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HEMATOLOGICAL PROFILE OF HIV/AIDS INDIVIDUALS WITH OPPORTUNISTIC RESPIRATORY MYCOSES AND IMMUNE STATUS: A CROSS SECTIONAL STUDY IN UYO NIGERIA

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ABSTRACT

Hematological abnormalities are strong predictors of morbidity and mortality among HIV infection. This study was aimed to determine hematological indices, abnormalities and the immune status of HIV/AIDS subjects having opportunistic pulmonary mycoses in Uyo, Nigeria. A cross sectional study was adopted using 230 subjects with pulmonary symptoms attending the Anti-retroviral clinics in University of Uyo Teaching Hospital and Saint Luke's Hosipital, Anua, Akwa Ibom State, Nigeria. The hematological parameters and CD4 counts was determined using blood and sputum was used for mycological examinations. Data was analysed using statistical package for the Social Sciences (SPSS) and was significant at p = 0.05. HIV subjects were more prevalent in female 98(68.89%) than male 56(31.11%). The most commonest fungi was *Aspergillus niger* (44.76%) and the least was *Cryptococcus* species (9.00%). The common hematological abnormality was anaemia with 86(86.9%), lymphopenia 33(33.3%) and thrombocytopenia 3(3.0%) among HIV/AIDS subjects with mycoses. The mean CD4 counts was 396.5±31.61 cells/µl (HIV) and 981.7±17.51 cells/µl (control individual). The CD4 counts below 200 cells/µl was observed in 19.4%(35) of AIDS patients. HIV/AIDS subjects with mycoses may develop hematological abnormalities such as anaemia, neutropenia and leucopenia due to low immune status.

KEYWORDS: Hematological parameters, Immunocompromised subjects, Cytopenias, CD4, HIV seropositive cases

INTRODUCTION

Human Immunodeficiency Virus (HIV) belongs to the lentivirus family (Derbie *et al*., 2018; Anjum *et al*., 2023) and if not properly treated, progressively damages the immune system which promotes opportunistic infections, immunological and haematological complications (Goni *et al*., 2017; Derbie *et al*., 2018; Vaswani *et al*., 2022). The weakening of immunity maybe due to HIV infection (Vaswani *et al*., 2022), drugs and opportunistic pulmonary infections (Udeani *et al*., 2018; Sani *et al*., 2020; Akpan and Umoyen, 2022). Researchers have reported high prevalence of anaemia and thrombocytopenia in asymptomatic HIV positive patients (Parinitha and Kulkarni, 2012; Ekeng *et al*., 2022). Hematological malignancies are common clinical conditions in Nigeria and HIV

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infections are common with 33% (Junior *et al*., 2017; Bergamasco *et al*., 2021; Akpan and Umoyen, 2022; Ekeng *et al*., 2022).

Untreated HIV infections lower CD_4 cells count; leading to opportunistic infections because of weak immunity (Servais *et al*., 2001). Invasive fungal infections are major cause of morbidity and mortality in patients with hematological malignancies; particularly in neutropenic and allogeneic haematopoietic cell transplants recipients (Junior *et al*., 2017; Osman *et al*., 2020). Hematologic abnormalities are important at every stages of HIV and involved blood cell lineages including leucocytes, haematopoiesis, thromphocytes (Osman *et al*., 2020; Vaswani *et al*., 2022). The hematologic profile of immuno-compromised individuals are indication of viral replication, with severe malignancies; especially in patients with low CD_4 count and high viral load (Abebe and Alemseged, 2009). These abnormalities worsen as the disease progresses to AIDS (Abebe and Alemseged, 2009; Raman *et al*., 2016). Opportunistic pulmonary infections with and malignancies in HIV/AIDS also contributes to the development of cytopenias; include red blood cells lymphocytes, monocytes, and macrophages (Kyeyune *et al*., 2014; Gunda *et al*., 2017).

Several studies have revealed anaemia as the commonest cytopenia among HIV-infected individuals (De Santis *et al*., 2011; Harding *et al*., 2020; Akpan and Umoyen, 2022), making hemoglobin an important biomarker of prognosis (De Santis *et al*., 2011; Nardo *et al*., 2012; Harding *et al*., 2020). Leucopenia and lymphopenia are known to raise the occurrence of opportunistic respiratory infections while neutropenia may allow HIV individuals to be susceptible to infections (Parinitha and Kulkarni, 2012; Udeani *et al*., 2018; Ekeng *et al*., 2022). Akwa Ibom State has the highest prevalence of HIV/AIDS in Nigeria (NACA, 2019). There is paucity of documented research on the hematologic abnormalities among HIV/AIDS patients having opportunistic pulmonary mycoses in Uyo. Therefore this study aimed to determine the hematological indices and abnormalities associated with HIV/AIDS sero-positive patients in Uyo, Akwa-Ibom State, Nigeria.

MATERIALS AND METHODS

Study design and population

Two years retrospective cross-sectional study (June 2019-November, 2022) was conducted using 180 HIV seropositive and 50 HIV-seronegative subjects with respiratory symptoms. Subjects were recruited from University of Uyo Teaching Hospital (UUTH) and Saint Luke's Hospital Anua, Uyo, Nigeria. All subjects were initially screened for anti-HIV antibodies before recruited into the study using Determine test kit (Abbott Chennai, India), Unigold test kit *(USA Exports Global,* New Jersey) and Statpak diagnostic kit (Chembio Diagnostic System Incorporated, New York) according to manufacturer's instructions. The inclusion criteria were the ability of participants to produce sputum and consented for the study. The exclusion criteria were inability to produce sputum and not giving consent.

Ethical approval

Ethical approval was obtained from the Health Research Ethics Committee (HREC), UUTH (UUTH/AD/S/96/VOL.XX1/553) and the State Health Research Ethics Committee (AKHREC/14/5/19/005; NHREC/19/4/2019). The rudiments of the research were followed accordingly.

Laboratory methods

Five millilitres of venous blood was aseptically obtained from each participant for hematological and immunological (CD4 estimation) by a phlebotomists. Also two repeated samples of early morning expectorate sputum were obtained from all the subjects enrolled for the study under universal aseptic precautions in suitable sterile container (Wadhwa *et al*., 2012).

Determination of hematological parameters

Hematologic indices were performed using automated blood analyzer (Sysmex XP-300). Hematological parameters investigated includes: total white blood cell count (TWBC), Haemoglobin (Hb), Packed cell volume (PCV) Mean haemoglobin concentration (MCHC), platelets count (PLT), neutrophils count (NC), Lymphocyte count (LC), eosinophils count, basophils count and monocyte count. Complete blood counts (CBC) vials were introduced to the chamber of the Sysmex XP-300 (manufactured by Sysmex corporation, China) and the complete blood counts analyzed. The various degrees of anaemia were classified using haemoglbin (Hbg/dl) values of <10.0/11.6g/dl: mild anaemia, 8.0/9.3g/dl: moderate anaemia and <8.0/9.3g/dl as severe anaemia respectively (Kaushansky *et al*., 2016).

Determination of CD4 T-lymphocytes count

The CD4 count was determined using flow cytometry. The blood was dispensed into corresponding sample tube and placed on the fluorescent activated cell sorter BD FACS Count System (Becton Dickinson and company, California). Leucopenia was define as total WBC count less than 300×10^9 cell/l. Neutropenia was defined as a neutrophil count <40% while lymphopenia was considered when lymphocyte count was less than 20%. Thrombocytopenia was defined as total platelet count of $<100\times10^9$ /L (Kaushansky *et al*., 2016; Woldeamanuel and Wondimu, 2018). The critical value of CD4 counts among HIV subjects was <200 cells/µl was defined as AIDS (stage 4), 200-349 cells/µl was defined as advanced HIV (stage 3), 350-449 cell/µl was defined as HIV infection (stage 2), ≥500 cell/µl was defined as HIV infection (stage 1) (WHO, 2017).

Microscopic examination

Direct microscopy was done using 10% Potassium Hydroxide (KOH) (Alexander and Pfaller, 2006). Sputum smears for each specimen was prepared by the addition of a loop full of the concentrated specimens to a drop of 10% Potassium Hydroxide (KOH), on a clean, grease free slide, covered with a cover slip. The slide was kept in a moist chamber at room temperature for 15 minutes. Wet preparations were examined under the microscope for yeast cells, hyphae, pseudohyphae and the presence of capsules with x10 and x40 objectives (Alexander and Pfaller, 2006; Jo Baron *et al*., 2013).

Culture

Sputum specimens were inoculated on Sabouraud dextrose agar with chloramphenicol at the concentration of 16µgml^{-1} in duplicates. The specimens were incubated at 25°C and 37°C. The cultures were examined every other day for growth up to 4–6 weeks before discarding as negative (38). Pure cultures of isolates were prepared before performing physiological tests. Isolates were sub-cultured on fresh SDA plates and incubated at 37°C and 25-28°C for 1 to 7 days (Deorukhkars and Sani, 2014; Forbes *et al*., 2021).

Lactophenol cotton blue staining for moulds

A drop of lactophenol cotton blue stain was placed on a clean grease-free glass slide (Forbes *et al*., 2021). A small fragment of the fungal colony was picked from the culture using a sterile inoculating needle to the lactophenol stain. A clean cover-slip was applied avoiding air bubbles. Excess stain was removed with blotting paper and the preparation examined using ×10 and ×40 objectives for conidial heads, hyphae and spores (Jo Baron *et al*., 2013; Deorukhkars and Sani, 2014; Forbes *et al*., 2021).

Slide culture for moulds identification

The slide cultures were done on all mould isolates for the identification as previously published (Wadhwa *et al*., 2012). The set-up was incubated at 28^{O}C and examined daily for sufficient growth. When good growth appeared, the cover slip from the slide culture set-up was removed using forceps for examination in lactophenol cotton blue mount using x40 objective. If the preparation showed insufficient developed structures, a second lactophenol mount was done using the slide after discarding the agar. Both preparations were preserved for future use by sealing the edges with nail polish (Wadhwa *et al*., 2012).

Germ tube test

Presumptive *Candida* species were subjected to germ-tube test using colonies from the purity plate in batches of three replicates per test; with each batch including a known positive and negative control as documented (Jo Baron *et al*., 2013). Germ tubes appeared as slender tubes with straight walls, and without constriction at the junction between the cells (Ochie and Kolhatkhar, 2005; Jo Baron *et al*., 2013).

India Ink preparation

India ink preparation was used to identify *Cryptococcus neoformans* polysaccharide capsules. The preparation was made in the center of a clean grease-free glass slide. A drop of the ink was placed on the slide and the specimen was emulsified in the ink. A cover-slip was gently dropped on the fluid so that air bubbles were not trapped. The smear was examined microscopically with x40 objective lenses (Chakrabarti *et al*., 2018).

Gram staining for yeast isolates

The isolates were smeared on clean grease free slides, air dried and heat fixed to preserve the morphology of the sample. Slides were flooded with crystal violet for one minute and then washed out with running water. Lugol's Iodine which act as mordant was added for 30 seconds. It was washed out with running water. The smear was decolorized with acetone for 30 seconds and washed with running water. The slide was counter-stained with safranin for two minutes and washed out with running water. The stained slide was examined using oil immersion objectives (Ochie and Kolhatkhar, 2005; Forbes *et al*., 2021).

Data analysis

Socio-demographic variables and clinical data were analyzed using SPSS. Clinical data were presented in simple percentages, frequencies, mean and standard deviation. Chi-square test was used to determine the degree of occurrence of variables and CD_4 counts. Student's t-test was used to compare hematological parameters and significance set at $p = 0.05$.

RESULTS

A total of 230 subjects were enrolled for this study and majority of subjects belonged to age group 35-44 years (29.4%). The mean CD_4 counts was 396.5±16.3 cells/µl and 991.7±17.5 cells/µl for HIV and control subjects respectively. *Apergillus niger* and *Cryptococcus* species 19(10.55%) and 2(1.11%) respectively among HIV subjects (Table 1). Mean PCV in HIV/AIDS subjects with mycoses and without pulmonary mycoses was 31.4±6.7g/dl and 34.3±11.3g/dl respectively, while haemoglobin was 10.7±2.9g/dl and 12.9±3.1g/dl respectively.

Table 1: Demographic distribution, CD_4 counts and fungal etiologic agents among subjects

Variables	HIV positive cases n=142 n (%)	AIDS cases n=38 n (%)	Controls n=50 n (%)	P-Value
Age group (years)				
15-24	17 (11.97)	3(7.89)	7 (14.00)	0.02
25-34	21 (14.79)	7 (18.42)	8 (16.00)	0.01
35-44	41 (28.87)	12 (31.57)	11(22.00)	0.24
45-54	38 (26.76)	6 (15.78)	19 (38.00)	0.36
55-64	17 (11.97)	6 (15.78)	3 (6.00)	0.01
65-75	8 (5.63)	4 (10.52)	2 (4.00)	0.00
Total	142 (78.88)	38 (21.11)	50 (100)	
Mean age (Years)	39.41	34.64	41.93	0.00
Sex				
Male	44 (30.98)	12 (31.57)	18 (36.00)	0.00
Female	98 (69.01)	26 (68.42)	32 (64.00)	0.00
Mean CD_4 counts (cells/µl)	396.5±31.61	342±28.33	981.7±17.51	0.05
Minimum CD_4 counts (cells/µl)	342.00	78.00	619.00	0.22
Maximum CD_4 counts (cells/µl)	1074.00	198.00	1913.00	0.01
Fungal etiologic agents				
Aspergillus flavus	15 (18.33)	4 (10.53)	1 (2.00)	
Aspergillus niger	19 (10.55)	13 (34.21)	5 (10.00)	
Aspergillus fumigatus	16 (8.80)	2 (5.26)	2 (4.00)	0.39
Candida species	14 (7.77)	11 (28.95)	3 (6.00)	
Cryptococcuss species	2 (1.11)	3 (7.89)	0 (0.00)	

Table 2: Haematological parameters of HIV infected subjects with and without mycoses

Haematological parameters	HIV positive subjects with mycoses (n=99)	HIV positive subjects without mycoses (n=81)	Statistics t-test	P-value
Haemoglobin (g/dl)	10.7±2.91	12.9±3.1	3.06	0.37
PCV (%)	31.4±6.73	34.3±11.3	2.17	0.32
RBC ($x10^{12}$/µl)	4.0±1.50	4.6±2.80	0.84	0.40
TWBC x 10^3/µl	5.2±2.22	7.4±6.14	0.31	0.76
MCV (%)	70.8±5.61	83.6± 7.11	1.44	0.15
MCH (%)	26.6±4.30	28.7±9.52	0.53	0.59
MCHC (%)	27.1±3.20	29.9±11.41	0.99	0.33
Platelets ($x10^3$/ µl)	201.1±1.41	223.3± 2.14	0.42	0.67
Lymphocytes (%)	42.9±2.23	45.5±3.00	0.48	0.63
Neutrophils (%)	50.1±23.62	56.6±24.11	0.25	0.98
Monocytes (%)	8.3±1.41	9.5±2.60	0.50	0.62
Eosinophils (%)	5.2±4.30	0.3040	0.30	0.76
Basophils (%)	1.0±0.31	1.5±1.70	0.50	0.62
CD_4 counts (cells/µl)	396.5±31.60	572.8±24.12	0.22	0.82

Table 3: Haematological abnormalities among mycoses positive and negative subjects

Haematological abnormalities	Mycoses positive subjects (n=99)	Mycoses negative subjects (n=81)	Total	t-test	P-value
Anaemia	86 (86.86)	68 (83.95)	154 (85.55)	9.18	0.01
Leucopenia	19 (19.19)	32 (39.51)	51 (28.33)	2.99	0.03
Neutropenia	11 (11.11)	29 (35.80)	40 (22.22)	3.89	0.01
Lymphopenia	33 (33.33)	26 (32.09)	59 (32.77)	1.18	0.24
Thrombocytopenia	3 (3.03)	0 (0.00)	3(1.66)	1.75	0.11

Table 4: The distribution of CD_4 counts in HIV/AIDS subjects by age

CD_4 Counts	**Age/ No (%) of subjects (Years)**						
Range (cells/µl)	15-24	25-34	35-44	45-54	55-64	65-74	**Total**
< 200	3(8.6)	3(8.6)	7(20.0)	10(28.6)	7(20.0)	5(14.3)	35(19.4)
200-349	1(11.1)	1(11.1)	1(11.1)	2(22.2)	2(22.2)	2(22.2)	9(5.0)
350-449	3(3.2)	2(10.0)	6(30.0)	4(20.0)	3(30.0)	2(10.0)	20(11.1)
500 & above	13(11.2)	22(19.0)	39(33.6)	28(24.1)	11(9.5)	3(2.6)	116(64.4)
Total	**20(11.1)**	**28(15.6)**	**53(29.4)**	**44(24.4)**	**23(12.8)**	**12(6.7)**	**180**

The mean neutrophils and mean CD_4 counts was 50.1±23.6% and 396.5±31.6 cells/µl respectively for HIV positive subjects with mycoses (Table 2). Anaemia was more prevalent (86.9%) in subject with mycoses while thrombocytopenia was least (3%) among HIV positive subjects (Table 3). Approximately, 19.4% had CD_4 counts <200 cells/µl and more than half of the subjects (64.4%) had CD_4 counts of 500 cells/µl and above (Table 4).

DISCUSSION

In this study, HIV/AIDS subjects were more of female (68.9%) than male (31.1%), correlating with previous study (Ofosu *et al*., 2019; Yoon *et al*., 2020), where higher proportions of subjects were females. In contrast, in Northern Nigeria higher infection rates were observed among males (63.5%) (Sani *et al*., 2020), which is not in tandem with our present results in Uyo. The mean age of HIV-seropositive subject in this study was 39.4 years, similar to 38.8±9.9 years reported in Uganda immunocompromised subjects (Njovu *et al*., 2021). A lower mean age of 35.6±9.65 years was reported in Zaria (Kusfa *et al*., 2017). A high of mean age of 40.62 years was published in Ghana (Ofosu *et al*., 2019).

The mean values of haemoglobin were 10.7±2.9 and 12.9±3.1(g/dl) among HIV-seropostive subjects with mycoses and without mycoses respectively, indicating decrease in haemoglobin value among HIV-seropostive subjects with mycoses. This finding is concomitant with other studies in Calabar (Ogba *et al*., 2013) and Nnewi (Chukwuanukwu *et al*., 2020); both in Nigeria. Similar mean hemoglobin value was documented among HIV subjects on HAART regimen in Ethiopia (Tilahun *et al*., 2022). In this current study, the mean value of red cell parameters decreased among HIV positive subjects with mycoses, agreeing with the results in Calabar, Nigeria (Ogba *et al*., 2013). This might be due to failure of the bone marrow and erythropoietin deficiency.

The most common cytopenia observed in our study was anaemia (47.8%) and in India, anaemia was between 38.8% - 84.0% (Parinitha and Kulkarni, 2012), 46.6%-48.6% in China (Bhardwaj *et al*., 2020) and 47.4% - 73.5% among immunocompromised subjects in South-South Nigeria (Akpan and Umoyen, 2022). The variation in the prevalence of anaemia among different populations may be due to malnutrition and non-adherent to medical treatments. In this study, neutropenia was 11.11% with mean neutrophil counts of 50.11±23.6% among HIV/AIDS subjects with mycoses. This is lower than 18.8% of neutropenia reported among HIV/AIDS subjects on HAART in Uganda (Njovu *et al*., 2021). In contrast, our finding is higher than 5.0% of neutropenia recorded in Africa (Tilahun *et al*., 2022). Neutropenia was one of the hematological disorder in HIV/AIDS patients with mycoses, corroborating with our results in Uyo. In this present study, leucopenia was lower in subjects with pulmonary mycoses (19.2%) than those without pulmonary mycoses (39.5%); with the mean total white blood cell counts of 5.2±2.2 x 10^3/µl in subjects with pulmonary mycoses respectively. Ciccacci et al reported 35.8% of leucopenia among their HIV positive subjects with mean white blood cell count of 4.55±1.2x10^9/l in Africa. This is higher than 19.2% observed in our study, but lower prevalence of 18.33% published in India (Thulasi *et al*., 2016). Leukopenia in HIV/AIDS subjects may be attributed to pulmonary infections and malignancies. Our study showed that some of the subjects had lymphopenia (32.8%) and was concurrent with previously documented among HIV/AIDS subjects (Parinitha and Kulkarni, 2012; Kusfa *et al*., 2017; Bhardwaj *et al*., 2020). Lymphopenia observed among HIV sero-positive subjects in this study may be due to the disease progression leading to AIDS.

In this research, thrombocytopenia prevalence was 3% among HIV/AIDS subjects with mycoses and was similar to 2.9% reported among Africans (Ciccacci *et al*., 2020). The mean platelet counts among the HIV/AIDS subjects with mycoses was 201.1±1.4x10^3/µl. Low prevalence (1.2%) of thrombocytopenia with a mean platelets count of 215.9±99.4x10^3/µl was previously reported in

Calabar (Ogba *et al*., 2013), while 13.1% and 15.83% were reported Africans (Bhardwaj *et al*., 2020; Njovu *et al*., 2021). Decreased in platelets production usually occurs during advanced stages of AIDS (Obirikorang and Yahoah, 2009; Marchionathi and Parisi, 2021). This study observed 19.4% (35) of the HIV/AIDS subjects with CD4 count ≤ 200 cells/µl and most of the subjects 17/35(48.6%) were aged 35-54 years. Munyazesa *et al*., (2012) reported CD4 counts of ≤ 200 cells/µl in 55% HIV positive adult women aged 30-40 years. These young and middle age subject constitute the workforce of a nation. Immunosuppression in this age-group may result to reduction in workforce and loss of productivity. In Nigeria, CD4 cell counts of healthy people range between 500-1500 cells/µl of blood (FMOH, 2007). In this present study, the mean CD4+T lymphocyte counts of 396.5±31.6 cells/µl and 342.8±28.33 cells/µl among HIV and AIDS subjects respectively. This finding is in concurrent with the study conducted in Calabar (Ogba *et al*., 2013) and Nnewi (Iroezindu *et al*., 2013). Lower mean CD4 counts among pulmonary mycoses positive subjects may be pointing to destruction of mature CD4+T lymphocyte in the peripheral lymphoid system and inhibition of mature lymphoid precursors due to HIV infection (Vidya *et al*., 2017). The CD4 counts ≤ 200 cells/µl was one of the clinical parameter identified as determinant of pulmonary opportunistic infections (Ogba *et al*., 2013; Iroezindu *et al*., 2013; Vidya *et al*., 2017).

In conclusion, the prevalence of anaemia and other hematological abnormalities were predominant among HIV-positive subject with mycoses than those without mycoses. Cytopenias were hematological abnormalities and could serve as clinical indicators for determining pulmonary opportunistic infections. Most of the subject had CD_4 count of <200 cells/µl and were at high risk of infections.

Limitation

Small sample size and this study only focused on HIV/AIDS subjects.

Competing interests

The authors declare no competing interest.

REFERENCES

Abebe, M and Alemseged, F., 2009. Hematologic abnormalities among children on HAART, in jimma university specialized hospital, South Western Ethiopia. Ethiop J Health Sci. 19(2):83-89.

Akpan, N.G. and Umoyen, A.J., 2022. Prevalence of anaemia and pulmonary mycoses in immunocompromised subjects: A review of Nigeria perspective. International J Pathogen Res. 9(1):34-48.

Alexander, B.D. and Pfaller, M.A., 2006. Contemporary tools for the diagnosis and management of invasive mycosis. Clin Infect Dis. 43(1):15-27.

Anjum, A., Rehman, A.U., Siddique, H., Rabaan, A.A., Alhumaid, S., Garout, M., et al., 2023. Evaluation of hematological, biochemical profiles and molecular detection of envelope gene (gp-41) in human immunodeficiency virus (HIV) among newly diagnosed patients. Medicina. 59:93-103.

Bergamasco, M.D., Pereira, C.A., Arrais-rodrigues, C., Ferreira, D.B., Baiocchi, O., Kerbauy, F., et al., 2021. Epidemiology of invasive fungal diseases in patients with hematologic malignancies and hematopoietic cell transplantation recipients managed with an antifungal diagnostic driven approach. J Fungi. 7(8):588-599.

Bhardwaj, S., Almaeen, A., Wani, F.A. and Thirunavukkarasu, A., 2020. Hematologic derangements in HIV/AIDS patients and their relationship with the CD4 counts: A cross-Sectional Study. Int J Clin Exp Pathol. 13(4):756-763.

Chakrabarti, A., Li, R., Sun, P., Tan, B., Chua, M., Wahyuningsih, R., et al., 2018. Survey of laboratory practices for diagnosis of fungal infection in seven Asian countries: An Asia Fungal Working Group (AFWG) initiative. Medical Mycol. 56:416–425.

Chukwuanukwu, C.R., Nkemjika, U., Mbagwu, S., Chukwuanukwu, O.T. and Onyenekwe, C., 2020. Cryptococcus neoformans seropositivity and some haematological parameters in HIV seropositive subjects. J Infect Publ Health. 13(7);1042-1046.

Ciccacci, F., Lucaroni, F., Latagliata, R., Marciano, L., Mondlane, E., Balama, M., et al., 2020. Hematologic alternations and early mortality in a cohort of HIV positive Africans. Plos One. 15(11),1-14.

De Santis, G.C., Brunetta, D.M., Vilar, F.C., Brandão, R.A., De Albernazmuniz, R.Z., De Lima, G.M.N., et al. (2011). Hematological abnormalities in HIV-infected patients. Int J Infect Dis. 15(12):808–11.

Deorukhkar, S. and Saini, S., 2014. Laboratory Diagnosis of candidiasis through ages. Inter J Cur Microbiol and Appl Sci. 4:949-958.

Derbie, A., Ayalew, W., Mekonnen, D., Alemu, M. and Mulugeta, Y., 2018. Magnitude of cryptococcal antigenemia among HIV infected patients at a referral hospital, Northwest Ethiopia. Ethiopian J Health Sci.; 28(4):369-374.

Ekeng, B.E., Akaba, K., Ide, C. and Oladele, R., 2022. Opportunistic infections in patients with haematological malignancies in Nigeria. J Clin Scient Res. 11(3):175-180.

Federal Ministry of Health (FMOH), 2007. National guidelines for HIV and AIDS treatment and care in adolescents and adults. Abuja. Federal Ministry of Health Press, Nigeria.

Forbes, B.A., Sahm, D.F. and Weissfeld, A.S., 2021. Laboratory methods in basic mycology Bailey and Scott's Diagnostic Microbiology (15th edition). Tille, Patricia.

Goni, B.W., Kida, I.M., Saidu, I.A., Brown, M., Bakki, B., Ayaji, B., et al., 2017. Cryptococcal neoformans antigenemia among HIV infected patients in North Eastern Nigeria. J Trans Dis and Immunol. 1(7):1-8.

Gunda, D.W., Godfrey, K.G., Kilonzo, S.B. and Mpondo B.C., 2017. Cytopenias among ART-naïve patients with advanced HIV disease onenrolment to care and treatment services at a tertiary hospital in Tanzania: A cross-sectional study. Malawi Med J. 29(1):43–52.

Harding, B.N., Whitney, B.M. and Nance, R.M., 2020. Anaemia risk factors among people living with HIV across the United States in the current treatment era: A clinical cohort study. Biomed Central Infect Dis. 20(1):238-248.

Iroezindu, M.O., Ofondu, E.O., Hausler, H. and Wyk, B.V., 2013. Prevalence and risk factors for opportunistic infections in HIV patients receiving antiretroviral therapy in a resource-limited setting in Nigeria. J Immune Deficiency Synd Clin Res. 3(2):1-9.

Jo Baron, E., Michael, M.J., Weinstein, M.P., Richter, S.S., Gilligan, P.H., Thomson Jr, R.B., et al., 2013. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2013 updates by the infectious diseases society of America (IDSA) and the American Society for Microbiology. Clin Infect Dis. 57(4):22–121.

Junior, M.C., Silva, H.M, Arantes, A.M., Costa, C.R., Ataides, F.S., Silva, T.C., et al., 2017. Invasive fungal infection in patients with hematologic disorders in a Brazilian tertiary care hospital. Rev Soc Bras Med Trop. 50:80-85.

Kaushansky, K., Lichtman, M.A., Prchal, J.T., Levi, M.M., Press, O.W., Burns, L.J., et al., 2016. Williams hematology (9th edition). New York, McGraw Hill Education.

Kusfa, I.U., Abubakar, A.A., Muktar, H.M., Ibrahim, I.N., Awwalu, S., et al., 2017. Comparative analysis of some hematological and immunological paratemters of HIV-positive patients at a tertiary HIV treatment center in Zaira, Nigeria. Sub-Saharan African J Med. 4:15-19.

Kyeyune, R., Saathoff, E., Ezeamama, A.E., Loscher, T., Fawzi, W. and Guwatudde, D., 2014. Prevalence and correlates of cytopenias in HIV-infected adults initiating highly active antiretroviral therapy in Uganda. BMC Infect Dis. 14:496.

Marchionatti, A. and Parisi, M.M., 2021. Anaemia and thrombocytopenia in people living with HIV/AIDS: A narrative literature review. International Health. 13:19-109.

Munyazesa, E., Emile, I., Mutimura, E., Hoover, R.D., Shi, Q., Mcginn, P.A., et al., 2012. Assessment of haematological parameters in HIV-infected and uninfected Rwandan women: A cross-sectional study. BMJ Open. 2:1-8.

Nardo, M., Brunetta, D.M., Vilar, F.C., Machado, A.A. and De Santis, G.C., 2012. Hemoglobin concentration increment is associated with a better prognosis in HIV patients with anemia. Int J Infect Dis. 16(9):703.

National Agency for the control of AIDS (NACA), 2019. Nigeria Prevalence rate. UNAIDS, Government of Nigeria, Abuja. https://naca.gov.ng/

Njovu, I.K., Musinguzi, B., Mwesigye, J., Kassaza, K., Turigurwa, J., Nuwagira, E., et al., 2021. Status of pulmonary fungal pathogens among individuals with clinical factors of pulmonary tuberculosis at Mbarara Teaching Hospital in Southwestern Uganda. Therapeutic Advs infect Dis. 8:1-11.

Obirikorang, C. and Yahoah, F.A., 2009. Blood hemoglobin measurements as a predictive indicator for the progression of HIV/AIDS in resource-limited setting. J Biomedi Sci. 16:102-110.

Ochie, J. and Kolhatkhar, A., 2005. Laboratory techniques in mycology examination of Sputum, Medicine Laboratory Science, Theory and Practice. New Delhi, Corporation Limited.

Ofosu, D.N., Marfo-Debrekyei, Y., Duah, J., Donkor, L. and Owiredu, E-W., 2019. Haematological profile of HIV patients in relation to Immune Status in Kumasi: A Case Study. International J Medical Science Clinical Invent. 6(8):4554-4558.

Ogba, O.M., Abia-Bassey, L.N., Ekpoke, J., Mandor, B.I., Akpotuzor, J., et al., 2013. Hematological profile of HIV infected patients with opportunistic respiratory mycoses in relation to immune status – a hospital based cohort from Calabar, Nigeria. Trop Med Surg. 1(3):1-5.

Osman, M., Al Bikai, A., Rafei, R., Mallat, H., Dabboussi, F. and Monzer Hamze, M., 2020. Update on invasive fungal infections in the Middle Eastern and North African region. Braz J Microbiol. 51:1771–1789.

Parinitha, S.S. and Kulkarni, M.H., 2012. Haematological Changes in HIV Infection with Correlation to CD4 Cell Count. Australian Med J. 5:157-162.

Raman, R.T., Manimaran, D., Hemanathan, G., Afroz, T. and Sagar, R., 2016. Hematological abnormalities in HIV infected individuals in correlation to CD4 counts and ART status. Asian J Med Sci. 7(4):14-18.

Sani, F.M., Uba, A., Tahir, F., Abdullahi, I.N., Adekola, H.A., Mustapha. J.N., et al., 2020. Spectrum of pulmonary fungal pathogens, associated risk factors, and anti-fungal susceptibility pattern among persons with presumptive tuberculosis at Gomba, Nigeria. Inter J Mycobacteriol.9:144-149.

Servais, J., Nkoghe, D., Schmit, J.C., Arendt, V., Robert, I., Staub, T., et al., 2001. HIV-Associated hematologic disorders are correlated with plasma viral load and improve under highly active antiretroviral therapy. J Acquir Immune Defic Syndro. 28(3):221-225.

Thulasi, R., Manimaran, D., Hemanathan, G., Afroz, T. and Sagar, R., 2016. Hematological abnormalities in HIV infected individuals in correlation to CD4 counts and ART status. AJMS. 7:14-8.

Tilahun, M., Gedefie, A., Ebrahim, E., Seid, A., Ali, A., Shibabaw, A., et al., 2022. Haematological abnormalities of HIV-Infected patients before and after initiation of highly active antiretroviral therapy in the antiretroviral therapy clinics of six health facilities at Dessie Town, Northeast Ethiopia. J Bld Med. 13:243–253.

Udeani, T.K., Asogwa, V.N. and Ezenwaka, U., 2018. Assessment of systemic fungal infections among diabetic patients in Enugu, Nigeria. J Infectious Dis Epidemiol. 4(2):1-5.

Vaswani, P.P.M., Senga-Tang, I.R., Catapiaa, J.R.M., Abadb, C.I.R. and Dumagaya, T.E., 2022. The hematologic profile of Filipino HIV-infected individuals and its association with CD4 counts. Hematol Transfus.4(3):307–313.

Vidya, K.V., Karthigeyan, K.P., Tripathi, S.P. and Hanna, L.E., 2017. Pathophysiology of CD4+ T-cell depletion in HIV-1 and HIV-2 infections. Front Immunol. 8:580.

Wadhwa, V, Rai, S., Thukral, T. and Chopra, M., 2012. Laboratory quality management system: Road to accreditation and beyond. Indian J Med Microbiol. 30(2):131-140.

Woldeamanuel, G.G. and Wondimu, D.H., 2018. Prevalence of anemia before and after initiation of antiretroviral therapy among HIV infected patients at black lion specialized hospital, Addis Ababa, Ethiopia: A cross sectional study. BMC Hematol. 18:1-7.

World Health Organization, 2017. Policy brief: Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. World Health Organization 2017. https://apps.who.int/iris/bitstream/handle/10665/258967/WHO-HIV-2017.05-eng.pdf?sequence=1&isAllowed=y. Retrieved on 28th of January, 2023.

Yoon, H.A., Felsen, U., Wang, T. and Pirofski, L-A., 2020. *Cryptococcus neoformans* infection in human immunodeficiency virus (HIV)-infected and HIV-uninfected patients at an inner-city tertiary care hospital in the Bronx. Med Mycol. 58(4):434–443