PREVALENCE OF THROMBOCYTOPAENIA IN HUMAN IMMUNODEFICIENCY VIRUS-1 INFECTION IN ZARIA

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ABSTRACT

Background: Thrombocytopaenia is relatively common during the course of HIV infection and it may serve as the first evidence of infection. It has been associated with clinical or immunological severity of the disease. Multiple interacting factors may contribute to this haematological manifestation of HIV infection.

Aim: To determine the prevalence of thrombocytopaenia and its relationship to CD4+ T lymphocyte count in antiretroviral naïve HIV-1 infected patients.

Methodology: Four hundred consecutive HIV-1 infected patients undergoing pre treatment investigations for staging were recruited over a one year period, at the HIV subspecialty clinic of Ahmadu Bello University Teaching Hospital, Zaria. All the patients were confirmed HIV-1 infected, repeatedly reactive by ELISA. Platelet count was determined by standard manual method and CD4+ T cell enumeration by Dynal® (Oslo Norway) manual method.

Results: Of the 400 patients studied, the prevalence of thrombocytopaenia was 6.25% with a male to female ratio of 1:1.7. There is a significant positive correlation between platelet count and CD4 + T lymphocyte count r 0.086, P 0.043 ($p < 0.05$), however this association is weak by clinical/immunological staging.

Conclusion: Thrombocytopaenia is not an uncommon finding in HIV infected patients in our setting and often occurs in the severely immunocompromised individual. Platelet count cannot be used as a substitute to determine the severity of immunosuppression.

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INTRODUCTION

Thrombocytopaenia is a frequently reported complication of HIV infection [1, 2, 3] and has been described in both adults and children.[4] Two forms of HIV-related thrombocytopenia are recognized: that associated with the pancytopaenia seen in AIDS and solitary thrombocytopaenia which occurs prior to development of AIDS in seropositive individuals.[5] Thrombocytopaenia is common at all stages of HIV disease which may be asymptomatic and in some cases it may be the presenting feature .[1] Sacchi et al at the first division of infectious disease in Italy reported 88 cases within a population of 1000 HIV positive patients.[6] High prevalence of 3-12% in adults with asymptomatic HIV infection has been reported and even higher prevalence of up to 30% have been found in adults with AIDS.[7] Beattie R M et al reported a series of 3 cases in children aged between 7 months to 2 years who developed thrombocytopaenia as an early feature of HIV infection.[8] She recommended HIV testing should be considered in the investigation of a child with thrombocytopaenia. In Nigeria Adetifa et al reported a lower prevalence of 2.5% in 2006 in a study of 68 children with confirmed HIV infection in the department of paediatrics, Lagos university teaching hospital.[9]

The mechanism involves both quantitative and qualitative marrow defects, which are a direct result of HIV infection, while the varied assault of opportunistic infection, lymphoma and a myriad of drugs against infection (trimethoprim/sulfomethoxazole, pentamidine, ganciclovir, rifabutin), or malignancy play an important role.[1] HIV-related thrombocytopaenia (HIV-RT) may also result from the effects of splenomegaly as shown by high response rate to splenectomy even in patients with advance disease.[1,]

One third of patients with HIV-RT present with a history of bleeding abnormalities although, significant spontaneous clinical bleeding does not occur.[10] Thrombocytopaenia in seropositive individuals is not a prognostic indicator for the development of AIDS.[11,12] Interestingly, in as high as 11-50% of patients thrombocytopaenia will regress spontaneously without therapy.[11] Modalities of treatment include, HAART, corticosteroids, intravenous gammaglobulin, danazole, anti-Rh immunoglobulin, dapsone, splenectomy or low dose splenic irradiation.[1, 5, 10, 13, 14] Vincristine has also been reported to improve the platelet count in a small number of patients with thrombocytopaenia.[14] Several reports have also shown responses to Zidovudine and Didanosine in approximately 50% of patients with HIV-RT.[1,14]

MATERIALS AND METHODS

Patients referred to Ahmadu Bello University Teaching Hospital, Haematology HIV sub-specialty clinic (from May 2003 to October 2004) for care were studied while undergoing evaluation for commencement of HAART. An informed written consent was obtained. The study was approved by the hospital's ethical committee. Pregnant women and paediatric patients were excluded from the study. All the patients were reactive for HIV-1 antibodies by both Genie II and Capillus. Platelet count was determined by manual cell count adopted from Dacie and lewis. [15] Thrombocytopaenia was defined as a platelet count of less than 100 X 10^9/L. CD4+T Cell Counts were determined by using monoclonal antibody labeled microspheres (Dynal manual method) developed in Oslo Norway. The patients were assessed clinically, immunologically and categorized into three clinical stages A, B, and C according to CDC criteria.[16] All analysis was conducted using Microsoft excel, computerized statistical software SPSS version 17, to determine the means, correlation coefficients, test of significance and scattered diagrams.

RESULTS

A total of 400 HIV positive patients comprising 187 (46.8%) males and 213 (53.2%) females, were recruited into the study. The mean age was 34.8 ± 8.9 years with a mean weight of 58.1 ± 12.2kg. There were 108(27%) of the patients in stage A, 153 (38.5%) in stage B, and 139 (34.8%) in stage C. The haematological and immunological parameter is shown in Table 1. Of the 400 patients recruited, only 25 (6.25%) had thrombocytopaenia.

Of the total number of patients with thrombocytopaenia, 16 (64%) and 9 (36%) were females and males respectively. Their age ranges from 22 to 56 years with a mean of 33.0 ± 10.7 years with a mean weight of 56.8 ± 11.7kg. The haematological and immunological parameter is shown in Table 2. They were also assessed clinically and immunologically, and categorized into three clinical stages, only 2 (8%) patients were in Stage A, 5 (20%) in stage B and 18 (72%) in stage C (figure 1).

The platelet count of all the patients was correlated to their CD4 cell count and a statistically significant positive correlation was obtained r 0.086, p 0.043 and is presented in the scatter diagram (figure 2). However platelet count was weakly and insignificantly correlated to the CD4 cell count in all the stages and is shown in scattered diagrams (figures 3, 4, and 5).

DISCUSSION

This study has shown that thrombocytopaenia is common in HIV infected patients in our setting with a prevalence of about 6.3% and platelet count is not invariably an indicator of severity of the disease. In Nigeria, Adetifa et al reported a lower prevalence of 2.5% in 2006 in a study of 68 children with confirmed HIV infection in the department of paediatrics, lagos university teaching hospital.[9] Sullivan et al reported a prevalence of 8.7% in persons with clinical AIDS using surveillance data from a longitudinal survey of the medical records of 30,214 HIV-infected patients, who received medical care from January 1990 through August 1996 in more than 100 medical clinics in 10 United States cities. [17] A high prevalence of 38% in seropositive individuals has been reported by several other workers.[18, 20] However an incidence of 0% was reported by Karpatkin et al in 1987 in a study of asympmptomatic group of 26 seropositive homosexual men.[21] Our study also shows that a greater proportion of the patients with thrombocytopaenia were in the symptomatic or immunocompromised stages B (20%) and C (72%) with only 8% in the asymptomatic or immunocompetent stage A (figure 1). Our finding is similar to several reports in the literature[1, 2, 3] findings that HIV related thrombocytopaenia is a common finding occurring in all stages but predominantly in the symptomatic patients. This therefore means that thrombocytopaenia in HIV infected patients may not be unconnected with the severity of the infection as shown by the large percentage of these patients in the severely immunocompromised/symptomatic stages B and C. Direct infection of the megakaryocytes by HIV[22, 23] may be responsible for this.

Megakaryocytes have been shown to express CD4 molecules and to be able to bind HIV.[24] Although megakaryocytes are typically increased in HIV-related thrombocytopaenia, they are characteristically dysplastic ('neglected megakaryocytes') and kinetic analysis has shown a decrease in platelet production due to ineffective thrombopoiesis.[25] Thrombocytopaenia may also result from immunologically mediated decrease in platelet survival due to increase in platelet-associated immunoglobulin, complement, and circulating immune complexes.[25]

Although no gender predilection has been reported we found 64% of females with thrombocytopaenia, this may be due to the sample size of which females constitute a larger percentage of about 53%. This finding is in agreement with the increasing rate of women living with HIV globally, [26] which appear to be closing up with those of males and this can be attributed to an increasing health seeking behaviour of female as a result of educational, economic empowerment and the ready access to available information on HIV/AIDS. This observation is in line with the finding by Piot et al who reported a male to female ratio of 5:6.[27]

Although a number of drugs frequently used in the management of HIV infection may cause thrombocytopaenia[1, 5], these cannot be implicated fully in this study since these patients are antiretroviral naïve, and it is very unlikely that they were exposed to the commonly implicated agents.

Furthermore, correlation of platelet count to CD4 cell count shows a

positive and a statistical significant correlation r + 0.086 p < 0.05 as shown by the scatter diagram (figure 2). However this correlation was weak following stratification of the patients by clinical and immunological stages (figures 3, 4 and 5). This therefore means that platelet count cannot be used as a surrogate of CD4 cell count, although thrombocytopaenia may be common in patients with low counts. Other studies have reported an inverse association.[18] On the contrary thrombocytopaenia during acute HIV infection as part of acute retroviral syndrome has been reported.[28]

The degree of thrombocytopaenia was mild to moderate, with a mean platelet count of 86×10^9/L and a range of 55 to 99×10^9/L (table 2). A severe reduction to levels less than 10×10^9/L was not recorded. None of the patients with thrombocytopaenia presented with a history of bleeding abnormalities and this is in agreement to reports in literature that spontaneous bleeding or bruising does not normally occur until the platelet count has fallen below 10 to 20 $\times 10^9$/L.[1, 29] In 20% of cases thrombocytopaenia occurred in association with anaemia (PCV < 0.30L/L) and 12% in association with Neutropaenia (Absolute Neutrophil count < 1500 cells/mm^3). This means that in about 80% to 88% of the patients, thrombocytopaenia occurred alone with no other associated cytopaenias. Thus it means that thrombocytopaenia (HIV-RT) frequently occurs as an isolated haematological abnormality contrary to other reports where cytopaenias are said to occur frequently in combination.[1, 9, 17] In no case was pancytopaenia recorded.

CONCLUSION

Thrombocytopaenia is commonly seen in immunocompromised HIV infected individuals, occurring often as an isolated haematological abnormality. Platelet count correlates weakly with CD4 cell count and therefore cannot be used as a surrogate of CD4 cell count to determine the severity of infection.

RECOMMENDATION

Platelet count evaluation prior to initiation of HAART and opportunistic infection treatment and prophylaxis is mandatory to avoid life threatening haemorrhagic state. The differences observed in this study as compared to others may be largely due to methods of cells enumeration. Most studies use automated techniques for cell counts and Flow cytometry as the standard technique used in determining CD4+ T lymphocyte subset. Further studies are also necessary using automated analyzers for cell counts and to identify aetiological factor/s of thrombocytopenia, their effect on survival and whether HAART may have a positive impact on reducing their prevalence in HIV/AIDS patients.

LIMITATION

The inherent errors associated with manual method is large, coefficient of variation for blood cells count for manual method is 16% and for automated analytical method is 1.5%. The presence of co-infections (Tuberculosis, Malaria, Enteric fevers, Hepatitis B, C, HTLV 1 and Syphilis) will also influence the CD4+ LC. These were not studied.

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