Clinical and immunologic features of HIV-infected children in South Kalimantan, Indonesia

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***Background**: Human Immunodeficiency Virus (HIV)-infected children is a global problem which should be addressed. The increasing prevalence of pediatric HIV become a burden for many countries.*
***Objective**: To compare of clinical stage and degrees of immunology in children with HIV infection*
***Materials and Methods**: This retrospective cross sectional study was conducted at two referral hospitals in Banjarmasin, South Borneo. Data collected from medical record of pediatric HIV infection patients diagnosed from January 2006 until January 2017. Diagnosis performed by three times serology test. Each variables was performed normality data test. Comparison test between variables were evaluated by Mann Whitney U test. Microsoft excel and SPSS 21 were used for data analysis.*
***Results**: There were 40 patients with the median age was 6.9 years old. Male to female ratio was 1.2:1. Perinatal as risk factor of transmission occurred to 37 patients (92.5%). The most frequent clinical presentation and diagnosed condition were severe malnutrition in 62.5%, pulmonary tuberculosis (TB) in 50%, pneumonia in 25%, and oral candidiasis in 25%. Six (15%) children were asymptomatic. The median CD4 cell count at presentation was 431.94 cells/µL. Four (10%) children had advanced immunodeficiency and 18 (45%) children had severe immunodeficiency. Mortality rate at presentation was 30%. There were significantly differences of CD4 count between clinical stage I and II (p=0.002) and clinical stage II and III (p=0.011)*
***Conclusion**: HIV-infected children had sex equal distribution. Most frequent risk factor of transmission was perinatal infection. Pulmonary TB was the most frequent co-infection condition. Most of HIV-infected children in this study were immune-suppressed. There were differences of CD4 count between each clinical stage.*

***Keywords**: HIV-infected children, malnutrition, Pulmonary TB, immunodeficiency, perinatal infection.*

Introduction

Human Immunodeficiency Virus (HIV) infection and Acquired Immunodeficiency Syndrome (AIDS) remain as global health problem challenges. HIV is an RNA virus, including to retroviruses which attack white blood cells especially CD4 lymphocyte cells. Patients with HIV infection require antiretroviral therapy to reduce the amount of virus in the body so as not to fall into AIDS. Patients with AIDS require antiretroviral therapy to avoid opportunistic infections which can lead to complications causing death. [1-3]
HIV in children is a global problem which still needs to be addressed. According to WHO, in worldwide by 2015, an estimated 1.8 million (1.5-2 million) children under 15 years old live with HIV. There are 150,000 newly HIV-infected children each year. Every day there are 400 new cases of children with HIV. One hundred thousand children die each year from AIDS and related illnesses and 12 children died because of AIDS every hour. More than 90% of children get HIV infection through mother-to-child transmission. Of the total children with HIV, only 49% were receiving antiretroviral therapy (ART). Without ART, 26% of infected children at the postnatal and 52% of infected children at the perinatal died in the first year of infection. In Indonesia, the cumulative number of HIV patients from 1987 to September 2014 was 150,296 and for AIDS patients 55,799. There was an addition of 39% of new cases of HIV patients from September 2014 to June 2016 and 47.95% of new cases of AIDS patients. Six point two percent of them aged 0-19 years. Risk factor for AIDS were 2.7% from perinatal. In South Kalimantan, the total accumulative cases of HIV infection reported since 1987 to second quarter 2016 were 1,036 patients. [3-8]
Opportunistic infections (OIs) from HIV infection were the causes of mortality in HIV-infected children. CD4 count cell play role to the degree of immunity of HIV-infected children. This is in line with the OIs of HIV-infected children. Meta-analysis and systematic review in 2016 said that the highest incidence of OIs were both pulmonary TB and extra-pulmonary, oral and esophageal candidiasis, and cryptosporidium diarrhea. Platt L et al mentioned that hepatitis C infection was six times higher in patients with HIV infection. TB and bacterial infections were a major cause of HIV/AIDS patients hospitalized. The highest mortality among adult and pediatric HIV/AIDS patients were also caused by TB and bacterial infections. Co-trimoxazole administration as prophylaxis may decrease the incidence of IOs of HIV/AIDS patients [9-13]. HIV infection increases the risk of malnutrition in children. Metabolic changes and abnormal cytokine production also play a role in the incidence of malnutrition in HIV patients. Caloric requirement in HIV-infected children is higher than uninfected children. Children with HIV infection are usually thinner, lower in weight, and shorter than malnourished children without HIV infection. [14-15]

Methods

Subjects

This retrospective cross-sectional study was conducted in two referral hospitals that have VCT policlinic facilities in South Kalimantan, which are Ulin General Hospital and Ansari Saleh General Hospital. It was approved by the Ethics Commission of the Faculty of Medicine, Lambung Mangkurat University, Banjarmasin, South Kalimantan, Indonesia. The study was conducted from January to June 2017. Data taken from the medical records of pediatric patients diagnosed with HIV infection from January 2006 to January 2017. Diagnosis performed by serology three times and all of them were positive. The sampling method was total sampling.

Samples collection

Names, number of medical record, age and date of birth, gender, address, date of diagnosis, risk factors, start date of ART , type of antiretroviral drugs, opportunistic infections acquired, the weight, determination of nutritional status, CD4 cell count at diagnosis, and mortality status were recorded in this study. Determination of clinical and immunology stage of HIV infection were according to WHO criteria[2].

Statistical analysis

Data entered in tables in Microsoft Excel. Comparison test between clinical stage and immunologic stage were performed by Mann Whitney U test. Data analysis using SPSS for Windows version 21.

Results

There were 40 patients HIV-infected children in VCT policlinic during January 2006 to January 2017. Twenty two (55%) patients were boys. Male to female ratio in this study were 1.2:1. There were 37 (92.5%) patients with perinatal risk factor.

Table 1. Baseline characteristic of children with HIV

No.	Variables		n(%)
1.	Gender	Male	22 (55)
		Female	18 (45)
2.	Ages	< 2 years old	4 (10)
		2-10 years old	27 (67.5)
		>10 -18 years old	9 (22.5)
3.	Nutritional status*	Well-nourished	7 (15.79)
		Malnourished	3 (5.26)
		Severe malnourished	25 (71.42)
4.	Risk factor	perinatal	37 (92.5)
		Blood transfusion	2 (5)
		Unknown	1 (2.5)
5.	ARV	on ARV	24 (60)
		not/yet	13 (32.5)
		Unknown	3 (7.5)
6.	Type of ARV	FDC for children	17 (70.8)
		AZT+3TC+NVP	6 (25)
		AZT+3TC+EFV	1 (4)
6.	Mortality	Male	7 (17.5)
		Female	5 (12.5)
		Total	12 (30)
7.	Alive	Male	14 (35)
		Female	14 (35)
		Total	28 (70)

*data were not complete due to loss of follow up patients.

FDC is the most widely used type of antiretroviral (60%) as an option for HIV therapy in children. The mortality rate of HIV-infected children in this study was 30%. Most of HIV-infected children (62.5%) were severe malnourished. Pulmonary TB is the most common type of clinical symptom and opportunistic infection (50%) in pediatric HIV patients and followed by pneumonia (25%). There was 2.5% HIV-infected children with Global Developmental Delayed (GDD). Fifteen percent of children with HIV were asymptomatic. The mean Hb in HIV-infected children was 11.99 g/dl. There was a two-time increasing of SGOT/AST in two patients

and a double increasing of SGPT/ALT in one patient. Twenty-two (50%) of pediatric patients are at advanced stage and severe immunodeficiency. There were significant difference in CD4 cell count between children with clinical stages one and three (p = 0.002), and in children with clinical stages two and three (p = 0.011).

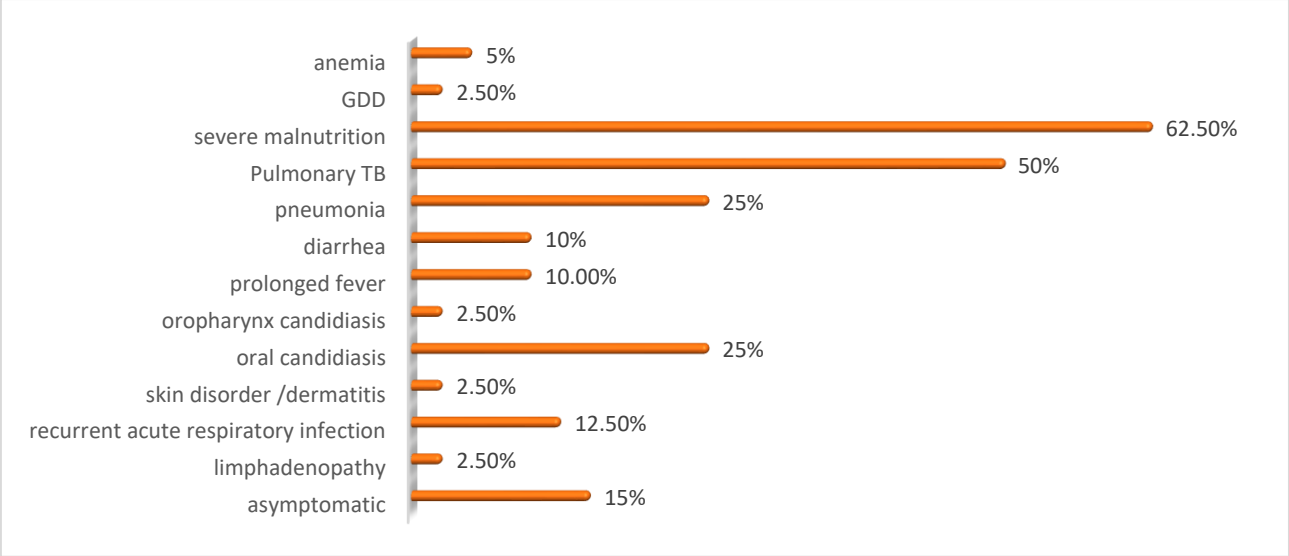

Figure 1. Clinical manifestation of children with HIV

Table 2. Mean of routine blood test and liver enzyme

No	Variables	Mean	±	SD
1.	Hb	11,99	±	2,56
2.	Leucocytes	7115,56	±	1685,61
3.	Platelet	327111,11	±	148108,4
4.	SGOT/AST	60	±	42,82
5.	SGPT/ALT	41,4	±	36,26

Table 3. Comparison between immunologic parameter and WHO clinical stage in children with HIV

Variables	n (%)	Median CD4 count* (min-max)	Immunodeficiency classification of WHO *(%)*			
			NS	*Mild*	*Advanced*	*Severe*
Clinical stage						
1	9 (22.5)	833,56 (127-2622)	4 (44.44)	2 (22.22)	2 (22.22)	1 (11.11)
2	9 (22.5)	436,78 (11-1068)	2 (22.22)	5 (55.55)	0 (0)	2 (22.22)
3	16 (40)	156,43 (9-730)	1 (6.25)	0 (0)	2 (12.5)	12 (85.71)
4	5 (12.5)	593,50 (6-2168)	1 (20)	0 (0)	1 (20)	3 (60)

**baseline* CD4 before ART. NS: *non-specified* (CD4 >500/mm^2), *Mild*: CD4 350-499/mm^2, *Advanced*: CD4 200-349/mm^2), *severe*: <200/mm^2 atau < 15%.[16]

Table 4. Comparison between CD4 count and clinical stage

no.	Variables		p-value*
1.	CD4	Clinical stage 1 Clinical stage 2	0,489
		Clinical stage 1 Clinical stage 3	0,002
		Clinical stage 1 Clinical stage 4	0,199
		Clinical stage 2 Clinical stage 3	0,011
		Clinical stage 2 Clinical stage 4	0,414

*Mann Whitney U test was performed

Discussion

This study demonstrated basic characteristics, clinical presentation features, laboratory features, and clinical stage in pediatric HIV-infected patients in two referral hospitals with VCT policlinic facilities in Banjarmasin. This study showed that 55% of patients with HIV were male. Research conducted in Iran in 2015 showed a number that did not differ much, as 56% in male patients[17]. Similar findings were made in research conducted in Nigeria and Zimbabwe, 54.4% and 53% respectively. [18-19]

A study by TREAT conducted in five countries in Southeast Asia, Cambodia, Indonesia, India, Thailand, and Vietnam showed that the risk of exposure to HIV during childhood at perinatal was 94.1% [20]. This was not much different from the results of this study which was 92.5% of children with HIV were acquired through perinatal infection.

Mortality rate of HIV in children in the Cohort study in Nigeria was 18.2% [19]. In this study, mortality rate was 30%. The Differences can be caused by the research method undertaken. In this study, a retrospective method was conducted by collecting data since 2006. Therefore, mortality rates were higher due to long periods of time. While in study in Nigeria was a prospective study which only followed the patient for the last six months.

The most common clinical features of children with HIV were cough, weight loss, and hepatomegaly [19]. In Ferrand et al study found 59% of children diagnosed with HIV infection and pulmonary TB infection [18]. There were 100% weight loss children at the time of HIV diagnosis in a study conducted in Iran [17]. Research in India mentioned that the most common clinical features were fever and chronic diarrhea. There were 18.6% of HIV-infected children with pulmonary TB [21]. Clinical symptoms of cough can be caused by TB co-infection or pneumocystis carinii pneumonia (PCP) infection. The diagnosis of pulmonary TB in 50% of patients in this study based on thorax X-rays and TB scores. Several existing studies did not mention the comorbid diagnosis obtained in children with HIV. The low rate of pulmonary tuberculosis infection in the Indian study compared to this study, since the majority of patients were found in clinical stages one and two with a mean CD4% greater than 15%. [21]

The mean Hb concentration in this study was 11.99 g/dl with a standard deviation of 2.56. The TREAT study conducted in Asia Pacific showed the mean Hb was 10.4 g / dl [20]. A study in Uganda showed a median Hb value was 10.5 g/dl. The lowest Hb was 4.3 g / dl [22]. The lowest Hb in this study was 7.4 g/dl. Low levels of hemoglobin or anemia in children with HIV are caused by many factors. Poor nutrition in patients can lead to micronutrient deficiency resulting in anemia. Chronic infection, autoimmune hemolysis, drug side effects, and persistent B19 parvovirus infection can cause anemia in HIV infection. Zidovudine (AZT) administration can have side effects of bone marrow suppression that may cause anemia[23].

A study conducted by Agarwal et al in 2007 showed a significant difference in CD4% between clinical stages. The decrease in CD4 cell count may lead to a decrease in the immune system resulting in opportunistic infections[21]. WHO clinical stage is a degree of clinical features in HIV patients demonstrated by the accumulation of symptoms including the number of opportunistic infections acquired. The more opportunistic infections acquired, the higher the clinical stage[16]. In this study, there were only significant differences in CD4 counts between clinical stages one and two, and clinical stages two and three.

Weakness of study

This study could not be analyzed by Kruskall Wallis test because the data did not meet the criteria.

Conclusion

In conclusion, HIV-infected children had sex equal distribution. Most frequent risk factor of transmission was perinatal infection. Pulmonary TB was the most frequent co-infection condition. Most of HIV-infected children in this study were immune-suppressed. There were differences of CD4 count between each clinical stage

Conflict of interest

We declare that we have no conflict of interest.

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