FREQUENCY OF PERIPHERAL BLOOD COUNT ABNORMALITIES IN PATIENTS WITH CHRONIC ACTIVE HEPATITIS C

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ABSTRACT

Liver disease causes a greater range of hematological changes than does disease in any other organ. Viral hepatitis and its sequel are the important hepatic disorders. Hepatitis C virus (HCV) is considered to be the main etiological factor for chronic liver disease. Present study was done to determine the frequency of peripheral blood count abnormalities in chronic active hepatitis (CAH) caused by Hepatitis C virus (HCV). It was a cross sectional study which was conducted in Department of Haematology, Shaikh Zayed Hospital Lahore from June to December 2010. In this study the frequency of anemia was found to be 41.3%, neutropenia 16.6% and thrombocytopenia 22.6 % in CAH caused by HCV. Patients who develop hematological abnormalities during treatment need hematological growth factor support so that treatment could be continued without hindrance.

Key Words: Blood counts, chronic active Hepatitis, Hepatitis C.

INTRODUCTION

Liver disease causes a greater range of hematological changes than does disease in any other organ, Viral hepatitis and its sequel are the important hepatic disorders.[1]

Chronic active hepatitis (CAH) is defined as symptomatic with biochemical or serological evidence of continuing or relapsing hepatic disease for more than six months with histologically documented inflammation, necrosis and eventually fibrosis.[2] Hepatitis C virus (HCV) is considered to be the main etiological factor for chronic liver disease and accounts for about 70 – 75% cases of chronic hepatitis and 15 – 20% cases of cirrhosis and hepatocellular carcinoma.[3] Although HCV principally replicate in the liver, evidence of HCV replication also has been reported in peripheral blood cells, and abnormal blood counts have been noted in patients with HCV infection.

Anemia occurs in up to 75% of patients with chronic liver disease,[1] the causes are multiple and include dilution, gastrointestinal blood loss, impaired bone marrow production, increased destruction and antiviral treatment. Neutropenia is a fairly constant feature of chronic liver disease; it is seen in 87% of patients during treatment.[4] Thrombocytopenia is also a complication in patients with chronic liver disease.[5,6] Which has been observed in 76% of cases, this occur due to splenic platelet sequestration, bone marrow suppression by chronic hepatitis C and antiviral therapy.[7]

The objective of present study is to determine the frequency of peripheral blood count abnormalities in patients with chronic active hepatitis (CAH) caused by Hepatitis C virus (HCV).

METERIALS AND METHODS

It is a cross sectional study conducted in Department of Haematology, Shaikh Zayed Hospital Lahore, one hundred and fifty patients were included during a period of six months. Sampling was non probability purposive in type. Patients of chronic active hepatitis (CAH) caused by HCV (diagnosed by HCV – RNA), were included in the study. Adults patients (> 15 yrs) of both genders were included. Patients of hepatitis C with cirrhosis, hepatocellular carcinoma, autoimmune diseases, alcholism, Wilson's disease and hepatitis B positive cases were excluded from the study. Anemia is defined as hemoglobin less than 10 g/dl, Neutropenia is defined as neutrophil count less than $2.0 \times 10^9/l$ and thrombocytopenia is defined as platelet count less than $150 \times 10^9/l$.[13]

Informed consent was taken and socio-demographic data like name, age, and address were collected. Patients were investigated for complete blood count (CBC) including hemoglobin, (Hb), total leucocytes count (TLC), differential leucocytes count (DLC), absolute neutrophil count (ANC) and platelet count (Plt). These all were performed on haematology analyzer Sysmex XT 1800i. All collected information was entered into SPSS version 10.0 and was analyzed through its statistical package. Age was presented in terms of mean and standard deviation, gender in terms of frequency and percentages. Peripheral blood count abnormalities like anemia, neutropenia, and thrombocytopenia were analyzed and were expressed as frequency and percentages.

RESULTS

There were 99 (66%) female patients and 51 (34%) male patients in the cohort. Age ranged from 18 to

78 years. Mean age was 41.9 ± 12.8 years. Most of the patients were in 4th decade of life.

Mean Hb was 11.0 ± 2.58 g/dl (range 4.8 – 16.7 g/dl). Eighty – eight of 150 (58.6%) patients had Hb > 10 g/dl while anemia (Hb ≤ 10 g/dl) was seen in 62 of 150 (41.3%) patients. Fourteen of 62 (22.6%) were male patients, 48 of 62 (77.4%) were female patients. Anemia was more common in female patients as compared to males and this difference was statistically significant (p<0.05). Mean Hb in anemic male patients was 8.75 ± 1.21 g/dl, mean Hb in anemic female patients was 8.37 ± 1.39 g/dl, the difference was not significant.

Mean TLC was 6.02 ± 2.13 × 10^9/l (range 1.56 – 13.0 × 10^9/l). Mean ANC was 3.48 ± 1.50 × 10^9/l, (range from 0.52 – 9.24 × 10^9/l). Most of the patients (125 of 150) had a normal ANC. Neutropenia was seen in only 25 of 150 (16.6%) patients. Six of 51 male patients (11.8%) and 19 of 99 female patients (19.2%) had neutropenia. Neutropenia was more common in female patients as compared to males but this difference was not statistically significant (p = 0.355). Mean ANC in neutropenic male patients

Table 1: *Blood Count Changes in 150 Patients.*

Sr. No.	Haematological parameters	Mean values ± SD	Value of Haematological Parameters	No. and Percentages of Patients
1.	Hemoglobin	11.0 ± 2.58	≤ 10.0 g/dl	62 (41.3%)
			> 10.0 g/dl	88 (58.6%)
2.	ANC	3.48 ± 1.5	≤ 2.0 × 10^9/l	25 (16.6%)
			> 2.0 × 10^9/l	125 (83.3%)
3.	Platelet	198.8 ± 77.3	≤ 150 × 10^9/l	34 (22.6%)
			> 150 × 10^9/l	116 (77.3%)

Table 2: *Comparison of Frequencies of Blood Counts Abnormalities in 2 Genders of 150 Patients.*

Sr. No.	Blood Count Abnormalities (Cytopenia)	Gender	Patients without Cytopenia	Patients with Cytopenia	P-value*
1.	Anemia	M	37 (72.5%)	14 (27.5%)	0.021*
		F	51 (51.5%)	48 (48.5%)	
2.	Neutropenia	M	45 (88.2%)	6 (11.8%)	0.355
		F	80 (80.8%)	19 (19.2%)	
3.	Thrombo-cytopenia	M	35 (68.6%)	16 (31.4%)	0.104
		F	81 (81.8%)	18 (18.2%)	

Total no. of male patients = 51. Total no. of female patients = 99
*Statistically significant p value < 0.05

Table 3: *Comparison of Mean Value of Blood Count Abnormalities in Both Genders.*

Sr. No.	Blood Count Abnormalities (Cytopenia)	Total No. of Patients	Gender	Patients with Cytopenia	Mean Value of Blood Count	SD	P-value*
1.	Anemia	62	M	14	8.75 g/dl	1.21	0.358
			F	48	8.37 g/dl	1.39	
2.	Neutropenia	25	M	6	1.30 × 10^9/l	0.46	0.379
			F	19	1.39 × 10^9/l	0.42	
3.	Thrombocytopenia	34	M	16	98.75 × 10^9/l	28.73	0.823
			F	18	95.88 × 10^9/l	42.72	

* Statistically significant p value < 0.05

was (1.30 ± 0.92 × 10^9/l). It was not significantly different from mean ANC in neutropenic female patients (1.39 ± 0.84 × 10^9/l).

Mean platelet count was 198.8 ± 77.3 × 10^9/l (range 12 – 411 × 10^9/l). Thrombocytopenia were

present in 34 (22.6%) patients in the total cohort. Sixteen of 51 (31.4%) were male patients, 18 of 99 (18.2%) were female patients. Thrombocytopenia was slightly more common in female patients as compared to males but this difference was not sta-

tistically significant (p=0.104). Mean platelet count in thrombocytopenic male patients was 98.75 ± 28.73 × 10^9/l, and mean platelet count in thrombocytopenic female patients was 95.88 ± 42.72 × 10^9/l, this difference was not significant.

The blood count abnormalities (cytopenias) were further analyzed by dividing the total cohort in two groups according to age of patient i.e. A (age ≥ 40 yrs) and B (age < 40 yrs). It was seen that frequency of anemia was almost equal in group A and B (41.4% and 41.3% respectively). However, the mean hemoglobin value was lower in group A, but the difference was not statistically significant (p = 0.243).

Table 4: *Comparison of Frequencies of Blood Count Abnormalities in Age Groups.*

Sr. No.	Blood Count Abnormalities (Cytopenia)	Group	Patients without Cytopenia	Patients with Cytopenia	p value*
1.	Anemia	A	51 (58.6%)	36 (41.4%)	0.989
		B	37 (58.7%)	26 (41.39%)	
2.	Neutropenia	A	74 (85.1%)	13 (14.9%)	0.657
		B	51 (81%)	12 (19%)	
3.	Thrombo-cytopenia	A	64 (73.6%)	23 (26.4%)	0.272
		B	52 (82.5%)	11 (17.5%)	

Total no. patients in group A (age ≥ 40 yrs) = 87
Total no. patients in group B (age < 40 yrs) = 63
*Statistically significant p value < 0.05

Table 5: *Comparison of Mean Values of Blood Counts Abnormalities in Age Groups.*

Sr. No.	Blood Count Abnormalities (Cytopenia)	Total No. of Patients	Group	Patients with Cytopenia	Mean Value	SD	p* value
1.	Anemia	62	A	36	8.28 g/dl	1.57	0.243
			B	26	8.69 g/dl	0.97	
2.	Neutropenia	25	A	13	1.28 × 10^9 /l	0.44	0.253
			B	12	1.48 × 10^9 /l	0.40	
3.	Thrombocytopenia	34	A	23	90.78 × 10^9 /l	28.3	0.136
			B	11	110.72 × 10^9 /l	47.82	

*Statistically significant p value < 0.05

Neutropenia was more common in group B (age < 40 yrs) i.e. 19.0% as compared to group A (age ≥ 40 yrs) i.e. 14.9% but mean ANC was lower in group A (table 4). Neither the difference in frequency of neutropenia nor in mean ANC value was statistically significant.

Thrombocytopenia was more common in group A (age ≥ 40 yrs) i.e. 26.4% as compared to group B (age < 40 yrs) where only 17.4% of patients had thrombocytopenia. Mean platelet count was also lower in group A as compared to group B. The greater frequency and degree of thrombocytopenia in group A did not appear statistically significant when values were analyzed using chi square and t-test respectively.

DISSCUSSION
The present study was done to determine the frequency of peripheral blood count abnormalities in patients with chronic active hepatitis (CAH) caused by Hepatitis C virus (HCV). A considerable percen-

tage of patients i.e. 41.3% were anemic (Hb less than 10 g/dl). ANC was below normal in 16.6% of patients and platelets were below normal in 22.6% of patients. In our study the mean Hb in CAH patients (HCV positive) was lower than the standard reference ranges for both genders .Total Leucocyte Count, Absolute Neutrophilic Count and platelet count were comparable to normal reference value.

The frequency of anemia was compared in two genders and two age groups, it was seen that females were more anemic than males patients with statistically significant difference (p < 0.05), but there was no difference in mean Hb in two genders.

In a study by Nachnani JS et al[8] the frequency of anemia was not significantly different in two genders (p = 0.82). The high frequency of anemia in females in our study can be explained by high prevalence of iron deficiency anemia in our female population.

Nicholas and Norris [9] reported that anemia (Hb < 10 g\dl) was seen in 20% of Hepatitis C patients on

treatment, they reported that female gender, age more than 60 years and reduced creatinine clearance were the predictors of development of anemia. This is in accordance to present study where anemia was more common in females (p < 0.05). However there was no difference between frequency of anemia in two age groups (p = 0.98) in our study.

In contrast to our results, a study by Streiff et al[6] showed that there was no significant difference in Hb, Hct, RBC indices and RDW between hepatitis C positive and negative persons. However, this study was a population based study and Strieff et al[6] themselves described the limitation of their study that they might have underestimated the severity of hematological findings, due to the fact that advanced hepatitis patients were likely to be hospitalized and thus not available for their population based study. Neutropenia was seen in 16.6% of patients in the study. In a study by Koirala et al,[10] 18.4% of hepatitis C patients (30 of 163) developed neutropenia (ANC < 1.0). In our study neutropenia was more common in female patients than male patients (19.2% vs. 11.8%, p = 0.35), but mean ANC was not considerably different in two genders. Neutropenia is more common in group B than in group A in our study (19% vs. 14.9%) however mean ANC was lower in group A (p = 0.25). In a study by Streiff et al[6] neutropenia was seen in 9% of anti HCV positive patients. Age groups < 60 vs. > 60 yrs showed difference in incidence of neutropenia in their study, while gender was not associated with difference in the incidence of neutropenia among HCV patients. Our study showed some difference in incidence of neutropenia between two genders, and in young (< 40 yrs) versus older (> 40 yrs) patients but differences were mild and not statistically significant. In a community based study by Soza et al,[11] absolute neutrophil count (ANC) in whites was 4.47×10^9/l, this is in accordance to our results where mean ANC was $3.48 \pm 1.5 \times 10^9$/l.

In our study thrombocytopenia was seen in 22.6% of CAH HCV positive patients. It was more common in males than in females (31.4% vs. 18.2%) and in group A than group B (26.4% vs. 17.5%) but the difference are not statistically significant. In a community based study by Wang CS et al[12] in Taiwan, frequency of thrombocytopenia in HCV positive was 10.2%. Our study showed a higher percentage of patients with thrombocytopenia (22.6%). The platelet count to define thrombocytopenia was lower i.e. 100×10^9/l in their study than used in our study i.e. 150×10^9/l. In their study mean platelet count in HCV positive was 180×10^9/l which was close to mean platelet count of 198.8×10^9/l in present study. They also reported that mean platelet count in HCV positive patients was lower than HCV negative persons (234×10^9/l, p = < 0.001).

Wang CS et al[12] also reported that among HCV positive, older people (> 65 yrs) were 3 times more likely than the persons in younger age group to have thrombocytopenia. Our study also revealed higher frequency of thrombocytopenia, in patients > 40 yrs than the younger ones (26.4% vs.17.5%) the milder difference may be due to the division of age groups at an earlier age of 40 yrs in our study as compared to 65 yrs in Wang CS study. A study by Streiff et al,[6] among HCV positive patients 4% had thrombocytopenia (platelets < 100,000) this shows a much lower frequency than our study. This study was a population based study where no HCV positive patients were on treatment and they had lower cut off platelet count to define as thrombocytopenia i.e. 100×10^9/l instead of actual reference range of 150×10^9/l. In the study of Strieff et al[6] the severity of hematological findings were under – estimated due to the fact that advanced hepatitis positive infected patients were likely to be hospitalized and thus not available for population based study.

It is ***concluded*** that anemia in CAH HCV positive patients was more common in females, which may be due to prior iron deficiency. Western studies show hematological changes in elderly patient as compared to the young ones, but this difference was not statistically significant in our study. Pretreatment blood counts are needed to identify high risk patients who are more likely to develop hematological abnormalities and require haematinics or growth factors during treatment for chronic hepatitis C. Another practical implication of the fact that considerable percentage of patients show hematological abnormalities is that persons with unexplained neutropenia and thrombocytopenia should be tested for HCV infection.

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