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RESEARCH

Anaemia in pregnancy in a setting of high HIV prevalence rates

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Background: Although there is much literature on anaemia in pregnancy, there are limited data on anaemia specific to HIV in pregnancy. The aim of this study was to determine the prevalence of anaemia among HIV-infected antenatal attendees at their first visit.
Methods: This was a secondary analysis of 2 000 antenatal attendees enrolled into a study on anaemia in pregnancy and was carried out at a regional hospital from 2012–2014. Demographic and clinical data including anaemia, perinatal and maternal outcomes of HIV infected women were analysed.
Results: Of the 2 000 recruited, 854 (42.7%) were anaemic, 943 (47.2%) were infected with HIV, and 609 (64.6%) HIV-infected women had anaemia.
There was a significant difference in the prevalence of anaemia in HIV-infected patients on antiretroviral (ARV) treatment compared to untreated patients (41.4% vs 92.1%; $p < 0.0001$). Mild grades of anaemia were common in HIV-infected patients on ARVs, while moderate to severe grades were most common in patients who were not on ARVs. Besides birthweight and hypertensive disorders of pregnancy, there was no significant difference in neonatal and maternal outcomes irrespective of duration of ARV treatment.
Conclusions: There was a high prevalence of anaemia among HIV-infected, untreated pregnant women. Assessment of anaemia at the first antenatal visit is, therefore, essential.

Keywords: anaemia, HIV, pregnancy

Introduction

Anaemia and HIV infections are important public health issues affecting millions of people globally.[1,2] Pregnant women in particular are vulnerable to both anaemia and HIV infections.[1,2] Recently, Oladeinde *et al*. reported that the prevalence of HIV and anaemia in a rural community in Nigeria was 11.7% and 49.3%, respectively.[3] Similar reports originate from other west and east African countries.[4–6] Okeudo *et al*. also showed that HIV infection increased the frequency of anaemia in a Nigerian population.[4] South Africa (SA) has higher rates of HIV infection than that reported from Nigeria, while rates of anaemia are similar.[7–10] In a South African rural province, the overall prevalence of anaemia (<10 g/dl) was 19.7%,[8] while that in an urban setting serving a low socio-economic population was 42.7% (< 11 g/dl).[7]

The prevalence of HIV infection in antenatal attendees in SA is approximately 30%.[10] Reports from other countries in Africa including SA show increased rates of anaemia in HIV-infected women, and it has been suggested that the increased prevalence may be explained by the fact that this viral infection is associated with low serum folate, vitamin B12 and ferritin levels in pregnancy.[4,11,12] In addition, the use of anti-retroviral agents such as zidovudine either for the prevention of mother to child transmission or treatment of HIV have also been implicated in the development of anaemia.[12] Furthermore, anaemia associated with HIV and AIDS may arise from destruction or inhibition of haematopoietic cells and it is reported to be a marker of disease progression.[5] Thus, HIV is independently reported to cause anaemia.[5,13] A recent retrospective study by Nandlal *et al.* in pregnant women with advanced HIV and AIDS showed that 64.2% had anaemia.[9] There is, however, limited data on anaemia in HIV pregnant women with high CD4 cell counts in South Africa.

Methods

Following institutional regulatory permissions (Biomedical Research Ethics Committee of the University of KwaZulu-Natal: BE 306/12) venous blood samples for complete blood counts were obtained from 2 000 consenting antenatal attendees at their first antenatal visit. All women except those who were infected with HIV, or were not on any other medications at the time of the study, were entered into the study. The standard practice at the study site was to offer all women a HIV screening blood test and a complete blood count. In addition, all women had syphilis and rhesus testing. Those who tested HIV-positive and those known to be HIV infected on treatment had CD4 cell counts performed. Relevant demographic and clinical information were entered in a structured data sheet.

Anaemia in pregnancy was defined according to the WHO classification of a haemoglobin (Hb) concentration of < 11 g/d.[2] All women received prophylactic iron therapy (oral ferrous sulphate, 200 mgs daily) and folic acid, 5 mgs daily. The haemoglobin (Hb) concentration levels were arbitrarily divided into the following groups: (i) > 11 g/dl; (ii) between 10–10.9 g/dl; (iii) between 7–9.9 g/dl; and, (iv) <7 g/dl and below, for the purposes of the study. The incidence of smoking in the population studied was low (approximately 3% according to hospital statistics) and the study site was a regional hospital in an urban setting at sea level serving a low socio-economic population.

Statistical Analysis

Data was entered into a computer database using Microsoft Excel software and was analysed using SPSS (version 23). Continuous variables were described as mean and standard deviation, whereas categorical variables were expressed by frequency and percentage. A *p*-value of < 0.05 was judged to be statistically significant.

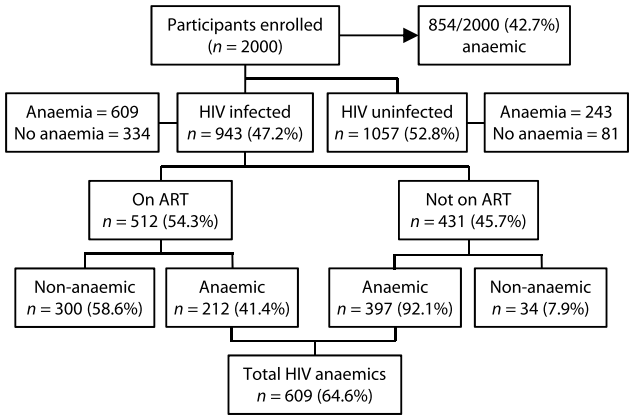

Figure 1: All HIV-infected women with anaemia.
ART=antiretroviral therapy.

Table 1: Demographic and obstetric data of HIV Infected anaemic participants at booking

Variable	Total (*n* = 609)	HIV infected on ARVs (*n* = 212)	HIV infected ARVs naive (*n* = 397)	*p*-value
Mean age years (range)	25.3 (17–40)	27.5 (24–40)	24.5 (17–31)	0.01
Age groups (years)				
≤19	84 (13.8%)	21 (9.9%)	63 (15.9%)	0.02
20–24	249 (40.9%)	89 (41.9%)	160 (40.3%)	0.7
25–30	154 (25.3%)	46 (21.7%)	108 (27.2%)	0.1
31–34	81 (13.3%)	42 (19.8%)	39 (9.8%)	0.0005
≥ 35	41 (6.7%)	14 (6.6%)	27 (6.8%)	0.9
Mean parity	2 .1 ± 1.0 (1–4)	2.1 ± 1 (1–4)	2.2 ± 1.1 (1–3)	0.4
Mean gestation				
Age at booking (weeks)	24.2 ± 3.1 (17–34)	26.4 ± 2.1 (24–34)	24.2 ± 1.1 (17–32)	0.2

ARV–antiretroviral drugs.

Results

Two thousand antenatal attendees were enrolled in the initial study. The mean (SD) age was 27.6 ± 7.6 years; the mean parity was 2.0 ± 1.1 and the mean (SD) gestational age at first visit was 24 ± 2.24 weeks. Eight hundred and fifty-four of the 2 000 antenatal participants were anaemic with a prevalence of 42.7% at entry into the study.

Figure 1 shows that of the 2 000 women enrolled, 943 (47.2%) patients were HIV infected and of these 609 were anaemic giving a prevalence rate of 64.6%. Five hundred and twelve of the 943 HIV infected patients (54.3%) were on antiretroviral (ARV) agents of which 212 (41.4%) patients were anaemic. Four hundred and thirty-one (45.7%) were ARV-naive, of which 397 (92.1%) were anaemic. There was significant difference in the incidence of anaemia in HIV infected patients on ARV treatment compared to HIV-infected ARV-naive patients (41.4% vs 92.1%; $p < 0.0001$).

Table 1 shows the demographic data of the 609 HIV-infected anaemic patients. The mean (SD) age was 25.3 (17 – 40) years compared to 27.5 (24 – 40) years in participants on ARV treatment and 24.5 (17 – 31) years in ARV-naive participants. The mean (SD) parity and gestational age of the HIV-infected participants at first visit was 2.1 ± 1.0 and 24 ± 3.1 weeks, respectively. The highest prevalence of HIV infection (40.9%) was in the age group 20–24 years.

Table 2: Stratified Haemoglobin levels of HIV-infected patients with anaemia at booking

Grades of anaemia	Hb levels (g/dl)	HIV-infected on ARVs (*n* = 212)	HIV-infected ARV-naive (*n* = 397)	*p*-value
Mild	10.0–10.9	123 (58%)	92 (24.4%)	0.0001
Moderate	7–9.9	89 (42%)	295 (74.3%)	0.0001
Severe	<7.0	0 (0%)	5 (12.6%)	0.0001

Five hundred and twelve (56.3%) participants were on HIV treatment for 1 to 3 years prior to pregnancy, of which 212 (41.4%) were anaemic.

Four hundred and thirty-one HIV-infected women were ARV-naive, of which 397 (43.7%) were anaemic and received HIV treatment at diagnosis, namely with zidovudine (ZDV) prophylaxis or triple ARV. ARV therapy was started at a mean gestational age of 26.2 ± 3.1 weeks.

Table 2 shows the grades of anaemia. The mild type was more common in HIV-infected patients on treatment, while moderate to severe anaemia was more common in ARV-naive patients.

In HIV-infected women, the main types of anaemia were hypochromic microcytic (*n* = 7; 1.1%), normochromic normocytic (*n* = 424; 69.6%), hypochromic normocytic (*n* = 108; 17.7%) and normochromic microcytic (*n* = 70; 11.5%) (Table 3). There was no

Table 3: Types of anaemia in HIV-infected participants at booking

Types of anaemia	HIV infected on ARVs (*n* = 212)	HIV infected ARV-naïve (*n* = 397)	*p*-value
Hypochromic microcytic	1 (0.5%)	6 (1.5%)	0.2
Normochromic normocytic	147 (69.3%)	277 (69.8%)	0.8
Hypochromic normocytic	44 (20.8%)	64 (16.8%)	0.2
Normochromic microcytic	20 (9.4%)	50 (12.6%)	0.2

Table 4: Maternal and neonatal morbidity and mortality of the HIV-infected anaemic participants (*n* = 609) based on duration of HIV treatment

Variable	HIV positive on ARVS 1–3 years (*n* = 212)	HIV positive on ARVs <1 year (*n* = 397)	*p*-value
Preterm labour	24 (11.3%)	43 (10.8%)	0.8
Stillbirths	5 (2.4%)	11 (2.8%)	0.2
Birthweight (kg)	3.2 ± 0.8	2.87 ± 0.4	0.0001*
Neonatal mortality	1 (0.5%)	4 (1%)	0.5
Hypertensive disorders	11 (5.2%)	4 (1%)	0.0001*
Abruptio placentae	2 (0.9%)	7 (1.8%)	0.3

*$p < 0.0001$.

difference in the type of anaemia between patients who received ARV treatment compared to ARV-naive patients. Normocytic normochromic anaemia was the most common. Normochromic microcytic anaemia was least common.

Table 4 lists the neonatal and maternal morbidity and mortality of HIV-infected patients based on the duration of HIV treatment. Except for neonatal bodyweight and hypertensive disorders of pregnancy, there was no significant difference in neonatal and maternal morbidity between patients who received ARV treatment for 1–3 years compared to those who had treatment for < 1 yr.

Discussion

The major findings in this study are an antenatal prevalence rate of HIV of 47.2% and a high prevalence of anaemia at entry of 42.7% of the study participants to this study.[7] The high prevalence rate in the study site may be a reflection of an increase in the awareness and acceptance of HIV screening. Similar prevalence rates of anaemia have been reported from other low and middle income countries, such as Nigeria where Oladeinde *et al*. and Okeudo *et al.* reported that the prevalence rates among pregnant women were 49.3% and 59.9% respectively.[3,4] Our population was a low socio-economic urban community and probably similar to that of the Nigerian studies, except malarial infection rates are low in the South African (SA) province in which the study site was situated. The Saving Mother's Report 2011–2013 also found that 42.4% of maternal deaths occurred in women who were anaemic (< 10 g/dl). In addition, the 2014 annual Saving Mothers Report published by the SA Department of Health indicated that of all women who died from non-pregnancy related infections, mainly HIV/AIDS, 58.2% were anaemic.[14]

The prevalence of anaemia in HIV-infected women in our study was 64.6%. This is in keeping with the study of Nandlal *et al.* who did a retrospective cohort data analysis of anaemia in a similar population group.[9] These authors found a prevalence rate of 64.5% but most of their study participants had advanced HIV (CD4 < 200 cells/mm^3; WHO grades 3 and 4) while on antiretroviral therapy. None of our study population had co-morbid diseases, such as tuberculosis, and all were healthy antenatal attendees with no previous history of admissions to a health facility during the current pregnancy. Furthermore, all the participants in our study had lesser severity of HIV infection, with a median CD4 cell count of 486 cells/mm^3 (range: 422–546 cells/mm^3).

The prevalence of anaemia in our study of those patients who tested HIV-seropositive for the first time was 34.5% and may be a more accurate reflection of their Hb concentration levels. The women who were seropositive at first testing were not on any HIV antiretroviral drugs and were not on multivitamin, iron or folic acid prophylactic supplementation. Antiretroviral drugs (ARVs), especially zidovudine, has been reported to cause anaemia,[5,6,13] which may be related to the duration of the use of these drugs. In a study from Thailand, comparing maternal anaemia between HIV-infected pregnant women receiving zidovudine-based and zidovudine-free highly active antiretroviral therapy (HAART); the outcome showed that both zidovudine-based and zidovudine-free HAART exposure was associated with substantial risk of maternal anaemia during pregnancy two to three months after exposure.[15,16] Similarly, Sartorius *et al*. conducted a randomised trial in three African countries, including SA, showed that severe anaemia occurred at a similar rate in women receiving a zidovudine-containing ARV regimen with a short or long duration.[5] Moreover, it appeared that women with severe anaemia reduced their Hb concentrations after a few months of treatment with ARV therapy. Overall, we found that 41% of HIV-positive pregnant women with anaemia were on ARV treatment, compared to 92% of HIV-infected pregnant women with anaemia who were not on ARV treatment. Thus, it seems that ARV therapy may have a positive impact on Hb levels.[5,12] However persistent low Hb levels may signify deterioration in the disease process.[15] Odhiambo *et al*. had similar findings in a mother-to-child ARV prevention study in which they found resolution amongst 550 women who continued with ARV therapy for up for 2 years from the time of child birth.[12] Berhane *et al.* also showed similar results with at least 6 months of ARV usage.[17] Thus, it seems that ARV therapy certainly increases the resolution of anemia and this might be due to the effects of ARVs on inflammation and chronic infection. However, it can be argued that women receiving ARVs also receive iron, folic acid, multivitamin and other nutritional supplements, which may have an overall positive impact on health.

Most of the types of anaemia in our study were normocytic normochromic in type suggesting that iron deficiency is not a major factor in the aetiology of the anaemia. Similar findings were reported from Uganda who evaluated serum ferritin levels and transferritin receptor levels to establish the contribution of iron and common infections in pregnant women. Baingana *et al*. indicate that chronic infections and inflammation have a greater role in the aetiology of anaemia.[6]

Previous studies have shown that anaemia had an impact on neonatal and maternal morbidity and mortality. Tunkyi *et al.* reported that anaemia is an important obstetric complication which affects both mother and child.[7] In our study, Table 4 shows the neonatal and maternal morbidity and mortality outcomes in HIV-infected women; and, except for birthweight and hypertensive disorders of pregnancy, there were no significant differences in perinatal and maternal morbidity between patients who received and did not receive HAART.

There was a high incidence of anaemia among HIV-infected pregnant women at entry. There was a significant difference in the incidence of anaemia in HIV-infected patients on ARV treatment compared to HIV-infected ARV-naive pregnant women at booking. There was no difference in perinatal and maternal morbidity between patients who received antiretroviral treatment irrespective of duration of treatment.

In conclusion, anaemia is a common finding in pregnant women diagnosed with HIV with high perinatal and maternal morbidity rates. Assessment of anaemia at the first antenatal visit is therefore essential as it affords one the opportunity to establish the exact cause of low Hb concentration levels, and institute interventions to prevent complications. It must be recognised, however, that anaemia is not a diagnosis and must prompt detailed investigations for the underlying cause in particular chronic infections.

Conflict of interests – The authors have neither conflict of interests nor financial declarations to declare.

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