Immune Thrombocytopenic Purpura Associated With Hepatitis C Virus

Qamar U.,[1] Naeem S.[2]
Address for Correspondence: *Department of Pathology, K.E.M.U., Lahore*

Introduction: Immune thrombocytopenic purpura (ITP) is a frequent cause of thrombocytopenia, especially in children. It can be Idiopathic or secondary to their diseases. The commonest cause of thrombocytopenia in Chronic Liver Disease has been reported to be platelet pooling and destruction in the spleen. The aim of the present study was to investigate the frequency of thrombocytopenia in Anti-HCV+ve patients excluding patients who had progressed to CLD.

Materials/Methods: Thrombocytopenia (<150,000/uL) was diagnosed in 60 (20%) out of 300 patients of Anti-HCV+ve status. Bone marrow examination (aspirate +trephine biopsies) was subsequently done on which the adequacy of megakaryocytes was noted.

Results: The ages of the patients ranged from between 18-65 years with an equal male to female ratio. Patients who had had splenomegaly were excluded to rule out Hypersplenism as a cause of Thrombocytopenia. Bone marrow biopsy showed adequate/increased megakaryocytes in 41 (68%) patients.

Conclusion: HCV infection is strongly associated with thrombocytopenia and may produce significant peripheral destruction of platelets related to autoimmune mechanisms.

Background: There has been an association between Hepatitis C virus infection and the development of autoimmune diseases in several studies conducted to date.[1] Autoantibodies against platelet membranes can also develop in Hepatitis C infection. These antibodies are involved in the pathogenesis of Immune thrombocytopenic purpura. The antibodies coating the platelet membranes result in the splenic sequestration and phagocytosis of the platelets by macrophages. Hence thrombocytopenia in Immune Thrombocytopenic Purpura is caused by the reduced lifespan of the platelets in circulation alongwith incomplete compensation by the bone marrow megakaryocytes.[2] The diagnosis of Immune thrombocytopenic Purpura can only be established if other causes of thrombocytopenia such as Leukemia, Myelophthisic bone marrow infiltration Myelodysplasia, Aplastic anemia adverse drug reactions have been excluded.[3] The estimated annual incidence of Immune Thrombocytopenic Purpura is approximately 5 cases per 100,000 Children and 2 cases per 100,000 adults.[4] Hepatitis C is endemic in Pakistan. The estimated prevalence of Hepatitis C in Pakistan ranges from 5 to 8%.[5] Most recently, there, there has been emerging evidence that Immune thrombocytopenic Purpura is a frequent cause of thrombocytopenia in Hepatitis C virus infection.[6] So In a country hyperendemic for hepatitis C like Pakistan this association might even be more significant. Thrombocytopenia in Hepatitis C can result from number of causes: 1. Hypersplenism. 2. Aplastic bone marrow associated with Hepatitis C. 3.Dysregulation of host Immune mechanisms.[7]

Key Words: Immune thrombocytopenic purpura, Hepatitis C.

Aim/Objectives

The aim of the present study was to investigate the frequency of thrombocytopenia in Anti-HCV +ve patients excluding patients who had progressed to CLD.

Materials And Methods

The study was conducted at King Edward Medical University, Lahore from January 2009 to November 2009.

Inclusion Criteria

1. Asymptomatic blood donors.
2. 18-65 years age.
3. Patients of both genders.
4. Hepatitis C positive on ELISA.

Exclusion Criteria

1. Splenomegaly, Ascites, Eosophageal varices or other signs of chronic liver disease.
2. Patients who have received or were under antiviral therapy.
3. Any other co-morbidity.

Blood samples of all persons were drawn for complete blood counts.

All persons with platelet counts less than 150,000/µL (cutoff for thrombocytopenia according to BCSH guidelines) underwent bone marrow examination (Aspirate+ Trephine).

Adequacy of Megakaryocytes was assessed on bone marrow examination. The number of the Megakaryocytes was categorized as:

1. Normal (1/1-3LPF),
2. Increased (>2/LPF) o.
3. Decreased (1/5-10LPF).[8]

Results

Out of 1500 patients 300 patients were found to be Anti

HCV+ve.

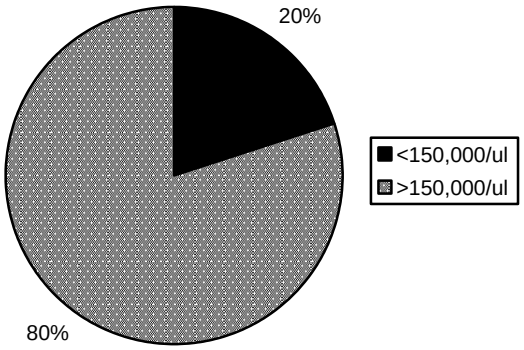

Fig. 1: *Results Platelet count in Anti-HCV +Ve patients <150,000=Thrombocytopenia (according to BCSH Guidelines).*

The Mean platelet count of Anti HCV+ve Patients was 130,000/µL± 46.67.

The mean platelet count of persons not found to be HCV +Ve was 210,000µL ±47, which is significantly higher than that of anti HCV+ve persons (P Value < 0.001).

Mean Platelet Count of the HCV +ve patients, who were THROMBOCYTOPENIC, was 56,000/µL ± 23.56.

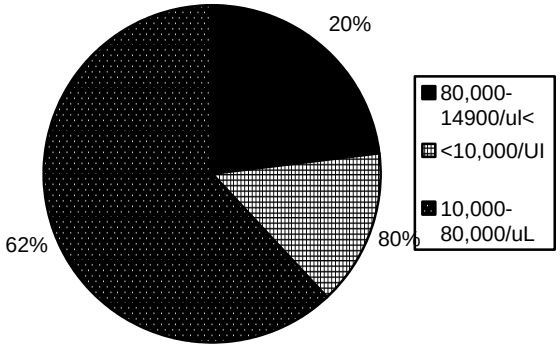

Fig. 2: *Distribution of Severity of Thrombocytopenia in Anti HCV +Ve Patients (N = 60).*

Table 1: *Results of Bone Marrow Biopsy (N = 60).*

Results of Bone Marrow Biopsy	No.	% ages
Increased megakaryocytes (>_2 (LPF)	41	(68)
Normal no. of megakaryocytes (1/2-3 LPF)	16	(25)
Decreasd megakaryocytes (1/5-10 LPF)	3	(5)

All patients with a reduced number of Megakaryocytes also had a reduced Bone Marrow cellularity for age.

Table 2: *Gender Distribution of ITP in HCV +Ve Patients.*

	Male	Female
HCV+ (300) (i) no.	198	102
(ii) % age	66	34
Thrombocytopenia in HCV+ patients (60)		
(i) no.	39	21
(ii) % age	65	35
HCV+ patients with ITP (57)		
(i) no.	39	18
(ii) % age	19.6%	17.6%

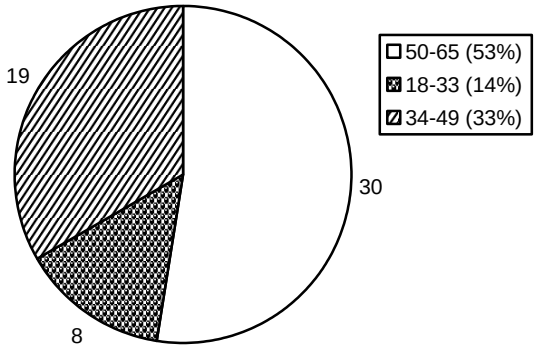

Fig. 3: *Age Distribution of Anti HCV +Ve Patients with Normal / Increased Megakaryocytes (N = 57).*

Mean age of thrombocyopenic Anti HCV+ve patients was 47.67±11.52.

The mean age of patients with ITP, according to one large study, has otherwise reported to be is 33.4 ± 23.1[9]

Discussion

The MEAN PLATELET COUNT of HCV +ve persons was significantly **LOWER** than in HCV -ve persons ($p < 0.001$). Houweriji E,Bloom N[8] conducted a study which also showed similar results. Since in our study patients with hypersplenism were excluded the low platelet count could be either because of hypocellular bone marrow or ITP. In our study, excluding patients with marrow hypoplasia, 6.33% of the Anti HCV +Ve patients showed ITP.

Frequency of ITP in general population in adults (18-65 years age) is 0.0096%.[10] Hence ITP might be more common in patients who are anti HCV+ve.

Although the platelet count tends to be low in Anti HCV+ patients as compared to that in general population but when it comes to severity, we observed in our study that. The severity of ITP in HCV +Ve persons seems to be less than of ITP in the general population (56,000/µL ± 23.56 Vs 31,500/µL ± 22.437). But a study by Khan A A[5]

showed that no such differences between Hep C +ve patients and Normal population with ITP exist.

In the present study the mean age of HCV +Ve persons with ITP was HIGHER than in the general population with ITP.

47.67 ± 11.52 Vs 33.4 ± 23.1. Liebman, H[10] also reached the same conclusion in their study.

Conclusions

ITP occurs more commonly in patients with chronic HCV infection than would be expected by chance. This should be considered in patients with liver disease and unexplained thrombocytopenia, as well as in patients with newly diagnosed ITP. The present study showed ITP to be frequent cause of thrombocytopenia in the clinically asymptomatic HCV positive population.

Prevalence of Hepatitis-C is quite High in Pakistan. So in this backgroung it might be logical to conclude that All the patients with Hepatitis-C should be investigated for ITP.

References

1. Kiser J. Trends in the Treatment of Chronic Hepatitis C Virus Infection. *Journal of Pharmacy Practice* 2007; 22: 405-418.
2. Cines D, Bussel J, Liebman H, Luning E. The ITP syndrome: pathogenic and clinical diversity. *Blood* .2007; 113: 6511-6521.
3. Pereboom I, de Boer M. Platelet Transfusion During Liver Transplantation Is Associated with Increased Postoperative Mortality Due to Acute Lung Injury. *Anesth. Analg.* 2009;108: 1083-1091.
4. Desmond A, O'Regan K, Curra C, McWilliams S, Fitzgerald. Crohn's disease: factors associated with exposure to high levels of diagnostic radiation. *Gut; 2008;* 57: 1524-1529.
5. Khan A A.Endemic transmission of Hepatitis C. JCPSP. 1995; 5 (1): 11-13.
6. George J, Terrell D. Novel thrombopoietic agents: a new era for management of patients with thrombocytopenia. *haematol*. 2008; 93: 1445-1449.
7. Lawson A, Zimmer J, Hentges F. Eltrombopag in thrombocytopenia. *NEJM.* 2008; 358: 1072-1072.
8. Houweriji E, Bloom N. Ultrastructural study shows features of apoptosis and para-apoptosis in megakaryocytes from patients with ITP. Blood. 2004; 103: 500-6.
9. Liebman H.Viral-Associated Immune Thrombocytopenic Purpura. *ASH Education Book* 2008: 212-218.
10. Gernsheimer T. The Pathophysiology of ITP Revisited: Ineffective Thrombopoiesis and the Emerging Role of Thrombopoietin Receptor Agonists in the Management of Chronic Immune Thrombocytopenic Purpura. *ASH Education Book* 2008: 219-226.

NOTE:

This Paper was Presented at 12TH National Pakistan Society of Haematology Conference
(13th February 2010)