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STUDY TO KNOW THE PREVALENCE OF VARIOUS TYPES OF BLEEDING DISORDERS

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Abstract:

Objective: *To determine the frequency and type of various bleeding disorders in hematology patients who enter the medical ward.*

Study Design: *A Cross-sectional and observational study.*

Place and Duration: *In the West Medical ward and Hematology department of Mayo Hospital Lahore for Six months period from august 2014 to Febraury 2015.*

Methodology: *All patients who had bleeding episodes and who admitted in the medical and hematology department during the study were included in the study with undesirable probability sampling. Fifty patients were found to meet the diagnostic criteria for the study.*

Results: *There are many underlying causes of bleeding disorder. In 50 cases, idiopathic thrombocytopenic purpura is the most common bleeding disorder, followed by bone marrow failure, coagulation disorders and liver diseases.*

Conclusion: *Bleeding disorder with different etiologies in patients with excessive bleeding in medical and hematology department had been investigated. Further studies are needed to investigate these underlying disorders.*

Key words: *Chronic liver disease, idiopathic thrombocytopenic purpura, activated partial thromboplastin.*

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INTRODUCTION:

Excessive bleeding is a common medical emergency in any hospital. Heavy bleeding is associated with high morbidity and mortality. Among the patients in medical wards, various hematologic disorders such as platelet defects and bone marrow diseases are associated with acute and chronic liver diseases. In a country like Pakistan, the prevalence of hepatitis C is high and this is the main cause of bleeding by causing liver cirrhosis. Liver is the important site for the synthesis of coagulation factors, proteins, factor VIII, coagulation inhibitors and proteins in the fibrinolytic system. In addition, platelets are affected by increased consumption and decreased production due to bone marrow failure. This is a cross-sectional, descriptive study conducted by the Department of Medicine and Hemtology.

MATERIALS AND METHODS:

This Cross-sectional and observational study was held in In the West Medical ward and Hematology department of Mayo Hospital Lahore for six months period from august 2014 to Febraury 2015. All patients who had bleeding episodes and admitted in the medical and hematology department during the study were included in the study with undesirable probability sampling. Fifty patients were found to meet the diagnostic criteria for the study.

A detailed history of bleeding episodes was taken, fever, weight loss (about 10% in the last six months); minor trauma, nosebleed, gingival bleeding, hematemesis, hemoptysis, hematochezia, malena, hematuria, menorrhagia, cuts or excessive bleeding after surgery. General physical examination including pallor; signs of bleeding on the skin (eg, bruising and purpura), nasal bleeding, oral cavity, vagina, anal canal, accessible lymphadenopathy in the cervical, axillary and inguinal region. Abdominal examination revealed hepatomegaly and splenomegaly and was confirmed by abdominal ultrasound. The cause of bleeding at each time was established with the help of the following research. Venous blood samples (2 ml) were taken and analyzed in Sysmex KX 21 to make a complete blood count (CBC). Blood films were stained with May-Grunwald stain-Giemsa, peripheral smear was performed and examined for any evidence of thrombocytopenia, abnormal platelet morphology and bone marrow failure. Another 1.8 ml of venous blood were taken and prothrombin time (PT) , partial thromboplastin time (PTT) was tested and the international normalization index (INR) was calculated. For long-term coagulation results, correction studies were performed at normal 1: 1 ratio with 0 h and after incubation at 37 ° C for 120 minutes to eliminate inhibitors. The deficiencies of clotting factor assays were confirmed by factor analysis studies for factor XIII, platelet function, factor VIII and vWF levels, and von Willebrand disease diagnosis (VWD). Bone marrow aspirates were performed from the right posterior iliac crest. Staining-May-Grunwald Giemsa was performed in the aspiration, which is examined for evidence of dysplasia, red blood cells and marrow megakaryopoiesis. 500 myelograms cell were used to calculate the blast cells percentage. The blast cell line was confirmed by myeloperoxidase, non-specific esterase and periodic acid Schiff stains. Patients were divided into six groups according to the disease category given in Table I. Laboratory properties such as hemoglobin, total leukocyte count, platelet count for each group are shown in Table II.

RESULTS:

A total of fifty patients were identified in the critical or emergency care unit and their underlying causes were determined by various tests. Patients were divided into 6 groups as described in Table I, columns 1 and 2.

Table I (n=50)

Diagnostic group	=n	Final diagnosis	=n
Platelet disorders	17	ITP	12
		Evans syndrome	1
		Gestational thrombocytopenia	1
		Bernard Soulier Syndrome	2
		Essential thrombocythemia	1
Bone marrow failures	12	Aplastic anaemia	5
		MDS	4
		Leukemia	3
Coagulation factor deficiency	8	vWD	4
		Hemophilia	3
		fact 13 deficiency	1
Liver disease	7	Cirrhosis	5
		Fulminant hepatic failure	2
Drug side effect	5	Anticoagulant	3
		Platelet antagonists	2
Miscella-neous	1	Polycystic ovary	1

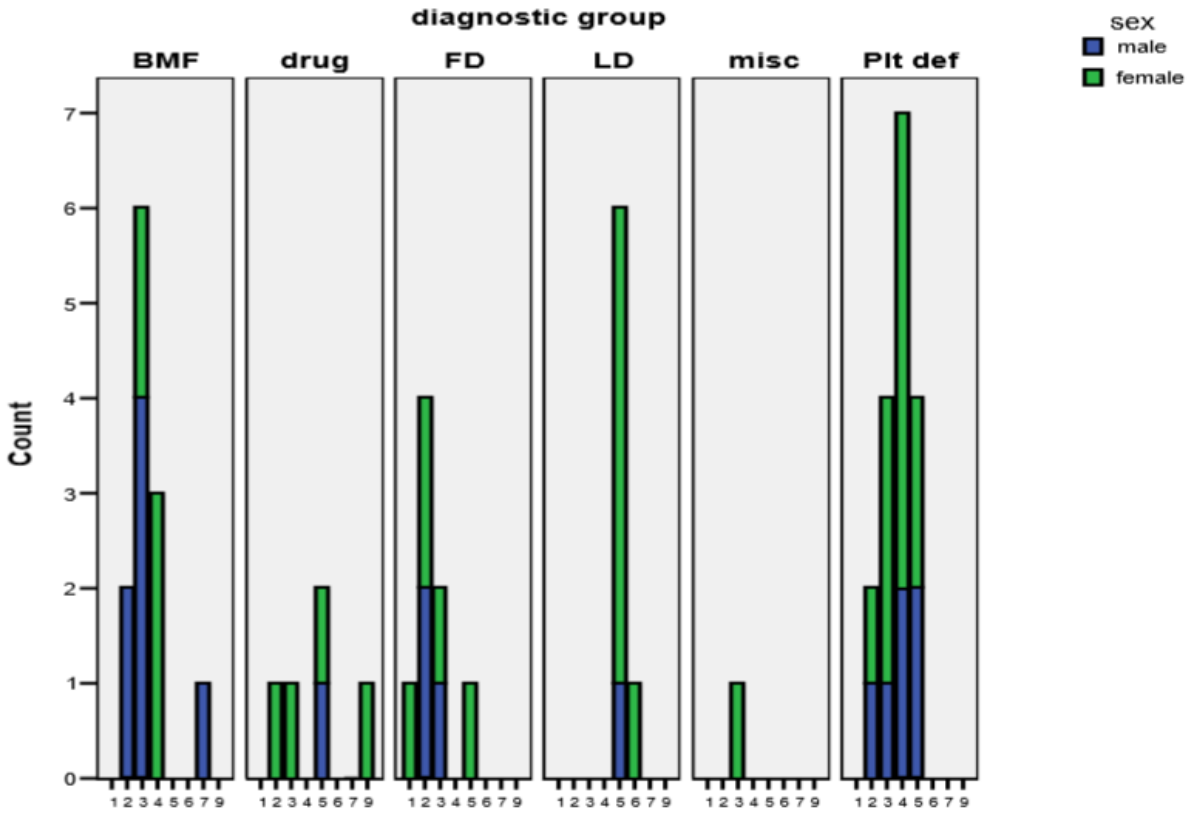
Specific diagnosis was also classified as shown in Table I column. Number of patients was observed in the group with Evans syndrome, idiopathic thrombocytopenic purpura, gestational thrombocytopenia, Bernard Soulier syndrome and essential thrombocythemia.

Table II

Diagnosis group	=n	age	Haemoglobin g/dl	TLC x 10^9/l	Platelet count x 10^9/l
Platelet disorders	17	32.2+/-10.2	9.8+/-2.7	7.6+/-3.1	70190+/-21394
Bone marrow failure	12	29.9+/-12.9	5.5+/-1.99	5.4+/-0.6	66500+/-180
Factor deficiency	8	19.6+/-9.8	8.2+/-2.9	5.5+/-0.9	262125+/-90308
Chronic liver disease	7	50.7+/-4.49	9.1+/-1.4	8.9+/-4.2	105142+/-30333
Drugs	5	44.6+/-2.3	6.5+/-3.2	11.3+/-2.7	353800+/-15193
Miscellaneous	1	25+/-0	10.9+/-0	6.7+/-0	350000+/-0
Total	50	33.4+/-15	8.15+/-2.9	7.3+/4.2	138864+/-19140

The second most common category for hemorrhage was aplastic anemia which was found to be the most frequent followed by myelodysplastic syndrome and leukemia. The underlying pathology was chronic liver disease with

cirrhosis in 5 cases and acute liver failure was only in two cases. The most common coagulation factor deficiency was von Willebrand disease, followed by hemophilia A and factor xiii deficiency. Iatrogenic group included drugs such as anticoagulants and platelets antagonists seen in 5 cases. Distribution by sex showed that there were 18 males and 32 females. In males, in the first 2 years of life, in 2nd or 4th decade, they presented with bone marrow failure, von Willebrand disease or platelet defect. In women, bone marrow failure was seen in the second and third decades, including drug overdose, factor deficiency, and platelet defects.



When the meaning of the two tails of the paired t-test was calculated for the age and type of presentation, the p value was less than 0.001. Secondary bone marrow failure and ITP causes were found in 3rd decade and the hereditary causes of coagulation factor deficiency were seen in the second decade of life. The main underlying disease was von Willebrand disease (vWD), the most common case was menorrhagia in 2 cases and intraperitoneal bleeding in 2 cases due to luteal cyst. One patient with factor xiii deficiency presented with intracranial hemorrhage and hemophilia in 2 cases after trauma and in one case after tooth extraction. The most common diagnosis was ITP. The average age of ITP was 30.55. Hemoglobin was 9.49 +/- 2.8; TLC was 6.93x109 / L; the platelet count was 13454.5 +/- 9092.5 and severe menorrhagia in women and in males as upper GI bleeding. Liver Cirrhosis in 5 cases with underlying disease and fulminant hepatic insufficiency and significant coagulopathy in 2 cases resulting in bleeding of the gastrointestinal tract.

DISCUSSION:

Recent research suggests that a change in our previous understanding of the pathophysiology of immune thrombocytopenia is evident. It is strongly believed that thrombocytopenia is due to the destruction of platelets mediated by antibodies. The new information developed is that the same antibodies that

causing platelet destruction are also damaging megakaryocytes and decrease platelet production by inhibiting the ability to release platelets . CD8 cytotoxic reactive cells are clearly present, but their

clinical significance is unknown. In our study, ITP was observed mainly in women with a mean age of 30 years. It is concluded that the predominance of ITP in younger women with bleeding seen in 12 cases. The deficiencies of the coagulation factor were observed in 8 patients. Bone marrow disorders were seen in 12 patients who had severe symptomatic thrombocytopenia. The mean platelet count for this group was 16000 / mm. The average Hb for this group was 5.5 g / dl. The number of platelets less than 10000 / microliter is associated with spontaneous bleeding. Abnormalities of coagulation and thrombocytopenia are often observed in patients with chronic liver disease, or in carriers of HCV. Such patients have a higher incidence of bleeding events. Severe coagulopathy is seen in both acute and chronic liver disease. This explains the higher morbidity and mortality among these patients. Chronic liver disease is responsible for various hematological and coagulation disorders by various mechanisms. Thrombocytopenia due to increased splenic sequestration and low thrombopoietin levels is common in patients with chronic liver disease. Both leukopenia and leukocytosis are associated with a decrease in the survival of red blood cells that cause hemophytic anemia. In our study, we included a total of seven patients with liver diseases who were diagnosed with bleeding disoders. Five patients had chronic liver disease and two of them had acute liver failure. All of them had thrombocytopenia. Therefore, retrospective studies show that bleeding disorders examined for any patient with bleeding in any part of the body are common. Bleeding diathesis contributes to the definitive diagnosis.

CONCLUSION:

Platelet disorders were the most common diseases in the selected patient population with bleeding and idiopathic thrombocytopenic purpura stood at top than other platelet defects. Twelve cases of bone marrow failure were the next common etiology for bleeding. In our patients, von Willibrand disease, hemophilia and factor XIII deficiency were diagnosed as coagulation defect. Coagulopathy was observed in patients with acute and chronic liver disease.

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