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Risk of anaemia in HIV positive pregnant women in Ibadan, South West Nigeria.

O Adesina[1], A Oladokun[1], O Akinyemi[2], T Akingbola[3], O Awolude[1] and I Adewole[1]

Departments of Obstetrics and Gynaecology[1], Epidemiology, Medical Statistics and Environmental Health[2] and Haematology[3], College of Medicine, University of Ibadan, Nigeria

Summary

Anaemia in pregnancy is an important cause of maternal and neonatal mortality. It is a recognized co-morbidity of HIV infection. This study aimed to determine the risk of anaemia in HIV positive pregnant women. Methodology- This is a cross sectional study of healthy pregnant women attending Adeoyo Hospital, a secondary health centre in South-western Nigeria over a 1- month period (January 2007). During the study period, 2,737 eligible women presented for antenatal care. About 98% (2,682) of these women consented to HIV testing. Over all, their mean (± S.D) packed cell volume was 30.96% (±4.13). The prevalence of HIV infection was 2.9% (95% CI 2.3% - 3.6%) and the overall prevalence of anaemia was 33.1%. Frequency of anaemia was significantly higher in HIV +ve women (57.3% vs. 42.7%, p= 0.00. OR=2.81., CI=1.72-4.58). HIV +ve women presented more frequently with moderate or severe anaemia. In the logistic regression analysis only HIV infection (OR=2.4, 95%CI=1.37-4.21) and primigravidity (OR=1.25, 95% CI=1.04-15.2) remained independently associated with anemia. Anaemia is common in HIV positive pregnant women in this environment. Care providers must endeavor to determine the HIV status of every pregnant woman especially if she presents with anaemia with a view to providing appropriate interventions.

Keywords: *HIV, anaemia, pregnancy, etiology, risk*

Résumé

L'anémie pendant la grossesse est l'une des causes importantes de la mortalité maternelle et néonatale. Il est reconnu des cas de souffrance des doubles infections au VIH. Cette étude a pour but de déterminer les risques d'anémie chez les femmes séropositives enceintes. Ceci est une étude sectionnaire croisée des femmes enceintes bien portantes atteignant l'hôpital Adeoyo, un centre de sante secondaire au sud oust du Nigeria pendant une période d'un mois (janvier 2007). Pendant cette période d'étude, 2.737 femmes présentées pour les soins prénatal. Environs 98% (2.682) de ces femmes ont acceptes le test du VIH. Au total, leur moyenne en hématocrite était de 30.96% (±4.13). La prévalence aux infections du VIH était 2.9%(95% CI 2.3%-3.6%) et la prévalence a l'anémie était significativement élevé chez les femmes séropositives (57.3% contre 42.7%, P=0.00, OR= 2.81, CI=1.72-4.58). Les femmes séropositives présentaient plus fréquemment une anémie sévère ou modéré. Dans les analyses de régression logistique, seule l'infection du VIH (OR=2.4, 95%CI=1.37- 4.21) et la primigravide (OR=1.25, 95% CI=1.04-15.2) restaient indépendamment associes avec l'anémie. L'anémie est fréquente chez les femmes enceintes séropositives dans cet environnement. Des dispositions de soins doivent être mises sur place pour déterminer le statut sérologique de toutes les femmes enceintes précisément si elle présente une anémie en vue d'apporter une intervention appropriée.

Introduction

Anaemia in pregnancy is an important direct and indirect cause of maternal death [1]. It is associated with adverse fetal outcomes such as intrauterine growth restriction, low birth weight and still birth [2]. During pregnancy, severe anaemia may result in circulatory changes that are associated with an increased risk of heart failure [3]. During labour, women with anaemia are less able to endure even moderate blood loss [4]. Anaemia in pregnancy is common in Nigeria and other developing countries of the world [5], where it's effects may be more marked due to conditions such as lack of balanced dietary intake, short inter-pregnancy interval and prolonged lactation coupled with women's daily routine of heavy physical exercise [5,6].

Correspondence: Dr. Olubukola Adesina, Department of Obstetrics and Gynaecology, College of Medicine, Univerity of Ibadan, Ibadan, Nigeria. E-mail: bukiadewole@yahoo.com, bukiadewole@hotmail.com

The definition of what constitutes anemia in pregnancy has been the subject of lively debate for several years. The World Health Organization defines anaemia as a haemoglobin concentration lower than 11gm/dl or a haematocrit lower than 33% [7]. If this definition were however to be applied in Nigeria, more than two-thirds of women attending antenatal clinics in the country will require to be investigated for anaemia [8]. In practice, it has been found that a large number of pregnant Nigerian women with haematocrit values between 30% and 33% get through pregnancy without any apparent ill effects to themselves or their offsprings. Thus, only anemia with haematocrit lower than 30% is deemed worthy of further investigation and treatment in this environment [8].

The etiology of anaemia in sub-Saharan Africa is complex and multi-factorial. While malaria is a major cause of anaemia, particularly in first and second pregnancies [9], it may also result from nutritional deficiency (most commonly iron deficiency), congenital blood cell disorders (e.g. sickle cell disease) and infections (such as hookworm and the Human Immunodeficiency Virus) [10]. Indeed, in HIV positive individuals, anaemia is the most common hematological abnormality that is encountered [11]. There are numerous potential etiologies for HIV- associated anaemia. The most frequent cause of anaemia in HIV-infected patients is anaemia of chronic disease [11]. Other possible etiologies include opportunistic pathogens infecting the bone marrow (e.g. parvovirus B19), medications (e.g. zidovudine) and autoimmune haemolsysis [11, 12, 13]. Other factors implicated include haemolytic micro-angiopathies, malignancies and chronic renal failure [11, 14]. Anaemia in HIV positive patients adversely affects functional capacity and quality of life, and it has been associated with decreased survival [15]. In addition, studies have reported an association between maternal anemia and vertical transmission of HIV [16, 17]. Thus, it is important for clinicians providing care for this group of pregnant women to be aware of the problem and prevent the morbidity associated with it. Thus, this study aimed to determine the risk of anaemia in HIV positive pregnant women presenting at a major health facility in Ibadan.

Patients and methods

This was a cross sectional study of apparently healthy pregnant Nigerian women attending Adeoyo Maternity Hospital (AMH). AMH is a secondary health centre in Ibadan, the capital of Oyo State in the South-West of Nigeria. Joint UI/UCH institutional review board ethical approval was obtained from the institutional review board.

The case record of every pregnant woman who presented for care over a 1-month period (January 2007) was reviewed. Women presenting newly for care had their data recorded, while those previously booked had their data at their first presentation retrieved and similarly recorded. These data included selected demographic, anthropometric measurements and obstetrics information. Pregnant women with multiple pregnancies, known history of glucose 6-phosphate deficiency, recent history of a febrile illness, chronic medical ailments (e.g. hypertension), bleeding in early pregnancy and blood disorders (e.g. haemoglobinopathies) at first presentation were excluded from the study. The women were categorized into the traditional first, second or third trimesters. Eligible participants were assigned serial numbers by a research assistant. This was discretely documented on the case files to avoid duplication of data collection.

All women were offered several investigations at their first antenatal visit including packed cell volume and HIV testing. Anaemia was defined as packed cell volume less than 30%. Mild, moderate and severe anaemia were defined as packed cell volume 27- 29%, 19 -26% and <19% respectively [18]. HIV testing, as recommended by the national prevention of Mother-to-Child transmission of HIV protocol, was offered in an opt-out approach. Three milliliters (3ml) of venous blood was obtained from the ante-cubital vein after the patient consented to HIV testing. The blood was placed into vacutainer tubes containing di-potassium ethylene diamine tetra-acetic acid (K2-EDTA) as the anti-coagulant. HIV testing involved the use of 2 rapid test methods: Determine (Abbott Laboratories) and Capillus HIV 1/HIV-2 (Cambridge Diagnostics, Wicklow Ireland). HIV sero-positivity was defined as a reactive result on both rapid tests. In case of an inconclusive result, a third rapid test and/or Western Blot test was performed as a tie-breaker to decide the status of the patient.

The statistical program, SPSS (SPSS for windows versions 12.0, SPSS Inc., Chicago IL) was used for analysis. For all statistical tests, p value less than 0.05 was considered significant. Differences in means were compared by student's t-test. Differences in proportions were analyzed using the chi-square test or Fisher's exact test when appropriate. Logistic regression was used to examine the association between

anemia and maternal characteristics that were found to be significant in the univariate analysis.

Results

From January 1st to January 31st 2007, two thousand seven hundred and thirty seven eligible women (2,737) sought antenatal care, at Adeoyo Maternity Hospital Yemetu, Ibadan. About 98% of these women consented to HIV testing, two percent declined HIV testing. Reasons for declining usually included having recently had an HIV test, requiring husband's consent before testing, etc. The records of the 2,682 women who therefore consented to HIV testing are analyzed and presented here.

Table 1 shows the distribution of selected maternal characteristics. The modal parity was 0. In this population the prevalence of HIV infection was 2.9% (n = 77; 95% confidence interval 2.3% - 3.6%). There were no significant differences between the HIV positive and HIV negative women in terms of characteristics such as age, height and gestational age. Table 2 shows distribution of maternal packed cell volume and VDRL result. The prevalence of anemia (defined as <30%) in this obstetric population was 33.1%. The HIV positive and HIV negative women were different in terms of mean packed cell volume and frequency of anemia. These differences were statistically significant. HIV +ve women presented more frequently

Table 1: Selected maternal characteristics

Variable	All women, n=2682	HIV-ve, n=2605	HIV +ve, n=77	p value
Mean age	27.36 ± 5.34	27.33 ± 5.38	27.04 ± 3.98	0.91
Mean height	159.1 ± 6.51	159.09 ± 6.5	158.9 ± 5.59	0.81
Mean weight	63. 84 ± 11.69	63.9 ± 11.71	61. 72 ± 11.71	0.16
Mean gest. age	26.38 ± 6.38	26. 37 ± 6.35	26.65 ± 7.05	0.73
Mean BMI	25. 20 ± 4.32	25. 25 ± 4.33	24. 41 ± 4.0	0.15
Age group				
≤ 19	134 (5.0%)	133 (5.1%)	1 (1.3%)	0.07
20-24	654 (24.4%)	638 (24.5%)	16 (19.5%)	
25- 29	964 (35.9%)	930 (35.7%)	34 (42.8%)	
30- 34	595 (22.2%)	573 (22.0%)	22 (29.9%)	
≥35	335 (12.5%)	331 (12.7%)	4 (6.5%)	
Parity				
0	973 (36.3%)	943 (36.2%)	30 (39.4%)	0.85
1-4	1672 (62.3%)	1626 (62.4%)	46 (59.2%)	
≥ 5	37 (1.4%)	36 (1.4%)	1 (1.4%)	
Body mass index				
≤ 19	74 (2.7%)	70 (2.7%)	4 (5.3%)	0.33
20- 29	2247 (83.8%)	2180 (83.7%)	67 (86.6%)	
≥29	361 (13.5%)	355 (13.6%)	6 (8.1%)	

Table 2: Selected maternal parameters

Variable	All women, n=2682	HIV-ve, n=2605	HIV +ve, n=77	p value
Mean PCV	30.96 ± 4.13	31. 05 ± 4.05	27.88 ± 4.7	0.01
Presence of anaemia				
PCV ≥ 30%	1794 (66.9%)	1761 (67.6%)	33 (42.7%)	0.00
PCV < 30%	888 (33.1%)	844 (32.4%)	44 (57.3%)	OR2.81
			(95% CI 1.72- 4.58)	
PCV 27-29 %	542 (20.2%)	524 (20.1%)	18 (22.7%)	0.01
PCV 19-26 %	340 (12.7%)	315 (12.1%)	25 (33.3 %)	
PCV ≤ 18 %	6 (0.2%)	5 (0.2%)	1 (1.3%)	

with moderate anemia or severe anaemia. These differences were also statistically significant.

multivariate analysis. Women with higher BMI were however noted to be less likely to have anaemia.

Table 3: Comparison of anemic women and women without anaemia

Variable	Nil anemia, n=1794	Anemic women, n=885	p value
Age grouping			
≤ 19 (134)	77(57.5%)	57 (42.5%)	0.001
20-24 (654)	393 (60.3%)	261 (39.7%)	
25-29 (964)	661 (68.6%)	303 (31.4%)	
30-34(595)	414 (69.7%)	181 (30.3%)	
≥ 35(335)	249 (74.4%)	86 (25.6%)	
Trimester			
1st trimester (88)	68(77.3%)	20 (22.7%)	0.08
2nd trimester (1209)	815 (67.4%)	394 (32.6%)	
3rd trimester (1385)	911 (65.8%)	474 (34.2%)	
Parity			
0 (973)	604(62.1%)	369 (37.9%)	0.001
1-4 (1672)	1161 (69.4%)	511(30.6%)	
≥ 5 (37)	29 (78.4%)	8 (21.6 %)	
BMI range			
≤ 19 (74)	41 (55.4%)	33 (44.6%)	0.001
20- 29 (2247)	1473 (65.6%)	774(34.4%)	
≥5 (361)	280 (77.6%)	81 (22.4%)	

Table 4: Factors predisposing to anemia in the multivariate logistic regression analysis model

Factors	Odds Ratio	95% Confid. Interval	P-Value
HIV status (positive vs negative)	2.40	1.37 – 4.21	0.002
BMI			
<19 vs 20 – 29	1.51	0.89 – 2.56	0.125
>29 vs 20 – 29	0.57	0.42 – 0.77	0.001
Parity			
0 vs 1 – 4	1.25	1.04 – 1.52	0.021
> or = 5 vs 1-4	0.72	0.31 – 1.69	0.453
Age group			
≤19 vs 20 -34	1.24	0.83- 1. 88	0.30
≤ 35 vs 20 - 34	0.92	0.68- 1. 25	0.60

Table 3 shows maternal characteristics that were associated with higher prevalence of anaemia on univariate analysis. Anaemia was seen more frequently in women aged ≤19 years, women with BMI ≤ 19 and primigravidae. These differences were statistically significant. In the logistic regression analysis, only HIV infection and primigravidity remained independently associated with anaemia (see table 4). Women with BMI d" 19 were more likely to have anaemia but these differences were not sustained when subjected to

Discussion

Anaemia remains a problem among pregnant women in this urban population of West Africa. Dairo and Lawoyin [19] working in the same state obtained a prevalence of anaemia of 32.8 %. Published figures in other parts of Africa have shown a great variability in the prevalence of anemia. These have ranged from 55% in western Kenya [20], to78% in Liberian women in their 3rd trimester of gestation [21]. The prevalence of anaemia was higher among the HIV positive women

compared to the HIV negative women. This finding is similar to previous studies by other workers [6, 10, 19]. As previously noted several factors may account for the anaemia seen in HIV positive individuals [11, 12, 13, 14], and the care provider must endeavour to identify same with the goal of offering appropriate intervention. The prevalence of severe anaemia was low, 0.2%.

In this study, we found that primigravidity remained independent risk factor for anaemia in this obstetric population. Generally, anaemia is more common in the primigravidae than in the multigravidae in sub-Saharan Africa [3]. Although one might expect that anaemia in pregnancy would tend to increase with rising parity owing to repeated drain on iron stores [22, 23], various workers have observed a progressive decline in iron stores but increasing mean haemoglobin levels with increasing parity and attributed these differences to a greater risk of malaria in the primigravida [23, 24, 25]. Thus, in malaria endemic communities, malaria parasitemia which is an important risk factor for anaemia in pregnancy is a frequent finding in primigravidae [9]. In addition, several studies have shown the association between HIV infection and malaria parasitemia [10, 19, 27, 28]. Indeed, these two conditions may have synergistic effects on anaemia.

Anaemia was also found to be significantly higher in women with low BMI. The American College of Obstetricians and Gynecologists recommends that height and weight should be recorded for all women at the initial prenatal visit to allow calculations of the BMI [29]. This is necessary because of adverse pregnancy outcomes observed at extremes of the BMI. In addition, the HIV positive women in this obstetric population were observed to have lower BMI. HIV is associated with weight loss through various mechanisms [30]. Indeed, BMI maybe used as a proxy for the nutritional status of this obstetric population. This effect of low BMI on anaemia was however not sustained on multivariate analysis. A possible explanation is that it is that HIV contributes to both low BMI and anaemia. In contrast women with BMI <30 were actually 43% less likely to be anaemic.

Pregnant women 19 years and below, in this urban population, had higher proportion of anaemia than the other age groups. Adolescents in urban areas often face the problem of early marriage, early and/ or unwanted pregnancy, illegal and unsafe abortion, poverty and violence that compound the difficulties of adolescent physical and psycho-social development [31]. An adolescent girl is a child herself with significant nutritional requirements during the adolescent growth spurt. Various workers studying in urban areas have reported prevalence of anaemia in adolescent girls as 56%, 65- 75% [31, 32]. In an adolescent mother, the competing nutritional needs of pregnancy and growth may manifest as anaemia in pregnancy [33]. In addition, the vast majority of these adolescents are primigravidae and the effect of malaria in primigravidae may also contribute to the problem of anaemia.

It is important for clinicians providing care to HIV positive pregnant women to understand the risk of anaemia among this group of patients so that therapy can be provided. Therapy should be directed at the specific aetiological mechanism identified as being responsible for the anaemia. Correction of anemia leads to improved quality of life and survival and maximum benefits occur when haemoglobin is kept above 12g/dl [11]. HAART lowers the risk of developing anemia and increases resolution of pre-existing anemia [11]. Appropriate interventions may include nutritional supplementation, replacing antiretroviral agents and the treatment of infections or malignancies as appropriate. HAART, with restoration of humoral immunity against parvovirus B19, is also curative in some cases [11].

Traditionally, blood transfusion in pregnancy is indicated when the PCV is <18% at any gestational age, if the pregnant women becomes symptomatic with potential for cardiac/ pulmonary compromise and anaemia of any degree in the third trimester [8, 18]. However, for the HIV positive patient transfusion of red blood cells has been associated with a tendency towards accelerated HIV progression and decreased survival [34]. Possible explanation for this negative impact includes the transmission of infectious pathogens like cytomegalovirus and parvovirus. In spite of these concerns, blood transfusion is generally safe and should be given whenever it is indicated [11].

In conclusion, anaemia is common in HIV positive pregnant women in this environment. Every effort should be made to determine the HIV status of every pregnant woman and this is even more important in women presenting with anaemia in pregnancy. Appropriate interventions must be instituted to reduce the risk of morbidity.

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