

Characteristics of Cytopenia in HIV Positive Individuals

ABSTRACT

Background: HIV infection is an emerging issue all over the world. Bangladesh also experiencing increasing trend of infection over the time. Around 9500 infected individuals were in 2014 and it were only 500 individuals in 2000. Haematological manifestations are very common among those individuals whereas cytopenia is the commonest. Cytopenia may develop due to HIV itself or its sequel or due to drugs used for treatment. In Bangladesh, there is no available data regarding cytopenia and its association in HIV positive individuals till date. So, in our study, we tried to focus about the frequency of cytopenia and its associated factor. **Objective:** The objective of this study was to assess the characteristics of cytopenia in HIV positive individuals. **Methods:** This was a cross sectional analytical study where 100 of HIV positive individuals were enrolled. The study was conducted in the Department of Haematology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh with collaboration of Ashar Alo Society, Dhaka, a renowned NGO from January 2014 to December 2015. Cytopenia was identified by automated cell counter and re-evaluated by manual examination of peripheral blood film. CD4 count measured by flow cytometry. Multiple regression analysis was done to assess correlation of different variable. A p value of <0.05 was taken as significant. **Results:** Among total participants, 56% had at least one type of cytopenia. Anaemia was observed in 45% whereas leucopenia and thrombocytopenia were found in 10% and 17% respectively. Among all anaemic individual's, mild anemia was the commonest which was in 64.4%, 22% was moderately anemic and severe anemia was observed in 13.3 % cases. The most common type of anaemia was microcytic anaemia 51.1%, then normocytic anaemia was found in 44.4% while macrocytic variety were seen in only 4.4%. Bicytopenia was observed in 14% and only 1% had pancytopenia. Cytopenia were more prevalent in subjects aged between 20 and 40 years. Multiple regression analysis shows anemia was associated with gender ($p < 0.05$) and CD4 count ($p < 0.0001$). Thrombocytopenia was associated with CD4 count ($p < 0.05$), leukopenia was correlated with the CD4 count ($p < 0.05$) and age ($p < 0.05$) among the variables observed. According to proportion of cytopenia after HAART, neutropenia was at baseline 46.6%, at 6 months 18.0%, at 12 months 15.1% and at 24 months 11.3%. Anemia at baseline 57.1%, at 6 months 14.9%, after 12 months 9.2% and at 24 months 7.9%. Thrombocytopenia at baseline 19.3%, at 6 months 4.4%, at 12 months 4.3% and at 24 months 2.5%. Cytopenia at baseline 79.1%, at 6 months 25.4%, at 12 months 21.8% and at 24 months 17.7%. Finally, of bi-cytopenia baseline 18.2%, at 6 months 3.4%, at 12 months 2.6% and after 24 2% respectively. **Conclusion:** Anemia is the commonest cytopenia related to HIV infected individuals. Mild anemia and microcytic type are very common in Bangladesh. CD4 count is a unique variable for development of cytopenia.

Keywords: Characteristics, Cytopenia, HIV positive, Individuals, CD4 count, Anaemia.

INTRODUCTION

HIV infection is an emerging issue all over the world. According to WHO updated on December, 2015, HIV continues to be a major global public health issue, having claimed more than 34 million lives so far. There are 9500 (4100-97000) people living with HIV in Bangladesh (Effective date 27-11-2014). [1] HIV infection causes diverse haematological manifestations. Mechanism of these complication include immune-mediated cytopenia, impaired haematopoiesis, altered coagulation. [2] Cytopenia is the commonest complication which may occur as a result of HIV infection itself, as sequelae of HIV related infections or malignancies or as a consequence of therapies used for HIV infections. [3] Cytopenia has been associated with several factors including age, sex, geographical location, ethnicity, HAART therapy, CD4 count and co-morbidities like tuberculosis, fever, hepatitis B infection and oral candidiasis. Anaemia is found among 10-20% of individuals with HIV infection at diagnosis and prevalence can range from 66-85% during the course of the disease. [4] Anaemia in HIV may be result of nutritional deficiencies, GI bleeding, diminished erythropoietin response and opportunistic infections. [5] Neutropenia may occur in 10-30% of HIV patients. Bone marrow infiltration, drug toxicity and infection has been described as the pathogenesis of leukopenia. [6] On the other hand, thrombocytopenia is found in 3-40% of patients with HIV infection. Immune mediated destruction, impaired hematopoiesis, thrombotic thrombocytopenic purpura and toxic effects of medications and infections all are described as the underlying

mechanism of thrombocytopenia. [7] CD 4 lymphocyte count is an important predictor of HIV positive individual's treatment and prognosis. CD 4 count <200 cells/ μ l is used to define as poor prognosis. [8, 9]

OBJECTIVE

General Objective:

To assess the characteristics of cytopenia in HIV-positive individuals.

Specific Objective:

- To assess the demographic status of the participants.
- To assess the cytopenia with different variables.
- To evaluate the proportion of cytopenia at baseline and 6, 12, and 24 months after HAART.

METHODOLOGY

This was a cross sectional analytical study where 100 of HIV positive individuals were enrolled. The study was conducted in the Department of Hematology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh with collaboration of Ashar Alo Society a renowned NGO during the period from January 2014 to December 2015. A detailed history was obtained with a preformed questionnaire. Characteristics including marital status, disease duration, treatment duration were also obtained. Co-morbid illness which may cause cytopenia like tuberculosis, hepatitis of the participants was excluded. Complete confidentiality identity and address was concealed from study proforma and was maintained in a separate record. Cytopenia was identified by automated cell counter and re-evaluated by manual examination of peripheral blood film. CD4 count measured by flow cytometry. The total intervention was conducted in accordance with the principles of human research specified in the Helsinki Declaration [10] and executed in compliance with currently applicable regulations and the provisions of the General Data Protection Regulation (GDPR) [11]. The study was approved by the ethical review committee of Bangabandhu Sheikh Mujib Medical University (BSMMU) Hospital, Dhaka, Bangladesh. Data were recorded and then entered into the computer using Microsoft Excel program and analyzed by SPSS version 21.0 software package with the help of a statistician. Categorical variables were summarized as proportions, while means, median and standard deviations were used for continuous variables. In the multiple regression analysis, adjusted R square and p-value were used to determine the factors that were associated with cytopenia.

RESULTS

In this study, among total 100 participants, 54% were male whereas the rest 46% were female. So male participants were dominating in number. Among all the participants, the lowest number of patients were from <20 years' age groups which was 8%. Besides this, 28%, 34% and 30% were from 20-30, 30-40 and >40 years' age groups respectively. Majority of our participants were married which was 82%. Among total participants, 56% had at least one type of cytopenia. Anaemia was observed in 45% whereas leucopenia and thrombocytopenia were found in 10% and 17% respectively. Among all anaemic individual's, mild anemia was the commonest which was in 64.4%, 22% was moderately anemic and severe anemia was observed in 13.3 % cases. The most common type of anaemia was microcytic anaemia 51.1%, then normocytic anaemia was found in 44.4% while macrocytic variety were seen in only 4.4%. Bi-cytopenia was observed in 14% and only 1% had pancytopenia. Cytopenia were more prevalent in subjects aged between 20 and 40 years. Multiple regression analysis shows anemia was associated with gender ($p < 0.05$) and CD4 count ($p < 0.0001$). Thrombocytopenia was associated with CD4 count ($p < .05$), leukopenia was correlated with the CD4 count ($p < 0.05$) and age ($p < 0.05$) among the variables observed. In this study, in assessing the frequencies of anaemia, leukopenia and thrombocytopenia among the participants, considering genders, ages, marital status treatment status or even

CD4 count, we found anaemia as the most frequent among the patients. In this study, in assessing the proportion of cytopenia at baseline, 6, 12, and 24 months after HAART we observed gradually the frequencies of neutropenia, anemia, thrombocytopenia, cytopenia, bi-cytopenia and pancytopenia had been decreased by time durations of treatment. Finally, in comparing between the proportion of cytopenia of baseline and 24 months after HAART therapy, we observed that, after 24 months the frequencies of all the events had been decreased significantly where the P value was found as 0.003.

Table 1: Gender distribution of participants (N=100)

Variables	n	%
Gender distribution		
Male	54	54%
Female	46	46%
Age distribution		
<20 yrs.	8	8%
20-30 yrs.	28	28%
30-40 yrs.	34	34%
>40 yrs.	30	30%
Marital status		
Married	82	82%
Unmarried	18	18%

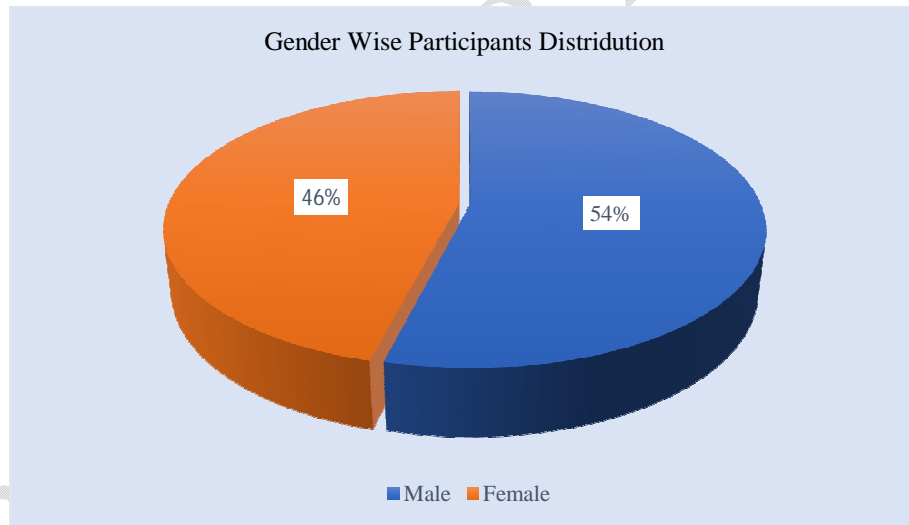


Figure I: Participants gender wise distribution (N=100)

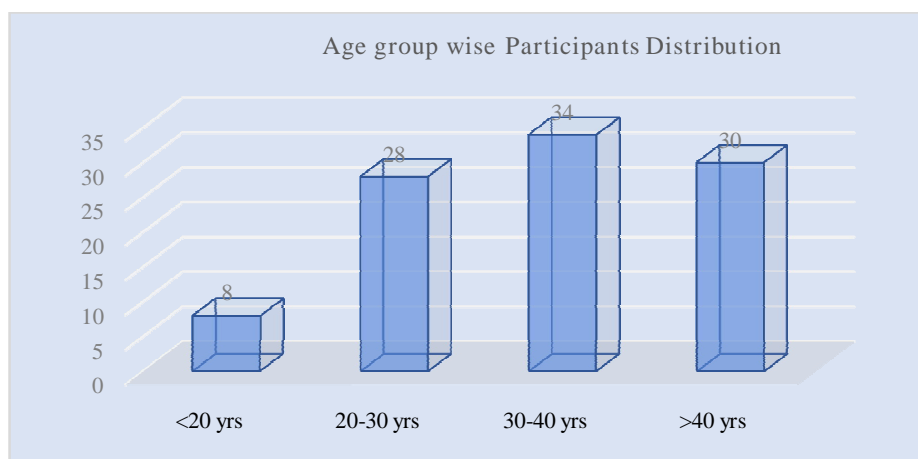


Figure II: Age group wise participant's distribution (N=100)

Table 2: Frequencies of cytopenia among participants with different features (N=100)

Parameter	Anemia	Leukopenia	Thrombocytopenia
	(n=55)	(n=15)	(n=30)
	n (%)	n (%)	n (%)
As per gender distribution			
Male	27(49.1)	10(66.7)	17(56.7)
Female	28(50.9)	5(33.3)	13(43.3)
As per age distribution			
<20 yrs.	5(9.1)	1(6.7)	2(6.7)
20-30 yrs.	18(32.7)	3(20.0)	7(23.3)
30-40 yrs.	20(36.4)	6(40.0)	8(26.7)
>40 yrs.	12(21.8)	5(33.3)	13(43.3)
As per the marital status			
Married	44(80.0)	13(86.7)	25(83.3)
Unmarried	11(20.0)	2(13.3)	5(16.7)
As per treatment status			
On treatment	31(57.1)	5(33.3)	22(73.3)
Not on Treatment	24(42.6)	10(66.7)	8(26.7)
As per CD4 count group			
<50	14(25.5)	2(13.3)	5(16.7)
50-200	10(18.1)	2(13.3)	3(10.0)
201-350	11(20.0)	3(20.1)	8(26.7)
351-500	9(16.4)	2(13.3)	3(10.0)
>500	11(20.0)	6(40.0)	11(36.6)

Table 3: The proportion of cytopenia at baseline, 6, 12, and 24 months after highly active antiretroviral therapy (HAART).

Cytopenia	Baseline	At 6 months	At 12 months	At 24 months
	%	%	%	%
Neutropenia	46.6	18.0	15.1	11.3
Anemia	57.1	14.9	9.2	7.9
Thrombocytopenia	19.3	4.4	4.3	2.5
cytopenia	79.1	25.4	21.8	17.7
Bicytopenia	18.2	3.4	2.6	2.0
Pancytopenia	2.6	1.0	0.5	0.2

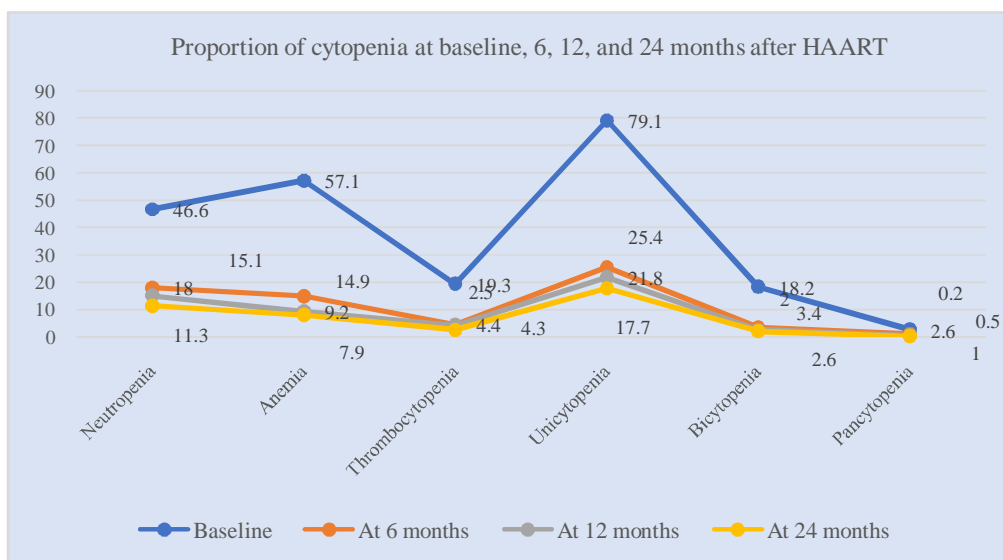


Figure III: Proportion of Cytopenia at baseline, 6, 12, and 24 months after HAART (N=100)

Table 4: Comparison between the proportion of cytopenia at baseline and 24 months after highly active antiretroviral therapy (HAART).

Cytopenia	Baseline	At 24 months	P value
	%	%	
Neutropenia	46.6	11.3	0.003
Anemia	57.1	7.9	
Thrombocytopenia	19.3	2.5	
Cytopenia	79.1	17.7	
Bicytopenia	18.2	2.0	
Pancytopenia	2.6	0.2	

DISCUSSION

The aim of this study was to assess the characteristics of cytopenia in HIV positive individuals. In our study, we have found 45% individuals to be anaemic which is consistent with the report on other country except in Mexico (20%). The possible cause may be different cut point value of haemoglobin to define anaemia. Our study also reveals 51% microcytic, 44% normocytic and only 4% macrocytic. Here microcytic anemia was found as a bit higher in comparison to the study of Mittal et al, 2014 (58.44%-normocytic) or Mathewa et al, 2013 (40.4%). [12, 13]. This odd to other results may be explained as cut-off value of MCV in our study was 83, but was 76 in above-mentioned study. Severe anaemia was found in 13.3%, moderate anaemia in 22.2% and mild anaemia was in 64.4%. The observation was good to other related studies like Ferede et al (2013) and Chandrakar et al (2015) [8, 14]. We have found significant correlation of anaemia with gender and CD4 count, about 85% individual anaemic when CD4 count is less than 50 cell/mm³. Subbaraman et al (2008) [15] also reported same, correlation of CD4 and female gender with anaemia in their study over 6996 pt upon 10 years. Qazi et al (2014) also observed significant $p < 0.05$ with CD4 count. [9] Leukopenia have been found to be associated with only CD4 count and age. A similar result was obtained by Attili et al (2008) and Mata-marin et al (2010). [16, 17] Thrombocytopenia had only associated with CD4 count among the variables we studied. This observation consistent with other international study of thrombocytopenia like Shen et al (2015) over 1948 of the Chinese population. [18] But a different result ($P > .05$) not significant for the CD4 count reported by Attili et al (2008)

[16]. The probable cause of this dispersion may be very low presence of thrombocytopenia (only 4%) to interpret with CD4 count in the study of Attili et al. [16]. CD4 count has been observed as the unique variable to correlate to develop any cytopenia. Same result was obtained by Chandrakar et al, 2015 over 400 participants. [8] All bicytopenic and pancytopenic individuals have found to be CD4 count less than 50 cell/mm³ and majority of them are below 20. Kyeyune et al (2014) had published similar observation over 400 individuals. They reported at least one form of cytopenia is present in 84.7% when CD4 count less than 50 cell/mm³. [3] Finally, in comparing between the proportion of cytopenia of baseline and 24 months after HAART we observed that, after 24 months the frequencies of all the events had been decreased significantly where the P value was found as 0.003.

Limitation of the study:

Though it was a single-centered study with a small sample size, so the findings of this study may not reflect the exact scenario of the whole country.

CONCLUSION & RECOMMENDATION

HIV is an emerging problem throughout the world and in Bangladesh, it is far more aggressive than our thinking. The magnitude of cytopenia in Bangladesh was grossly unknown. The purpose of this study was to shed some light over this issue. As far we have found, the rate of anaemia was 45%, thrombocytopenia was 17% and leucopenia was 10%. Mild anemia was more common (64.4%) than moderate anemia (22%) or severe anemia (13.3 %). Microcytic anaemia is more prevalent (51.1%) than normocytic anaemia (44.4%) and macrocytic anaemia (4.4%). Cytopenia were more prevalent in subjects aged between 20-40 years and when CD4 count less than 50 cell/ul. CD4 count had observed to be directly associated with anaemia, leukopenia and thrombocytopenia. As our study was a cross-sectional one, we did not have many scopes to determine the individual risk factor for cytopenia. So, we will suggest doing a prospective cohort study to evaluate such factor in future. For getting more specific findings we would like to recommend for conducting similar more studies with larger sized samples in several places.

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