EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 8
Issue: 12
215-221
Year: 2021

PATTERNS OF HEMATOLOGICAL MANIFESTATIONS IN PEOPLE LIVING WITH HUMANIMMUNE-DEFICIENCY VIRUS (HIV): A DESCRIPTIVE CROSS-SECTIONAL STUDY

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Article Received on 24/09/2021 **Article Revised on 14/10/2021** **Article Accepted on 04/11/2021**

ABSTRACT

Introduction: People living with Human Immune-deficiency Virus can have various clinical presentations. Hematological manifestations are one of the common clinical presentations, but often overlooked in day to day clinical practices. This study is done to find the patterns of hematological abnormalities in people living the Human Immune- deficiency Virus. **Methods:** One hundred participants were enrolled in this descriptive cross sectional study who were diagnosed as a case of confirmed Human-Immune deficiency Virus infection, from June 2018 to July 2020. All the detail data of various hematological abnormalities from investigations like complete blood count, peripheral smear and other relevant informations like CD4(cluster of differentiation) count, viral load, duration and treatment regime of antiretroviral treatment and staging were recorded after taking ethical clearance from the institute. Statistical analysis was done using Statistical Package for the Social Sciences. **Results:** We observed almost equal participation of male and female with median age of 39.9 years with mean duration of anti-retroviral therapy for 5.1 years. 62% of study participants had anemia, 21% had leucopenia and 22% had thrombocytopenia. Normocytic normochromic anemia was the most common finding (88%) followed by microcytic anemia (68%) in peripheral smear of blood. Most of the participants (69%) were in WHO stage 1. Most of them (69%) were on Tenofovir based treatment regimen. **Conclusion:** Young age people living with HIV under treatment have normocytic normochromic to microcytic anemia as the commonest hematological abnormality with normal level of leukocytes and thrombocytes.

KEYWORDS: Anemia; Hematological; Leucopenia; Human Immune-deficiency Virus; Thrombocytopenia.

INTRODCUTION

Hematologic abnormalities are considered as one of the commonest clinical manifestation in patients with advanced human immunodeficiency virus (HIV) infection, such as anemia, neutropenia, and thrombocytopenia.[1,2] Although cluster of differentiation 4(CD4) count and HIV RNA(Ribo-nucleic acid) concentration are taken as biomarkers of disease progression, many other factors can also predict the prognosis.[3,4,5] In developing countries with resource limited areas like Nepal, they can be taken as alternative indirect markers.[6] HIV itself can cause hematological manifestations by influencing survival and growth of hematopoietic progenitors.[7]

Anemia is considered as the one of the commonest hematological abnormalities in people living with HIV infection. As the severity of HIV diseases increases, the prevalence of anemia also increases.[8] In fact prevalence of anemia is more in HIV infection compared to general population.[9] There are many studies done in past which have shown that anemia has prognostic value. Anemia is associated with health related quality of life, progression of disease and mortality.[10] Many factors have been identified which are associated with anemia in HIV infection. Micronutrient deficiency, opportunistic infection, drug induced anemia, neoplastic diseases and chronic inflammation of the disease can cause anemia.[11]

HIV related leucopenia is also a common hematological abnormality. However, the prevalence of leucopenia among treatment naïve people are much higher compared to treated ones.[12] Although leucopenia is associated with the toxicities of drugs for HIV or associated conditions, studies have shown leucopenia is prevalent among untreated HIV infected people also.[13] Lower CD4 counts and higher HIV viral load were found to be associated with the development of neutropenia.[14] However there are few studies which have shown improvement in leucopenia with antiretroviral therapy (ART).[15]

In some HIV infected asymptomatic patients, thrombocytopenia may be the first clinical manifestation.[16] Severe thrombocytopenia can cause bleeding as the disease progresses.

Thrombocytopenia can occur due to a drug induced adverse event, HIV infection itself, effects of opportunistic infections and malignancies.

The main objective of this study is to evaluate the patterns of hematological manifestations in people living with Human Immune-deficiency virus which will help us to identify early disease progression, prognosis and timely management of cytopenias to improve quality of life.

MATERIALS AND METHODS

This is a hospital based cross-sectional study which was conducted in B.P. Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal in out-patient and ward, Department of Internal Medicine. The study protocol was submitted for ethical approval to institutional ethical review board (IERB) and ethical clearance to conduct the study was obtained. An informed verbal and written consent were taken. Patients were requested to participate in the study with assurance that consenting or refusing to participate in the study will have no effect on the treatment they receive. All consecutive patients more than 18 years of age diagnosed as cases of HIV infection was included for the study and those with co-infections with chronic hepatitis B and C, malaria, leishmaniasis, tuberculosis and previously diagnosed case of hematological cytopenias before the diagnosis of HIV infection were excluded as these condition can have their own effects on hematological abnormalities. The convenient sampling technique was used.

Data collection

A detailed socio-demographic data for every patient were collected and information was recorded in structured proforma. The data included were age, gender, duration of diagnosis of HIV, duration of initiation of ART (Anti-retroviral Therapy), clinical features at the time of presentation related to cytopenias (Easy fatiguability, Fever, Purpuric rash, Bleeding manifestations etc). Hematologicalinvestigations were done in all patients with complete blood count, reticulocyte count and peripheral smear for cytology. Other important lab values of CD4 count, HIV RNA level were recorded. Other important investigation to rule out co-infections were done including RK39 (recombinant kinase 39), HBsAg (Hepatitis B surface antigen), HCV (hepatitis C Virus) RNA and Chest radiography. HIV Staging was done as per WHO guideline and treatment regime for HIV was also recorded. Data were collected and entered in Microsoft Excel 2010. Analysis was done using Statistical Package for the Social Sciences.

RESULTS

Baseline Characteristics of the Study Population

In our study, we took 100 patients visiting to our hospital. The mean age in our study was 39.9 years. Among them 49% were female. Most of the study participants were asymptomatic at the time of presentation.

Table 1: Baseline characteristics and clinical profile of the study participants (N=100)

Description of variables	Frequency (n)	Percentage (%)
Age (yrs) (Mean ± SD)	39.9 ± 11.2	
□ 20 yrs	3	3.0
21 – 35 yrs	33	33.0
36 – 45 yrs	37	37.0
□ 46 yrs	27	27.0
Gender		
Male	51	51.0
Female	49	49.0
Presenting clinical features of participants		
A)Easy fatiguability	18	18.0
B)Other symptoms (fever, purpuric rashes)	9	9.0
C) Asymptomatic	73	73.0
Duration of HIV diagnosis (yrs) (Mean ± SD)	5.4 ± 4.6	
Duration of ART therapy (yrs) (Mean ± SD)	5.1 ± 4.3	

We looked for hemoglobin profile in our study where we found 62% of study participants had anemia (Hemoglobin levels <12.0 g/dL in women and <13.0 g/dL in men). Only 6% of study participants had severe anemia (Hb<8.0g/dl), Leucopenia (Total leucocytes count <4000/mm^3) was observed in 21% and thrombocytopenia (Platelets count<150000/mm^3) was observed in 22% of study participants.

We also observed Normocytic normochromic Red Blood Cell as the commonest peripheral smear finding (88%) followed by microcytic and hypochromic Red Blood Cell.

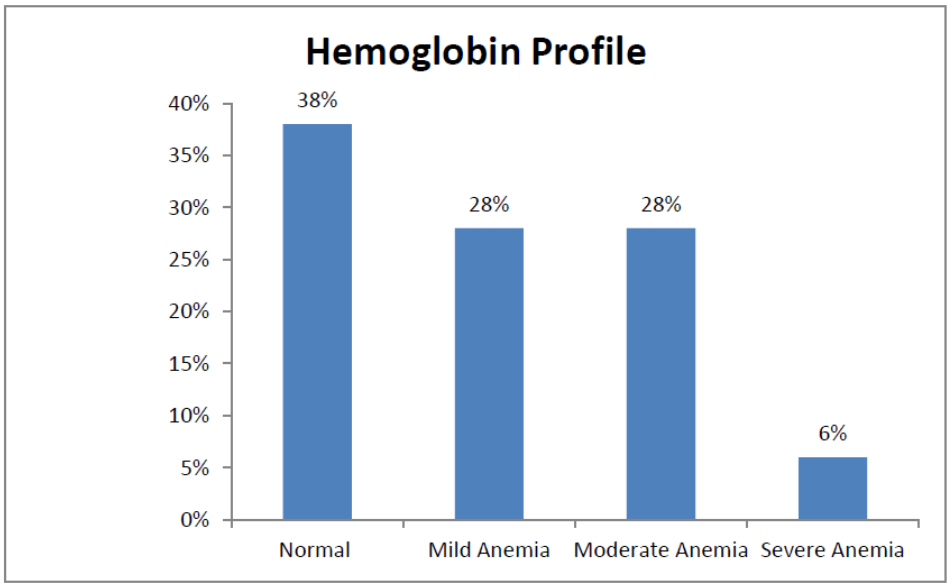

Fig 1: Hemoglobin profile of study participants (N=100).

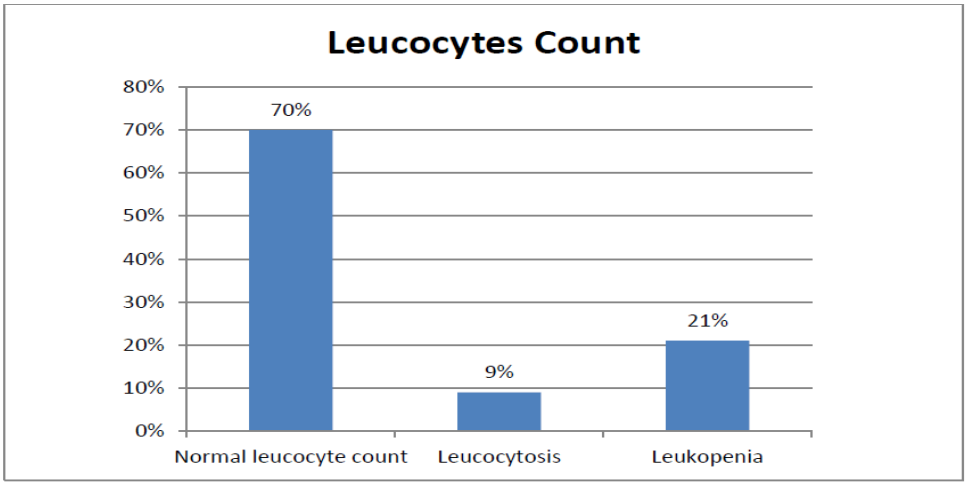

Fig 2: Leucocyte counts among study participants (N=100).

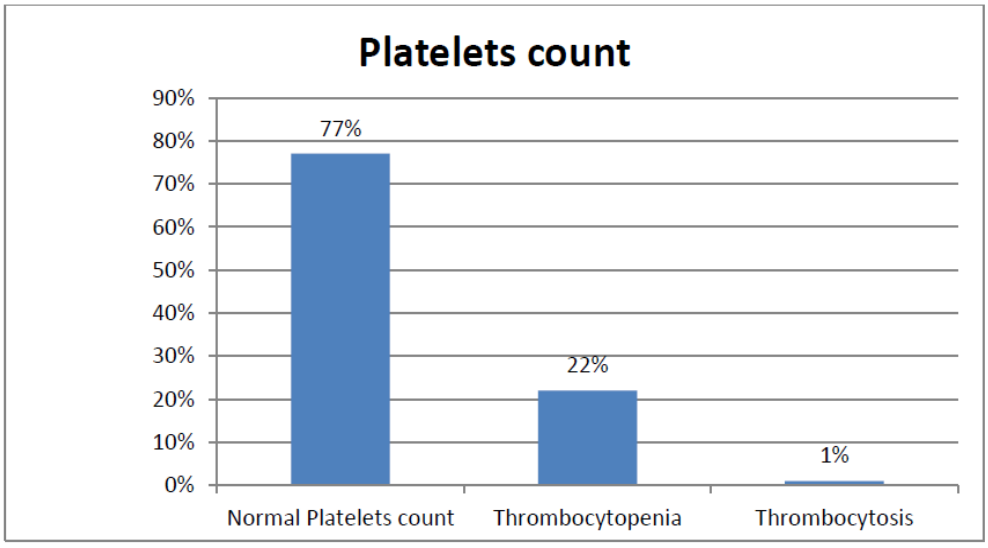

Fig 3: Platelets count among study participants (N=100).

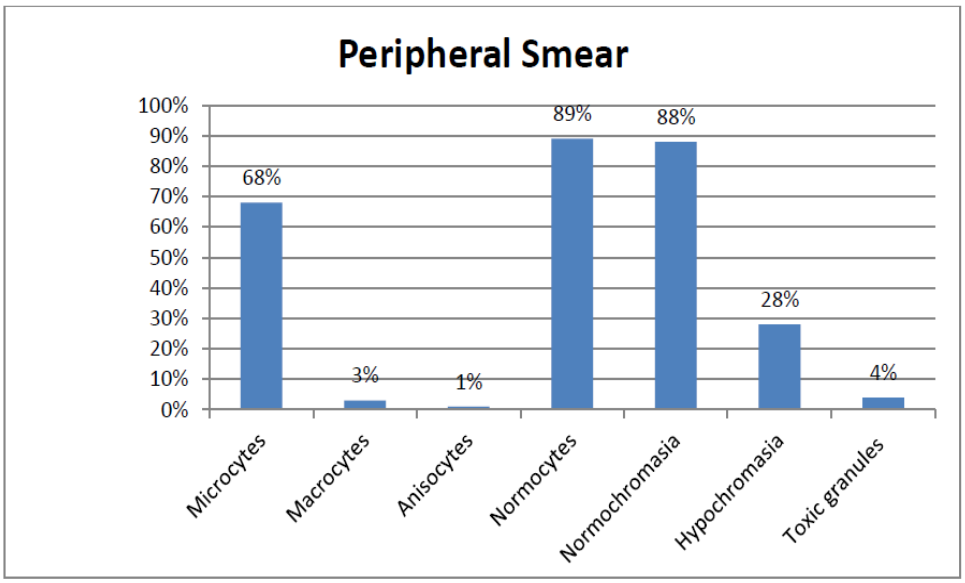

Fig 4: Peripheral smear among study participants (N=100).

Most of the study participants (87%) had undetectable viral load, however around 10% of studyparticipants had detectable viral load and 3% of study participants had viral load more than 10,000 copies/ml. We also found that most of our study participants (74%) had CD4 count more than 500 cells/mm^3. Study participants were also classified according to WHO clinical staging. Among study participants, most of them(69%) were in WHO stage 1and other study participants, 18%, 11% and 2% were in WHO stage 2,3 and 4 respectively.

Among study participants, most the them (69%) were on Tenofovir based anti-retroviral therapyand 31% were on Zidovudine based therapy. Besides antiretroviral medication, 31% of study participants were on Cotrimoxazole prophylaxis therapy.

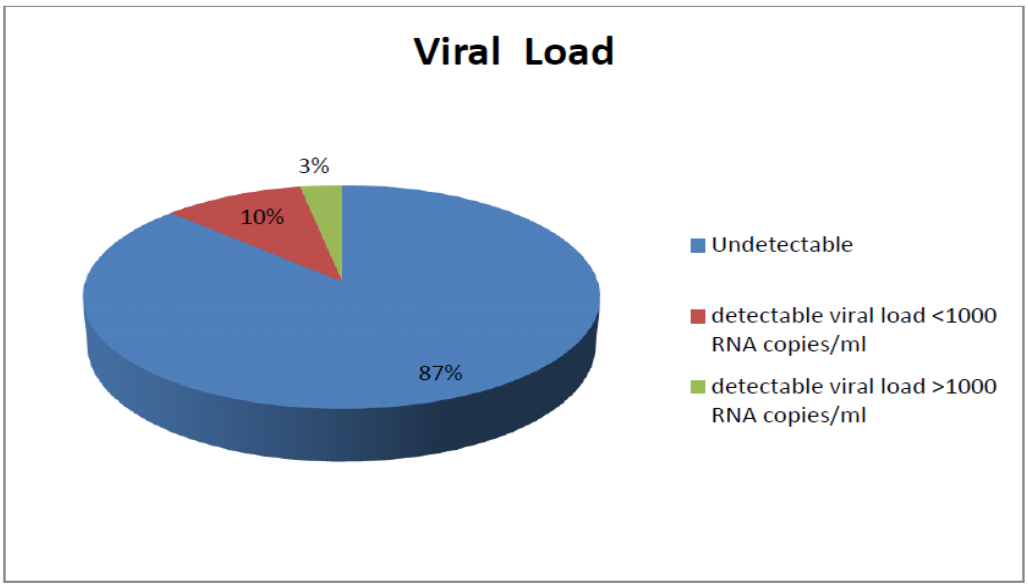

Fig 5: Viral load (RNA copies/ml) in study participants (N=100).

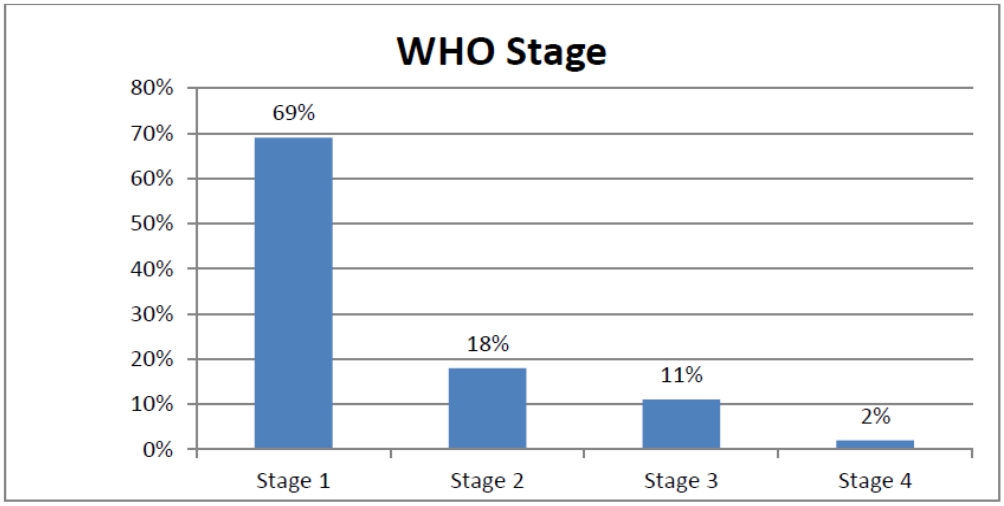

Fig 6: WHO staging in study participants (N=100).

DISCUSSION

In previous studies, among the various hematological abnormalities, anemia was the commonest clinical manifestation.[17,18] Anemia in HIV is associated with impaired quality of life, disease progression, and a higher mortality rate.[19,20] Our study also showed anemia as the most common hematological abnormality (62%). Anemia itself is prevalent in general population due to various nutritional deficiencies.[21] However it may have multiple etiologies like iron deficiency, drug related side effects (eg. Zidovudine's side effect) and increase loss of blood in females during menstruation It's very difficult to identify the etiologies as they all can contributeequally for decreased hemoglobin. But our study also showed normocytic normochromic Red Blood Cells as the most common cytological abnormality followed by microcytic Red Blood Cells, which can be the manifestation of anemia of chronic diseases and nutritional deficiencies.

Like any other viral diseases, HIV infection also can cause leucopenia. In previous study done by Gebreweld et al, it was found that up to 13.8 % of patients present with low leucocyte counts.[22] However in our study, most of the participants (70%) have normal leucocyte counts and we observed leucopenia in 21% of study participants. It might be due to anti- retroviral therapy or HIV infection itself. Studies have shown that low level of neutrophil count is associated with worsening of HIV disease itself.[23] Although low neutrophil counts usually reflect the toxicity of therapies for HIV infection, studies have shown high incidence of neutropenia of untreated patients too.[24]

A low platelet counts, sometimes can be the only hematological abnormality at presentation. Although thrombocytopenia doesn't seem to be of prognostic value, it is not uncommon among people with HIV infection. In previous study done by Taremwa et al, HIV related thrombocytopenia was found upto 17.8% of HIV patients during their course of disease.[25] But our study showed normal platelet count in most of the study participants (77%) and thrombocytopenia in 22% of study participants. We observed more participants with thrombocytopenia and leucopenia compared to previous studies.

Regarding treatment regimens, national guidelines recommend use of combination of Tenofovir, Lamivudine and Dolutregravir as the first line of therapy for HIV infection in Nepal. But we enrolled most of our participants prior to the new recommendation of national guideline. So in older recommended regimen, Tenofovir, Lamivudine and Efavirenz combination was the most common treatment regimen (55%) in study participant. Zidovudine based regimen were used in 31% of study participants which can also cause anemia as a side effect. However most of the participants (69%) were on non zidovudine based regimen.

CONCLUSION

Hematological manifestations are very common but often overlooked in people living with HIV. Early identification of abnormal hematological patterns like anemia, leucopenia and thrombocytopenia will help us to identify disease progression, need for change in medication, evaluation of many other important etiologies and search for drug related side effects. Although our study showed low viral load in 87% of study participants and high CD4 count of >500cells/mm^3 in 74% of study participants, we expected normal hematology study as the main pattern but we found anemia (predominantly normocytic normochromic to microcytic hypochromic) in 62% of study participants which indicates that there are many factors other than HIV itself, which are responsible for decreased hemoglobin. Also we observed more number of thrombocytopenia and leucopenia in our study participants compared to previous studies.

The main limitation of our study is that it didn't follow up for evaluation of etiologies of anemia, leucopenia and thrombocytopenia as this is an observational cross

sectional study only. But it will definitely help for future studies regarding etiological evaluation of hematological abnormalities, mainly anemia. Also this is a hospital based study, so the results obtained may not be generalized to whole population of people living with HIV, specially who do not visit hospital.

Conflict of Interest: No.

Source of Funding: non funded.

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