FREQUENCIES OF BLEEDING DISORDERS IN CHILDREN PRESENTING TO PEDIATRIC DEPARTMENT OF A TERTIARY CARE HOSPITAL AT PESHAWAR

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ABSTRACT

Objective: To determine the frequencies of various bleeding disorders in children presenting to pediatrics department of a tertiary care hospital at Peshawar.

Methodology: A descriptive cross sectional study was conducted in the admitted patients in the Department of Pediatrics and Neonatology, PGMI/LRH Peshawar; during one year period from Jan to Dec 2010. A total of 103 patients (aged from 1 day to 12 years, both male and female) were recorded as samples. The frequency of various bleeding disorders and etiological factors were scrutinized in children presenting with bleeding disorders.

Results: Out of 103 patients, 68.9% were males and 31.1% were females. Majority of patients 46.60% had defects in clotting factors, defects in platelet were found in 45.64% and defects in vessel wall were found in 7.76%. Among patients with defects in clotting factors; hemorrhagic disease of newborn recorded in 15.53% cases, diarrhea in 13.59%, liver parenchymal disease in 03.88%, disseminated intravascular coagulation (DIC) in 03.88%, biliary atresia in 0.97%, hemophilia "A" in 04.85%, von Willebrand disease (vWD) in 01.94% and factor VII deficiency in 01.94% cases respectively. Bleeding due to thrombocytopenia was found in 47 patients, aplastic anemia in 19.41%, idiopathic thrombocytopenic purpura (ITP) in 09.70%, acute lymphocytic leukemia (ALL) in 07.76%, megaloblastic anemia in 05.82%, and infection induced thrombocytopenia in 2.91% cases respectively. Defects due to vessels wall were found in 07.76% cases.

Conclusion: Majority of patients had defects in clotting factors, followed by defects in platelet and defects in vessel wall respectively. Bleeding disorders were common in majority of males with mean age of 05.68 years (age ranged from 1 day to 12 years).

Key Word: Bleeding disorders; AA; HDN; ITP; ALL; DIC; HA-etiology-diagnosis.

INTRODUCTION

Bleeding disorders can either be inherited or acquired and are due to defects in either primary or secondary hemostasis. Bruising with or without preceding trauma can be due to a defect in either primary or secondary hemostasis although deep palpable bruises are usually due to a clotting factor defect. Petechiae are usually due to a platelet or blood vessel defect.[1]

The bleeding disorders are known to treating physicians since 16th century.[2] Congenital bleeding disorders have worldwide distribution but very limited information is available in developing countries like Pakistan about their prevalence and so on. Among all, hemophilia A (HA), B (HB), and von Willebrand disease (vWD) are the commonest. Severity of bleeding is proportional to the severity of factor deficiency; therefore, HA and HB diseases, X-linked recessive disorders, are classified as mild, moderate, and severe according to concentration of factor present in the plasma.[3]

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Hemorrhagic disease of newborns (HDN) is an acquired condition due to vitamin k deficiency.[4]

Newborn infants are vulnerable to hemorrhagic disorders owing to limited transplacental transfer of vitamin K and limited fetal storage of vitamin K.[5] The current frequency of vitamin K deficiency bleeding in the first week of life in infants not receiving vitamin K prophylaxis has been estimated at 0.01% to 0.44%.[6] Incidence of bleeding complications in fully breast fed infants who did not receive vitamin K at birth is between 1 in 15 000 and 1 in 20 000 births.[7]

Higher incidence of platelet functional disorders has been reported from Middle East and India.[8] The incidence of HA (FVIII deficiency) is 1 in 5000 live male births and that of HB (FIX deficiency) is 1 in 30 000.[9] In contrast, the deficiency or dysfunction of vWF constitutes the most common bleeding disorder in females, the incidence of which may reach 1 in 1000 or even more.[10]

At present no cure, for these diseases is available. Clotting factor replacement therapy is the main stay in management of these patients. However, factor replacement therapy, exposes the patient to increased risk of transfusion transmitted diseases for example HCV, HBV, and HIV infections and also end up in alloan-

tibodies (inhibitor) formation against the missing factor. These antibodies ultimately make the patient resistant to conventional factor replacement therapy. Inhibitors develop with frequency of 20% to 30% in HA and 02% to 5% in HB.[11]

In Pakistan, there is no infrastructure available to look after this lifelong bleeding disorder. Laboratory diagnosis of hemophilia is limited to teaching hospital in the bigger cities like Peshawar, Lahore, Karachi, and Rawalpindi. Most patients get FFP or occasionally cryoprecipitate in the public sector hospitals in the bigger cities and only patients, who are registered with hemophilia societies, get appropriate treatments. Virally inactivated high-purity or intermediate purity factor concentrates are out of the reach for the majority of patients. In the smaller cities, towns, and villages they are not even diagnosed, leading to high morbidity and mortality among these patients. With this background, the study was designed to determine the frequency of bleeding disorders and assess the presenting features of the patients.[12] There is scanty data on the frequency of bleeding disorders in Pakistan.[13]

The objective of the study was to determine the frequencies of various bleeding disorders in children presenting to our department, which was helpful in earlier detection and in time proper management of patients with bleeding disorders.

MATERIAL AND METHODS

The study was conducted in admitted patients of Department of Pediatrics and Neonatology, Postgraduate Medical Institute, Lady Reading Hospital, Peshawar, during the one year period from January to December 2010.

Inclusion criteria: Neonates and children aged up to 12 years and who have a personal and family history of congenital bleeding disorders or a suspected bleeding tendency were included in the study confirmed by the relevant laboratory investigations.

Exclusion Criteria: Known patients of bleeding disorders like aplastic anemia, immune thrombocytopenic purpura (ITP), disseminated intravascular coagulation (DIC), or patients on anticoagulant therapy were excluded.

Methodology: Informed consent was obtained from parents, or legal guardians. A detailed history and clinical examination was recorded. Type and site of bleeding, and therapy including surgical intervention used, were also recorded. Baseline laboratory tests including Complete Blood Count, Bleeding Time, Prothrombine Time, APTT, fibrinogen, and blood grouping were carried out in all patients on same day. Further investigations were carried out on the basis of baseline results. If platelet count was reduced bone marrow biopsy and trephine biopsy were performed, to detect the cause of thrombocytopenia. If platelet count and Bleeding Time were normal, but P.T and APTT were prolonged then correction studies with adsorbed plasma and serum were performed. Clotting factor assays were done where needed. If coagulation profile was found to be normal then vessel wall defect was considered as a cause of bleeding. Henock Schonlen Purpura was confirmed by skin biopsy.

All the qualitative variables were analyzed for percentages and frequencies. Mean + standard deviation was calculated for quantitative variables like age. The results were presented through tables. All the data was analyzed by statistical program SPSS version 12 for windows.

RESULTS

In this study a total of 103 patients with bleeding disorders were included. Age range was from 1 day to 12 years with mean age of 05.6893 ± 3.4924 years.

Among the 48 patients with defects in clotting factors; etiology of coagulative disorders showed that hemorrhagic disease of newborn (HDN) was recorded in 16 (15.53%) cases, diarrhea in 14 (13.59%) cases, liver parenchymal disease in 04 (03.88%) cases, disseminated intravascular coagulation (DIC) in 04 (03.88%) cases, biliary atresia in 01 (0.97%) case, hemophilia "A" in 05 (04.85%) cases, von Willebrand disease (vWD) in 02 (01.94%) and factor VII deficiency in 02 (01.94%) cases respectively.

Bleeding due to thrombocytopenia was found in 47 patients, the aplastic anemia was etiology in 20 (19.41%) patients, idiopathic thrombocytopenic purpura (ITP) in 10 (09.70%) cases, acute lymphocytic leukemia (ALL) in 08 (07.76%) cases, megaloblastic anemia in 06 (05.82%) cases, and infection induced thrombocytopenia in 03 (2.91%) cases respectively. Defects due to vessels wall were found in 08 (07.76%) (Table 1).

DISCUSSION

Inherited platelet functional disorders constitute a large group of rare genetic defects diseases that can lead to bleeding symptoms of varying severity. This has been reported that autosomal recessive genes are hidden within the family for generations and only come to the surface (expressed phenotypically in children) after new consanguineous marriages within the family.[14]

Due to the lack of proper knowledge and diagnostic facilities even in large cities of Pakistan, a significant number of patients with bleeding disorders either are not diagnosed or misdiagnosed.[13]

In our study we have included a total of 103 diagnosed patients with bleeding disorders. Mean age was 05.6893±3.4924 years. Similar results are reported in a local study also carried out in this institute in which average age was 5.35 ± 3.7 years.[15]

In our study of 103 patients, 46.60% had defects in clotting factors, among these 37.86% had acquired and

Table 1: Frequency of various etiologies of bleeding disorders in patients (n=103)

Etiologies	No. of cases	Percentage
Defects in clotting factor:		
Hemorrhagic disease of newborn (HDN)	16	15.53%
Diarrhea	14	13.59%
Liver parenchymal disease	04	03.88%
Disseminated intravascular coagulation (DIC)	04	03.88%
Biliary atresia	01	0.97%
Hemophilia "A"	05	04.85%
von Willebrand disease (vWD)	02	01.94%
Factor VII deficiency	02	01.94%
Bleeding due to thrombocytopenia:		
Aplastic anemia	20	19.41%
Idiopathic thrombocytopenic purpura (ITP)	10	09.70%
Acute lymphocytic leukemia (ALL)	08	07.76%
Megaloblastic anemia	06	05.82%
Infection induced thrombocytopenia	03	02.91%
Defects due to vessels wall:	08	07.76%

8.73% had congenital, 45.64% had defects in platelet and 7.76% had defects in vessel wall. While in a local study out of 435 patients, 273 (62.8%) had coagulation factor deficiency, 81 (18.6%) had platelet function defects. Another 81 (18.6%) had vWF deficiency. Among the 273 coagulation factor deficiency patients, inherited coagulation factor deficiencies were found in 218 (79.9%) and acquired deficiency in the form of multiple factor deficiency was seen in 55 (20.1%) mainly due to vitamin K deficiency and liver disease.[13]

In a study of Peyvandi et al[16] on rare coagulation deficiencies, they have estimated that in countries where consanguineous marriages are frequent, such as Muslim countries and southern India, recessively inherited coagulation deficiencies are so frequent that they can surpass the prevalence of disorders like haemophilia B, representing an important clinical and social problem. The study done by Ahmed et al[17] has shown high frequency of platelet functional disorders (27.77%) as compared to factor IX and other rare coagulation disorder in a population of 1576 congenital bleeding disorder patients.

Patients with thrombocytopenia caused by various neoplastic and primary bone marrow diseases are susceptible to major hemorrhage.[18]

In our study aplastic anemia was the commonest bleeding disorder found in majority 19.41% of patients. It was also the most common disorder present in 20.2% cases of a local study done at the Pediatrics Department of PGMI/LRH, Peshawar.[15] Another recent local study reported the same results with an incidence of 20% cases of aplastic anemia in their study.[19]

Hemorrhagic Disease of the Newborn (HDN), now known Vitamin K Deficiency Bleeding Disorder (VKDBD), has been a recognized clinical entity for over 150 years. In the present study we have found that hemorrhagic disease of the newborn (HDN) was the second common disorder after aplastic anemia, found in 15.53% of patients. Our findings are incorporate with the national and international studies.[20]

Immune or idiopathic thrombocytopenic purpura (ITP) is one of the most common acquired bleeding disorders of childhood. In our study it was reported in 09.70% cases, majority was male, aged 1-6 years. Similarly a local study showed that idiopathic thrombocytopenic purpura (ITP) was present in15.7% cases.[15] A prospective study has documented a higher rate of acute ITP in boys than girls (54.8% vs. 45.2%) on all continents worldwide.[21] The other study reported that male/female ratio was highest in infants and decreased with age. Peak occurrence is between 2 and 5 years of age.[22]

In our study it was found that acute lymphocytic leukemia was reported in 07.76% cases. In a local study acute leukemia was the predominant malignant disorder present in 11.6% of the cases.[15]

In our study megaloblastic anemia was documented in 05.82% cases. In a local study megaloblastic anemia was reported in 14.6% cases.[15] Mild thrombocytopenia occurs in approximately 20% of patients with megaloblastic anemia resulting from vitamin B12 deficiency in the United States.[23]

One study has shown HA as the most common

bleeding disorder with decreased life expectancy when different age groups of patients with hemophilia are compared with normal population. Earlier study from Pakistan by Zafar et al[11] has shown similar findings. These figures are close to the figures found in neighboring countries such as Iran and India.[24,25] Karimi et al[24] have reported 367 patients with inherited coagulation disorders from Iran. A total of 272 (73.8%) patients had HA.

In a recent study done at Department of Hematology, Jagiellonian University School of Medicine, Krakow, Poland showed the prevalence of 14.9% of all severe haemophilia A patients.[26] In our study hemophilia A was documented in 04.85% cases, which is comparable with the national and international studies referenced above. Differences in results of incidence could be due to small and big sample sizes in these studies references above.

In the present study we have recorded only 03.88% patients with liver parenchymal disease.

In the present study we have found 02.91% cases of infection induced thrombocytopenia. The cause of this was due to measles which was evident from history of vaccine. No one was found having HIV among our patients.

One study done at Karachi in the tribe of Chandio has shown high prevalence of VWD (51.02%) and platelet functional disorders (48.98%) and no case of haemophilia A or B was detected.[27] Worldwide VWD prevalence is generally 1% of the normal population with higher frequency of type 1 but studies from East has shown higher frequency of type 2 and types 3 as compared to type 1.77 Comparable results were also found in our present study in which 01.94% patients had von Willebrand disease (vWD).

CONCLUSION

From the results of this study it is concluded that: Majority of patients had defects in clotting factors, followed by defects in platelet and defects in vessel wall respectively.

Bleeding disorders were common among in majority of males with mean age of 05.68 years (age ranged from 1 day to 12 years).

RECOMMENDATION

Bleeding patients should be investigated based on clinical patterns. Causes of multiple factor deficiency and acquired causes of platelet function defects should be identified so that they can be adequately corrected.

Cousin marriages should be avoided. All newborns should received vitamin K at birth which should be made a national policy.

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