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Risk factors associated with mortality in HIV-infected children at Dr. Soetomo Hospital, Surabaya

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Abstract

Backgrounds Morbidity and mortality among HIV-infected children in Indonesia are increasing. Risk factors for mortality in these children have not been well described.

Objective To analyze risk factors for mortality in HIV-infected children hospitalized in Pediatric Ward Dr. Soetomo Hospital ,Surabaya.

Methods A cross sectional study of HIV-positive children hospitalized in the pediatric ward Dr. Soetomo Hospital, Surabaya from January 2012 until April 2015 was conducted. Factors associated with mortality were analyzed using chi square test. Multivariate analysis was assessed using logistic regression analysis.

Results There were 100 admissions, 40 cases (readmission) and 14 others (incomplete data) were excluded. Out of the 46 admitted children (57% were male), 21 (45%) died. Median age of fatal cases was 30 (range 7-105) months and median length of stay (LoS) was 20 (range 1-60) days. Among death cases, 5 (23%) patients were new cases of HIV, belonged to clinical-stadium 4 (95%) and 12 (54,5%) were with severe immunological classification of HIV. Antiretroviral (ARV) therapy was administered in 9 (41%) patients. The most common cause of death was sepsis (64%), followed by respiratoy failure (23%). Mortality was significantly associated with severely wasted (P=0.026), PCP infection (P=0.036), and HIV clinical-stadium 4 (P=0.006). Logistic regression analysis revealed that HIV clinical-stage 4 was the only significant risk factor of mortality in HIV children (adjusted OR 9.167; 95% CI 1.003 to 83.767, P=0.05).

Conclusions Human immunodeficiency virus infection clinical-stadium 4 is a significant risk factor of mortality in HIV-infected children admitted to Dr. Soetomo Hospital.

Keywords: HIV-infected, children, mortality, risk factor

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Characteristics and clinical manifestations of infant dengue at Dr. Hasan Sadikin Hospital, Bandung

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Abstract

Background Dengue virus infection is a serious health problem all over the world. Infants in endemic areas are at risk for contacting dengue infection.

Objectives To observe the characteristics and clinical manifestations of dengue viral infection in infants.

Methods This is a retrospective, descriptive study which used medical records data of patients admitted in the pediatric ward of Dr. Hasan Sadikin Hospital, Bandung. The subjects were infants aged 1 to 12 months years old, with confirmed dengue virus infection, based on the WHO 2012 criteria, suggestive laboratory and serological findings of dengue infection.

Result Infant dengue was diagnosed in 22 of the 239 hospitalized children with clinical dengue, which was a considerable proportion (9.2%) ofthe total dengue infections. Dengue fever (DF), dengue haemorrhagic fever (DHF), dengue shock syndrome (DSS) were diagnosed in 9cases (42.8%), 6 cases (28.5%), and 1 case (4.7%) of 21 serologically confirmed infant dengue patients respectively. Three cases(14.2%) were dengue encephalopathy. Out of all the cases, 1 infant eventually died due to unusual manifestation of dengue. From physical examinations, we found that petechiae were present in 9 cases (42.8%), while pleural effusion was found in 3 cases (14.2%).The most common chief complaint was fever, while ptechiae were the most common evidence of bleeding manifestation.

Conclusion In this study, infant dengue is shown to have varied characteristics and clinical manifestations, ranging from self-limited disease to severe fatal illness, thus dengue infection remains difficult to recognize.

Keywords: characteristics, hemorrhagic fever, encephalopathy dengue, infant

Risk factors associated with mortality of HIV-infected children in Pediatric Ward Dr. Soetomo Surabaya

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Backgrounds: Morbidity and mortality among HIV-infected children in Indonesia are increasing. Risk factors for mortality in these children have not been well described.
Objective : To analyze risk factors for mortality of HIV-infected children hospitalized in Pediatric Ward Soetomo Hospital Surabaya.
Methods : A cross sectional study of HIV-positive children hospitalized in the pediatric ward Dr. Soetomo Hospital Surabaya from January 2012 until April 2015 was conducted. Factors associated with mortality were analyzed using chi square test. Multivariate analysis was assessed using logistic regression analysis.
Results : There were 100 admissions, 40 cases (readmission) and 14 others (incomplete data) were excluded. Out of the 46 admitted children (57% were male), 21 (45%) died. Median age of fatal cases was 30 (range 7-105) months and median length of stay (LOS) was 20 (range 1-60) days. Among death cases, 5 (23%) patients were new cases of HIV, belonged to clinical-stadium 4 (95%) and 12 (54,5%) were with severe immunological classification of HIV. Antiretroviral (ARV) therapy was administered in 9 (41%) patients. The most common cause of death was sepsis (64%), followed by respiratoy failure (23%). Mortality was significantly associated with severely wasted (p=0.026), PCP infection (p=0.036), and HIV clinical-stadium 4 (p=0.006). Logistic regression analysis revealed that HIV clinical-stage 4 was the only significant risk factor of mortality in HIV children (adjusted OR 9.167; 95% CI 1.003 to 83.767, p=0.05).
Conclusions: HIV clinical-stadium 4 was a significant risk factor of mortality in HIV-infected children admitted to Dr. Soetomo Hospital.

Keyword : HIV-infected, children, mortality, risk factor

INTRODUCTION

Since the early 1980s, more than 45 million people have become infected with Human immunodefficiency virus (HIV) worldwide and it is estimated that in 1998 alone nearly 6 million adults and children acquired HIV infection. More than 95% of all people living with HIV infection live in the developing world, mostly in sub-Saharan Africa.[1,2] The HIV epidemic among children is closely linked to that among women, since the vast majority of paediatric infections are the result of vertical transmission from mother to child. Vertical transmission of HIV infection can take place during pregnancy, delivery or postnatally through breastfeeding with the most stricking factor is viral load (VL). Rates of vertical transmission, in the absence of specific intervention range from 15-20% in Europe, 16-30% in the USA, 25-40% in Africa and 13-48% in South and South East. Indonesia has a relatively recent but rapidly growing globally, between 2002 and 2013, there was a 58% reduction in the number of new HIV infections among children (under 15 years of age).[3,4] Despite this, more than 240,000 children were infected with HIV during 2013 - around 700 new infections every day. In addition, millions more children every year are indirectly affected by the impact of the HIV epidemic on their families and communities. As prevalence of HIV infection in women of child bearing age increases, more children will be at risk of vertically acquired HIV infection.[5]

Human immunodeficiency virus (HIV) infection is a major cause of mortality and morbidity amongst children worldwide, with over five million women and 700,000 children having been infected since the start of the pandemic more than two decades ago (WHO, 2010).[5] Morbidity and mortality among HIV-infected children in Indonesia are increasing. Risk factors for mortality in these children have not been well described HIV epidemic that, apart from the Papua provinces, is concentrated in some key populations. According to the Indonesia AIDS Commission the number of HIVinfected individuals increased at least three-fold between 2009 and 2014. [3,5]
There were 3.2 million children living with HIV around the world at the end of 2013, 91% of these reside in sub-Saharan Africa. In the same year only 24% of children who needed antiretroviral treatment (ART) received it and 190,000 children died of AIDS-related illnesses.[1,2]

Recent studies in many children center care at a late stage of disease progression, such that mortality rates during the first few months of treatment are high. This study was undertaken to identify risk factor associated with mortality of HIV-infected children in Pediatric Ward Dr. Soetomo Surabaya.

SUBJECT AND METHODS

We evaluated medical records from all patients who were <18 years old when they hospitalized and got diagnose with HIV at Dr.Soetomo Hospital's Surabaya from January 2012 until April 2015. There were 100 admission we conducted to the study but only 46 were analyze (54 children was excluded because of readmission and incomplit data). The inclusion criteria were all childhood under 18 years old who were confirmed diagnose by PCR or rapid test or/and three serology methods, Pneumonia, Tuberculosis, PCP, Diarrhea, Urinary Tract Infection, Candidosis Oris, Enchepalitis, nutrition status, clinical stadium, imunological classification of HIV. The characteristic data including age, sex, parent"s HIV status, reason admitted, history of nutrition, age of fatal case, lenght of stay (LOS), HIV theurapy, CD_4 Counts performed, cause of the death were collected. We used chi square test with Fisher Test and $P<0.05$ considered significant as univariate analysis during collected data as recorded at the last hospitalized. Risk factors for mortality were evaluated using Logistic regression test and the multivariable model $P<0.05$ considered significant. All analyses were conducted in SPSS version 17.

RESULTS

During the study period, 100 admission with HIV-infected children were invited to participate and 46 were enrolled. The basic characteristic in this study (table 1) found that age of children were infected mostly in >1.5-5 (61.9%) years old. Female was 57.1% and mostly got breastfedding (85.7%). Median age of fatal case was at 30 (range 7-105) months were readmitted (76%). The median of CD_4 percent median 4.7 (range: 0.02-27.8) % with median CD_4 absolute median 60 (range: 1-1405) cells/m^2. Prevalence of the clinical stadium were stadium 4 95% and those with immunological classification of HIV was in Severe immunosupression (57%) and almost all of them got antibiotics because of the OI 89.1%, part of them got PCP

prophylaksis 73.9%, tuberculosis drug 69.6% and ARV 45.7%. Cause of the death mostly because of sepsis were 13 children (63.6%).

Table.1. Social Characteristics of mortality children with HIV infection admitted ward 2012-2014

Characteristics	(N=21)
Age (yr):	
<1.5	5 (23.8%)
≥ 1.5-5	13 (61.9%)
> 5	3 (14.3%)
Sex:	
Female	12 (57.1%)
Male	9 (42.9%)
Diagnosis:	
Serologic	45 (97.8)
PCR	1 (2.2)
Diagnosis:	
Presumptive	30 (65.2)
Confirmed	16 (34.8)
History of Nutrition	
Breastfedding	18 (85.7%)
Formula milk	3 (14.3%)
Nutritional status:	
Normal	1 (4.8%)
Wasted	2 (9.5%)
Severely wasted	18 (85.7%)
Age of fatal case	30 (range 7-105) months
LOS	20 (range 1-60) days
Reason Admitted	
New cases	5 (23%)
Readmitted	17 (76%)
Clinical-Stadium	
Stadium 3	1 (5%)
Stadium 4	20 (95%)
Immunological Classification of HIV	
Mild immunosupressive	1 (5%)
Moderate immunosupressive	8 (38%)
Severe immunosuppressive	12 (57%)
CD_4 Counts performed	31 (67.4%)
CD_4 percent	median 4.7 (range: 0.02-27.8) %
CD_4 absolute	median 60 (range: 1-1405) cells/m^2
Therapy	
ARV therapy	21 (45.7%)
TB drugs	32 (69.6%)
PCP prophylaxis	34 (73.9%)
Antibiotics	41 (89.1%)
ARV therapy	
Yes	9 (43%)
No	12 (53%)
Cause of Death	
Heart failure	3 (13.7%)
Respiratory failure	5 (22.7%)
Sepsis	13 (63.6%)

Table 2 and 3 show the risk factor of mortality in infected children with HIV among the subjects. These risk factors of mortality was seen in OI, clinical stadium and immunological classification of HIV, nutritional status, age, readmitted, ARV theuraphy were tested together in univariate and multivariate analysis, but were presentated in two tables for the purpose of clarity and easy understanding. In univariate analysis, severely wasted (p=0.026), PCP infection (p=0.036), and HIV clinical-stadium 4 (p=0.006) were found to be associated with mortality of children with HIV. However, at multivariate analysis HIV clinical-stage 4 was the only significant risk factor of mortality in HIV children (adjusted OR 9.167; 95% CI 1.003 to 83.767, p=0.05). the child's age, gender, CD4 counts, Tuberculosis, pneumonia, diarrhea, UTI, candidosis, Enchephalitis were not significantly associated with mortality of HIV in children.

Table 2. Mortality children with HIV infection

Variable	*OR (CI 95%)*	*P*
Age		0.98
Sex	1.00 (0.16-6.25)	1.000
Pneumonia	0.57 (0.10-3.27)	0.670
Tuberculosis	0.40 (0.06-2.80)	0.642
PCP	0.73 (0.04-13.45)	0.036
Diarrhea	0.50 (0.08-2.99)	0.660
Urinary Tract Infection	0.93 (0.03-2.19)	0.429
Candidosis Oris	0.40 (0.06-2.80)	0.642
Severely Wasted	0.06 (0.01-0.69)	0.026
Enchepalitis	0.40 (0.05-3.130	0.610
Clinical-stage 4	13.33 (1.54-115.83)	0.006
Severe Immunological Classification	0.06 (0.01-0.69)	0.550

Significant value is p<0,05 with *Chi square test/Fisher exact test*

Table 3. Multivariate analysis of risk factor Mortality children with HIV infection

Variable	*OR (CI 95%)*	*P*
PCP	4.909 (0.864-27.883)	0.073
Clinical-Stage 4	9.167 (1.003-83.766)	0.050

Significant value is p<0,05 with logistic regression test

DISCUSSION

In this present study, prevalence of mortality in children infected with HIV was 46 % among the subjects mostly cause by sepsis. The mortality risk factors identified in this study highlight several areas for potential improvement in pediatric treatment and monitoring algorithms. The increased mortality in younger children and those with low CD4 plus the growing body of evidence of improved outcomes in infant ART initiation argues for the early initiation of ART in HIV positive children.[6] In response, WHO treatment guidelines have recently been altered to recommend expansion of ART to all infants younger than 24 months and all young children with CD4 percentages lower than 25%. [4] As most HIV-infected children in our cohort were not enrolled at birth, our observed mortality rate is likely to underestimate the true mortality. Among children who enrolled within 3 months of birth, mortality was nearly eight times higher in HIV infected than HIV-exposed.[7] Causes of death among ARTnaive HIV-infected children and HIV-exposed children were similar and are the major causes of childhood mortality in developing countries.[8] As found elsewhere malnutrition was associated with mortality among HIV-infected children in our study, stressing the need to integrate nutritional rehabilitation into paediatric HIV care.[9]

Early initiation of ART during infancy is associated with reductions in mortality and HIV disease progression.[10] The lack of a significant effect of ART on mortality in our study is likely due to delays in starting ART, the small number of children that have been treated so far and the limited follow-up time among those on ART. The median age of fatal case was 30 (range 7-105) months with lenght of stay was 20 (range 1-60) days but only 43% got ARV and median CD_4 percent was median 4.7 (range: 0.02-27.8) % at initiation with CD_4 absolute median 60 (range: 1-1405) cells/m^2 this shows that many of these children were already severely immune suppressed and therefore had a poor prognosis even after starting ART. The WHO 2010 guidelines recommend initiating ART in all infants <2 years irrespective of CD4 counts. However, in reality, early ART initiation among infants still poses a great challenge particularly in rural settings given the unavailability of diagnostic PCR testing even in areas where PMTCT is offered. Although use of clinical symptoms symptoms to make a presumptive diagnosis of HIV is recommended in the absence

of virological testing, this requires trained personnel who are often lacking in rural areas.[4]

Lower CD_4 cell counts are associated with increased risk of mortality but also with increasing incidence of TB while the resence of TB disease is associated with reduced CD_4 cell counts. Consequently, a lower CD_4 cell count not only predicts and increases the risk of mortality but also influences the likelihood of developing TB and can play an intermediate role in the causal effect chain when assessing the impact of TB on mortality. [11] This may have resulted in underestimating the effect of TB on mortality by ignoring the effect that TB may have had on mortality through its mediation on CD_4 cell counts. Other potential time dependent confounders include TB treatment, HAART initiation, viral load or other time varying markers of immunosuppression.[11,12]

Resent research identified five significant and objective predictors ofmortality that are readily available at illness presentation. Except for the A–a O2 gradient, none of the significant predictors of mortality identified in multivariate analysis was strictly associated with the severity of underlying HIV disease or respiratory compromise from PCP. Instead, our results suggest that non-HIV-associated factors that reflect the presence of underlying medical co-morbidities and general severity of illness, namely age, injection drug use, serum total bilirubin and serum albumin, may be more accurate predictors of mortality from PCP than HIV-associated factors, such as CD4 cell count or history of opportunistic infection.[13] Age is a predictor that is widely used in risk stratification rules for community-acquired pneumonia, and correlates with the number of medical co-morbidities in HIV-infected patients. In addition, many studies have reported age and serum albumin as predictors of mortality not only for patients with PCP but also for HIV-infected patients requiring intensive care.[14]

CONCLUSION

In our conclusion, children with HIV clinical-stadium 4 was a significant risk factor of mortality in HIV-infected children admitted to Dr. Soetomo Hospital. While our prediction that oportunistic infection was potentially causing of mortality. So, this intitions need futher research to identifying patients who are at high and low risk for

death early in the hospital course, and therefore may assist clinicians in assessing severity of illness and more accurately deciding on management strategies.

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PERTEMUAN ILMIAH TAHUNAN KE-7 ILMU KESEHATAN ANAK IDAI (SURABAYA/ 31 OKT- 4 NOV 2015)

Tema: Enhancing The Equality of Quality in Pediatric Science

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