CAT/CLAMS examination in the HIV group

Developmental State	First examination				6th-month examination			
	CAT		CLAMS		CAT		CLAMS	
	70-85	85-120	70-85	85-120	70-85	85-120	70-85	85-120
Mental retardation (n)	1	0	1	0	1	0	1	0
Delayed speech (n)	1	1	3	0	1	1	2	0
Normal (n)	0	40	0	3	0	6	0	42
Suspect (n)	25	0	49	0	59	0	24	0

Table 4. The result of the CAT/CLAMS examination in the control group

Developmental State	First examination				6th-month examination			
	CAT		CLAMS		CAT		CLAMS	
	70-85	85-120	70-85	85-120	70-85	85-120	70-85	85-120
Normal (n)	0	62	0	64	0	68	0	68
Suspect (n)	6	0	4	0	0	0	0	0

Table 5. The difference in CAT/CLAMS scores between HIV and control groups

CAT/CLAMS scores	HIV group (median)	Control group (median)	p-value
First month			
CAT	86.6	91.0	0.01
CLAMS	86.35	92.45	0.01
Sixth month			
CAT	86.35	92.35	0.01
CLAMS	85.65	91.65	0.01

After the sixth month's examination, mental retardation was found in 1 patient (1.5%), the delayed speech was found in 2 patients (2.29%), while 25 patients were suspect (36.8%), and 40 patients (58.8%) were mostly in normal developmental milestone. Clinical manifestation in the HIV group was found in the gastrointestinal tract, such as diarrhea and vomiting, upper respiratory tract infection, skin hyperpigmentation and wasting syndrome, and others mainly without complaint. We selected HIV subjects in clinically stable conditions and controlled by antiretroviral treatment, and able to undergo the examination.

In Table 3, we showed the first CAT examination of the HIV group. We found one patient with mental retardation, one patient with delayed speech, 25 patients were suspects and 40 patients within normal limits. CLAMS examination resulted in 1 patient suffering from mental retardation, three patients with delayed speech, and 49 were in suspect criteria. After six months of CAT examination, we found the same patients still in mental retardation, one in delayed speech, and 59 in suspect criteria. There was an increasing number of subjects in suspect criteria. As a result of the CLAMS examination, one patient was still in mental retardation, and two patients were in delayed speech. There was an increase in normal subjects from 40 to 42 and a decrease in suspect subjects from 25 to 24. The milestone development in the HIV group tended to be abnormal or impaired, but in the control group, almost all subjects were within the normal limit (Table 4).

DISCUSSION

Using CAT/CLAMS assessment, this study breaks down neurocognitive and psychosocial functions among HIV-infected children using CAT/CLAMS assessment. Based on the characteristics of the subjects, the HIV group was predominantly male, but the control group was predominantly female. The same result was stated by Lindsey et al. (2007) that HIV-infected children were mostly males. Kube et al. (2000) found that male children tend to have cognitive problems. In contrast to a study by Whitehead et al. (2014), the HIV-infected children were primarily females. On the contrary, Nakasuja et al. (2012) stated that HIV-positive females suffered more severe cognitive impairments in comorbid psychosis.

We found that HIV children aged 12-24 months almost suffered delayed speech and were in suspect criteria. The first 24 months of life is technically denoted as the infancy period. It was the time when a child's brain underwent rapid development. During this phase, a child attains several motors, cognitive, and behavioral milestones.

Based on their socioeconomic status, HIV children were found to have poorer socioeconomic status, similar to the one found in the previous study by Bunyasi and Coetzee (2017). We found the educational level of their parents was the same in both groups. The result is concordance with a study by Smith et al. (2006) that no significant correlation was found between cognitive score and maternal educational level. Another study by Bunyasi and Coetzee (2017), Bello et al. (2013), and Ngoma et al. (2014) stated that the HIV child had low-educated parents, especially maternal educational level.

The difference in CAT/CLAMS scores between HIV and control group

We found a significant difference in CAT and CLAMS scores of the HIV group compared to the control group in the initial examination ($p<0.01$) and also in the sixth-month examination ($p<0.01$). This result was in contrast to that of Bruck et al. (2001), where there was no significant difference in CAT/CLAMS scores between positive and negative HIV groups.

This might be caused by the early treatment of ARV that could maintain CD4 levels and prevent brain damage due to encephalopathy HIV. Meanwhile, poor ARV adherence was correlated with poorer global neurocognitive functioning and a deficit in working memory.

Our finding was supported by Tahan et al. (2006), that observed significant differences in CAT/CLAMS scores between HIV with control groups, although the median score was still in the normal range. A previous study conducted by Nakasuja et al. (2012) found differences in cognitive function in individuals with HIV positive and HIV negative with psychosis. They found that the HIV group had higher cognitive function than the control group ($p <0.001$).

Bruck et al. (2001) observed significant differences in the mean of CLAMS scores between the HIV and control groups, and the HIV group had lower CLAMS scores than the control group. Both groups were followed for seven years. We also found significantly lower CLAMS scores in the HIV group than in the control group, both during the first and six-month examinations ($p<0.01$). As declared previously by Redmond et al. (2016), HIV exposure was the risk for persistent language impairment, such as delayed speech. Walker et al. (2013) stated that neurological impairment in HIV resulted from HIV encephalopathy. The decrease in CAT/CLAMS scores must be the result of neurophysiological damage that worsened with age. The difference in cognitive and psychosocial development between HIV and the control group must also be the result of brain abnormalities. Children perinatally exposed to HIV were at high risk for language impairment (Rice et al. 2012). Clinically and immunologically, stable HIV-infected children had more frequent behavioral problems and lowered developmental and cognitive scores than normal children.

Strength and limitation

The study had a large sample size of 136 children, increasing the statistical power of the results. The study focuses on an important issue affecting the quality of life of HIV-infected children.The study used a widely recognized and standardized assessment tool, the Capute scale, to evaluate cognitive, motor, and language development in both the HIV-infected and control groups. The study was conducted in a specific setting and population, limiting the generalizability of the findings to other contexts and populations.The study did not investigate the causes of the observed differences in Capute scores between HIV-infected and normal children, such as the effect of HIV on brain development.

CONCLUSION

The HIV group had lower cognitive, motoric, and language performance than a normal child by Capute scores assessment from the first- and sixth-month examination. Early detection and intervention of neurodevelopmental problems must be programmed to prevent progressive loss of cognitive, motoric, and language ability. Routine control of clinical manifestation and antiretroviral treatment in the HIV-infected group should also be continued to minimize the risk of neurological damage that could affect the neuro-developmental milestone.

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Conflict of interest

None.

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Author contribution

INS, KDKW, and DR were conseptual design and collected and analysis data. PIBA write and revised the

manuscript. All author was manuscript arrangement to the final content.

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