Treatment Outcomes of HIV Infected Children After Initiation of Antiretroviral Therapy in Southwest China: an Observational Cohort Study

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Abstract

Background: The number of HIV infected children receiving antiviral treatment in Guangxi is increasing. Understanding factors and trends of mortality and attrition in HIV-infected children under antiretroviral therapy (ART) was an urgently need to improve treatment outcomes. This study aimed to describe and assess mortality and attrition after ART initiation between 2004 and 2018 among children with HIV in Guangxi, China.

Methods: Cohort study data were extracted from the National Free Antiretroviral Treatment Program (NFATP) database, which has standard guidelines for core treatment indicators and other data at all HIV/AIDS treatment facilities of Guangxi. A total of 901 HIV-infected children who have started ART were included in the study. The study collected the following data: age, gender, WHO clinic stages before ART, CD4 cell count before ART, Cotrimoxazole prophylaxis (CTX) use before ART, initial ART regimen, malnutrition before ART, abnormal liver function before ART, abnormal kidney function before ART, severe anemia before ART, and time lag between a HIV diagnosis and ART initiation.

Results: HIV-infected children under ART had a mortality rate of 0.87 per 100 person-years, and an attrition rate of 3.02 per 100 person-years. Mortality was lower among children with CD4 count between 200-500 copies/ml (Adjusted Hazard Ratio (AHR) 0.22, 95% Confidence Interval (CI) 0.09-0.54), and CD4 count ≥ 500 copies/ml (AHR 0.09, 95% CI 0.03-0.27); but higher among children with late ART initiation at 1-3 months (AHR 2.37, 95% CI 1.10-5.08), and at ≥ 3 months (AHR 2.22, 95% CI 1.05-4.72). Attrition was lower among children with a CD4 count ≥ 500 copies/ml (AHR 0.61, 95% CI 0.40-0.93), but higher among children with late ART initiation at 1-3 months (AHR 1.63, 95% CI 1.10-2.42), and at ≥ 3 months (AHR 1.26, 95% CI 0.85-1.86).

Conclusion: Supportive programs are needed to educate children's families and parents on early ART, link HIV-infected children to care, and retain them in care among other programs that treat and manage physical conditions of HIV-infected children before ART initiation.

Introduction

Despite intensive efforts for the prevention of mother-to-child transmission (MTCT), HIV consistently impacts children. Globally 1.8 million children aged < 15 years living with HIV/AIDS, and approximately 150,000 children became newly infected and 95,000 children died of HIV/AIDS-related illnesses in 2019.(1) Children HIV disproportionately impacted middle- and low- income countries where HIV disease burden was high and resources were limited.(2, 3) China's MTCT prevention programs have achieved full coverage in 2015, although significant improvement has been made, the MTCT rate was as high as 5.7 in 2016%(4, 5) Moreover, the leading causes of death among infectious diseases in Chinese students aged 6 to 22 years shifted from rabies and tuberculosis in 2008 to HIV/AIDS in 2017.(6)

Without timely antiretroviral therapy (ART), the mortality of HIV-infected young children significantly increased (52.5% vs 7.6% uninfected at the age of 2).(7) On the other hand, early HIV diagnosis and early ART initiation substantially reduced infant mortality.(8) ART was recommended by World Health Organization (WHO) for children infected with HIV regardless of age, CD4 status, and clinical stage as of 2015.(9) However, children ART coverage remained low worldwide, only approximately 53% children aged < 15 years have received ART compared to 67% of people aged 15 and older in 2019.(10, 11) A nationwide study reported that as of 2018, only 5892 (73.4%) out of 8029 HIV-infected children ≤ 14 years have started ART in China.(12) Although ART had

significantly extended children's survival time,(12) HIV-infected children had much lower rates on the receipt of ART compared to the national average ART coverage of 80.4% in China.(13) Furthermore, HIV-infected children might encounter challenges such as parental death, school dropout, and stigma which in turn resulted in negative consequences.(7)

Southern and southwestern China reported the highest HIV disease burden nationwide.(14) Guangxi Zhuang Autonomous Region that is located in southern China sharing borders with "Golden Triangle" ranked 3rd for HIV cases in 2018.(14, 15) It was one of six provinces and autonomous regions that had an HIV prevalence in pregnant women of over 50 per 100,000 population.(14, 16) MTCT programs have been scaled up in Guangxi and contributed to a significant decrease of MTCT in recent years.(17) Although early ART has been proven to be effective and beneficial for HIV-infected children, limited studies examined factors associated with death and attrition among HIV-infected children who were receiving ART. This retrospective study aimed to investigate factors that were related to death and attrition among a cohort of HIV-infected children who initiated ART. The findings of this study could be used to design programs with the goals to improve treatment outcomes and maximize the benefits of ART in HIV-infected children.

Methods

Patient and public Involvement:

Participants and the public were not involved in the design and administration of the study.

Study design and participants

The observational cohort study was conducted in Guangxi. Eligibility criteria included: (1). HIV positive children younger than 14 years old; (2). Enrolled in the National Free Antiretroviral Treatment Program (NFATP) between January 1, 2004 and December 31, 2018; (3). Being willing to provide informed consent for study participation. The study did not include participants who have not started ART. NFATP included approximately all HIV-infected children who were receiving ART in Guangxi. The study was approved by the institutional review board of Guangxi Center for Disease Control and Prevention. The research was performed in accordance with approved procedures.

Data collection

Cohort study data were extracted from the NFATP database. The following baseline data of study participants were collected: age, gender, clinic stage before ART (using WHO's criteria), CD4 count before ART, cotrimoxazole prophylaxis (CTX) use before ART, initial ART regimen, malnutrition status before ART, liver function before ART, kidney function before ART, anemia status before ART, and time between a HIV diagnosis and ART initiation. Follow-up data that were collected included: death, cessation of ART, and loss to follow-up. Date of death was based on death certificate information. Lost to follow-up was defined as missing more than 90 days after the date of last ART clinic visit, which was also defined as the date of ART cessation. More details could be found at a previously published article that used the Chinese national HIV treatment cohort study databases.(18)

China has been providing free ART for all HIV-infected individuals. The most common ART regimens that were prescribed to HIV-infected children were zidovudine (AZT), lamivudine (3TC), and nevirapine (NVP)/efavirenz (EFV)/lopinavir; or abacavir (ABC), lamivudine (3TC), and nevirapine (NVP)/efavirenz (EFV)/lopinavir. We

categorized ART regimens into the following three groups: containing AZT, containing ABC, and others.(19) Malnutrition was defined as BMI-for-age Z-score (BMIZ) less than - 3SD that was recommended by WHO for children and adolescents.(20) Abnormal liver function was defined as either alanine transaminase (ALT) or aspartate transaminase (AST) was higher than lab references. A cutoff point for AST and ALT level was set at 40 IU/L.(21) Abnormal kidney function was defined when serum creatinine (Scr) was higher than the lab reference. Scr thresholds using the enzymatic method were set up for different age groups: 0–7 days, 1.19 mg/ml; 7 days-1month, 0.79mg/ml; 1 month-1 year, 0.50mg/ml; 1–10 years, 1.09mg/ml; and 10–19 years, 1.29mg/ml.(22) Severe anemia was defined as a less than 8 g/dl of hemoglobin concentration value.(23)

Statistical analysis

We performed a time-to-event cohort analysis. The primary study endpoints were death and attrition. Attrition was defined as lost to follow-up or cessation of ART as recorded in the NFATP database. Mortality and attrition rates were calculated based on Poisson distributions and their 95% confidence intervals (CI) were assessed with incidence densities per 100 person-years at follow-up. Data were censored on Dec 31, 2019.

Cox proportional hazard models were performed to evaluate treatment effect of initial ART regimens on death and attrition (cessation of ART or loss to follow-up) of HIV-infected children who started ART between 2004 and 2018, respectively. Competing risks for cause-specific hazard models were censored accordingly. A two-sided p-value of ≤ 0.05 was regarded as statistically significant. Statistical Analysis System (SAS 9.1™ for Windows; SAS Institute Inc., NC, USA) was used for all data analyses.

Results

Baseline characteristics of study participants

Of 911 HIV-infected children who started ART from 2004 to 2018 in Guangxi, 10 participants were older than 14 years at ART initiation. A total of 901 study participants were included in the final cohort study analyses. Regarding participants' characteristics at ART initiation, 55.8% of participants were less than 5 years old, more than half of participants were males (52.3%), and more than one third were at a clinic stage of III or IV (35.1%, Table 1). Prior to ART initiation, 38.0% participants had a very low CD4 cell count of < 200 copies/ml, one fourth had a CD4 count of 200–500 copies/ml, and 37% participants had a CD4 count of ≥ 500 copies/ml. Nearly half of HIV-infected children have used CTX before ART initiation (47.8%). The initial ART regimens used by participants included ART containing AZT (71.6%), ART containing ABC (20.5%), and other (7.9%). Furthermore, the proportions of HIV-infected children who met definitions of malnutrition, abnormal liver function, abnormal kidney function, and severe anemia were 6.0%, 43.6%, 14.9% and 4.1%, respectively. More than one third of participants initiated ART within 1 month after receiving a HIV diagnosis (36.5%).

Table 1
Characteristics of HIV infected children started ART in Guangxi, 2004–2018

Variable	Number	%
Total	901	100.0
Age before ART		
0–5 years	503	55.8
≥5 years	398	44.2
Gender		
Male	471	52.3
Female	430	47.7
WHO stage before ART		
1/2	585	64.9
3/4	316	35.1
CD4 count before ART		
<200 copies/ml	342	38.0
200–500 copies/ml	225	25.0
≥500 copies/ml	334	37.0
CTX use before ART		
No	431	47.8
Yes	470	52.2
Initial ART regimen		
Cotaining AZT	645	71.6
Cotaining ABC	185	20.5
Others	71	7.9
Malnutrition before ART		
No	847	94.0
Yes	54	6.0
Abnormal liver function before ART		
No	508	56.4
Yes	393	43.6
Abnormal kidney function before ART		

Variable	Number	%
No	767	85.1
Yes	134	14.9
Severe anemia before ART		
No	864	95.9
Yes	37	4.1
Time lag since HIV diagnosis and start of ART		
<1 month	329	36.5
1–3 months	244	27.1
≥3 months	328	36.4

Mortality

Among 901 HIV-infected children who started ART between 2004 and 2018, 47 of them died, the average mortality rate was 0.87 deaths per 100 person-years. The mortality rate per 100 person-years was 3.65 in the first year of ART, and it decreased thereafter (Table 2). Univariate Cox regression analyses indicated that several factors were significantly associated with mortality, including status before ART started such as disease severity (WHO clinic stage), CD4 count, malnutrition, and abnormal liver function, initial ART regimen, and time lag between a HIV diagnosis and ART initiation. In the multivariate model, higher levels of CD4 count were associated with reduced risks of mortality (200–500, AHR 0.22, CI 0.09–0.55; ≥500, AHR 0.10, CI 0.03–0.29, Table 3). Furthermore, longer time lag between a HIV diagnosis and ART initiation was associated with increased risks of mortality (1–3 months, AHR 2.30, CI 1.07–4.94; ≥3 months, AHR 2.22, CI 1.04–4.74).

Table 2
Mortality and attrition rates of HIV infected children started ART in Guangxi, 2004–2018

Variable	Number	Deaths	Person years	Deaths per 100 person years (95% CI)	Attritions	Attritions per 100 person years (95% CI)
Total	901	47	5394.48	0.87(0.63–1.11)	163	3.02(2.57–3.47)
Year post-ART initiation						
The first year	901	31	849.66	3.65(2.40–4.90)	44	5.18(3.69–6.67)
The second year	839	2	825.08	0.24(0.00-0.57)	24	2.91(1.77–4.04)
The third year	796	5	780.41	0.64(0.09–1.19)	20	2.56(1.47–3.66)
The fourth year	722	2	705.41	0.28(0.00-0.67)	23	3.26(1.96–4.56)
The 5th year	663	2	652.58	0.31(0.00-0.72)	19	2.91(1.64–4.19)
The 6th year	577	3	566.22	0.53(0.00-1.11)	14	2.47(1.21–3.74)
The 7th year	502	1	488.53	0.20(0.00-0.60)	10	2.05(0.81–3.28)
The 8th year	394	0	389.23	-	2	0.51(0.00-1.21)
The 9th year	321	0	316.96	-	2	0.63(0.00-1.48)
The 10th year	255	1	247.42	0.40(0.00-1.18)	2	0.81(0.00-1.90)
The 11th year	177	0	167.39	-	2	1.19(0.00-2.81)
The 12th year	113	0	109.48	-	0	-
The 13th year	50	0	47.32	-	1	2.11(0.00-6.15)
The 14th year	24	0	22.88	-	0	-
The 15th year	9	0	8.55	-	0	-

Table 3
Mortality rates and risk factors of HIV infected children started ART in Guangxi, 2004–2018

Variable	Number	Deaths	Person-years	Deaths per 100 person-years (95% CI)	HR (95%CI)	p	AHR (95%CI)	P
Total	901	47	5394.48	0.87(0.63–1.11)				
Age before ART								
0–5 years	503	25	3525.65	0.71(0.44–0.98)	Reference		Reference	
≥5 years	398	22	1868.83	1.18(0.70–1.66)	1.24(0.69–2.20)	0.473	0.71(0.38–1.34)	0.293
Gender								
Male	471	21	2948.97	0.71(0.42–1.01)	Reference		Reference	
Female	430	26	2445.51	1.06(0.66–1.46)	1.39(0.78–2.46)	0.267	1.77(0.97–3.23)	0.064
WHO stage before ART								
1/2	585	20	3457.10	0.58(0.33–0.83)	Reference		Reference	
3/4	316	27	1937.39	1.39(0.88–1.91)	2.56(1.44–4.57)	0.001	1.44(0.75–2.75)	0.269
CD4 count before ART								
<200 copies/ml	342	37	1857.02	1.99(1.37–2.62)	Reference		Reference	
200–500 copies/ml	225	6	1430.9	0.42(0.09–0.75)	0.23(0.1–0.54)	0.001	0.22(0.09–0.55)	0.001
≥500 copies/ml	334	4	2106.56	0.19(0.01–0.37)	0.10(0.04–0.29)	< 0.001	0.10(0.03–0.29)	< 0.001
CTX use before ART								
No	431	19	2107.14	0.90(0.51–1.30)	Reference		Reference	
Yes	470	28	3287.34	0.85(0.54–1.16)	1.23(0.68–2.20)	0.495	0.60(0.31–1.17)	0.132

HR: hazard ratio in univariate regression; AHR: adjusted hazard ratio in multivariate regression.

Variable	Number	Deaths	Person-years	Deaths per 100 person-years (95% CI)	HR (95%CI)	p	AHR (95%CI)	P
Initial ART regimen								
Cotaining AZT	645	27	4104.26	0.66(0.42–0.90)	Reference		Reference	
Cotaining ABC	185	12	836.28	1.43(0.64–2.23)	1.69(0.85–3.34)	0.132	1.17(0.54–2.55)	0.693
Others	71	8	453.94	1.76(0.57–2.95)	2.77(1.26–6.09)	0.012	1.49(0.62–3.57)	0.374
Malnutrition before ART								
No	847	41	5104.40	0.80(0.56–1.04)	Reference		Reference	
Yes	54	6	290.08	2.07(0.45–3.68)	2.45(1.04–5.76)	0.041	1.84(0.74–4.56)	0.188
Abnormal liver function before ART								
No	508	20	2826.21	0.71(0.41–1.01)	Reference		Reference	
Yes	393	27	2568.27	1.05(0.66–1.44)	1.71(0.96–3.05)	0.07	1.36(0.73–2.51)	0.331
Abnormal kidney function before ART								
No	767	37	4316.97	0.86(0.59–1.13)	Reference		Reference	
Yes	134	10	1077.51	0.93(0.37–1.49)	1.41(0.70–2.86)	0.334	1.23(0.54–2.80)	0.615
Severe anemia before ART								
No	864	44	5122.72	0.86(0.61–1.11)	Reference		Reference	
Yes	37	3	271.76	1.10(0.00–2.32)	1.47(0.46–4.75)	0.516	1.46(0.41–5.16)	0.557

HR: hazard ratio in univariate regression; AHR: adjusted hazard ratio in multivariate regression.

Variable	Number	Deaths	Person-years	Deaths per 100 person-years (95% CI)	HR (95%CI)	p	AHR (95%CI)	P
Time lag since HIV diagnosis and start of ART								
<1 month	329	11	2091.88	0.53(0.22–0.83)	Reference		Reference	
1–3 months	244	17	1433.91	1.19(0.64–1.74)	2.14(1.00–4.58)	0.049	2.30(1.07–4.94)	0.033
≥3 months	328	19	1868.69	1.02(0.57–1.46)	1.77(0.84–3.71)	0.134	2.22(1.04–4.74)	0.04
HR: hazard ratio in univariate regression; AHR: adjusted hazard ratio in multivariate regression.								

Attrition

Among 901 HIV-infected children who started ART between 2004 and 2018, 163 attritions were reported, and the average attrition rate was 3.02 deaths per 100 person-years. The attrition rate per 100 person-years was 5.18 in the first year of ART, and decreased after then (Table 2). Using univariate Cox regression analyses, factors that were significantly associated with attrition were determined: age before ART, disease severity (WHO clinic stage) before ART, CD4 count before ART, initial ART regimen, and time lag between a HIV diagnosis and ART initiation. In the multivariate model, a high CD4 level was associated with a reduced risk of attrition rate (≥ 500 , AHR 0.62; CI 0.41–0.91, Table 4). On the other hand, a delayed initiation of ART (≥ 3 months) was associated with an increased risk of attrition (AHR 1.55, CI 1.05–2.30).

Table 4
Attrition rates and risk factors of HIV infected children started ART in Guangxi, 2004–2018

Variable	Number	Attritions	Person-years	Attritions per 100 person-years (95% CI)	HR (95%CI)	p	AHR (95%CI)	P
Total	901	163	5394.48	3.02(2.57–3.47)				
Age before ART								
0–5 years	503	84	3525.65	2.38(1.89–2.88)	Reference		Reference	
≥5 years	398	79	1868.83	4.23(3.32–5.14)	1.56(1.14–2.13)	0.005	1.32(0.92–1.89)	0.131
Gender								
Male	471	76	2948.97	2.58(2.01–3.14)	Reference		Reference	
Female	430	87	2445.51	3.56(2.83–4.29)	1.33(0.98–1.81)	0.069	1.39(1.01–1.91)	0.041
WHO stage before ART								
1/2	585	94	3457.1	2.72(2.18–3.25)	Reference		Reference	
3/4	316	69	1937.39	3.56(2.74–4.38)	1.37(1.01–1.88)	0.046	1.22(0.86–1.73)	0.277
CD4 count before ART								
<200 copies/ml	342	77	1857.02	4.15(3.24–5.05)	Reference		Reference	
200–500 copies/ml	225	38	1430.9	2.66(1.83–3.48)	0.65(0.44–0.96)	0.030	0.66(0.44–1.01)	0.053
≥500 copies/ml	334	48	2106.56	2.28(1.65–2.91)	0.56(0.39–0.81)	0.002	0.62(0.41–0.95)	0.026
HR: hazard ratio in univariate regression; AHR: adjusted hazard ratio in multivariate regression.								

Variable	Number	Attritions	Person-years	Attritions per 100 person- years (95% CI)	HR (95%CI)	p	AHR (95%CI)	P
CTX use before ART								
No	431	70	2107.14	3.32(2.56–4.08)	Reference		Reference	
Yes	470	93	3287.34	2.83(2.27–3.39)	0.96(0.70–1.31)	0.793	0.87(0.60–1.24)	0.430
Initial ART regimen								
Cotaining AZT	645	115	4104.26	2.80(2.30–3.30)	Reference		Reference	
Cotaining ABC	185	24	836.28	2.87(1.75–3.99)	0.89(0.57–1.38)	0.602	0.75(0.47–1.20)	0.231
Others	71	24	453.94	5.29(3.22–7.35)	1.97(1.27–3.06)	0.003	1.72(1.06–2.78)	0.027
Malnutrition before ART								
No	847	155	5104.40	3.04(2.57–3.50)	Reference		Reference	
Yes	54	8	290.08	2.76(0.89–4.62)	0.92(0.45–1.86)	0.808	0.79(0.38–1.64)	0.53
Abnormal liver function before ART								
No	508	85	2826.21	3.01(2.38–3.63)	Reference		Reference	
Yes	393	78	2568.27	3.04(2.38–3.69)	1.08(0.79–1.47)	0.619	1.07(0.77–1.49)	0.686
Abnormal kidney function before ART								
No	767	134	4316.97	3.10(2.59–3.62)	Reference		Reference	
Yes	134	29	1077.51	2.69(1.74–3.65)	0.99(0.66–1.49)	0.968	1.00(0.63–1.59)	0.996

HR: hazard ratio in univariate regression; AHR: adjusted hazard ratio in multivariate regression.

Variable	Number	Attritions	Person-years	Attritions per 100 person-years (95% CI)	HR (95%CI)	p	AHR (95%CI)	P
Severe anemia before ART								
No	864	159	5122.72	3.10(2.63–3.57)	Reference		Reference	
Yes	37	4	271.76	1.47(0.07–2.88)	0.50(0.19–1.36)	0.176	0.53(0.19–1.48)	0.226
Time lag since HIV diagnosis and start of ART								
<1 month	329	49	2091.88	2.34(1.70–2.98)	Reference		Reference	
1–3 months	244	53	1433.91	3.70(2.73–4.67)	1.54(1.04–2.27)	0.030	1.55(1.05–2.30)	0.029
≥3 months	328	61	1868.69	3.26(2.47–4.06)	1.30(0.89–1.90)	0.169	1.19(0.81–1.77)	0.378
HR: hazard ratio in univariate regression; AHR: adjusted hazard ratio in multivariate regression.								

Discussion

Globally, 14% of HIV-related deaths were children under the age of 15 although they only accounted for 5% of all people living with HIV/AIDS.(10) It is urgently needed to improve treatment outcomes for children with HIV. The study reported a mortality rate of 0.87 per 100 person-years in Guangxi HIV-infected children who have started ART. This result was lower than comparable reports from other Asian regions (2.1–2.86 per 100 person-years) for HIV-infected children.(24, 25) Also this mortality rate was much lower than HIV-infected adults who were receiving ART in Guangxi (5.94 per 100 person-years).(26, 27) Moreover, mortality reached the peak of 3.65 per 100 person-years within the first year, and dramatically reduced from the 2nd year, and reached nearly 0 at the 8th year of ART initiation. The trends were consistent with previous studies that reported generally higher mortalities in the first 3–6 months of ART initiation and decreasing over time.(24, 28) It could be explained that infections and other complications related to advanced HIV disease and late clinic stages were the possible major causes of the first-year deaths because medication-related deaths were generally low.(28)

ART has significantly reduced HIV-infected children's mortality in this sample and initiating ART at a high CD4 level of ≥ 500 contributed to the lowest mortality. On the other hand, low CD4 count and late ART initiation resulted in an increased mortality. In addition to a weakened immune system and its consequences, previous studies reported that a higher CD4 count could reduce the odds of virologic failure and HIV drug resistance mutations.(29) However, 63.5% participants have started ART after one month of a HIV diagnosis, and 38%

started ART with a very low CD4 count (< 200 copies/ml) in this sample. And numbers of children have other physical conditions when they started ART, such as malnutrition, abnormal liver function, abnormal kidney function, and severe anemia. It suggested that supportive programs, such as nutritional support, routine examination, lab test are needed in addition to ART promotion.

The overall attrition rate was 3.02 per 100 person-years in this study (18.1%). The result was consistent with the reports of Thailand (2.9 per 100 person-years) and Zambia (16%) for HIV-infected children,(25, 30) but much lower than HIV-infected adults who started ART in Guangxi (10.86 per 100 person-years).(26) More than 25% attritions occurred in the first year of ART initiation. High attrition rates can result in suboptimal treatment outcomes, increased mortality, increased cost of care, and excess infections.(31) Therefore, future interventions can provide retention support, such as case management, and follow-ups to help retain HIV-infected children in care. Moreover, health education and linkage to care services are needed to educate families with HIV-infected children to start ART as early as possible and remove possible barriers for ART initiation.

One strength of the study was it utilized a database which included approximately all HIV-infected children who were under ART in Guangxi. The study provided a profile of this group of children and assessed factors associated with mortality and attrition. The study also confirmed the effectiveness of pediatric ART. Therefore, the findings have important real-world implications to reduce mortality and attrition in HIV-infected children. The study has limitations. First, the study included HIV-infected children who were in NFATP between 2004 and 2018 in Guangxi, some groups were not covered such as, HIV-infected children who were not in ART. Therefore, the results cannot be generalized to these groups. Second, this sample and the number of events were relatively small (47 deaths), it possibly could cause over fitting of the Cox model to predict risk factors for mortality. Third, the retrospective study was limited by the existing information of the database. Some information that might be helpful to explain the study results was lacking, such as children's viral load, parental HIV status, and parental or families' attitudes or sociodemographic characteristics.

Conclusion

MTCT prevention efforts and ART have significantly reduced HIV-infected children's mortality although first-year mortality and attrition were relatively high after ART initiation. Low CD4 count and late ART initiation (> 1 month) were associated with increased mortality and attrition. The findings have implications to design interventions and programs that support linkage to care, early ART initiation, and first-year retention in care.

Abbreviations

AHR, adjusted hazard ratio; HR, hazard ratio.

Declarations

Ethics approval and consent to participate

The study was approved by the institutional review board of Guangxi Center for Disease Control and Prevention. The research was performed in accordance with approved procedures.

Consent for publication

All authors read and approved the final version of the paper.

Availability of data and materials

Data was extracted from the National Free Antiretroviral Treatment Program database. According to Chinese law, the original data can not be made public.

Conflicts of interest

The authors have no conflicts of interest to declare.

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The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the paper. The corresponding author has full access to all data in the study and takes final responsibility for the decision to submit for publication.

Author contribution

XZ, JZ and YR were responsible for study design and planning. QZ, ZS, GL, HC contributed to data collection and management. XZ, JZ, YR contributed to data analysis. XZ, JZ, HZ,YS, XZ and YR contributed to interpretation. XZ, JZ, XZ, YR contributed to writing the report.

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