

Clinico-Haematological Profile and its Correlation with CD4 Count in HIV and HIV-HCV co-infection

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Abstract

Background: Haematological abnormalities are a common complication of human immunodeficiency virus (HIV) infection and result from several influences on the haematopoietic tissue. These abnormalities reflect the underlying immune status and may be prevented or corrected by the use of highly active antiretroviral therapy (HAART). Hepatitis C infection (HCV) is one of the common co-infection in HIV infected person. Anaemia commonly occurs during HIV infection and has been associated with increased progression to acquired immune deficiency syndrome (AIDS) and co-infection with HCV and reduced survival.

Aims: The aims of the study is to analyse haematological manifestations in HIV and HIV-HCV infection and to also study correlation between haematological changes and CD4 level

Methods: One hundred HIV and another one hundred HIV-HCV patients, symptomatic as well as asymptomatic, diagnosed by enzyme linked immunosorbent assay (ELISA) method according to the National AIDS Control Organization (NACO) guidelines and anti HCV Antibody positive were included. Complete haematological profile was recorded. Relationship between CD4 counts and various haematological parameters was analysed. Descriptive statistics were applied. Association between two attributors was calculated by chi-square test, t-test, Pearson correlation coefficient and P value less than 0.05 was considered statistically significant.

Results: The most common haematological abnormalities were anaemia, seen in 64% of the patients. A strong association between anaemia and CD4 counts, HCV co infection was observed. Thrombocytopenia was the second common abnormality and has no significant relationship with CD4 counts.

Conclusion: HIV affects virtually all organ systems, with well-known abnormalities related to haematopoietic system. Anaemia being the most common abnormality has strong correlation with CD4 counts and HCV co-infection and therefore could be used to predict the development of a more advanced disease.

Keywords: HIV, CD4 counts, HCV, Anaemia, Thrombocytopenia

Date of Submission: 18-09-2019

Date of Acceptance: 05-10-2019

I. Background

HIV infection targets mainly the immune system and hence haematological abnormalities are among the most common clinic-pathological features. These haematological abnormalities vary from anaemia, leucopenia, and thrombocytopenia including bone marrow dysplasia. The pathophysiological basis for these haematological abnormalities may include impaired haematopoiesis, immune mediated cytopenia, drugs, opportunistic infections and/or coagulopathies especially in the advanced stage of the diseases^{1,2}. Haematological abnormalities progress in frequency and severity with the progression of the disease from the asymptomatic HIV carrier state to the advanced state of the disease³. About 15% of asymptomatic HIV carriers have mild anaemia. The prevalence of anaemia increases from 30% to 40% in those with the early disease to 70-90% in advanced patients⁴.

Due to the shared risk factors for infection of HIV and HCV, HCV infection is one of the common co-infection in HIV infected person. HIV infection influences the natural evolution of chronic HCV infection by higher rate of viral persistence, accelerating fibrosis, cirrhosis progressing to end stage liver disease⁵. In addition to liver involvement, chronic HCV infection can interestingly result in several extra-hepatic conditions with haematological problems being one of them. Haematological manifestations in HCV infection can range from benign cytopenia to malignant lymphoproliferative disorders.

To the best of our knowledge, the clinico-hematologic characteristic of patients presenting with HIV and HCV infection in the tertiary level hospitals of our state Manipur, has not been well defined till date. It will

be worthwhile to look into the patients' characteristic and their hematologic profile belonging in this north eastern part of the country.

II. Aims

The aims of the study is to analyse haematological manifestations in HIV and HIV-HCV infection and to also study correlation between haematological changes and CD4 level

III. Materials and method

The study was a cross sectional study done in the Department of Medicine , Jawaharlal Nehru Institute of Medical Sciences (JNIMS) , Manipur from August 2017 to August 2019. Known case of HIV and HIV-HCV co infection patients with age >13 years but < 75years were included in the study after giving consent. Patients with previously known haematological disorders, congenital haematological disorders, pregnant women, critically ill patients were excluded from the study. The target sample of the study was 100 patients of HIV and 100 HIV-HCV co-infected patients in this study.

Detailed history, general, and systemic examination was conducted with emphasis on signs suggesting haematological system involvement. The investigations included complete haemogram with peripheral blood picture and CD4 cells count by Flow cytometry. Anaemia was defined according to WHO as haemoglobin concentration < 13 g/dl for male and < 12g/dl for non pregnant female. Leucopenia was defined as total leukocyte count less than 4000cumm/dl. Thrombocytopenia was defined platelet count less than 1.5 lakh/dl. Pancytopenia was defined as reduction in the number of all cell lineages from normal values. Data were collected using a pre-tested Performa to meet the objectives of the study. Data collected were analysed using SPSS version 21. Descriptive statistics like percentages, mean and standard deviation were used. Analytical statistics: chi-square test and fisher's exact test were used. P value < 0.05 was considered significant

IV. Results And Observations

The study had been conducted during the period . A total of 200 patients suffering from HIV and HIV HCV coinfection were included the study. All the patients were analysed. In the study the general weakness was the most common symptom in (72%). It was followed by anorexia(62.5%), cough (59.0%), lymphadenopathy (48.5%), fever (46.5%), oral ulcer (45%), diarrhoea (28.0%), etc.as shown in table no 1. In the case of co infection with HIV and HCV also, generalised weakness, anorexia, lymphadenopathy, fever, oral ulcer, diarrhoea and tingling limbs was present. When compared to HIV infected alone there was significant difference in generalised weakness, anorexia among co infected patients (p=0.02).

Table 1: Distribution of the patients by signs and symptoms stratified by presence or absence of HCV co-infection

Signs and symptoms (present)	HIV only N(%)	HIV+HCV co-infection N(%)	Total N(%)	P value
Symptoms				
General weakness	62(62.0)	82(82.0)	144(72.0)	p-0.002
Anorexia	39(39.0)	86(86.0)	125(62.5)	p-0.000
Cough	61(61.0)	57(57.0)	118(59.0)	p-0.663
Lymphadenopathy	43(43.0)	54(54.0)	97(48.5)	p-0.120
Fever	43(43.0)	50(50.0)	93(46.5)	p-0.321
Oral ulcer	39(39.0)	51(51.0)	90(45.0)	p-0.088
Diarrhoea	23(23.0)	33(33.0)	56(28.0)	p-0.205
Headache	27(27.0)	16(16.0)	43(21.5)	p-0.058
Vomiting	13(13.0)	11(11.0)	24(12.0)	p-0.231
Tingling limbs	18(18.0)	22(22.0)	40(20.0)	p-0.480
Rash	3(3.0)	2(2.0)	5(2.5)	p-0.651
Total	100(100.0)	100(100.0)	200(100.0)	

Haemoglobin was significantly reduced in HCV co-infection group (9.87±2.6 vs10.98±2.9 g/dl) than HIV only group (p=0.06). TLC was almost similar in both the groups. Platelet count was reduced significantly among HCV co-infection group (p<0.05). For, ESR there was no significant difference observed shown in table 2. Anaemia and thrombocytopenia are more common in HIV HCV co infection group and statistically significant (p< 0.05) as shown in table 3.

Table 2: Distribution of the patients by haematological findings stratified by presence or absence of HCV co-infection

Hemogram parameters	HIV only Mean±SD	HIV+HCV co-infection Mean±SD	P value
Haemoglobin g/dl	10.98±2.9	9.87±2.6	p-0.006
TLC cells/mcl	5257.10±2962.7	5237.0±2998.4	p-0.962
Platelet count lakh/mm ³	2.1±0.78 lakh	1.0±0.40	p-0.001
ESR	71.21±38.4	64.72±36.8	p-0.224

Table 3: Distribution of the patients by haematological findings stratified by presence or absence of HCV co-infection

Hemogram parameters	HIV only Mean±SD	HIV+HCV co-infection Mean±SD	p value
Haemoglobin g/dl			
<12	56(56.0)	72(72.0)	p-0.018
≥12	44(44.0)	28(28.0)	
TLC cells/mcl			
<4000	39(39.0)	38(38.0)	p-0.949
4000-11000	56(56.0)	56(56.0)	
>10000	5(5.0)	6(6.0)	
Platelet count			
<1.5 cell/mm ³	19(19.0)	89(89.0)	p-0.001
≥1.5	81(81.0)	11(11.0)	
Total	100(100.0)	100(100.0)	

Haemoglobin and TLC had fair positive correlation with CD4 count which were statistically significant in only HIV infected group as shown in table no 4. Platelet count also have poor positive correlation but statistically insignificant. ESR had fair negative correlation with CD4 count and statistically significant.

Table 4: Relation between Haematological parameters and CD4 count among HIV only group

Haematological parameters among HIV only	CD4 count r _p (Pearson correlation coefficient)	p-value
Haemoglobin	0.363	0.001
TLC	0.345	0.001
Platelet count	0.168	0.96
ESR	-0.285	0.004

Table 5: Relation between Haematological parameters and CD4 count among HCV co-infection group

Haematological parameters among HIV and HCV co-infection	CD4 count r _p (Pearson correlation coefficient)	p-value
Haemoglobin	0.290	0.003
TLC	0.617	0.001
Platelet count	0.066	0.511
ESR	-0.211	0.035

While among HCV co-infection group, haemoglobin also had fair positive correlation with CD4 count which were statistically significant (p=0.03). For TLC, there was good positive correlation with CD4 count and was significant(p=0.001). Platelet count also have poor positive correlation but statistically insignificant. ESR had poor negative correlation with CD4 count and statistically significant as shown in table no 5.

V. Discussion

The mean age of the present study population was 39.5±10.4 years for HIV group and 43.3±8.4 years for HIV-HCV co-infection group which is similar to study of Devi CS et al.⁶ The commonest age group in both the groups was 41-50 years which constitute 35% in HIV and 47% in HIV-HCV co-infection group. As to compared to other study of Kumar et.al and Devi CS et.al, age group are little older but similar male and female ratio.⁷

Our study shows male predominance (p<0.05) more among HIV and HCV co-infection. This can be explained by high prevalence of IV drug user among males in our state. The present study also showed IVDUs, alcohol consumption and smoking was significantly (p= 0.001) more in HIV-HCV co-infection as found in study of Mohsen et al.⁸

Generalised weakness, anorexia, lymphadenopathy, fever, oral ulcer, diarrhoea and tingling limbs was more among HIV-HCV co-infection group. Pallor was significantly increased among HCV co-infection group.

The present study showed mean CD4 is lower in HIV-HCV co-infection group and significant ($p=0.036$) but failed to show that actual lower CD4 count is associated with HIV-HCV co-infection only ($p=0.087$). There may be many confounding factors for this.

Kasthuri et. al had reported anaemia in 61% (61/100) and 80% in advanced HIV disease⁹. In the present study anaemia was the most common presentation (64%). Anaemia is multifactorial in HIV infection, with causes including opportunistic infection, myelosuppressive drugs, nutritional deficiencies, and the direct effects of HIV on bone marrow progenitors and stromal elements

In our study, 112 (56%) of patients of cases were with CD4 count < 200 cell/microL. As expected, patients from the group with low CD4 count presented a significantly increased rate of anaemia (Pearson correlation coefficient=0.363 with $p=0.001$). CD4 cell count have been found to be significant variables that contributed to the incidence of anaemia. This association is most likely explained by the increasing viral burden as HIV disease progresses, which leads to cytokine-mediated myelosuppression and anemia according to Henry DH et al.¹⁰ Inflammatory cytokines released by lymphocytes such as tumour necrosis factor (TNF), interleukin-1 (IL-1) and interferon gamma play an important role in the pathogenesis of anaemia. These cytokines inhibit erythropoiesis in vitro¹⁰.

In this study, haemoglobin was significantly reduced in HCV co-infection group than HIV only group (9.87 ± 2.6 vs 10.98 ± 2.9 g/dl). Also among HIV-HCV co-infection group, haemoglobin had fair positive correlation with CD4 count ($p=0.003$)

In our study, 54% of the patients have thrombocytopenia. This may be due large amount of HCV-HIV co-infection. It was the most frequent cytopenia observed by Kasthuri et al and a feature seen in advanced disease⁹. But this study showed patients with a more severe disease (CD4 <200 CELLS/microL) presented a slightly lower platelet count but insignificant ($p=0.96$) like findings of Attili SVS et. al.¹¹ The mechanism of thrombocytopenia in HIV infection is mainly due to ineffective platelet production and at the same time increased platelet destruction.

Cacoub P et al¹³ and Obienu et al¹³ had shown that HCV/HIV coinfection is associated significantly with thrombocytopenia. In our study, among HIV-HCV co-infection, platelet count has poor positive correlation (Pearson correlation coefficient 0.168) but statistically insignificant ($p=0.96$)

Various studies have reported neutropenia in 13% to 44% of cases with progression of disease from HIV to AIDS¹¹. In the present study, 23% patients were detected to have neutropenia.

HIV infection can directly result in lymphopenia as the infection evolves, leading to a decrease in CD4+ lymphocytes and is one of the most important prognostic indicators for the risk of developing opportunistic infections¹⁴. There has been a variation in the frequency of lymphopenia reported in different studies which includes 28.9% (59/204) by Rahman et al¹⁵, 65.2% (163/250) by Parinitha et al¹⁶, 70% (14/20) by Treacy et al¹⁷ and in 25.6% (19/74) by Tripathi et al¹⁸ of the cases. In the present study, lymphopenia was seen in 46/ 200 (23%) of patients. Among HIV-HCV co-infection, TLC shows good positive correlation with CD4 count and was significant ($p=0.005$). TLC was almost similar in both the groups in the study.

VI. Conclusion

Haematological abnormalities are the common manifestations in patients with HIV infection. All the cell lines are affected by HIV, resulting in anaemia, thrombocytopenia, and leucopenia. Anaemia is the most common hematologic abnormality which is more prevalent among patients with declining CD4 count and HIV-HCV co infection and is strongly associated with progression of the disease. Early detection, exact cause and appropriate treatment of these abnormalities will reduce morbidity and mortality in HIV/AIDS patients

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Kh.Lokeshwar Singh. “Clinico-Haematological Profile and its Correlation with CD4 Count in HIV and HIV-HCV co-infection.” *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, vol. 18, no. 10, 2019, pp 16-20.