Prevalence of Anaemia and Pulmonary Mycoses in Immunocompromised Subjects: A Review of Nigeria Perspective

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Authors’ contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJPR/2022/v9i130218

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/81920

Received 20 November 2021
Accepted 25 January 2022
Published 28 January 2022

ABSTRACT

Anaemia and mycoses are being diagnosed with increasing frequency among immuno-compromised subjects. Fungal respiratory infections are important causes of mortality and morbidity among immuno-compromised individuals. The goal of this research was to systematically review the prevalence of anaemia and mycoses among immuno-compromised subjects in Nigeria based on published articles. We reviewed a total of 23 studies published between 2009 and 2021 comprising retrospective studies, cross-sectional studies and case reports. The overall prevalence of anaemia in this study was between 16.2%-75.5% while mycoses prevalence was between 8.7-73.6% among immuno-compromised subjects in reviewed Nigerian populations. This study revealed that the prevalence of anaemia in South-South, South-East and Abuja (North Central Nigeria) were between 47.4%-73.5%, 44.6%-75.5% and 16.2% respectively among immuno-compromised HIV/AIDS and/or TB co-infections. The prevalence of mycoses in South-South, South-East, Western Nigeria and Northern Nigeria were between 25.3%-36%, 22.4%-52.5%, 8.7-

*Corresponding author: Email: anthonyumoyen4000@gmail.com, anthonyumoyen2015@yahoo.com;
33% and 12.7%-73.6% respectively among immuno-compromised subjects. This study confirms that anaemia and mycoses are common among immuno-compromised subjects in Nigeria; with pulmonary mycoses and low CD4 being important risk factors.

Keywords: Prevalence; immunocompromised subject; anaemia; mycoses; opportunistic infections.

1. INTRODUCTION

People with immuno-compromised systems are vulnerable to secondary infections and malignancies that are generally termed as opportunistic infections [1,2]. Individuals susceptible to pulmonary mycoses include those with immuno-suppressive illnesses like HIV/AIDS [1-5], diabetes [6-8], tuberculosis [3,9,10], cancer [7], chronic obstructive pulmonary diseases (COPD), immune-modulator therapy for the prevention of rejection in solid organ and haematopoietic cell transplantation [7,11,12]. Fungal infections of the lung are among the most feared infections in immuno-compromised patients. Fungi like Aspergillus species, Candida species, Cryptococcus species are common ubiquitous opportunistic pathogens affecting the lung, especially in immuno-compromised people [1-5,7,9,10,13]. The Aspergillus species forms a genus of ubiquitous, molds present in soil, air, various types of organic debris, water, indoor environment and many other sites; forming commonest pathogens responsible for mycoses in immuno-suppressive individuals [1-4,7,9-13]. Aspergillus species caused pulmonary aspergillosis; especially in immuno-compromised subjects [14-16]. HIV is a multi-systemic infection that suppresses haematopoietic system [13,17]. HIV/AIDS is a global pandemic disease [1-3,18] contributing to health burden in developing countries [1-3]. Diabetes mellitus continues to be a global health problem with over 80% of affected people living in low-middle income countries (LMICs) where tuberculosis is widespread [2,6-8]. Nigeria is ranked fifth among the 22 nations with high tuberculosis burden [2, 6] with new and relapsed cases of tuberculosis occurring [7,8]. Anaemia is a major public health problem, especially in developing countries [18-20]. It is the most important clinical problem observed in people living with HIV/AIDS [18-20] and other immuno-compromised subjects; its severity increases as CD4 count declines [2-3,19,20] and with progression of HIV to advanced stage [18]. Additionally, the higher anaemia level is also a good opportunity for HIV/AIDS progression irrespective of CD4 counts level and viral load [18-21]. Moreover, anaemia influences the natural history of HIV/AIDS [18,21], resulting in the decrease of the survival rate [19-22]. HIV/AIDS and anaemic condition have significant consequences on health, social and economic development of individuals [18]. The most common causes of anaemia are chronic infections like TB, HIV/AIDS [3-5,18-20], deficiency of mineral, iron, and vitamin B12 [23] and genetic defects [24]. Prevalence of pulmonary mycoses and anaemic conditions among immuno-compromised subjects in Nigeria and other African countries are on the increased [1-5, 9-11]; resulting to public health burden in the region. Therefore periodic review of published articles on the prevalence of mycoses and anaemic conditions among immuno-compromised subjects in Nigeria is imperative to ascertain the prevalence in the region. This information will be useful for prompt actions to be taken by health practitioners. This study seeks to review relevant published researches on prevalence of pulmonary mycoses and anaemia among immuno-compromised subjects in Nigeria from 2009 to 2021.

2. MATERIALS AND METHODS

2.1 Study Design and Searching Strategy

Systematic review of relevant published articles in Nigerian populations were searched in accordance with the Preferred Reporting Items for Systematic Review and Meta-analysis [25]. All databases were searched from 2009 to 2021. Electronic databases search like Google Scholar, PubMed, EMBASE, MEDLINE, CAB HEALTH and Cochrane Library were performed. The search engine used detailed medical subject heading (MeSH), keywords/abbreviations such as: incidence/prevalence of opportunistic pulmonary mycoses (caused by Candida species, Aspergillus species, Cryptococcus species) among immuno-compromised subjects in Nigeria. The immuno-compromised subject included HIV/AIDS, diabetic patients and tuberculosis. Also, TB, Anaemia, hematological parameters, hemoglobin, Hb, the names of each states in Nigeria and her geopolitical regions were used for literature search.
2.2 Selection Criteria

Publications on retrospective study, cross sectional study, case study and case-control study conducted using primary data from Nigeria were selected for this study. From those studies meeting eligibility criteria, the first author’s name, publication year, study area, sample size, study design and effect measure of anemia for immuno-compromised subjects were extracted. Only literature published in English Language was used for this study. Review articles and cases with grossly missing data were excluded.

2.3 Brief Description of Study Area

Nigeria is one of the most densely populated countries in Africa, with approximately 200 million people in an area of 920,000 km² (360,000 square miles). She is one of the countries with the largest population in Africa and the seventh largest population in the world. Nigeria is situated in the West Africa region and borders Benin, Chad, Cameroon, and Niger. She has 36 states and the Federal Capital Territory (FCT) of Nigeria with diverse ethnic groups within six geopolitical zones as shown on Fig. 1 [26,27].

2.4 Data Extraction

The online data extraction was performed independently by authors and any discrepancies were solved via discussions. Data on study authors, study location (country, region in Nigeria), study period, sex and clinical presentation or risk factors were equally extracted.

2.5 Statistical Analysis

Data analysis was performed using Microsoft Excel 365 and using Statistical Package for Social Sciences (SPSS) version 20.0. Categorical characteristics of studies (example: study design, state/region, cases, highlight of results) were summarized. Individual cases of pulmonary mycoses were summed up to give an overall number of patients diagnosed with pulmonary mycoses in Nigeria used for the study. Pulmonary mycoses among immuno-compromised subjects were stratified by state and region.

3. RESULTS

This review retrieved 273 full texted publications initially from the database search and 30 identified from references of eligible studies. We then removed duplicates and 201 citations remained from which relevant studies were selected for review. Their potential relevance was examined using a title and abstract screening to remove studies that were clearly not related to scope of this review. A total of 280
publications were excluded and 23 were used for this review based on primary data on prevalence of anaemia and/or mycoses in immuno-compromised subjects (HIV/AIDS, TB and diabetic cases) in Nigerian populations between 2009-2021 (Fig. 2). The overall prevalence of anaemia in this review study was between 16.2%-75.5% while mycoses prevalence was between 8.7-73.6% among immuno-compromised subjects in Nigerian populations. This study revealed that the prevalence of anaemia in South-South, South-East and Abuja (North Central Nigeria) were between 47.4%-73.5%, 44.6%-75.5% and 16.2% respectively among immuno-compromised HIV/AIDS and/or TB co-infections. The prevalence of mycoses in South-South, South-East, Western Nigeria and Northern Nigeria were between 25.3%-36%, 22.4%-52.5%, 8.7-33% and 12.7%-73.6% respectively among immuno-compromised (Table 1).

Fig. 2. Literature selection flowchart
Table 1. Prevalence of anaemia and mycoses in Nigeria among immunocompromised subjects reviewed

<table>
<thead>
<tr>
<th>Study design</th>
<th>City/year</th>
<th>State/Region</th>
<th>subjects</th>
<th>Cases</th>
<th>Result highlight(s)</th>
<th>Reference</th>
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</table>
| Retrospective study   | Calabar, 2013 | Cross State/South-South | HIV patients                      | 272   | -31.6% pulmonary mycoses and patients with mycoses were relatively younger.  
- overall prevalence for anaemia was 47.4%.  
- 18.4% were anaemic for mycoses positive subjects  
- Mild, moderate and severe anaemia was 36.4%, 12.7% and 9.5% respectively in females.  
Leucopenia, neutropenia, lymphopenia, thrombocytopenia and CD4 <300 was 15.1%, 9.3%, 45.3%, 1.2% and 94.2% respectively for mycoses positive cases. | [19]      |
| Retrospective study   | Calabar, 2013 | Cross State/South-South | HIV patients with some TB co-infections | 272   | -Overall prevalence of mycoses was 36% and mixed mycoses/TB was 7.7%.  
- The commonest fungi was Candida species (32.7%), followed by Aspergillus species.  
The commonest clinical conditions were cough (86%), chest pain (25.5%) | [27]      |
| Cross-sectional study | Owerri, 2013 | Imo State/South-East | HIV subjects                      | 339   | - Overall prevalence of opportunistic infection (OIs) was 22.4% with more females having it.  
Candidiasis, cryptococcal meningitis and tuberculosis was 8.6%, 0.6% and 7.7% respectively.  
Baseline Hb<10 g/dl and CD4<200 for OIs was 46.1% and 50.7% respectively. | [28]      |
| Retrospective study   | Maiduguri, 2017 | Borno State/North-East | HIV/AIDS                          | 150   | -68% pulmonary mycoses with 69.3% and 66.1% for male and female respectively.  
The Candida species was more prevalent (38%), followed by Aspergillus species (18.6%).  
-HIV/TB coinfection was 90.2%. | [2]       |
| Cross-sectional study | Gomba, 2020 | Gomba State/North-East | TB                               | 216   | -73.6% pulmonary mycoses with 69.5% and 36.5% for male and female respectively.  
The Aspergillus species was more prevalent (61.1%), followed by Candida species (32%).  
-Prevalence was highest (27.7%) in younger age (30-38 years). | [29]      |
Table 1 Continued

<table>
<thead>
<tr>
<th>Study design</th>
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</table>
| Retrospective      | Kano, 2014         | Kano State/ North-East | TB        | 200   | -55.5% pulmonary mycoses, 63.06% were males and 36.94% were females.  
- Fungal species was highest in Aspergillus species (36.94%), followed by Candida spp. (36.04%)                               | [30]      |
| study              |                    |                    |           |       |                                                                                                                                                                                                                      |           |
| Retrospective      | Abeokuta, 2016     | Ogun State/ South-West | HIV/TB patients | 272   | - Male prevalence of pulmonary mycoses was 33% and female prevalence was 66.7%.                                                                                                                                     | [28]      |
| study              |                    |                    |           |       |                                                                                                                                                                                                                      |           |
| Retrospective      | Port Hacourt, 2020 | Rivers States/ South-South | TB subjects | 400   | - The overall TB Candida co-infections was 34.4%.  
- The prevalence of TB among females was 22.4% and males 24.4%  
- High prevalence of Candida (25.0%) were between 31 - 40 yrs                                           | [31]      |
| study              |                    |                    |           |       |                                                                                                                                                                                                                      |           |
| Case study         | Port Hacourt, 2016 | Rivers States/ South-South | Diabetes mellitus | 1     | Chronic pulmonary aspergillosis and pulmonary tuberculosis                                                                                                                                                    | [8]       |
| Cross-sectional    | Enugu, 2018        | Enugu State/ South-East | Diabetic patients | 120   | - 52.5% mycoses prevalence, Candida species was 20.8% while Aspergillus species accounted for 18.3%.  
- Co-morbid factors were HIV/AIDS, HBP and liver diseases with 1.7%, 30.8% and 0.8% respectively.                                                   | 6         |
| study              |                    |                    |           |       |                                                                                                                                                                                                                      |           |
| Retrospective      | Orlu, 2014         | Imo State/ South-East | HIV patients | 921   | - 75.5% were anaemic for HIV positive subjects.  
- 11.5% prevalence for HIV positive                                                                                                                                         | [32]      |
| study              |                    |                    |           |       |                                                                                                                                                                                                                      |           |
| Cross-sectional    | Enugu, 2020        | Enugu State/ South-East | TB        | 303   | - Prevalence of Aspergillus species causing pulmonary aspergillosis was 42.6% and other fungi was 13%.  
- Aspergillus fumigatus ranked highest (36.1%), others were A. niger (28.4%), A. flavus and A. nidulans (3.6%), A. oryzae and A. terreus (2.4%)  
- High prevalence of pulmonary mycoses (37.3%) were between 31 - 40 years                                       | [33]      |
| study              |                    |                    |           |       |                                                                                                                                                                                                                      |           |
### Table 1. Continued

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<thead>
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<th>Study design</th>
<th>City/year</th>
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<th>subjects</th>
<th>Case(s)</th>
<th>Result highlight(s)</th>
<th>Reference</th>
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<tbody>
<tr>
<td>Cross-sectional</td>
<td>Kebbi, 2009</td>
<td>Kebbi State/ North</td>
<td>HIV subjects</td>
<td>606</td>
<td>-Prevalence of 61.7% for OIs.</td>
<td>[34]</td>
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<td>-Prevalence of tuberculosis (TB) was 6.7% while candidiasis was 8.6%.</td>
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<td>HIV prevalence was 31.6%.</td>
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<tr>
<td>Case study</td>
<td>Lagos, 2018</td>
<td>Lagos State/ South-West</td>
<td>TB subjects</td>
<td>1</td>
<td>-Chronic pulmonary aspergillosis</td>
<td>[35]</td>
</tr>
<tr>
<td>Retrospective</td>
<td>Lagos, 2020</td>
<td>Lagos State/ South-West</td>
<td>HIV/AIDS</td>
<td>7034</td>
<td>-Opportunistic fungal infection was 18.6% and 21% had pulmonary TB.</td>
<td>[36]</td>
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<td>-Oral candidiasis was 0.3%, oesophageal candidiasis (8%), superficial mycoses (1.6%), Pneumocystis pneumonia (0.8%) and cryptococcal meningitis (0.4%).</td>
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<td></td>
<td>-The mean CD4 count was 184 cells/µl. HIV-1 viral load was 51,194 RNA copies/ml and 88% had initiated ART. Cohort death was 1.6%.</td>
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<tr>
<td>Cross-sectional</td>
<td>Lagos, 2017</td>
<td>Lagos State/ South-West</td>
<td>HIV</td>
<td>156</td>
<td>-Chronic pulmonary aspergillosis (CPA) prevalence was 8.7%; 6.5% were HIV infection and 14.5% were HIV-negatives.</td>
<td>[37]</td>
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<td>-Mean CD4 count was 169.5 cells/µl (range 4–593) in HIV-infected patients with positive Aspergillus IgG. Overall, 52.4% had documented TB, 67.3% had a productive cough and 50 had haemoptysis.</td>
<td></td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Maiduguri, 2018</td>
<td>Borno State/ North-East</td>
<td>HIV</td>
<td>150</td>
<td>-Pulmonary aspergillosis (PA) was 12.7% and 11% of these 19 specimens were positive for Aspergillus terreus, 4 (21%) were positive for Aspergillus flavus, 5 (26%) were positive for Aspergillus niger and 8 (42%) were positive for A. fumigatus.</td>
<td>[38]</td>
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<td>-PA was diagnosed in 12 of 35 participants (34.3%) with CD4+ cell counts &lt;200 cells/µl, 5 of 52 (9.6%) with counts of 200–350 cells/µl and 2 of 63 (3.2%) with counts &gt;350 cells/µl</td>
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<td>-PA male prevalence was 22.6% and female was 5.7%</td>
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Table 1 Continued

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<tr>
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</table>
| Cross-sectional    | Owerri, 2020 | Imo State/ South-East | HIV subjects | 350     | -The prevalence of anemia in HIV positive was 44.6%.
-The mean hemoglobin statuses at booking was 9.92±1.8g/dl for HIV positive
-The mean CD4+ at booking for HIV positive group was 478±251µl                                                                                                                                       | [39]      |
| Retrospective study| Port Hacourt, 2021 | Rivers States/ South-South | HIV subjects | 200     | -Overall anaemia was 73.5% in HIV cases with 38% of the cases having mild anaemia, moderate anaemia (25.5%) and 10% had severe anaemia.
-The prevalence of leucopenia was 26% and thrombocytopenia (32%).
-Haematological indices were WBC 1.3-11.9 x109L, Lymphocyte 0.3-6.4 x109L, Monocyte 0.2-2.6 x109L, Granulocyte 0.1-5.1 x109L and Platelet 30-550 x109L.
-HIV infection comes with its health challenges, included anaemia, leukocytopenia, and thrombocytopenia.                                                                                   | [17]      |
| Retrospective study| Calabar, 2017 | Cross State/ South-South | HIV patients | 321     | -The overall prevalence of anaemia was 76%.
-Mild anaemia in female was 57%, moderate anaemia (71.4%) and severe anaemia (55.6%) in HIV subjects
-Sex, living in an urban area and low CD4 cell count are risk factors that were associated with anaemia among HIV patients.                                                                                 | [40]      |
| Retrospective study| Port Hacourt, 2016 | Rivers States/ South-South | TB subjects | 200     | -Candida species prevalence was 25.3% and Male incidence of candida infections was (27.1%) and female (23.1%).
-The incidence of Candida co-infection was high in TB patients with complications (28.4%) than TB patients without complications (20%).
-The Candida species isolated, Candida albican was 16.3% and most prevalent, followed by Candida tropicalis (8.9%) and Candida stellatoids (3.2%).                                                                 | [41]      |
| Cross-sectional    | Abuja, 2020 | Abuja/           | HIV       | 420     | The overall rate of anaemia was 16.2% while the overall                                                                                                                                                           | [42]      |
Table 1 Continued

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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Retrospective study</td>
<td>Jos, 2016</td>
<td>Plateau State/ North-Central Nigeria</td>
<td>HIV patients</td>
<td>96</td>
<td>-21.9% HIV positive subjects had Candida pathogens</td>
<td>[43]</td>
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<td>17.7% had Candida albicans isolated from their sputum and 11.5% had a CD4 count of &lt;200 cells/μl. Risk of pulmonary candidiasis occurring in HIV infected patients with CD4 count &lt;200 cells/μl and Candida species contributed to chronic cough in HIV infected patients.</td>
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</table>
4. DISCUSSION

This study recorded a prevalence of 8.7%-73.6% among immuno-compromised subjects. The prevalence of 55.6% was reported in Sao Paulo, Brazil among AIDS patients [44], 55.5% in Kano, Nigeria among HIV and TB co-infected subjects [30], 78.6% in Gombe, Nigeria among TB patients [29], 70.7% in Mbarara, South-Western Uganda [45]. 12.8% in Beijing, China by Shailaja et al. [46], 47.6% in South African [47]. The differences in the prevalence of pulmonary mycoses in various populations may be attributed to the differences in sample size of recruited subjects, variations in the risk factors common to a particular environment, mode of sample collection/processing after collection and diagnostic approaches used. The high prevalence of 61.7-73.6% observed in some studies conducted in Western and Northern Nigeria may be due to high prevalence of HIV/AIDS patients in the regions and non-compliance of HIV/AIDS subjects to routine medical care/ regimens.

The prevalence of fungi isolates was higher in female subjects than male subjects in most articles reviewed; especially in Southern and Western Nigeria. This result is concomitant to the finding in South-Western Uganda [9], Calabar [3, 19] and Imo State [28]. The high prevalence of fungi isolates in females among HIV/AIDS subjects could be attributed to more females presenting with HIV/AIDS in the hospital settings where this study was conducted. High prevalence of fungi isolates causing mycoses were detected among males subjects than females in Madagascar [1], Northern, Nigeria [2, 29, 30, 38], which are not in agreement with our present review study.

Aspergillus species was the commonest etiologic agent causing mycoses among immuno-compromised subjects in the articles reviewed for this study. This findings is in agreement with the work of Hussein et al. in Iraq [48], Punjab, India [49] and Northern Nigeria [29] where Aspergillus species was the predominant fungal agent associated with respiratory mycoses among immuno-compromised subjects; followed by Candida species. The high prevalence of Aspergillus species in these regions of Nigeria may be due to their ability to produce small easily aerosolized conidia which penetrates deep into the lung cavity as previously reported [50]. This study differs from the work in Calabar [3] and in Asia [46] where Candida species was the most common aetiologic agent isolated among immuno-compromised subjects with respiratory infections.

Pulmonary mycoses occurred more frequent between 30-40 years; comprising youths and middle aged subjects in majority of the reviewed articles in this current study. This agreed with previously published results in Benin City, Edo State, Nigeria [51], Gombe State [29], Calabar [3, 5] and Mbarara, South-Western Uganda [9], were pulmonary mycoses was more prevalent in youths and middle aged individuals. Possible reason for high prevalence within these age brackets may be due to their active outdoor activities leading to exposures of these fungi pathogens [2]. Also another possible reason for this high prevalence of pulmonary mycoses associated with these aged brackets may be related to high unprotected sexual activities in such individuals (youths and middle aged people), as HIV infection primarily occurs through sexual transmission [52].

This study recorded the prevalence 16.2%-75.5% for anaemia among subjects and was more prevalence among females than males subjects. Higher prevalence of 42.2%-97% was documented in Malawi [20] and 38.8-84% in India [53]. The prevalence of 39.5% for anaemia among HIV sero-positive subjects was documented in Javanese, Indonesia [54], 7.2%- 84% among subjects living with HIV/AIDS by reviewing documented research in different continents [18], 59.6% in Soweto, South Africa [55], 57.5% before HAART administration in North Eastern Nigeria [56], 63% and 46% before and after HAART administration respectively in Ghana [57] and 40.46% in Tanzania [58]. Additionally, the anaemic prevalence were 31.8-51% in North Central and South-East Ethiopian populations [59-61], 27.6%-44.3% in Chinese populations [62], 20.5% in Rwanda [63], 20.8% in Zauditu [64] and Addis Ababa [65]; both in Ethiopian populations, 12% using subjects from Africa, Asia, South America, Caribbean and United States of America [66].7.2% in United State of America [67], 6.9% in Denmark [68] and 6.3% in Uganda [69]. The variations in the prevalence of anaemia in different populations may be due to the sample size of recruited subjects, inclusion and exclusion criteria used in the research methodology, differences in the level of poverty, malnutrition and overall poor economic status of the countries especially in underdeveloped and developing countries [18, 66]. Lower prevalence of anaemia were...
frequently documented in developed nations among immuno-compromised subjects [67-68], confirming that economic status, good/functional health facilities and good standard of living in a nation contributed to low prevalence of anaemia and mycoses in such developed countries.

5. CONCLUSION

Fungal infections due to immuno-compromised systems of HIV/AIDS, TB and diabetic patients are on the increased. The overall prevalence of anaemia in this study was between 16.2%-75.5% while mycoses prevalence was between 8.7-73.6% among immuno-compromised subjects in reviewed Nigeria populations. Immuno-compromised systems can induce pulmonary mycoses, several hematological manifestations like anaemia, neutropenia. Anemia and pulmonary mycoses are treatable comorbidities associated with increased mortality among immuno-compromised subjects; important to clinicians. Hemoglobin levels, platelet and CD4+ T lymphocyte counts should be monitored routinely, especially CD4+ T lymphocyte count of <200 cells/μl.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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DOI:https://dx.doi.org/10.4314/ahs.v20i4.9
DOI:10.5588/ijtld.17.0060.
DOI:10.4103/tcmj.tcmj_46_18
DOI:https://dx.doi.org/10.18203/2320-1770.ijrcog20205216
DOI:https://dx.Doi.org/10.4314/Gjpas.v23i1.19
DOI:10.1177/1178636120947680
DOI:http://dx.doi.org/10.4314/ajcem.v17i1.6


