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Prevalence of Some Hematological Abnormalities among HIV Positive Patients on Their First Visit to a Tertiary Health Institution in Ethiopia; A Cross Sectional Study

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Authors' contributions

This work was carried out in collaboration between all authors. Author ZA designed the study, wrote the protocol, and wrote the first draft of the manuscript. Author GY performed immunohematological analysis of blood samples. Author BT managed the literature search and data analysis. All authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Aim: The main objective of this study was to identify the magnitude of hematological abnormalities among HIV patients on their first visit to antiretroviral treatment (ART) centers.
Methods: A cross sectional study was conducted among 189 HIV positive patients, visiting University of Gondar Hospital, Ethiopia. Blood sample was analyzed for hematological parameters and CD4 count. Frequencies (%), mean (SD) or median (IQR) were used to summarize data according to the type of variable. Independent sample t-test and chi-square test were used as appropriate and in all cases $P<0.05$ was considered significant.
Results: The mean (±SD) age of the participants was 33.2 (±9.3) years. The prevalence of anemia, leucopenia and thrombocytopenia were 42.3%, 4.8% and 12.7% respectively. Immunosupression was found in 83.1% of the individuals. CD4 count with leucopenia ($P<0.0001$) was the factor that showed significant association.

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Conclusion: The prevalence of hematological abnormalities in this study was high and nearly half of the patients were eligible to start antiretroviral therapy. Researches that explore the clinical presentations of HIV positive patients on their first visit to ART centers and hematological changes after initiation of treatment need to be conducted.

Keywords: Anemia; leucopenia; therombocytopenia; antiretroviral therapy.

1. INTRODUCTION

Acquired Immunodeficiency Syndrome (AIDS) is a systemic disorder caused by Human Immunodeficiency Virus (HIV), and characterized by severe impairment and progressive damage of both cellular and humoral immune responses. Besides immunological complications of HIV disease, hematological abnormalities, involving all lineages of blood cells, have been documented as strong independent predictors of morbidity and mortality in HIV-infected individuals [1,2]. These abnormalities have been documented to be the second most common causes of morbidity and mortality in HIV positive patients [3].

Hematological complications among HIV patients are generally marked with cytopenias such as anemia, neutropenia, lymphopenia and thrombocytopenia [4]. The incidence and severeity of cytopenias correlate to the stage of the disease, anemia being the most frequent hematological abnormality occurring in more than 70% of the infected individuals leading to transfusion [4,5]. Anemia has been associated with progression to AIDS and shorter survival times in HIV-infected patients [6]. Anemia may be resulted from an indirect effect of HIV infection or it may be caused by the direct effect of HIV on bone marrow stromal cells [7-9].

Thrombocytopenia is another frequent disorder occurring in about 30-40% of individuals with HIV infection [1,10,11]. The pathogenesis of thrombocytopenia is not well under stood but immune mediated destruction of platelets is expected to be the possible mechanism [10]. Leucopenia is one of the hematological abnormalities that occur in the course of HIV disease progression. The most common form of leucopenia usually encountered is neutropenia, occurring in 10-30% of the HIV infected individuals [1,10]. Neutropenia is caused by decreased production of cells because HIV will suppress the bone marrow by changing the marrow microenvironment and by altering the cytokine expression [12].

Hematological abnormalities are common manifestations of HIV infection and AIDS, and may have considerable impact on patients' well-being, treatment and care [2]. Especially in developing countries where access to the health institutions is low, people will visit these institutions after the disease progressed to a severe state, accompanied by cytopenias. Hence, investigating the magnitude of cytopenias is very important, especially at the first encounter of patients to the health institutions, because specific interventions other than antiretroviral treatment may be indicated for its correction [10]. So the aim of this study is to assess the hematological abnormalities of HIV positive patients on their first encounter to the antiretroviral therapy (ART) clinic at University hospital of Gondar, North West Ethiopia.

2. METHODS

2.1 Study Setting and Study Period

This cross-sectional study was conducted at University hospital of Gondar from November, 2011 to May 2012. The hospital is a tertiary level teaching hospital and has a separate ART

clinic where HIV positive individuals will attend their follow up care. There are more than 9000 HIV positive individuals who attend their follow up care in the clinic.

2.2 Study Population

During the study period a total of 189 newly diagnosed adult (age >18 years) HIV positive individuals visited the clinic and all of these individuals were included in the study.

2.3 Data Collection

The sociodemographic characteristics of the study participants were collected by a simple format prepared for the purpose of this study by direct interview of the patients. About 4ml of venous blood was collected from each study participant using EDTA coated test tubes. Hematological parameters (total white blood cell (WBC) count, differential WBC count, platelet count, hematocrit determination and hemoglobin measurement) were determined using Cell-Dyn 1800 hematology analyzer (Abbott Laboratories Diagnostics Division, USA) and the immunological parameter (CD 4 count) was analyzed using BD FACSCOUNT system (Becton Dickenson and Company, California, USA). Quality control samples were run along with patient sample to assure the quality of instrument function.

2.4 Data Analysis and Interpretation

Data was entered and analyzed using SPSS version 16 statistical software. Categorical variables were summarized in frequencies and percentages. Continuous variables were presented in mean (±SD) or median (IQR) as appropriate. Differences in the hematological parameters between males and females were assessed using independent sample t-test. Chi-square test was used to assess the presence of statistically significant association between hematological abnormalities and some sociodemographic variables and level of CD4 count. In all cases P-value less than 0.05 was considered as statistically significant.

2.5 Definition of Hematological Abnormalities

Anemia was defined as a hemoglobin concentration of <13g/dl for males and 12g/dl for females and a hemoglobin level <8mg/dl was considered as severe anemia. Mild anemia was defined as a hemoglobin level of 8-12mg/dl for females and 8-13mg/dl for males [13]. A platelet count of less than 150,000cells/µl was considered as thrombocytopenia and leucopenia was defined as a total WBC count of less than 4000cells/µl [14,15]. Neutropenia was considered when the absolute neutrophil count was less than 1500cells/µl and lymphopenia was defined as absolute lymphocyte count of less than 100cells/µl [16,17]. Immunosupression was defined based on the CD4 count as per the WHO guideline. Accordingly a CD4 count <200, 200-349 and 350-499 were considered as severe immunosupression, advanced immunosupression and mild immunosupression respectively [18].

2.5 Ethical Consideration

The study was ethically approved by the institutional ethical review board of University of Gondar. All study participants were involved on voluntary basis after giving informed consent. All results were kept confidential and only important results were communicated with the patients' physician.

3. RESULTS

3.1 General Characteristics and Immunohematological Profile of Study Subjects

A total of 189 HIV positive individuals (91 males and 98 females) were assessed for the presence of hematological abnormalities during their first visit of ART clinic. The mean (±SD) age of the participants was 33.2 (±9.3) years. Majority, 55.8% and 87.9% of the study participants were in the age range from 30-49 years and urban dwellers respectively. There was no statistically significant difference in hemoglobin, total white blood cell count (WBC), hematocrit, absolute neutrophil count (ANC), absolute lymphocytre count (ALC), platelet count and CD4 count between male and female participants (Table 1).

Table 1. Demographic and immunohematological characteristics of HIV positive patients on their first visit to ART clinic

Characteristics	Men (mean±SD)	Women (mean ±SD)	P-value
Age (Years)	36.1±9.4	30.5±8.38	< 0.0001
Hemoglobin (mg/dl)	13.4±4.53	12.5±1.87	0.089
Total WBC (x 10^3 cells/µl)	6.378±2.25	6.084±2.23	0.386
Hematocrit (%)	40.9±8.2	39.4±5.6	0.131
	Median (IQR)	**Median (IQR)**	
ANC (cells/µl)	3456(2435.25-5749.8)	3150(2428.75-4672.8)	0.212
ALC (cells/µl)	1681(1293.25-2227)	1626(2365.75-1295.55)	0.868
Platelet (x 10^3 cells/µl)	264(199.5-307)	270(217.25-355.25)	0.405
CD4 count (cells/µl)	187(118.5-378)	271.5(120-414.5)	0.110

3.2 Prevalence of Immunohematological Abnormalities and Associated Factors

Table 2 shows the prevalence of immunohematological abnormalities of HIV positive individuals during their first visit to the ART clinic. Accordingly 19% and 12.2% of the study participants had leucopenia and thrombocytopenia respectively. Anemia was observed among 42.3% of the study participants. Leucopenia and lymphopenia were observed among 4.8% and 12.7% of the study participants. The most common abnormality observed was immunosupression (CD4 count < 500 cells/mm^3) which is found in 83.1% of the individuals, majority, 43.7%, being severeely immunosupprssed (Table 2).

Fifty eight individuals (30.7%) had a combination of two of either of leucopenia, thrombocytopenia and anemia. Though not statistically significant, the occurrences of combination of hematological abnormalities were more common among females than their male counter parts (Fig. 1).

Sex, age, residence and CD4 count were assessed for the presence of association with individual hematological abnormalities. None of these factors showed statistically significant association with thrombocytopenia, but CD4 count was significantly associated with leucopenia (Table 3).

Table 2. Prevalence of immunohematological abnormalities among HIV positive individuals during their first visit to the ART clinic

Immunohematological Abnormalities	Frequency	Percentage (%)
Leucopenia	36	19
Neutropenia	9	4.8
Lymphopenia	24	12.7
Thrombocytopenia	23	12.2
Anemia (Hemoglobin <12mg/dl for men; <13mg/dl for women)	80	42.3
Severe (<8)	5	6.25
Mild (8-13 for men & 8-12 for women)	75	93.75
Immunosuppression (CD4 <500cells/mm^3)	157	83.1
Severe (<200)	83	52.7
Advanced (200-349)	49	31.2
Mild (350-499)	25	15.9

Table 3. Association of age, sex, residence and CD4 count with hematological abnormalities

Factors	Leucopenia			Thrombocytopenia			Anemia		
	Yes N (%)	No N (%)	P-value	Yes N (%)	No N (%)	P-value	Yes N (%)	No N (%)	P-value
Sex									
Male	14 (7.4)	77 (40.7)	0.22	11 (5.8)	80 (42.3)	0.97	38 (20.1)	53 (28)	0.878
Female	22 (11.6)	76 (40.2)		12 (6.3)	86 (45.5)		42 (22.2)	56 (29.6)	
Age									
<20	2 (1.1)	8 (4.2)	0.29	1 (0.5)	9 (4.8)	0.98	5 (2.6)	5 (2.6)	0.33
20-29	9 (4.8)	53 (28)		7 (3.7)	55 (29.1)		21 (11.1)	41(21.7)	
30-39	18 (9.5)	51 (26.9)		9 (4.8)	60 (31.7)		34 (17.9)	35(18.5)	
>39	7 (3.7)	41 (21.7)		6 (3.2)	42 (22.2)		20 (10.6)	28 (14.8)	
Residence									
Urban	32 (16.9)	135(71.4)	0.91	18 (9.5)	149(78.8)	0.11	68 (31.7)	99 (52.4)	0.29
Rural	4 (2.1)	18 (9.5)		5 (2.6)	17 (8.9)		12 (6.3)	10 (5.3)	
CD4 count									
<200	28 (14.8)	55(29.1)	<0.0001	14 (7.4)	69 (36.5)	0.15	41 (21.7)	42 (22.2)	0.25
200-349	3 (1.6)	46 (24.3)		4 (2.1)	45(23.8)		19 (10)	30 (15.9)	
350-499	4 (2.1)	21(11.1)		4 (2.1)	21 (11.1)		7 (3.7)	18 (9.5)	
>499	1 (0.5)	31(16.4)		1 (0.5)	31(16.4)		13 (6.9)	19 (10)	

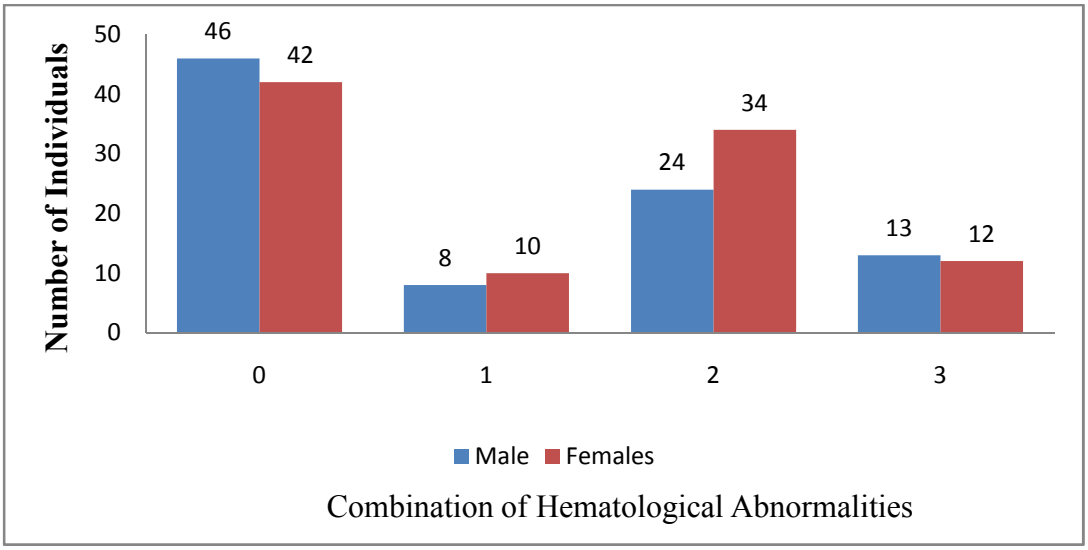

Fig. 1. Occurrence of combination of hematological abnormalities (leucopenia, thrombocytopenia and anemia) among the two sex groups (0 = No abnormality, 1 = single abnormality, 2 = combination of two types of abnormalities, 3 = combination of three abnormalities

4. DISCUSSION

In this study we evaluated the hematological manifestations of 189 consecutive HIV positive patients on their first visit to ART clinic of University of Gondar. High rates of hematological abnormalities were also found in this study; immunosupression being the most commonly encountered followed by anemia, leucopenia and thrombocytopenia.

The prevalence of anemia in this study was 42.3% which is lower than a study conducted in India that showed a prevalence of 65.5% from a total of 200 study participants [1]. A study from Ghana has also reported anemia prevalence of 63.5% among 276 HAART naïve patients which is higher than the current report [19]. On the other hand studies from Iran and Nigeria reported a prevalence of 10.3% from 642 individuals and 24.2% from 205 individuals [6,10] which are lower than the current report. Differences observed may be attributed to the difference in the demographic profile, sample size difference and variability in the definition of anemia. A relatively similar result was reported previously by Ferede et al. from the study area among HAART naïve patients [20]. The anemia prevalence among female participants was 22.2% in our study and this was similar with a study from Rwanda that reported a prevalence of 20.5% [2]. In this study prevalence of anemia was not significantly associated with different characteristics of the study participants which is different from other studies where associations with some factors like sex and CD4 count were reported [6,20].

The prevalence of leucopenia in this study was 19% which is lower than a follow up study conducted in Nigeria that reported a prevalence of 26.8% [21]. On the other hand a lower prevalence, of 5.5%, was also reported [22]. In this study high rate of leucopenia was significantly associated with immunosupression (low CD4 count) as reported elsewhere in the world [23,24]. About 43.9% of the study participants were severeely immunocompromised (had a CD4 count of less than 200 cells/µl) requiring immediate

initiation of ART as per the WHO guideline [18]. Lymphopenia was observed in about 12.2% of the study participants which was similar to a report by Ogba et al. [4]. About 4.8% of the study participants had neutropenia and are hence at great risk of developing infections at different sites including the skin, mucosa and the lungs [16].

In the current study, thrombocytopenia was reported among 12.2% of the study participants. This result is higher than a previous report in the study area that showed a prevalence of 5.9% [25]. An Indian study has also reported a lower prevalence (4.65%) of thrombocytopenia [26]. Higher results in our study may be due the difference in the study population. Because the current study participants were newly diagnosed HIV positive individuals who might had visited the ART clinic after the disease has progressed to a severe state that will increase the prevalence of thrombocytopenia. A thrombocytopenia prevalence of 20% was reported from Iran which higher than our report [27]. The low cut of value used to define thrombocytopenia in the Iranian study may contribute to higher prevalence rates. Similar to the study conducted by Wondimeneh etal, neither the sociodemographic factors nor the CD4 count of the study participants showed significant association with the prevalence of thrombocytopenia [25].

In this study more than one fourth (30.7%) of the patients had more than one hematological abnormality and 13.2% had cytopenia. The result is lower than a report from Nigeria that indicated an overall cytopenia prevalence of 20% [10]. Though the result seems smaller as compared to the Nigerian study, it indicates that large numbers of HIV positive individuals are at great risk for HIV associated morbidity and mortality as the larger population is considered. Hence great attention should be given to this group of individuals and the various reasons behind the cytopenia need to be investigated for better management of the patients.

This study was limited in that it couldn't assess the clinical profile of the study participant which could possibly add the level of knowledge by relating clinical profile with the hematological abnormalities. Despite this the report provides valuable information about the hematological characteristics of HIV positive patients on their first encounter to the ART clinic.

5. CONCLUSION

The hematological abnormalities observed in this study are very high, especially the rate of immunosupression and anemia. This high prevalence may be associated with delayed visit to ART providing institutions. Hence the association of health seeking behavior or HIV positive patients and the state of hematological manifestations need to be understood. Moreover further research that will assess the clinical profile of HIV positive patients in the first visit to the ART centers and their association with hematological profile need to be researched as it will provide more important information for the care and management of these patients.

CONSENT

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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