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HIV as an additional risk factors for anaemia in pregnancy: evidence from primary care level in Ibadan, southwestern Nigeria

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Summary

Anaemia in pregnancy has serious consequences including maternal morbidity and impairment of infant cognitive development. Several authors have however reported inconsistent findings on risk factors for anaemia in pregnancy. This study was carried out to determine risk factors for anaemia in pregnancy among women at primary care level and document the contribution of HIV/AIDS to anaemia in pregnancy in low risk pregnant women at primary care level. A prospective study carried out among pregnant women attending the booking clinics of primary health care centres in Ibadan, Nigeria. HIV positive and HIV negative mothers were followed throughout pregnancy till delivery of their babies. History of use of iron, folate, Vitamin B complex and daraprim were obtained. Haemoglobin, malaria parasitaemia, and HIV serostatus were determined. Use of iron ($P < 0.006$), folate ($P = 0.032$), vitamin B complex ($P = 0.001$) and treatment for malaria ($P = 0.05$) significantly reduced the risk for anaemia in pregnancy. Malaria parasitaemia ($P = 0.0001$) significantly increased the risk of anaemia. However, use of daraprim and HIV seropositivity increased the risk of anaemia in pregnancy but not significantly. In a logistic regression analysis, iron ($P = 0.001$) and folate supplementation ($P = 0.015$) significantly protected against anaemia in pregnancy while malaria parasitaemia ($P = 0.006$) and HIV seropositivity ($P = 0.015$) were significant adverse risk factors. HIV is an additional risk factor for anaemia in pregnancy. Voluntary counseling and testing of pregnant women for HIV is therefore also indicated at primary care level to detect asymptomatic anaemia in pregnancy that may be due to HIV.

Keywords: *Anaemia, HIV/AIDS, risk factor, iron and folate supplementation, malaria,*

Résumé

L'anemie dans la grossesse a des consequences serieuses qui incluent la morbidite maternelle et l'affaiblissement du developpement cognitive de l'enfant. Plusieurs auteurs ont rapporte des conclusions inconsistentes sur les facteurs de risqué de l'anemie dans la grossesse parmi les femmes au niveau des dispensaires et de documenter la contribution du VIH/SIDA a l'anemie dans la grossesse chez les femmes enceintes a risqué faible. Une etude propective parmi les femmes enceintes qui se sont inscrites au niveau des dispensaires d'Ibadan, Nigeria. Les meres seropositives et negatives du VHI ont ete suivies pendant la grossesse jusqu'a l'accouchement. L'histoire de l'utilisation du fer, du folate de la vitamine B complexe et du daraprim de la malaria et le serostatut VHI ont ete determines L'utilisation du fer (0,0006) du folate (p=0,032), de vitamine B complexe P=0,0001) et le traitement de la malaria de malaria (p=0,05) ont reduit assez considerablement le risque de l'anemie dans la grosesse. La parasitemie de la malaria (p=0,0001) a augemente le risque d'anemie. Cependant, l'usage du daraprim et la seropositivete du VHI ont augmente le risqué d'anemie dans la grossesse mais pas considerablement. Dans une analyses du retour en arriere logistique, fer (p=0,001) et la supplementation du folate (p=,015) a considerablement protégé contre l'anemie dans la grossesse alors que la parasitimie de la malaria (p=0,006) et la seropositive VHI (p=0,015 etaient des facteurs de risques adverses considerables. Le VHI est un facteur de risqué supplementaire d'anemie dans la grossesse. Des conseils volontaires et le test des femmes enceintes en ce qui concerne le VHI est indique aussi au niveau des dispensaries pour detecter l'anemie asymptomatique qui peut etre due au VHI.

Introduction

Anaemia in pregnancy is a condition in which there is a reduction in the amount of circulating haemoglobin. This is usually defined as haemoglobin less than 11g/dl or a packed cell volume of 33% [1]. Anaemia in pregnancy causes adverse effects on both the mother and the foetus and also known to contribute to stillbirths, abortion and severe respiratory infections in the mothers. In the foetus, effect of anaemia is uncertain although studies have demonstrated significant impairment of foetal cognitive development even up to infancy [2-3].

Anaemia in pregnancy is common in Nigeria and other developing countries of the world [1,3,23]. World wide the prevalence of anaemia in pregnancy is 51%. Prevalence of anaemia in pregnancy in the developed world is about 20%, however, higher prevalence rates were found in the developing world. In Africa, an overall rate of 52% has been found while prevalence rate up to 35% has been found in South Africa, 56% in West Africa, and 53% in

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North Africa. In Nigeria, hospital-based prevalence of 22% was found in the west, 34% in the east and 46% in some parts of the north [1,3]. Thus, given the adverse effect and the magnitude of anaemia in pregnancy, its control in pregnancy has become imperative to combat the grave associated morbidity and mortality in both mothers and infants.

Several risk factors have been identified as predisposing to anaemia in pregnancy among which are iron deficiency, folate deficiency, malaria and HIV infection [1,3,9,22-24]. Evidence of the role of these factors in the development of anaemia in pregnancy are well established in some instances as in malaria parasitaemia but controversies still exist on the role and effect of some other factors especially HIV/AIDS. This study among low risk pregnant women at primary care level was done to determine the risk factors for anaemia in pregnancy and document evidence of association if any between HIV infection and anaemia in pregnancy. The study is part of a larger study on determinants of anaemia in pregnancy [4].

Patients and methods

Study areas

The study areas were health centres in two randomly selected urban and one rural local government areas (LGAs) in Oyo State. Ibarapa central LGA is rural while Ibadan north and Ibadan northwest LGAs are urban. The local government areas are populated mainly by the Yorubas, but a significant population of Fulani and Hausa settlers can be found in Ibarapa central and Ibadan northwest respectively.

Study population

All consenting pregnant women attending the antenatal clinics of randomly selected primary health care centres in the chosen local government areas were enrolled in the study at booking and followed till delivery of their babies. The primary health care centres were selected by simple random sampling using a sample frame of lists of health centres in the respective Local Government Areas. The women attending primary health care centres are those with low risk for poor pregnancy outcome. High risk pregnancies are normally referred to the secondary health care level in the city.

Study Design

The study is a prospective study of cases of anaemic women at booking and comparable controls attending the chosen antenatal clinics. Cases were defined as pregnant women with haemoglobin values below 11g/dl (PCV 33%) [3]. Pregnant women with multiple pregnancies, known history of glucose 6 phosphate deficiencies, haemoglobinopathy and blood dyscrasias were excluded from the study. The cases were compared with controls drawn from pregnant women from the same booking clinic who had similar age at last birthday, educational status, gestational age and parity. Data was collected by means of prepared proforma administered by the community health officers and nursing staff of the health centres. Demographic and obstetric information were collected from the women by means of open and closed ended questions. Haemoglobin and malaria parasitaemia were determined for all the cases and controls. HIV serostatus was determined for 60 cases and 120 controls that gave consent. For each participant the mean heamoglobin at the third trimester was used to define anaemia[4].

Laboratory methods

Haemoglobin estimation was by means of venous blood drawn from the antecubital vein into potassium EDTA bottles. Haemoglobin was then determined by the Sahli acid haematin method [5]. Malaria parasitaemia was determined by means of thick blood film on a slide stained with Giemsa stain and then examined with the light microscope under oil immersion illumination and 1000 magnification [6]. HIV serostatus was determined by means HIV Cassette test kit by Clinotech Diagnostics limited Canada [7]. The kit is a rapidly applied diagnostic screening test kit with a sensitivity of 99.9 % and specificity of 99.8%. The HIV test was performed at room temperature and results read within 30 minutes. Consent of each woman was obtained before any procedure was performed on her. The study protocol was approved by the Joint UI/UCH Institutional Review Board.

Statistical analysis

Anaemia was defined as haematocrit of 33% (11g/dl) according to WHO criteria [3]. Education was grouped into high or low. High education includes those with secondary level of education or more. Low education includes those with primary education or less. Qualitative demographic variables such as education level and marital status were compared using the Chi square statistic while quantitative variables such as age and parity were compared with the t test. Data was entered into the Epi Info version 6 statistical software and later exported to Systat for regression analysis [8,9]. In the univariate analysis levels of statistical significance were determined at 95% confidence interval. Variables significant at the 0.08 levels of significance were entered into the stepwise logistic regression model and odds ratio were determined at the 95% confidence limit. An odd ratio (O.R) less than one indicates a protective effect of the characteristic while odds ratio more than one indicate an adverse risk factor. An odds ratio of one indicates no risk.

Results

There were 196 women with anemia and 399 women without anaemia who acted as unmatched controls in this study. One hundred and thirty eight (70.4%) cases and 301(75.4%) controls had nil or low education. Cases and controls thus

had comparatively similar levels of education ($P > 0.05$) (Table 1). The ages of the cases ranged from 15 - 45 years while that of controls was 14 - 40years. The mean age of cases (25 ± 5.5 years) was not statistically significantly different from that of controls (25± 5.3years) ($P > 0.05$). The parity of the women ranged from 0-7 for cases and 0-8 for controls. Similarly, the mean parity of cases (1.4 ±1.3) was not statistically significantly different from that of controls (1.5±1.4) ($P > 0.05$) (Table 1). The gestational ages of the cases at booking ranged from 16-36weeks while that of controls ranged from 12 –38 weeks. Mean gestational ages of cases was 26.9 ± 4.6 while that of controls was 26.4 ± 4.3 and are not statistically significantly different ($P > 0.05$).

Table 1: Characteristics of respondents

Characteristic	Cases N=196	Controls N=399	p value
Marital Status			
Married	173(29.3)	344(58.2)	
Never Married	23(3.6)	55(9.0)	>0.05
Education			
Nil or low education	138(70.4)	301(75.4)	
High education	58(29.6)	98(24.6)	>0.05
Mean Age	25.2 ±5.5	25.7 ± 5.3	>0.05
Mean parity	1.5 ± 1.3	1.5 ± 1.4	>0.05
Gestational age at booking	26.9 ± 4.6	26.4 ± 4.3	>0.05

malaria {O.R = 3.24 ((1.86-5.63), $P < 0.0001$} and HIV seropositivity {O.R = 4.46(1.2 -18.57), $P < 0.026$, Table 3}. The prophylactic use of pyrimethamine was associated with a statistically insignificant increase in the risk of anaemia {O.R = 1.22(0.708 – 1.90), $P > 0.05$}.

Table 3 also shows that among the cases HIV prevalence rate was 13.3% compared to 3.3% among the controls. This was statistically significant ($P < 0.026$).

Table 3: Association between HIV infection and Anaemia

HIV infection	Cases (Anaemic) N= 60	Control (Non Anaemic) N= 120	Odds ratio (Confidence interval)	P
Positive	8(13.3)	4(3.3)		
Negative	52(86.7)	116(96.7)	4.46(1.15-18.57)	< 0.026

In a logistic regression analysis, iron supplementation ($P = 0.001$) and folate supplementation ($P < 0.015$) were associated with significantly lowered risk of anaemia in pregnancy while malaria parasitaemia ($P < 0.006$) and HIV seropositivity ($P < 0.015$) was associated with significantly increased risks (Table 4).

Table 2: Risk factors for anaemia in pregnancy in a bivariate analysis

Risk factor	Cases N=196	Control N=399	Odds ratio (Confidence interval)	P
Iron supplementation	39(19.9)	135(33.8)	0.49(0.3-0.7)	< 0.006
Prophylactic Pyrimethamine	37(18.9)	64(16.0)	1.22(0.78-1.90)	>0.05
Therapeutic Chloroquine	8(4.1)	33(8.3)	0.47(0.21-0.94)	<0.058
Folate supplementation	36(18.4)	105(26.3)	0.63(0.41-0.96)	<0.032
Use of Vitamin B complex	27(13.8)	106(26.6)	0.44(0.28-0.70)	<0.0001
Malaria parasitaemia	39(19.9)	23(5.8)	3.24(1.86-5.63)	<0.0001

Table 2 shows the risk factors for anaemia. One hundred and thirty five (33.8%) of the controls were on iron supplementation compared with only 39 (19.9%) of cases. The risk of anaemia is thus less for those using iron supplements than for those not on iron supplement {O.R = 0.49 (0.3-0.7), $P < 0.006$}. Similarly, the risk of anaemia was significantly reduced for women on folate supplements {O.R = 0.63(0.41 –0.96) $P < 0.032$}, vitamin B complex supplements {O.R = 0.44 (0.28 – 0.70), $P < 0.0001$} and women treated for malaria in the course of the pregnancy {O.R = 0.47(0.21 –0.94), $P < 0.058$}

The risk of anaemia however is significantly increased among women who had positive blood film for

Discussion

In this study the use of iron supplements was shown to reduce the risk of anaemia in pregnancy by two thirds. This corroborates the observation of several investigators. Sing *et al* in Singapore found a significant reduction in the prevalence of anaemia among women on iron supplementation compared with those not on iron supplementation. He further demonstrated that women not on iron supplements had 11 times increased risk of anaemia compared with their counterparts in the placebo group [10]. Likewise Beaufrere *et al* and Mahommed *et al* and showed in several randomized controlled trials that use of iron supplements reduced the risk and prevalence of anaemia in

pregnancy in women in the iron supplemented group compared to those in the placebo group [11-14].

Table 4: Adjusted Odds ratio for Anaemia in pregnancy

Variable	Adjusted odds ratio	Confidence interval	P value
Iron supplementation			
Yes	0.39		
No	1.00	0.29-0.52	<0.001
Folate Supplementation			
Yes	0.69		
No	1.00	0.51-0.93	<0.015
Use of Vitamin			
Vitamin B complex			
Yes	0.88	0.65-1.19	>0.05
No	1.00		
Prophylactic pyrimethamine			
Yes	1.00	0.899-1.59	>0.05
No	1.19		
Therapeutic Chloroquine			
Yes	1.26	0.76-2.10	<0.05
No	1.00		
Malaria parasite			
Positive	2.50	1.29-4.84	<0.006
Negative	1.00		
HIV			
Positive	1.00	0.51-0.93	<0.015
Negative	0.69		

Folate supplementation likewise also reduced the risk of anaemia as shown in this study. Women on folate supplements had their risk of anaemia reduced by one third compared with those not using folate supplements. Fleming *et al* had shown earlier that malaria in pregnancy caused an increase in the demand for folate occasioned by the haemolysis of parasitized red cells. Mahommed K *et al* also found in a review of 21 controlled trials of folate supplementation that use of folate supplements was associated with a reduction in the percentage of pregnant women with anaemia and low haemoglobin in pregnancy [14-16].

Another factor that was associated with anaemia in pregnancy in this study was malaria parasitaemia. Anaemia was two and half times more likely in those who had malaria parasitaemia in pregnancy compared with those who did not. This study corroborates the findings by several authors that malaria parasitaemia is an important risk factor for anaemia in pregnancy. Fleming in his work in Ibadan found that malaria was a common cause of anaemia in pregnancy [17]. Similar observations had been noted in other works in Africa. A rise in the percentage of cases of anaemia in pregnancy in areas endemic for malaria had been found by Rougermount, while van Eijk et al in their study of Kenyan population found that malaria was associated with anaemia in primi- and secondigravidae [18,19]. Therefore the use of malaria prophylaxis is expected to reduce the risk of anaemia in pregnancy. However, in this study, use of prophylactic daraprim was not found to reduce the risk of anaemia. The women were also found using Chloroquine often in the course of pregnancy, an indication of being infected with malaria. The risk of anaemia was also found significantly reduced with the treatment for malaria during pregnancy. Prompt treatment of malaria in pregnancy reduces the risk of developing complications such as anaemia [20,21].

HIV seropositivity was associated with an increase in the risk of anaemia. Pregnant women who were HIV negative had one -third reduction in the risk of anaemia compared with those who are HIV positive. This is in consonance with the findings of Rammon et al in Abidjan and Meda N. *et al* in Burkina Faso who also demonstrated similar findings [22,24].

In summary, the adverse risk factors for anaemia in pregnancy are non-use of iron and folate supplements, malaria parasitaemia and HIV seropositivity. Routine voluntary counseling and testing (VCT) for HIV has become necessary at primary care level in view of the growing HIV sero-positivity among pregnant women. Training of health workers on VCT and provision of VCT and antiretroviral drugs at primary care level becomes necessary to reduce mother to child transmission of HIV infection in pregnancy. A limitation of this study is that HIV serostatus was determined by means of a screening test. Although the specificity and sensitivity of the test kit is high and therefore the result of the test are reliable, studies employing confirmatory tests to determine HIV serostatus are recommended in further studies. A further limitation of this study is that the role of diet in the development of anaemia was not examined in this study. The dietary history of these women was not determined thus the relationship between the nutritional status of the women and anaemia cannot be studied. Also the malaria density was not determined. Thus association between the degree of anaemia and malaria density was not quantified

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