Platelets distribution width is common hematological finding in HIV infection

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Abstract
Aim and Objectives: Discuss relevant laboratory findings raised PDW with age and sex distribution. Establish care guidelines for HIV infected person and altered haematopoiesis resulting in with raised red cell distribution width. Review the pathogenesis of the haematological manifestations of human immunodeficiency virus (HIV).
Method: Blood was collected in a sterile EDTA containing tube and processed following our established laboratory protocol and by universal precaution as per the guideline of National aids control organization (NACO, India). A complete blood counting including HB%, PCV, Red cell indices, platelet count, Red cell distribution width and total white cell count and differential was done by Automated blood cell counter analyzer of all the patient on antiretroviral therapy. The all cell count indices including WBC count with differential and platelet count, was further confirmed by manual oil immersion smear study method. Peripheral smears study was done with field A and B Stain and Leishman stain.
Result: In our study out of 300 HIV cases 189 cases (63%, n=300) shows increased PDW in which male cases are 125 cases (66.48%, n=188) and female cases are 64 (57.14%, N=112).
Conclusion: PDW is commonly affected haematological parameter in HIV infective cases. Higher red blood cell distribution width is associated with a worse virologic and clinical situation in HIV infected.

Introduction
All peripheral blood cells have been observed in patients with HIV infection with the exception of thrombocytopenia, which can occur in asymptomatic individuals with relatively mild immune deficiency, anaemia and leucopenia are both more frequent and severe in patients with advanced immunodeficiency. Peripheral red blood cells in patients with anaemia are typically normochromic and normocytic and exhibit a varying degree of anisocytosis and poikilocytosis. The perturbation in red cell size and shape is reflected in an increased red cell distribution width. Macrocytosis is rarely seen. However, in patients receiving therapy with zidovudine, macrocytosis
is present in the majority of patients, occasionally with mean corpuscular volumes as high as 120 or greater. Rouleux formation and increased background staining may also be seen; this likely reflects the presence of concomitant hypergammaglobulinemia. As noted previously, schistocytes and nucleated red cells are present in patients with HIV-associated TTP.

Peripheral blood neutrophils are showed striking dysplastic features, which included detached nuclear fragments, acquired Pelger-Huet anomaly chromatin clumping, neutrophils with strangely shaped nuclei, and a high nucleocytoplasmic ratio and macropolycytes.

The presence of detached nuclear fragments in neutrophils is particularly suggestive. The range of changes seen differ from those that are usual in myelodysplastic syndromes. Hypogranularity is less common whereas bizarrely shaped nuclei and a high nucleocytoplasmic ratio in mature cells are more common. but they are quite uncommon whereas they are characteristic of HIV infection. Typically left-shifted and may exhibit a number of morphologic abnormalities, including enlarged size, hyposegmentation, and Pelger-Huet anomalies. Atypical plasmacytoid lymphocytes are occasionally seen in asymptomatic individuals but are particularly common in lymphopenic patients with AIDS and during acute HIV infection. Large atypical monocytes have also been described with prominent vacuolization and fine nuclear chromatin. Anaemia is the most common haematological abnormality found in children and adult with HIV infection. The etiology of anaemia in adult with HIV infection is multifactorial, and managing anaemia can involve a variety of modalities. HIV infection and its direct effects on HSCs and stromal elements can lead to anaemia. Opportunistic infection and myelosuppressive drugs might also cause anaemia.

Material & Methods
Study area and design: The present study was conducted at the Department of Pathology MGM Medical College associated with M.Y. Hospital Indore, M.P. The study was designed as an observational hospital based study over a period of time from 2010.

Ethical consideration: Detailed general, systemic examination along with complete details of patient and informed consent was obtained from all study participant do from ART Center of M.Y. Hospital Indore during the time of registration at center.

Patients selection criteria: The study targeted medically diagnosed HIV positive cases with the help of ELISA technique and confirmed by western blot under the guideline of National aids control organization (NACO, India) over period of time from 2010

All studied 300 cases registered at ART Center and on HAART between the age of 5 to 69 years who are schedule to visit the hospital at regular intervals of time for routine medical review was studied.

Laboratory investigations: Blood was collected in a sterile EDTA containing tube and processed following our established laboratory protocol and by universal precaution as per the guideline of National aids control organization (NACO, India). A complete blood counting including HB%,PCV, Red cell indices, platelet count, PDW and total white cell count and differential was done by Automated blood cell counter analyzer of all the patient on antiretroviral therapy. The all cell count indices including WBC count with differential and platelet count, was further confirmed by manual oil immersion smear study method. Peripheral smears study was done with field A and B stain and leishman stain.

Complete Blood Count (CBC) and Peripheral Smear
Materials: Purple vacutainer tube or capillary collector (EDTA),Slides and blue capillary tube, Needle or lancet, Vacutainer holder, Alcohol swab, Cotton balls, Absorbent materials, Slide case.
Procedure
1. Specimen is collected into EDTA (purple) vacutainer. (5 or 7ml volume)
   - Blood smears must be made from freshly collected specimen and must be prepared within four hours of collection. A well-made peripheral smear is thick at the frosted end and becomes progressively thinner toward the opposite end. The “zone of morphology” (area of optimal thickness for light microscopic examination) should be at least 2 cm in length. The smear should occupy the central area of the slide and be margin-free at the edges.

Hematological examination
Hematological examination including HB%, PCV, Red cell indices, platelet count and total white cell count with differential count should be done on peripheral smears stained with field A and B stain

Following Base line investigation were done for all 300 patients.
Hemoglobin in grams/dl–(Cyanmethhaemoglobin method of automated blood cell counter analyzer) and further confirmation by Sahli’s manual method in case of suspicious readings.RBC counting and RBC indices parameters MCV, MCH, MCHC, PCV & PDW - automated cell counter analyzer RBC morphology study under oil immersion manual stained smear study method .Total and differential leukocyte count - automated cell counter analyzer & confirmed by oil immersion manual stained smear study method, Platelets counts - automated cell counter analyzer & confirmed by oil immersion manual stained smear study method Other counting parameters and morphological changes done under automated cell counter analyzer & confirmed by manual oil immersion smear study method

Results
Table 1 Sex distribution of study cases

<table>
<thead>
<tr>
<th>Sex</th>
<th>Case (%) n=300</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>188 62.66%</td>
</tr>
<tr>
<td>Female</td>
<td>112 37.34%</td>
</tr>
<tr>
<td>Total Case –</td>
<td>300 100%</td>
</tr>
</tbody>
</table>

Out of 300 study cases males are more commonly affected (62.66%) (n=300) than female 37.34% (n=300)

Table 2 Age distribution of study cases

<table>
<thead>
<tr>
<th>Age</th>
<th>No. of cases</th>
<th>% (n=300)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>9</td>
<td>3.00%</td>
</tr>
<tr>
<td>11-20</td>
<td>19</td>
<td>6.33%</td>
</tr>
<tr>
<td>21-30</td>
<td>62</td>
<td>20.66%</td>
</tr>
<tr>
<td>31-40</td>
<td>132</td>
<td>44.00%</td>
</tr>
<tr>
<td>41-50</td>
<td>57</td>
<td>19.00%</td>
</tr>
<tr>
<td>51-60</td>
<td>14</td>
<td>4.66%</td>
</tr>
<tr>
<td>61-70</td>
<td>7</td>
<td>2.33%</td>
</tr>
</tbody>
</table>

Out of 300 study cases HIV positive patients are most commonly i.e.44% (n=300) in age group of 31-40 years while least common (1%, n=300) in age of above 60 years.

Sex distribution of different age groups

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>11-20</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>21-30</td>
<td>35</td>
<td>27</td>
</tr>
<tr>
<td>31-40</td>
<td>78</td>
<td>54</td>
</tr>
<tr>
<td>41-50</td>
<td>40</td>
<td>17</td>
</tr>
<tr>
<td>51-60</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>61-70</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>

- Among male most commonly affected age group is found to be 31-40 years with 41.48% involvement (n=188). Among female also most commonly affected age group is found to be 31-40 (48.21%, n=112).
- In Our study youngest HIV infected male 5 year old boy (our case serial no =11 and art reg. No.225072 and oldest male is 65 year (our case Serial No =292, Art Reg. No. 318651).
- Our study youngest HIV infected female 5 year old girl (our case serial no =89 and Art reg. No=317521 and oldest female is 69 year (our case serial no =33, art reg. No. = 316130).

Platelet count in the blood can be rapidly measured using an automated haematologic analyser. Platelet indices are biomarkers of platelet activation. They allow extensive clinical investigations focusing on the diagnostic and
prognostic values in a variety of settings without bringing extra costs. Among these platelet indices, plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW) are a group of platelet parameters determined together in automatic CBC profiles; they are related to platelets’ morphology and proliferation kinetics. PDW is an indicator of volume variability in platelets size and is increased in the presence of platelet anisocytosis (17). PDW is a distribution curve of platelets measured at the level of 20% relative height in a platelet-size distribution curve, with a total curve height of 100% (18). PDW directly measures variability in platelet size, changes with platelet activation, and reflects the heterogeneity in platelet morphology (13,20). Under physiological conditions, there is a direct relationship between MPV and PDW; both usually change in the same direction (20). Meanwhile, there are conflicting reports in the literature about the relationship between platelet volume and numbers, which suggests that they are affected by different mechanisms (5,21-25).

**Hematological examination:** Hematological examination including HB%, PCV, Red cell indices, platelet count and total white cell count with differential count should be done on peripheral smears stained with field A and B stains.

<table>
<thead>
<tr>
<th>VALUE</th>
<th>Prognosis</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDW high</td>
<td>Poor prognosis</td>
<td>63</td>
<td>63.00%</td>
</tr>
<tr>
<td>PDW normal</td>
<td>Good prognosis</td>
<td>36</td>
<td>36.00%</td>
</tr>
<tr>
<td>PDW low</td>
<td>Not significant</td>
<td>01</td>
<td>01%</td>
</tr>
</tbody>
</table>

- Data analysis in increased PDW with the difference of sex distribution under the Upton's "N-1"chi-sq.x2 value = 2.980, P=0.084 and Pearson's chi-square x2 value = 2.998 P = 0.083.

**Discussion**

PDW is also commonly affected haematological parameter in HIV infective cases. In our study out of 300 HIV cases 189 cases (63%, n=300) shows increased PDW in which male cases are 125 cases (66.48%, n=188) and female cases are 64 (57.14%, N=112). So increased PDW is also very significant finding in our study. Defined Increased PDW is defined when red cell distribution width is > 14.5%. Cut-off value of increased PDW reference by Dacie and Lewis practical haematological book 10/e and Shirish M Kothalkar Essentials of haematology and various other studies. A “higher red blood cell distribution width is associated with a worse virologic and clinical situation in HIV infected .Increase PDW also with the reference of Hoffman haematology text book and various other study.

**Conclusion**

**Age & Sex**-In our study of 300 cases, where 188 (62.66%.n=300) are males while 112 (37.34%, n=300) are females, highest prevalence of hematological manifestation of HIV positive patient i.e. 44% is found between 31-40 years of age.

**Platelets Distribution Width (PDW)**- PDW is also commonly affected haematological parameter in HIV positive cases. In our study out of 300 HIV cases 189 cases (63%, n=300) shows increased PDW in which male cases are 125 (66.48%, n=188) and female cases are 64 (57.14%, N=112).

**Acknowledgement**

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