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Prevalence of anemia and associated factors in HIV-1 infected children before and after initiation of antiretroviral therapy in Burkina Faso: A retrospective study

Serge Theophile Soubeiga[1,2]*, Albert Theophane Yonli[2,3], Bapio Valerie Jean Telesphore Elvira Bazie[2,3], Henri Gautier Ouedraogo[1] and Jacques Simpore[2,3]

[1]Research Institute for Health Sciences (IRSS), Ouagadougou, Burkina Faso.
[2]Pietro Annigoni Biomolecular Research Centre (CERBA), Ouagadougou, Burkina Faso.
[3]Molecular Biology and Genetics Laboratory (LABIOGENE), University Joseph Ki-Zerbo, Ouagadougou, Burkina Faso.

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Anemia is a public health problem and has significant adverse health consequences in HIV-infected persons. In Burkina Faso, there are little data on anemia in HIV-1 infected children. This study aimed to describe the prevalence of anemia and its associated factors in HIV-infected children before and after their highly active antiretroviral therapy (HAART). This was a retrospective study that involved a cohort of 151 HIV-1 infected children on HAART at the pediatric service of Saint Camille Hospital, from January 2018 to October 2018. Data were collected before and after their HAART initiation and analyzed using SPSS version 21.0. The prevalence of anemia was 81.46% before treatment and 48.34% 12 months after initiation of treatment. There was a significant association between gender, BMI, TB, and CD4 counts before HAART initiation While, after HAART initiation, only gender, age, and CD4 T cell count were significantly associated with anemia. Children with a CD4 count <200 Cell/µl had a risk of developing anemia before HAART initiation but no longer had a risk of developing anemia 1 year after HAART initiation [OR=0.35 (0.14-0.89); p=0.028 vs. OR=1.54 (0.67-3.51); p=0.300].This study showed that antiretroviral treatment contributes strongly to improving the hemoglobin level in persons living with HIV.

Key words: HIV, anemia, prevalence, highly active antiretroviral therapy (HAART), Children, Burkina Faso.

INTRODUCTION

The number of children (0-14 years) infected with HIV was estimated to be 1.7 million [1.2 million- 2.2 million] in 2020 (UNAIDS, 2021). HIV infection causes several complications, including anemia (Cao et al., 2022). Anemia defined as reduced hemoglobin levels of red blood cells may carry less oxygen to skeletal muscle and impair physical performance (Tsai et al., 2019). Anemia is a risk factor for death in HIV-1 infected individuals (Harding et

*Corresponding author. E-mail: theo.soubeiga@gmail.com. Tel: +226 70 01 30 58.

al., 2020). In Burkina Faso, the prevalence of anemia in children aged 6-59 months was 87.0% in 2020 (Muriuki et al., 2020). In children, depending on the hemoglobin level, anemia can be considered severe (Hb level<7 g/dL), moderate (Hb level [7-9.9] g/dL), and mild (Hb level [10-11] g/dL). According to WHO, Africa represented the continent with the highest rate of anemia in children aged 6-59 months (60.2%), followed by Southeast Asia (49.0%) (WHO, 2021a).

In Africa, anemia remains the most frequently observed hematologic abnormality and an independent predictor of disease progression in people living with HIV, particularly in children and most people infected with HIV-1 are anemic (Abioye et al., 2020; Duffy et al., 2020). However, the risk of anemia is reduced after the initiation of highly active antiretroviral therapy (HAART) (Yesuf et al., 2019). Indeed, studies have shown that antiretroviral therapy helps to improve anemia and reduce mortality in children (Haider et al., 2019; Duffy et al., 2020). Moreover, antiretroviral treatment (ART) is known to profoundly suppress viral replication. It increases CD4 cell count, delays disease progression and death; patients on highly active antiretroviral therapy commonly suffer from side effects of the drugs (Geletaw et al., 2017; Mouhari-Toure et al., 2018). Each antiretroviral (ARV) drug is associated with specific adverse effects and among the ARV drugs, zidovudine (AZT) remains the most widely used drug, resulting in myelosuppression (Leroi et al., 2017) and has been associated with anemia (Tamir et al., 2018).

Studies have identified factors associated with anemia in HIV-infected children such as age, low CD4 percentage, WHO clinical stage, and Iron deficiency (Bisong et al., 2017; Lai et al., 2018; Huibers et al., 2020). A study in Uganda showed that in patients who started or continued ARV therapy, CD4 counts increased significantly over 18 months of follow-up, and the improvement did not differ by baseline ferritin level or anemia status (Ezeamama et al., 2019).

In Burkina Faso, there are little data on the effect of ARV treatment on anemia in HIV-1 infected children as well as the associated factors. However, having information on this would help in the better therapeutic and clinical management of children. So, the objective of this study was to describe the prevalence and associated factors of anemia in HIV-infected children before and after their HAART.

MATERIALS AND METHODS

Study population and data collection

This was a retrospective study whose data were collected from the records of HIV-1 children on HAART at the pediatric ward of Saint Camille Hospital in Ouagadougou, Burkina Faso during the period from January 2018 to October 2018. This study involved 151 HIV-1 infected children. Data were collected before and 12 months after initiation of HAART and included: socio-demographic, clinical, hemoglobin (Hb), and immunologic characteristics. Hemoglobin and CD4 T cell counts were determined using the CELL-DYN Ruby (Abbott, Illinois, USA) and the BD FACSCOUNT (Becton Dickenson, California, USA) respectively. To ensure good quality results, the data were collected through a questionnaire form and incomplete data were eliminated during processing.

Definition of variables and data analysis

Based on hemoglobin level, anemia was classified as severe (Hb level<7 g/dL), moderate (Hb level [7-9.9] g/dL), and mild (Hb level [10-11] g/dL). Body mass index (BMI) was classified into normal body weight (18.5 - 24.9), underweight (<18.5), and overweight (≥25) according to WHO, and the calculation was based on the formula BMI= (weight in Kg/height in m^2) (WHO, 2021b). Bivariate analysis and multivariate logistic regression were performed using IBM SPSS version 21.0 software and any value was considered statistically significant for $p<0.05$. Odds ratios with confidence intervals (95% CI) were used to determine the association between anemia and potential risk factors.

RESULTS

General characteristics of the study population

The socio-demographic and clinical characteristics of the study population at the time of initiation of ARV treatment are shown in Table 1. Female children were more represented (54.3%) than males (45.7%) with a sex ratio of 0.84 and the mean age was 10.04±3.7 years. The most represented age group was 5-11 years (58.28%). The majority of HIV-1 infected children (70.86%) were underweight at the start of ARV treatment. Approximately, 64.9% of the children were in WHO clinical stages I and II and 25.83% of them had a CD4 count below 200 cells/µl (Table 1).

Prevalence of anemia before and after HAART initiation

Figure 1 shows the severity of anemia in HIV-1 infected children before and after initiation of HAART. The prevalence of anemia was 81.46% (123/151) before treatment and 48.34% (73/151) 12 months after initiation of treatment. About 5.96% of the children had severe anemia, 50.33% had moderate anemia and 25.16% had mild anemia before initiation of HAART (Figure 1). Among the children with anemia before starting ARV treatment, 97.10% (67/69) were male and 68.29% (56/82) were female. This study shows that all children under 5 years of age (100%) and 86.92% of those who were underweight developed anemia. Also, anemia was found in all HIV-1 infected children with CD4 T cell count between 200 and 350 cells/µl (Table 2). In contrast, 12 months after initiation of HAART, the prevalence of anemia decreased overall. It was 63.49% (40/63) in male children and 37.5% (33/88) in female children. The age group of 5-11 years was the most anemic (60.23%).

Table 1. Sociodemographic and clinical characteristics of HIV-1 infected children.

Characteristics		Number	Percentage
Sex	Male	69	45.7
	Female	82	54.3
Age (years)	< 5	16	10.6
	5-11	88	58.28
	12-14	47	31.12
WHO clinical stage	I and II	98	64.9
	III and IV	53	35.1
BMI (Kg/m^2)	Normal weight	37	24.5
	Underweight	107	70.86
	Overweight	7	4.64
Tuberculosis	Yes	7	4.64
	No	144	95.36
CD4 (cell/µL)	< 200	39	25.83
	200-350	33	21.85
	≥ 350	79	51.32

BMI; Body Mass Index.
Source : Serge Theophile Soubeiga.

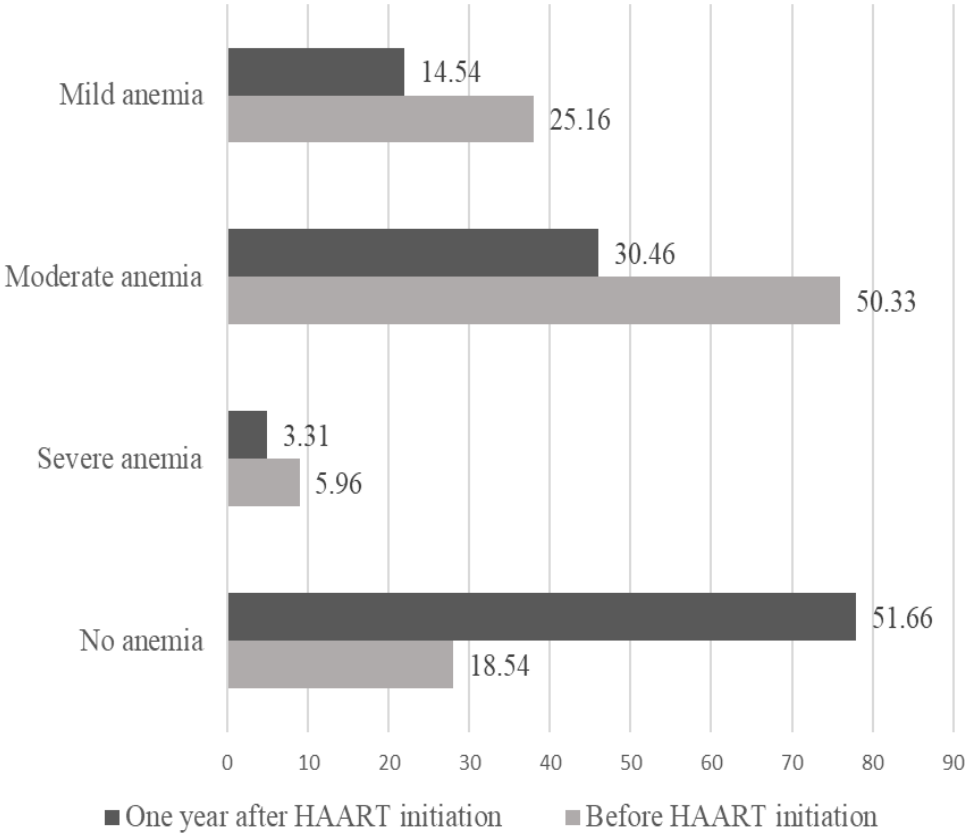

Figure 1. Severity of anemia in HIV-1 infected children before and after HAART initiation.

Table 2. Sociodemographic and clinical characteristics by anemia before ART initiation in HIV-1 infected children.

Characteristics		Anemic (n=123)	Non- anemic (n=28)	p-value
Sex	Male	67 (97.10)	2 (2.90)	<0.001
	Female	56 (68.29)	26 (31.71)	
Age (years)	< 5	16 (100)	0 (0,00)	0.110
	5-11	71 (80.7)	17 (19.3)	
	12-14	36 (76.6)	11 (23.4)	
WHO clinical stage	I and II	81 (82.65)	17 (17.35)	0.607
	III and IV	42 (79.25)	11 (20.75)	
BMI (Kg/m^2)	Normal weight	17 (79.91)	6 (26.09)	0.054
	Underweight	102 (85.00)	18 (15.00)	
	Overweight	4 (57.14)	3 (42.86)	
Tuberculosis	Yes	3 (42.86)	4 (57.14)	0.028
	No	120 (81.08)	24 (18.92)	
CD4 (cell/µl)	< 200	31 (79.5)	8 (20.5)	0.007
	200-350	33 (100)	0 (0.00)	
	≥ 350	59 (74.7)	20 (25.3)	

Source : Serge Theophile Soubeiga.

Similarly, 46.97% (31/68) of HIV-1 infected children in whom treatment was not AZT-based developed anemia (Table 3).

Factors associated with anemia before and after HAART

Analysis of the data showed a significant association between gender, BMI, TB, and CD4 counts before HAART initiation, but there was no association between age, WHO clinical stage, and anemia (Table 2). After HAART initiation, gender, age, and CD4 T cell count were significantly associated with anemia. However, there was no association between WHO clinical stage, BMI, ARV treatment, and anemia (Table 3). Female children had a 16-fold [OR=16.07 (3.65-70.71; p<0.001] risk of developing anemia before HAART initiation but this risk significantly decreased 1 year after HAART [OR=0.41 (0.19-0.85), p=0.017]. Children with a CD4 count <200 Cell/µl had a risk of developing anemia before HAART initiation but no longer had a risk of developing anemia 1 year after HAART [OR=0.35 (0.14-0.89); p=0.028 vs. OR=1.54 (0.67-3.51); p=0.300] (Table 4).

DISCUSSION

This study showed a high prevalence (81.46%) of anemia in HIV-1 infected children before initiation of HAART, which is lower than the prevalence of 87.0% found in children in 2020 from Burkina Faso in a study conducted in African children but higher than the prevalence of anemia found other countries (70.0% in Kenya; 49.7% in Uganda; 60.1% in Gambia) (Muriuki et al., 2020). This high prevalence of anemia confirms that the situation remains concerning in Central and Western Africa. Indeed, children in developing countries have a high prevalence of anemia due to poverty, a high burden of infectious diseases whose inflammation is a primary contributor to anemia (Mantadakis et al., 2020). In this study, the prevalence of anemia decreased 12 months after treatment initiation. It decreased from 81.46 to 43.34%, that is, a reduction of 33.90% in one year. This prevalence is nevertheless higher than that found in several countries: 11.4% in Southern Ethiopia (Fenta et al., 2020); 54.2% in Nigeria (Ahumareze et al., 2016) but remains lower than 49.6% found in Cameroon (Bate et al., 2016) and 88% in Mozambique (Duffy et al., 2020). These differences could be due to the methodologies used, the heterogeneity of the populations, and the nutritional status of the children. Indeed, a study conducted in Sub-Saharan Africa among children aged 6-59 months revealed a difference in the prevalence of anemia between countries. West Africa had the highest prevalence (70-88%), followed by Central Africa (63-67%) and East Africa (38-69%) (Tesema et al., 2021). In this study, the decrease in anemia after 1 year of HAART truly demonstrates the involvement of ARV therapy in improving hemoglobin levels. Indeed, studies have shown that ARV therapy contributes to improved anemia

Table 3. Sociodemographic and clinical characteristics according to anemia 12 months after initiation of HAART in HIV-1 infected children.

Characteristics		Anemic (n=73)	Non- anemic (n=78)	p-value
Sex	Male	40 (63.49)	23 (36.51)	0.001
	Female	33 (37.5)	55 (62.5)	
Age (years)	< 5	5 (45.45)	11 (54.55)	0.002
	5-11	53 (60.23)	35 (39.77)	
	12-14	15 (31.91)	32 (68.09)	
WHO clinical stage	I and II	43 (45.74)	51 (54.26)	0.411
	III and IV	30 (52.63)	27 (47.37)	
BMI (Kg/m^2)	Normal weight	56 (44.07)	62 (55.93)	0.627
	Underweight	13 (56.52)	10 (43.48)	
	Overweight	4 (40.0)	6 (60.0)	
Treatment	AZT based	42 (49.41)	43 (50.59)	0.501
	Non AZT based	31 (46.97)	35 (53.03)	
CD4 (Cell/µl)	< 200	25 (65.79)	13 (34.21)	0.001
	200-350	12 (27.27)	32 (72.73)	
	≥ 350	36 (52.17)	33 (47.83)	

Source : Serge Theophile Soubeiga.

Table 4. Logistic regression of risk factors for anemia in HIV-1 infected children before and 1 year after initiation of HAART.

Characteristics		Before HAART initiation		1 year after HAART initiation	
		Odds ratio (IC 95%)	p-value	Odds ratio (IC 95%)	p-value
Sex	Male	1.00		1.00	
	Female	16.07 (3.65-70.71)	**<0.001**	0.41 (0.19-0.85)	**0.017**
WHO clinical stage	I and II	1.00		1.00	
	III and IV	0.80 (0.34-1.86)	0.667	1.48 (0.61-3.56)	0.382
CD4 (cell/µl)	≥350	1.00		1.00	
	200-350	0.50 (0.10-2.50)	0.403	5.76 (1.83-18.11)	**0.003**
	<200	0.35 (0.14-0.89)	**0.028**	1.54 (0.67-3.51)	0.300

Source : Serge Theophile Soubeiga.

and reduced mortality in children (Haider et al., 2019). This is confirmed by the decrease in the rate of severe anemia (5.96% before HAART vs 3.31% after HAART). Our results are in agreement with other studies (Geletaw et al., 2017; Beletew et al., 2020). Authors have shown the reduction of anemia 6 months, 12 months, 18 months, 24 months, and 30 months after AZT-based ART treatment (Getaneh et al., 2021). While our study found a higher rate of anemia in children on HAART with AZT (64.2%) than in those on non-AZT HAART (51.11%). The factor that may have contributed to the observed high prevalence of anemia is the possible effect of AZT. Side effects such as myelotoxicity, mitochondrial toxicity, myopathy, and incidence of anemia associated with AZT use in people living with HIV have been reported in several studies (Tamir et al., 2018). AZT is known to be associated with life-threatening hematological toxicity like anemia due to early long-term higher-dose therapy. AZT also causes bone marrow suppression, which causes anemia (Getaneh et al., 2021).

In this study, the under-5 years' age group was most affected by anemia before HAART initiation. This confirmed that children under 5 years of age in developing countries are more vulnerable to severe anemia (Kejo et al., 2018) certainly due to malnutrition, malaria, and opportunistic infections (Bate et al., 2016; Wagnew et al., 2019). The 5-11-year-old was most affected 1 year after HAART treatment in contrast to the under 5-year-old. This was also found in a study conducted in Cameroon (Bate et al., 2016). There was an association between gender, BMI, tuberculosis, and CD4 T-cell count with anemia before initiation of HAART in children. Indeed, opportunistic infections and immune system failure are factors that can promote anemia. One study reported that tuberculosis and malaria were associated with anemia in HIV-1 infected children (Huibers et al., 2020). In terms of BMI, anemia was found most in underweight HIV-1 infected children. Indeed, the hemoglobin level is an important biological parameter that, when it is reduced, can affect growth, especially in children (Ibrahim et al., 2017).

Children with CD4 counts < 200 Cell/µL and 200-350 Cell/µl had a 0.35- and 5.76-fold risk of developing anemia before initiation and 1 year after HAART, respectively, as a study in Ethiopia showed that immunocompromised children were at higher risk of developing anemia than those with normal immunity (Techane et al., 2020). Tuberculosis, zidovudine-based drugs, severe immunosuppression, and undernutrition have remained predictors of anemia among children on antiretroviral therapy (Atalell et al., 2018; Techane et al., 2020).

In general, HAART reduces the incidence of anemia by suppressing viral replication and increasing CD4 cell counts (Beletew et al., 2020; Getaneh et al., 2021). In addition to HAART, all HIV-infected children received Cotrimoxazole prophylaxis to prevent other opportunistic infections. This treatment could contribute to the reduction of anemia in children. Indeed, cotrimoxazole may have a direct impact on erythropoiesis by reducing the number of red blood cells (Bouyou Akotet et al., 2018). This study showed important results but has presented some limits. Outside of tuberculosis, there was no existing data on other diseases that could influence the hemoglobin level of children before their treatment and we did not identify the exact cause of anemia. This study confirmed with many authors that antiretroviral treatment contributes strongly to improving the hemoglobin level in persons living with HIV. However, there is the need to enhance the management of HIV-infected children to restore their immune system, monitor their nutritional status, and prevent opportunistic infections.

Ethics approval

This study received approval from the Burkina Faso Health Research Ethics Committee (deliberation N° 2014-7-084). Anonymity and confidentiality were respected and the results were used to improve the clinical management of the children included in the study.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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