High CD_4 + T-cells Percentage and/or Low Viral Load are Predictors of 1-5 Years Survival in HIV-1 Vertically Infected Thai Children

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Abstract

Objective : Enrolling pediatric HIV children into the clinical trial of when to initiate antiretroviral therapy is a crucial ethical issue. CD_4 + T-cells percentage and /or viral load were able to identify potential cases of survival through 5 years of age.

Method : HIV infected cohort from 1992 to 1994 from Children's and Siriraj Hospitals were followed from 1 through 5 years of age. The outcome was survival or death. The predictors were CD4 percentage and viral load (without age and clinical status adjustment).

Result : 16 of 35 (45.71%) of the cohort survived through 5 years of age. The probability of survival increased to almost 100 per cent either with CD_4 + T-cells percentage of over 22 or viral load of less than 500,000.

Key word : CD_4 + T-cells Percentage, Viral Load, HIV-Infected Children, Survival

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Pediatric HIV infection has been recognized as one of the major public health problems. Before antiretroviral agents were available, most of the infected infants died earlier despite good quality of symptomatic and supportive care. When antiretroviral agents became available they were expensive, and were not affordable by everyone. Although life was extended, the quality of life was not perfect. The combination of antiretroviral agents which had a bad taste as well as inappropriate formulation for

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infants and children created poor compliance and adherence. Viral resistance was predicted in the near future. Physicians had to deal with more adverse reactions and disclosure problems. On the contrary, some infected children without antiretroviral agents still carried on normal life. It is not always clear which individuals would benefit from or need immediate antiretroviral agents. In designing the study trial answering the above question of when to initiate antiretroviral therapy by randomization of infected children to either antiretroviral agents or no treatment. The authors had to identify the cohort of low risk for disease progression to be enrolled into the study for ethical reason. Viral load and CD_4 + T-cells percentage are widely recognized as predictors

MATERIAL AND METHOD

The infected cohort from a prospective perinatal transmission study at Siriraj, Rajvithi, and Children's Hospitals in Bangkok enrolled from 1992 to 1994 were reviewed. The study was conducted before the AIDS Clinical Trials Group 076 study ended. Antiretroviral prophylaxis was not yet used to prevent mother-infant transmission and primary prophylaxis against pneumocystis carinii pneumonia was not used routinely for HIV exposed infants. Infants were considered HIV-infected if they had two positive DNA PCR tests or one positive PCR test and an AIDS-defining condition according to the CDC case definition(1).

The infants had study visits and blood specimens were drawn at birth, 1, 2, 4, 6, 9, 12, 24, 30, 36, 42, 48, 54 and 60 months of age for viral load and lymphocyte subset count according to published methods(2).

Low risk for disease progression were considered among those who survived through 1-5 years of age. The determination variables of predictive value of 100 per cent 5 years survival were independently analysed as

1. Cut off point of viral load giving 100 per cent specificity of death
2. Cut off point of per cent CD_4 + T-cells giving 100 per cent specificity of death

RESULT

Of the 295 children born in the cohort, 68 were infected (66 were subtype E). Twelve infants died within 1 month. Twenty one infants were lost to follow-up and their outcome could not be determined. Thirty five infants were included for analysis. In October 2000, sixteen infected children were still in follow-up and all of them were over 5 years of age. 19 died during 1-5 years of age. Two by two tables were constructed to identify the cut off point of viral load and CD_4 + T-cells percentage giving 100 per cent specificity of death in the following Table 1 and 2.

At any time point Log viral load of under 5.67 as well as CD_4 + T-cells per cent over 22 predicted an almost 100 per cent chance of survival through 5 years of age.

DISCUSSION

Virologic, immunologic and clinical status all provide information regarding disease progression risk as well as mortality risk. Kalish et al from New England Research Institutes demonstrated viral load in 165 HIV-1 infected children followed from birth to 24 months of age to be the important factor for monitoring pediatric disease progression to class C or death in all analyses, even after adjusting for immunologic and clinical status. CD_4 + T-cells count reflected immediate risk more than long term risk(3).

Mofenson et al demonstrated in 218 HIV infected children enrolled in a trial of intravenous immunoglobulin prophylaxis of bacterial infections that CD_4 + T-cells percentage was associated with mortality. In every 5 per cent decrement in baseline CD_4 + T-cells percentage there was a 1.5 fold increase in the mortality risk ratio(4).

Table 1. Log viral load.

		5 Yr	Death
	Lowest		
Log viral load	VL <5.67	7	0
	VL >5.67	9	19
	Highest	16	19

Table 2. CD4 percentage.

		5Yr	Death
	Highest		
CD4 per cent	> 22	11	0
	< 22	5	19
	Lowest	16	19

Table 3. Predictors of US. cohort (PACTG 152).

Age	CD_4 + T-cells percentage	Viral load
3-30 months	>25	<500,000
30-72 months or over	>25	<100,000

Palumbo et al identified practically the criteria of low risk for disease progression and mortality from US pediatric cohort (PACTG 152) as Table 3.

82 South African HIV-infected children over 1 year of age who did not receive antiretroviral were followed more than 2 years. The cut off point of high and low mortality (not disease progression) had a CD_4 + T-cells percentage lower than 15 and viral load over 250,000.

In the present study, the authors examined only mortality between 1-5 years of age in 35 infected children. Viral load and CD_4 + T-cells percentage were independently analysed from 1 year of age and there were at least 3 measurements for each indivi-dual. No adjustment for time or age of the children as well as clinical status had been made for viral load and CD_4 + T-cells percentage. At any point in time either CD_4 + T-cells percentage of over 22 or viral load of less than 500,000 was able to predict survival through 5 years of age in the present cohort of baseline survival 45.71 per cent.

For current HIV infected children, almost all of them were on the antitretroviral prophylaxis for vertical transmission regimen. The authors really do not know the effect of the regimen on viral load, CD_4 + T-cells percentage and mortality. Enrolling them into the clinical trial of when to initiate antiretroviral therapy might be justified but it would be better if the result of the current cohort was available.

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จำนวนร้อยละของซีดี$_4$ + ที ลิมโฟซัยท์ ที่สูง และ/หรือปริมาณไวรัสที่ต่ำทำนายโอกาสรอดถึงอายุ 5 ปี ของเด็กไทยที่ติดเชื้อเอ็ชไอวีจากมารดา

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แม้เป็นที่ยอมรับว่ายาต้านเรโทรไวรัสมีประโยชน์ในการรักษาผู้ป่วยเด็กที่ติดเชื้อเอ็ชไอวี แต่ก็ยังไม่มีข้อมูลยืนยันว่าควรเริ่มยาเมื่อใด จึงจะก่อประโยชน์สูงสุดกับผู้ป่วย เพราะมีเด็กบางกลุ่มที่ไม่ได้ยาแต่มีคุณภาพชีวิต และรอดมาถึงอายุ 5 ปี ร้อยละซีดี$_4$ + ที ลิมโฟซัยท์ และหรือปริมาณไวรัส น่าจะเป็นตัวทำนายได้ดี

ในปี พ.ศ. 2535 ถึง 2537 กลุ่มทารกที่ติดเชื้อเอ็ชไอวี จากมารดาที่โรงพยาบาลเด็ก และโรงพยาบาลศิริราช ในการศึกษาอุบัติการของการถ่ายทอดเชื้อจากมารดาสู่ทารก โดยธรรมชาติคือไม่ได้ยาต้านเรโทไวรัสป้องกัน มีชีวิตรอดอยู่จนอายุ 1-5 ปี ได้รับการติดตามดูร้อยละ ซีดี$_4$ + ที ลิมโฟซัยท์ และปริมาณไวรัสเป็นระยะ 35 ราย อยู่รอดถึงอายุ 5 ปี 16 ราย คิดเป็นร้อยละ 45 การติดตามดูซีดี$_4$ + ที ลิมโฟซัยท์ ถ้ายังเกินร้อยละ 22 หรือปริมาณไวรัสมากกว่า 500,000 ก๊อปปี้ต่อลูกบาศก์มิลลิเมตร ทำนายโอกาสอยู่รอดถึงอายุ 5 ปี ได้ทั้งหมด

คำสำคัญ : ร้อยละซีดี$_4$ + ที ลิมโฟซัยท์, ปริมาณไวรัส, เอ็ชไอวี, เด็ก, มีชีวิตรอด

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