Anaemia and iron deficiency in peri-urban school children born in a National HIV Prevention Programme in Zimbabwe: A cross-sectional study

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Abstract

***Objective*:** To determine the prevalence of anaemia, iron deficiency and iron deficiency anaemia in school children who were born in a national HIV prevention programme.
***Design*:** This was a community based cross-sectional study.
***Setting*:** A resource poor peri-urban setting with high prevalence of HIV infection.
***Subjects*:** School aged children six to 10 years old who were born in a national mother-to-child HIV prevention programme.
***Main Outcome Measures*:** Haemoglobin (Hb), serum Ferritin (F) and serum Transferrin receptor (sTfR) levels.
***Results*:** Three hundred and eighteen children were recruited including 21 HIV positive. The prevalence of anaemia (Hb <11.5 grams per litre), iron deficiency (F<15 micrograms per litre) and iron deficiency anaemia (Hb < 11.5 g/L and either F <15μg/L or sTfR > 8.3μg/L) were 15%, 4% and 2% respectively. When a higher cut-off for ferritin of 30 micrograms per litre was applied to adjust for high infection disease burden, iron deficiency prevalence increased to 32% and iron deficiency anaemia increased to 5%. Anaemia was 4.9 (C.I 1.9-12.4) times more likely to occur in HIV infected children compared to the HIV uninfected children. Maternal HIV status at birth was not related to presence of anaemia in the school children.
***Conclusion*:** Anaemia was of mild public health significance in this cohort of children. Iron deficiency anaemia contributed less than a quarter of the cases of anaemia. HIV infection was an important determinant for presence of anaemia. Therefore continued efforts to eliminate paediatric HIV infection as a way of reducing anaemia in children are essential.

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Introduction

Anaemia is a problem of public health importance because 25% of the world population[1] is affected by this disorder. Anaemia can result from reduced red blood cell production, increased red cell destruction or increased red cell loss from the body. Several factors, which include nutritional deficiencies, infectious diseases and inherited diseases, are known to cause anaemia in children. Iron deficiency (ID) is the commonest micronutrient deficiency leading to anaemia. Human immunodeficiency virus (HIV) infection has become an important factor associated with the development of anaemia in sub-Saharan Africa, because of the high prevalence of HIV infection in the region. The current prevalence of HIV in the reproductive age in Zimbabwe is 15%.[2] This has decreased from a higher prevalence of 29.3%[3] reported in the previous decade. HIV infection can, through many mechanisms, contribute to anaemia.[4]

In 2011, 56% of Zimbabwean children below 60 months of age were reported to be anaemic (Haemoglobin < 11 grams/decilitre).[2] However, this national survey did not report on the prevalence of anaemia in children of school age. According to the World Health Organization 2001 estimates, the global prevalence of iron deficiency anaemia (IDA) in children between 5 and 14 years was estimated to be 48%.[5]

Iron deficiency has important health and economic consequences. It is a multisystem disorder that has both haematological and non-haematological effects. ID has a negative impact on psychomotor development and cognitive function.[6-8] Altered iron accumulation in the brain results in altered myelination, neurotransmitter metabolism and changes in the hippocampus. These changes may explain the effect of ID on the brain and, if not corrected early at critical periods of brain development, may result in irreversible changes.[9] In addition, iron supplementation in non-anaemic adolescent children improved verbal learning and memory in a randomised control trial.[10] It improved red cell indices and learning achievement in children of school age.[11] Improving iron status and general childhood nutrition could be a way of increasing access to education and improving school performance.[12]

The prevalence of anaemia and ID in children of school age and above five years is unknown in Zimbabwe. This is because most health programmes including the national demographic health survey, report only on children below five years. In addition, the effect of HIV infection and exposure to HIV on the occurrence of anaemia in children over five years of age is also unknown. This article presents findings from a cross-sectional study which determined the prevalence of anaemia and ID in HIV infected and uninfected children above five years who were born in a national mother to child HIV prevention programme.

Materials and Methods

Study Design

A cross-sectional study was carried out from August 2011 to June 2012 at three primary care peri-urban clinics (Epworth clinic, St Mary's clinic, and Seke North clinic) offering maternal and child health services around Harare, the capital city of Zimbabwe. The study participants were children born to mothers who participated in a national programme for prevention of mother to child transmission of HIV infection between 2002 and 2004. The design of this cohort is described in detail in a previous publication.[13] In summary, the original birth cohort had 1050 babies born to 571 HIV negative and 479 HIV positive mothers. However, as of June 2009, only 237 babies born to HIV negative mothers and 215 born to HIV positive mothers could be identified. The rest had either been lost to follow up or had died.[14] The minimum sample size required for estimating the prevalence of anaemia in this population of children with a confidence interval of 95% and a margin of error of 0.05 was 208 at 80% power. It was assumed that the prevalence of anaemia was 50% since it was unknown for this particular population of children between 5 and 10 years of age in Zimbabwe.

The care givers and the children were contacted in the community and given information about the study. Children who were the initial siblings born in the cohort, above the age of five years and whose care givers were interested in taking part in the research were asked to come to the local clinic for recruitment. Participants were recruited every Thursday between 8am and 6pm as they presented to the local clinic. A questionnaire was administered to collect socio-demographic data including age, gender, household monthly income, primary care giver (defined as person who took care of the child during most of the day) and whether parents of the child were alive. All the children had a physical examination performed by a paediatrician. HIV test results available from a previous study were used to define the HIV infection status of the children.[13]

Anaemia was defined as a haemoglobin level of less than 11.5 grams per decilitre(g/dl). ID was defined as a serum ferritin level of less than 15 micrograms per litre (µg/L). IDA was defined as a haemoglobin level of less than 11.5 g/dland either ferritin below 15 µg/Lor a serum transferrin receptor (sTfR) level of more than 8.3 µg/L (above manufacturer' reference limit).

Blood Samples Collection

Participants' hands were washed thoroughly with soap, rinsed well with warm water and dried with paper towel. The middle finger was massaged and a lancet was pressed on the fleshy part of the finger tip. The finger was gently squeezed to produce a drop of blood. The initial drop of blood was wiped away with cotton wool. Blood was collected in a micro cuvette slide and the haemoglobin level was determined by using a

The prevalence of all- cause anaemia in the children was 15% (n= 48) and that of IDA was 2%. There was no difference in the prevalence of all-cause anaemia between the girls and boys (p = 0.94). Only one child had severe anaemia. The prevalence of ID was 4%. The World Health Organization recommends using a higher cut off level for ferritin of 30 µg/L in children below five years in areas with a high infectious disease burden. However, there is no recommendation for children above five years in similar settings. When the higher cut off of ferritin was applied, it resulted in a higher prevalence of ID of 32%.

Table III: Haemoglobin, Ferritin, All-cause Anaemia (ACA) and Iron Deficiency Anaemia (IDA) stratified for Gender, Age and HIV Status in Zimbabwean School-aged children.

Characteristic	Sub Category	Frequency (n)	[1]Haemoglobin (g/dl) n=317	[2]Ferritin (µg/L) n=316	ACA n (%)	[3]IDA n (%)
Gender:	Female	181	12.5 (±1.10)	46.1 (±26.5)	27 (15)	2 (1)
	Male	137	12.5 (±1.23)	47.2 (±39.5)	21 (15)	5 (4)
Total		**318**	**12.5 (±1.16)**	**46.6 (±32.7)**	**48 (15)**	**7 (2)**
Age (Years):	7	21	12.7 (±1.04)	48.3 (±25.2)	3 (14)	0 (0)
	8	105	12.4 (±1.08)	48.8 (±41.7)	21 (20)	2 (2)
	9	186	12.6 (±1.19)	45.3 (±27.7)	23 (12)	5 (3)
	10	6	12.3 (±1.42)	41.8 (±24.5)	1 (17)	0 (0)
HIV Status:	Negative	296	12.6 (±1.14)	46.4 (±32.7)	39 (13)	6 (2)
	Positive	21	11.9 (±1.25)	51.0 (±34.0)	9 (43)	1 (5)

[1] Mean haemoglobin (standard deviation)
[2] Mean ferritin (standard deviation)
[3] IDA defined as Hb< 11.5 g/dland either F < 15 µg/Lor sTfR level > 8.3 µg/L

The comparison of the prevalence of ID and IDA for the two cut off values of ferritin are presented in Table IV. Anaemia was more likely to be present in HIV infected children (p-value<0.001) with an odds ratio of 4.9 (CI 1.9- 12.4). Maternal HIV status at birth was not related to presence of anaemia in the children aged 7 to 10 years.

Table IV: Prevalence of iron deficiency (ID) and iron deficiency anaemia (IDA) using a Ferritin cut-off value of 15µg/L and 30µg/L respectively in Zimbabwean school-aged children.

Characteristic		Frequency (n)	ID Ferritin <15µg/L n (%)	ID Ferritin <30µg/L n (%)	IDA[1] Ferritin <15µg/L n (%)	IDA[2] Ferritin <30µg/L n (%)
Gender	Female	181	7 (4)	50 (28)	2 (1)	6 (3)
	Male	137	6 (4)	52 (38)	5 (4)	10 (7)
Total		**318**	**13 (4)**	**102 (32)**	**7 (2)**	**16 (5)**

[1] IDA defined as Hb< 11.5 g/dland either F < 15 µg/Lor sTfR level > 8.3 µg/L
[2] IDA defined as Hb< 11.5 g/dland either F < 30 µg/Lor sTfR level > 8.3 µg/L

Discussion

The 15% prevalence of anaemia was of mild public health significance as it falls between 5 and 19.9%.[18] In spite of this, anaemia has important effects at the individual level in school going children. Very few children had IDA but when a higher ferritin cut off of 30 µg/L was applied the prevalence of IDA became of mild public health significance in this cohort. A small proportion of anaemia was caused by ID in these children. ID increased almost 8 fold when the higher cut off, of 30 µg/L was used. As previously observed by others, HIV infection increased the likelihood of anaemia in the children.[19-21] Our study agrees with the studies that have shown that HIV infection increased the odds of anaemia in children. Maternal HIV status at birth was not related to presence of anaemia in the children after five years of age.

This study had a much lower prevalence of anaemia, ID and IDA anaemia compared to a study done by Midzi *et al* in a rural area in Zimbabwe with a high prevalence of malaria, *schistosomiasis* and soil helminths.[22] The prevalence of anaemia and IDA reported were 48% and 38% respectively. The study on

which the present article is based was conducted in a peri-urban area around Harare, the capital city of Zimbabwe, with no malaria,[23-24] *schistosomiasis* and a very low soil helminths[25] burden. Another difference is that Midzi *et al* included preschool children below five years. Our study alsodiffers from other African studies done in areas with high parasite burden which also reported high prevalence of anaemia and IDA.[26-28] Some researchers from Africa and Europe have found that boys had more ID compared to girls[27-29] in a similar age group to our participants, while in an Asian study ID was higher in girls.[28] In our study there was no gender difference in the occurrence of anaemia or IDA. However, our result on prevalence of anaemia concurs with the global estimates from WHO were Zimbabwe is estimated to have an anaemia prevalence of mild public health significance.[18]

Anaemia is important in school going children as it has been associated with reduced physical work capacity, reduced cognitive function and reduced intellectual performance.[1] ID has also been shown to negatively affect physical growth,[30] since iron is necessary for growth and metabolism.[31] Furthermore, ID negatively affects learning, memory, affective and social behaviour.[6,32-33] It also affects physical work performance, cognitive function, language development and causes poor grades at school.[34-39] ID is associated with increased gut uptake of other heavy metals like lead.[40] The brain should be protected from the effects of ID as these may persist for a long time.[33] The importance of identifying individual children with anaemia, ID and IDA should be emphasized as they all can result in children failing to achieve their full potential at school. This impacts on their future economic performance and can result in poverty. Programs should be in place to identify school children with anaemia, ID and IDA for intervention purposes. These should be continuous with the programs for infants and children under five years so as to have an impact in preventing the long term consequences of anaemia, ID and IDA.

Limitations

This study used haemoglobin level and serum ferritin complemented with sTfR levels to make a diagnosis of IDA, which is the WHO recommendation.[41] The gold standard would have been doing bone marrow iron studies but this is invasive and difficult to justify in well school going children. Some studies have shown that having unstainable bone marrow iron may not equal ID.[42-43] C-reactive protein levels were not measured in our study. C-reactive protein has been used by others to identify inflammation and improve reliability of ferritin in diagnosis of ID. Although thresholds of C-reactive protein levels that make ferritin unreliable are not clearly defined, thresholds of 10-30 nanograms per litre are used.[44] The combination of ferritin and sTfR level may allow some differentiation between ID and inflammation.[44] Conversely, there are studies that found sTfR level to be affected by inflammation.[45] On the other hand, there are also studies that have found sTfR to be relatively independent of inflammation.[46-47] Not using C-reactive protein or sTfR level to define ID resulted in underestimation of prevalence of ID in our study. The fact that this was a cross sectional study meant we could not discuss causality of anaemia in these children. Nevertheless, this is one of the few studies that have looked at anaemia in school children born in a national mother-to-child HIV prevention programme beyond the age of 5 years in an area with a high prevalence of HIV infection.

Conclusion

This study found that the prevalence of anaemia and ID was of mild public health significance in the school children born in a national HIV prevention programme in a resource poor setting with a high burden of HIV infection. IDA contributed 15% of all cases of anaemia. IDA should be addressed easily and cheaply through iron fortification of basic food stuff such as mealie-meal and teaching the public to consume iron rich food. HIV infection was an important determinant for the presence of anaemia. Therefore HIV prevention programs for children should be strengthened to eliminate paediatric HIV infections as this may also reduce the cases of anaemia in school children in areas with high burden of HIV infection.

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