THE PREVALENCE AND RISK FACTORS ASSOCIATED WITH ANAEMIA AMONG HIV PATIENTS AttENDING CLINIC AT THE UNIVERSITY OF CALABAR TEACHING HOSPITAL, CALABAR, NIGERIA

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ABSTRACT

Introduction: Anaemia is one of the haematological complications of HIV, and most of the studies in Nigeria and outside Nigeria have shown prevalence above 50%. Also, anaemia in HIV patients has been shown to be associated with morbidity and mortality. Our study therefore aimed to determine the prevalence and the likely risk factors associated with the development of anaemia among HIV patients attending the special treatment clinic in the University of Calabar Teaching Hospital, Calabar, Nigeria.

Methods: This was a cross–sectional study conducted over a period of 6 months from June to November, 2010. A total of 321 patients were recruited but only 300 met the inclusion criteria, and their haemoglobin levels were measured with the use of Drabkin Cyanide method. Data obtained was analyzed with SPSS version 20 with statistical significance at p < 0.05.

Results: There were more females than males in the study (70.0% vs 30.0%). Majority of the participants were in the 30 – 39 years age category (35.0%), closely followed by those in the 40 – 49 years age category (21.0%). The overall prevalence of anaemia was 76%. Female sex, living in an Urban Area and low CD4 cell count are risk factors that were associated with anaemia among HIV patients. However, in a multivariate logistic regression analysis, female sex was the only predictor of anaemia.

Conclusion: Anaemia is a common complication seen among HIV patients in view of the prevalence rate of 76% observed in our study. The risk factors associated with anemia were female sex, living in urban area and low CD4 cell count.

KEYWORDS: Anaemia, HIV, Prevalence, Risk factors, Nigeria.

INTRODUCTION

Since the beginning of the Human Immunodeficiency Virus (HIV) epidemic, about 71 million people have been infected with the virus and about 34 million people have died of HIV (Global Health Observatory (GHO) Data 2016). Globally, 36.9 million (34.3-41.4 million) were living with HIV at the end of 2014 (Global Health Observatory (GHO) Data 2016). An estimated 0.8% (0.7-0.9%) of adults aged 15-49 years worldwide are living with HIV, although the burden of the epidemic continues to vary considerably between countries and regions (Global Health Observatory (GHO) Data 2016). Sub-Saharan Africa remains the most severely affected, with nearly 1 in every 20 adults (4.8%) living with HIV and accounting for nearly 70% of the people living with HIV worldwide (HIV and AIDS in sub-Saharan Africa. Regional Overview 2016). In 2013 there were an estimated 1.5 million new HIV infections and 1.1 million AIDS related deaths in sub-Saharan Africa. Of all people with HIV globally, 9% of them live in Nigeria (HIV and AIDS in sub-Saharan Africa. Regional Overview 2016). Nigeria, together with South Africa and

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Uganda, account for almost half of all annual new HIV infections in sub-Saharan Africa (HIV and Aids in sub-Saharan Africa. Regional Overview 2016). Critically, significant haematologic abnormalities are common in persons with HIV infection. These abnormalities may occur as a result of HIV infection itself, as sequelae of HIV related opportunistic infections / malignancies or as a consequence of therapies used for HIV infection and associated conditions (Donald W. N. 2016).

Anaemia is a frequent complication that occurs in 20-80% of HIV infected persons and is associated with faster disease progression and mortality (Belperio P.S. & Rhew DC. 2004). Anaemia is a condition in which the number of red blood cells in the body or their oxygen-carrying capacity is insufficient to meet physiologic needs, which vary by age, sex, altitude, use of cigarettes and pregnancy status (WHO 2011).

HIV positive patients with anaemia are at a greater risk of mortality compared to their non-anaemic counterparts, even after controlling for CD4+ cell count and viral load (Lundgren JD, & Mocroft A. 2003, Median M. et al 2012). HIV disease and treatment are believed to result in decreased and ineffective red blood cell (RBC) production as well as an increased RBC destruction thus increasing the prevalence of anaemia among people living with HIV/AIDS (PLWHA) (Volderbing P. 2000).

Several factors have been identified that put PLWHA at an increased risk of developing anaemia namely later stage of HIV disease, increased viral load, CD4 count of less than 200 cells/ul, female sex, being pregnant, injection drug use and use of zidovudine and ganciclovir (Sullivan P.S. et al 1998). In developing countries like Nigeria, lower levels of education, poorer housing, rural residence, unemployment, poor diet, lower body mass index (BMI), increased age and presence of other infections have also been associated with increased level of anaemia (Thein M. & Ershier WB, MOHP Nepal Country Progress Report 2012).

The introduction of highly active antiretroviral therapy (HAART) has improved the quality and life expectancy of HIV infected individuals. The HAART regimen suppresses the HIV virus and improves the immune function with attendant increase in the CD4 count levels. However, the use of HAART has been shown to be linked to the development of anaemia among HIV patients (Sullivan P.S. et al 1998).

This study was conducted to determine the prevalence and risk factors associated with anaemia among HIV patients attending the special treatment clinic (STC) of the University of Calabar Teaching Hospital (UCTH), Calabar, Nigeria.

MATERIALS AND METHODS

The study was conducted in the HIV special clinic of the UCTH over a period of 6 months from June to November, 2010. This was a cross-sectional study in which consecutive adult HIV positive patients aged 18 years and above were recruited in the clinic after signing an informed consent form. A total of 321 patients were recruited but only 300 met the inclusion criteria in terms of complete data for analysis. Pregnant women were excluded from the study. Ethical approval was obtained from the Health and Research Ethical Committee of the UCTH before commencement of the study.

An interviewer administered questionnaire was issued detailing subjects socio-demographic characteristics in the first part and details of HIV diagnosis, duration, medications and associated variables in the second part. Diagnosis of HIV infection was done using determine HIV 1 & 2 by Abbott Japan Co. Ltd for screening purposes. Confirmation was done using Unigold by Trinity Biotech Plc Bray, Ireland. Haemaglobin estimation of participating subjects was analyzed using the Drabkin Cyanide method.

The World Health Organization (WHO) criteria for the definition of anaemia was used in this study (WHO 2011). Anaemia for males was defined as haemoglobin (Hb) concentration less than 13g/dl while for females it was less than 12g/dl. Mild anaemia was defined as haemoglobin level of 8-13g/dl and 8-12 g/dl for men and women respectively. A haemoglobin level of less than 8g/dl was defined as severe anaemia for both sexes.

All data obtained was entered into and analyzed with Statistical Package of Social Sciences (SPSS) version 20.0 software (SPSS Inc, Chicago Illinois, USA). The mean ± standard deviation (SD) was computed for the quantitative variables, while frequency and percentages were generated for qualitative variables. Logistic regression was used to determine the predictors of anaemia. A p – value of < 0.05 was taken as statistically significant.
Table 1: Demographic characteristics of participants (N = 300)

| Values                  | Frequency (N, %) |
|-------------------------|------------------|
| Sex                     |                  |
| Male                    | 90 (30.0%)       |
| Female                  | 210 (70.0%)      |
| Age category (years)    |                  |
| < 20                    | 5 (1.7%)         |
| 20 – 29                 | 92 (30.7%)       |
| 30 – 39                 | 106 (35.3%)      |
| 40 – 49                 | 63 (21.0%)       |
| 50 – 59                 | 31 (10.3%)       |
| 60 above                | 3 (1.0%)         |
| Marital status          |                  |
| Single                  | 106 (35.3%)      |
| Married                 | 142 (47.3%)      |
| Divorced                | 12 (4.0%)        |
| Widowed                 | 40 (13.3%)       |
| Occupation              |                  |
| Trader                  | 97 (32.3%)       |
| Farmer                  | 22 (7.3%)        |
| Student                 | 25 (8.3%)        |
| Civil servant           | 58 (19.3%)       |
| Artisan                 | 90 (32.7%)       |
| Religion                |                  |
| Christian               | 296 (98.7%)      |
| Muslim                  | 4 (1.3%)         |
| Educational level       |                  |
| No formal education     | 19 (6.3%)        |
| Primary                 | 73 (24.3%)       |
| Secondary               | 120 (40.0%)      |
| Tertiary                | 88 (29.3%)       |
| Residence               |                  |
| Urban                   | 215 (71.7%)      |
| Rural                   | 85 (28.3%)       |

Table 1 shows that majority of the participants were females and more than two-thirds of the participants were in the younger age group below 40 years. Married participants constituted (47.3%) of the study population, (32.7%) were artisans and most had secondary level of education (40.0%), and majority resided in an urban region (71.7%).

Table 2: Risk factors for anaemia among HIV patients

| Values                  | Anaemia present (N = 228), %, Mean ±SD | Anaemia absent (N = 72), %, Mean ±SD | p-value |
|-------------------------|-----------------------------------------|--------------------------------------|---------|
| Sex                     |                                         |                                      |         |
| Male                    | 79 (34.6%), 295.93±212.95               | 11 (15.3%), 354.94±227.93            | 0.002   |
| Female                  | 149 (65.4%), 295.93±212.95              | 61 (84.7%), 354.94±227.93            |         |
| Age category (years)    |                                         |                                      |         |
| < 20                    | 3 (1.3%), 33.3±23.3                    | 2 (2.8%), 33.3±23.3                  | 0.717   |
| 20 – 29                 | 69 (30.3%), 245.93±212.95              | 23 (32.4%), 245.93±212.95            |         |
| 30 – 39                 | 82 (36.0%), 330.93±212.95              | 24 (33.3%), 330.93±212.95            |         |
| 40 – 49                 | 51 (22.4%), 245.93±212.95              | 12 (16.9%), 245.93±212.95            |         |
| 50 – 59                 | 21 (9.2%), 245.93±212.95               | 10 (14.1%), 245.93±212.95            |         |
| 60 above                | 2 (0.9%), 245.93±212.95                | 1 (1.4%), 245.93±212.95              |         |
| CD4 levels (cells/µl)   |                                         |                                      |         |
| < 200                   | 91 (39.9%), 295.93±212.95              | 23 (31.9%), 354.94±227.93            | 0.225   |
| ≥200 above              | 137 (60.1%), 295.93±212.95             | 49 (68.1%), 354.94±227.93            |         |
| CD4 levels (cells/µl)   | 295.93±212.95                          | 354.94±227.93                       | 0.045   |
| ARV exposure            |                                         |                                      |         |
| Yes                     | 159 (69.7%), 295.93±212.95             | 47 (65.3%), 295.93±212.95            | 0.568   |
| No                      | 67 (29.4%), 295.93±212.95              | 24 (33.3%), 295.93±212.95            |         |
| Defaulted               | 2 (0.9%), 295.93±212.95                | 1 (1.4%), 295.93±212.95              |         |
| Duration of ARV exposure|                                         |                                      |         |
| No exposure             |                                         |                                      |         |
| < 6 months              | 69 (30.3%), 295.93±212.95              | 25 (34.7%), 295.93±212.95            | 0.462   |
| > 6 months              | 46 (20.2%), 295.93±212.95              | 10 (13.9%), 295.93±212.95            |         |
| Residence               |                                         |                                      |         |
| Urban                   | 156 (68.4%), 295.93±212.95             | 59 (81.9%), 354.94±227.93            | 0.026   |
| Rural                   | 72 (31.6%), 295.93±212.95              | 13 (18.1%), 354.94±227.93            |         |
In table 2, anaemia was commoner in females as compared to males, \( p < 0.05 \). Also, participants with higher levels of CD4 count from 200 and above, exposure to ARV and longer duration of exposure to ARV had anaemia, but these were not statistically significant \( (p > 0.05) \). However, participants with mean lower CD4 count levels and those in urban region had anaemia, and these were statistically significant \( (p < 0.05) \).

| Variables                      | Mild Anaemia (11 – 12.9g/dl) N = 86 | Moderate Anaemia (8 – 10.9g/dl) N = 133 | Severe Anaemia (< 8g/dl) N = 9 | p-value |
|--------------------------------|--------------------------------------|------------------------------------------|-------------------------------|---------|
| Sex                            | 37 (43.0%)                           | 38 (28.6%)                               | 4 (44.4%)                     | 0.075   |
| Male                           | 49 (57.0%)                           | 95 (71.4%)                               | 5 (55.6%)                     |         |
| Female                         |                                      |                                          |                               |         |
| Age Category                   |                                      |                                          |                               |         |
| < 20                           | 1 (1.2%)                             | 1 (0.8%)                                 | 1 (11.1%)                     | 0.362   |
| 20 – 29                        | 27 (31.4%)                           | 39 (29.3%)                               | 3 (33.3%)                     |         |
| 30 – 39                        | 29 (33.7%)                           | 51 (38.3%)                               | 2 (22.2%)                     |         |
| 40 – 49                        | 19 (22.1%)                           | 30 (22.6%)                               | 2 (22.2%)                     |         |
| 50 – 59                        | 10 (11.6%)                           | 11 (8.3%)                                | 0 (0.0%)                      |         |
| 60 above                       | 0 (0.0%)                             | 1 (0.8%)                                 | 1 (11.1%)                     |         |
| Residence                      |                                      |                                          |                               |         |
| Urban                          | 59 (68.6%)                           | 93 (69.9%)                               | 4 (44.4%)                     | 0.310   |
| Rural                          | 27 (31.4%)                           | 40 (30.1%)                               | 5 (55.6%)                     |         |
| CD4 count (cells/µl)           |                                      |                                          |                               |         |
| < 200                          | 23 (26.7%)                           | 61 (45.9%)                               | 7 (77.8%)                     | 0.001   |
| ≥ 200                          | 63 (73.3%)                           | 72 (54.1%)                               | 2 (22.2%)                     |         |
| ARV exposure                   |                                      |                                          |                               |         |
| Yes                            | 67 (77.9%)                           | 89 (66.9%)                               | 3 (33.3%)                     | 0.036   |
| No                             | 19 (22.1%)                           | 42 (31.6%)                               | 6 (66.7%)                     |         |
| Defaulted                      | 0 (0.0%)                             | 2 (1.5%)                                 | 0 (0.0%)                      |         |
| Duration of ARV exposure (months) |                                    |                                          |                               |         |
| No exposure                    | 19 (22.1%)                           | 44 (33.1%)                               | 6 (66.7%)                     | 0.029   |
| < 6 months                     | 17 (19.8%)                           | 27 (20.3%)                               | 2 (22.2%)                     |         |
| >6 months                      | 50 (58.1%)                           | 62 (46.6%)                               | 1 (11.1%)                     |         |

In table 3, more patients with CD4 count < 200 cells/µl had severe anaemia (77.8%) as compared to those with values that were up to 200 and above. While patients with ARV exposure (77.9%) had mild anaemia as compared to those without ARV exposure and defaulters on ARV, and these are statistically significant \( (p< 0.05) \). On the other hand, patients with no duration of exposure (66.7%) to ARV had severe anaemia compared with those that had duration of ARV exposure, and this is statistically significant \( (p< 0.05) \). However, the sex, age category and residence are not statistically significant.

| Values                      | Odds ratio | 95% CI OR | p-value |
|-----------------------------|------------|-----------|---------|
| Sex                         | 0.334      | 0.163 – 0.684 | 0.003   |
| Age (1)                     | 1.559      | 0.075 – 32.358 | 0.774   |
| Age (2)                     | 0.740      | 0.063 – 8.691 | 0.811   |
| Age (3)                     | 0.685      | 0.058 – 8.049 | 0.763   |
| Age (4)                     | 0.622      | 0.051 – 7.612 | 0.710   |
| Age (5)                     | 1.316      | 0.103 – 16.790 | 0.832   |
| CD4 count levels            | 0.782      | 0.427 – 1.430 | 0.424   |
| ARV exposure(1)             | 0.690      | 0.057 – 8.371 | 0.771   |
| ARV exposure(2)             | 0.692      | 0.057 – 8.340 | 0.772   |
| Duration of ARV exposure    | 0.624      | 0.277 – 1.402 | 0.253   |
In this regression model as shown in table 3, with anaemia as the dependent variable; female sex was significantly associated with the presence of anaemia ($p < 0.05$). The other variables in the model were not statistically significant.

**DISCUSSION**

Anaemia is one of the haematological complications of HIV, and most of the studies outside Nigeria and in Nigeria have shown a prevalence above 50% (Median M. et al 2012, Grace R.P. et al 2015). The overall prevalence of anaemia in our study is 76%. This was similar to the findings by Mukund et al from a cross sectional Indian Study (Mukund B.K. et al 2015). It was slightly higher than studies in Iran and Ethiopia with rates of 70.1% and 71% respectively (Mukund B.K. et al 2015, Alem M. et al 2013). Comparatively the prevalence rate is higher than that in similar Nigerian studies at Keffi and Benin City with rates of 64% and 60.61% respectively (Grace R.P. et al 2015, Omoregie R. et al 2009). However it was lower than findings obtained by Panwar et al in an Indian study with 86.4% prevalence rate of anaemia among HIV positive subjects (Panwar A. et al 2016). The differences in the prevalence between our study and others may be attributable to different socio-demographic characteristics of participants. As compared to our study, other studies had more males, farmers, participants with no formal education and lower percentage of rural dwellers (Median M. et al 2012, Grace R.P. et al 2015, Alem M. et al 2013, Panwar A. et al 2016). The majority of patients with anaemia had a moderate type (58.3%), closely followed by the mild grade (37.7%), while a few had severe grade of anaemia (4%). The findings are in keeping with that from other similar studies (Mukund B. K. et al 2015, Alem M. et al 2013).

Anaemia was commoner in females (84.2%) than males (34.6%), $p < 0.05$. A similar finding was reflected in other studies (Mukund B.K. et al 2015, Alem M. et al 2013). Most of our study participants were below 40 years of age, which is the most sexually active age in the society (Mukund B.K. et al 2015). A multitude of factors increase women’s vulnerability to HIV acquisition, including, biological, behavioural, socioeconomic, cultural and structural risks (Gita R, Brodie D. 2013). In Sub-Saharan Africa, women bear the brunt of the HIV epidemic (UNAIDS 2013). The high prevalence of anaemia in females may be largely attributed to menstrual blood loss and to the drains on iron stores that occur with pregnancy and delivery (Muluken A. et al 2015). There was no statistical significant difference between HAART experienced and HAART naïve study subjects with anaemia. This finding was replicated in a similar study (Panwar et al 2016). In a contrast study, exposure to HAART has been shown to be a predictor of anaemia in HIV positive subjects (Gedefaw L. et al 2013). Some HAART regimens containing zidovudine have been associated with anaemia (Phe T. et al 2013).

The mean lower CD4 count levels were significantly associated with anaemia. This is in conformity with other studies where lower CD4 levels was associated with increased risk of anaemia (Grace R.P. et al 2015, Ernest A. 2016). Patients with low CD4 count are known to be at risk of multiple opportunistic infections which are known to cause anaemia and such patients are also likely to have high HIV viral load which could lead to viral infiltration of the bone marrow subsequently causing anaemia (Hermela M. et al 2017). As in a similar study, the severity of anaemia increased with decrease in CD4 Count (Panwar A. et al 2016). Urban residence was a predictor of anaemia in our study. This may be due to poorer nutritional habits of urban dwellers, most of whom have abandoned traditional feeding habits due to urbanization and its attendant pressures. They often eat junk and fast foods which may be less nutritious. However, a study in southwest Ethiopia had rural residence as a predictor of anaemia among HAART naïve participants (Gedefaw L. et al 2013) which contrasts with our own findings. The HAART naïve subjects in our study were those who were on the verge of commencing HAART.

**LIMITATIONS**

This study had limitations which may have affected some of the conclusions drawn from it. The income of participants could have been evaluated as this has a direct effect on ability to afford necessary food items. Also the type of HAART regimen should have been documented as not all agents are associated with anaemia. The BMI should have been assessed because a lower BMI has been shown to be associated with anaemia in HIV positive subjects (Median M. et al 2012). Other common causes of anaemia in our study environment such as hookworm infestation should have been screened for.

**CONCLUSION**

The prevalence rate of anaemia in our study is 76%. Female sex, living in an urban area and having a low CD4 cell count were risk factors for anaemia in our study. Age, marital status, occupation, religion, educational level, being on HAART or not and HAART duration were not risk factors for anaemia in the study population.

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