Original Article

To study the clinicoetiological profile of children admitted with bleeding diathesis

Kapil Bhalla[1], Poonam Mehta[1], Sanjiv Nanda[1], Shuchi Mehra[2]

From Departments of [1]Pediatrics, and [2]Microbiology, Pandit B D Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India

Correspondence to: Kapil Bhalla, Department of Pediatrics, Pandit B D Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India. E-mail: kavashu@gmail.com

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ABSTRACT

Background: Bleeding complications in children may be caused by disorders of secondary hemostasis or fibrinolysis. A child who presents with bleeding warrants evaluation for a significant bleeding problem. **Objectives:** The aim is to study the clinicoetiological profile of children admitted with bleeding diathesis. **Materials and Methods:** Children up to the age of 14 years presenting in the Department of Pediatrics, Pandit B D Sharma Postgraduate Institute of Medical Sciences, Rohtak, with hemorrhagic diathesis, that is, non-traumatic spontaneous bleeding, suspected to be either due to the defective primary hemostatic mechanism (platelet–blood vessel interaction) or defective secondary hemostatic mechanism, were enrolled for this study. Frequency distribution of various bleeding disorders in various age groups was studied. **Results:** A total of 92 children up to the age of 14 years were taken up for study, of which, maximum cases with bleeding presented with hematemesis (23.9%) followed by melena (22.8%). A total of 73 children (79.34%) presented with skin and joint bleeds. We were able to make diagnosis in 82 children (89.1%). Among 82 patients, 31 (37.8%) had bleeding secondary to infections, 11 (13.4%) had coagulation disorder, 9 (10.97%) had Henoch–Schonlein purpura (HSP) and immune thrombocytopenic purpura (ITP) each, 6 (7.3%) had hypoplastic bone marrow, 2 (2.4%) had chronic malaria, 4 (4.9%) had leukemia, 6 (7.3%) had liver diseases, and 6 (7.3%) had hemorrhagic disease of newborn (HDN). Almost half of the children with bleeding manifestations in each age group had thrombocytopenia. The most common causes of bleeding in <1 year were septicemia with thrombocytopenia and HDN; among 1-7 years were infections, ITP, and coagulation disorders; and in more than 7 years were HSP, ITP, liver disease, and hemolytic-uremic syndrome. **Conclusion:** Our study found that the gastrointestinal tract was the most common site of bleeding in children presenting with non-traumatic spontaneous bleed, and thrombocytopenia was present in 50% of the cases in each age group. We also found that infections were the most common cause of bleeding in younger children, whereas immunological causes and coagulation disorders predominate in older children. Hence, while evaluating any child with bleeding, age at presentation is also an important parameter to find the etiological diagnosis.

Key words: *Age, Bleeding diathesis, Coagulation disorders, Non-accidental injury*

Bruising and bleeding are commonly seen in children and are usually associated with minor injury and trauma [1-3]. However, in two subsets of children, bleeding may be more significant than expected: Those having underlying hemostatic abnormalities such as an inherited bleeding disorder or those who have been subjected to non-accidental injury (NAI) [4-6]. The presentation of an infant or child with symptoms of bruising and/or bleeding commonly causes considerable anxiety to both pediatricians and hematologists. These symptoms may be due to a hemostatic disorder or due to NAI or both and making an accurate assessment and diagnosis is vital to ensure that the further management of that child is appropriate and the correct treatment is given if necessary [7-11]. Various studies in the past have tried to pick any one component of coagulation pathway or in isolation a single bleeding problem and tried to study it in detail [12-17]. However, this attempt by authors has been an effort to bring out the profile of children presenting in the Department of Pediatrics with bleeding manifestations.

MATERIALS AND METHODS

This prospective study was carried out on consecutive patients from newborn to children up to 14 years of age admitted to the Department of Pediatric from December 2013 to November 2014 at Pandit B D Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana. Children presenting with non-traumatic spontaneous bleeding or significant bleeding following trivial trauma were studied. Newborns requiring neonatal intensive care and children who developed bleeding during hospital stay were excluded from this study. Patients were divided into four age groups (Group A to D) ranging 0-1 month, >1 month-1 year, >1 year-7 year, and >7-14 years. Ethical clearance was taken from the Institutional Ethical Committee. Both the written and verbal consents were obtained from the parents. Their detailed history and physical examination were recorded.

The following investigations were done in all patients on the day of admission and repeated as and when required: Complete

hemogram with absolute platelet count, standard bleeding time (BT), prothrombin time (PT), partial thromboplastin time (PTT), and clotting time (CT). Bone marrow examination was done in cases who presented with either pancytopenia or hemogram with peripheral smear showing atypical cells or patients in whom immune thrombocytopenic purpura (ITP) was suspected. Fibrin degradation product (FDP) levels were assessed in patients in whom disseminated intravascular coagulation (DIC) was suspected. All these hematological investigations were performed by the standard techniques (Dacie and Lewis) [18].

Leukocytosis was defined as total leukocyte count (TLC) >11000/mm^3 and leukopenia as TLC <4000/mm^3. The WHO criteria for anemia were used to define anemia, that is, neonates (hematocrit <45%), children 6-59 months age (hemoglobin [Hb] <11 g/dl), children 5-11 years (Hb <11.5 g/dl), and children 12-14 years (Hb <12 g/dl). The detailed history was recorded and cases were investigated as per the standard neonatal and pediatric guidelines. Transfusion of the blood products was done according to the standard pediatric transfusion guidelines. Statistical methods such as frequencies, descriptive were used to analyze the data, employing the SPSS 11.0 package.

RESULTS

A total of 92 children, admitted in pediatric ward, fulfilled the inclusion criteria and taken up for this study. The age and sex distribution of cases in different pediatric age groups are shown in Table 1. More number of male children presented with bleeding in <7 years age; however, after 7 years, no sex predominance was seen. Out of 92 patients, 78 children (84.8%) presented with bleeding symptoms (Table 2). Among the bleeding symptoms, the most common were hematemesis in 22 cases (23.91%), melena in 21 cases (22.8%) followed by epistaxis in 15 cases (16.3%). The age-wise distribution of the bleeding symptoms is depicted in Table 2. On examination, about 73 children (79.34%) had bleeding signs in the form of skin, subcutaneous, and joint bleed (Table 2). Maximum cases had purpura and ecchymotic spots (28 cases, 30.4% each), followed by petechial bleeds (12 cases, 13%) and hemarthrosis in 5 cases (5.4%).

Anemia was present in 90 cases (97.8%). Out of these, 13 cases (l4.1%) had severe anemia. Leukocytosis was present in 13 cases (14.1%), whereas leukopenia was present in 10 cases (10.9%). 34 children (36.96%) had neutrophilia, whereas 5 (5.4%) children had lymphocytosis. 42 cases (45.67%) had thrombocytopenia (platelets <50,000/mm^3) while one case had thrombocytosis (platelets >450,000/mm^3). Almost half of the children with bleeding manifestations in each age group had thrombocytopenia. Of all thrombocytopenic children, 5 cases (11.9%) had platelet count <25,000/mm^3, whereas 22 children (52.4%) had platelet counts between 25,000/mm^3 and 55,000/mm^3. Out of a total of 42 cases of thrombocytopenia, 4 cases (9.5%) expired due to massive bleeding. 38 cases (90.5%) of thrombocytopenia recovered.

Table 1: Age and sex distribution of the cases

Group	Age	Male n=65 (%)	Female n=27 (%)	Total n=92 (%)
A	0-1 month	13 (20)	4 (14.8)	17 (18.5)
B	>1 month-1 year	18 (27.7)	4 (14.8)	22 (23.9)
C	>1-7 years	21 (32.3)	4 (14.8)	25 (27.2)
D	>7-14 years	13 (20)	15 (55.6)	28 (30.4)

The platelet count returned to normal earliest in Group D (5.2 days) while in group B, it took longest for the platelet count to normalize (12.6 days) and the average number of days (of the total cases) when the platelet count became normal was 8.48 days. PT was deranged in 26 children (28.3%). PTT was deranged in 33 children (35.9%). BT was prolonged in 2 children (2.2%) and CT was prolonged in 5 children (5.4%). FDP levels were elevated in 4 children (4.3%). Bone marrow examination was done in 16 cases. Out of these, 6 had hypoplastic, 6 had megakaryocytic thrombocytopenia, and 4 had leukemia.

The age-wise distribution of the final diagnosis of the patients is shown in Table 3. We were able to made diagnosis in 82 children (89.1%). Among 82 patients, 31 (37.8%) had bleeding secondary to infections, 11 (13.4%) had coagulation disorder, 9 (10.97%) had Henoch–Schonlein purpura (HSP) and ITP each, 6 (7.3%) had hypoplastic bone marrow, 2 (2.4%) had chronic malaria, 4 (4.9%) had leukemia, 6 (7.3%) had liver diseases, and 6 (7.3%) had hemorrhagic disease of newborn (HDN). Among patients with HDN, 3 had classical and 3 had late-onset disease. Among the coagulation disorders, nine cases (81.8%) had hemophilia A and two cases had hemophilia B. Out of these, 5 manifested with hemarthrosis (45.45%). Family history was positive in 7 cases (77.8%) of hemophilia A. The most common manifestations in patients with hemophilia were epistaxis, gingival bleed, hemarthrosis, and ecchymotic spots. The most common clinical manifestations in patients with ITP were bruises in 6 cases (66.6%), epistaxis in 3 (33.3%), and petechial rash in 5 cases (55.6%). The most common clinical presentation in HSP patients was purpuric rash (8 cases, 88.8%), arthralgia (5 cases, 55.6%), and abdominal pain (3 cases, 33.3%).

Maximum incidence of thrombocytopenia was due to infective causes (17 cases, 40.47%) followed by ITP (9 cases, 21.43%), hypoplastic anemias (6 cases, 14.28%), leukemias (4 cases, 9.52%), and other causes (14.3%). The maximum incidence of bleeding in 0-1 month age group was due to infective causes, that is, 10 cases (58.8%), out of which, maximum cases were associated with thrombocytopenias and rest of the neonates (17.6%) had HDN. The predominant cause of bleeding in >1 month-1 year of age group was sepsis. Of the total 22 cases, 9 cases were of infective origin (40.9%), followed by HDN and coagulation disorders (3 cases each) and one case (4.5%) of hypoplastic anemia. In the age group of >1-7 years, the most common cause of bleeding was coagulation disorders in 6 cases (24%) followed by 5 cases of ITP (20%), 5 cases of infection (20%), 3 cases of hypoplastic anemia (12%), 2 cases each of HSP, acute leukemia, and liver disease (8% each). In children >7-14 years, maximum number presented with HSP in 7 cases (25%) and infections in

Table 2: Frequency relationship of bleeding symptoms and signs at admission in different age groups

Clinical features	Group A (n=17)	Group B (n=22)	Group C (n=25)	Group D (n=28)	Total (n=92)
Bleeding symptoms at admission					
Epistaxis	0	2 (9.1)	9 (36)	4 (14.3)	15 (16.3)
Gingival bleeding	0	1 (4.5)	3 (12)	3 (10.7)	7 (7.6)
Hematemesis	6 (35.3)	6 (27.3)	6 (24)	4 (14.3)	22 (23.9)
Melena	8 (47.1)	7 (31.8)	4 (16)	2 (7.1)	21 (22.8)
Hemoptysis	0	0	0	1 (3.6)	1 (1.1)
Hematuria	1 (5.9)	0	1 (4)	4 (14.3)	6 (6.5)
Intracranial bleed	1 (5.9)	4 (18.2)	1 (4)	0	6 (6.5)
Total	16 (94.1)	20 (90.9)	24 (96)	18 (64.3)	78 (84.8)
Bleeding signs on examination					
Petechia	1 (5.9)	1 (4.5)	4 (16)	6 (21.4)	12 (13)
Purpura	3 (17.6)	3 (13.6)	10 (40)	12 (42.9)	28 (30.4)
Ecchymosis	4 (23.5)	10 (45.5)	7 (28)	7 (25)	28 (30.4)
Hemarthrosis	0	0	3 (12)	2 (7.1)	5 (5.4)
Total	8 (47.1)	14 (63.6)	24 (96)	27 (96.4)	73 (79.3)

Table 3: Frequency distribution of etiology of bleeding in different age groups

Diagnosis	Group A (n=17)	Group B (n=22)	Group C (n=25)	Group D (n=28)	Total (n=92)
HSP	0	0	2 (8)	7 (25)	9 (9.8)
Hypoplastic anemia	0	1 (4.5)	3 (12)	2 (7.1)	6 (6.5)
Infections					
Sepsis with thrombocytopenia	7 (41.2)	5 (22.7)	1 (4)	0	31 (33.7)
Sepsis with DIC	3 (17.6)	3 (13.6)	0	1 (3.6)	
Renal TB	0	0	1 (4)	1 (3.6)	
Viral hemorrhagic fever	0	0	1 (4)	0	
HUS	0	1 (4.5)	1 (4)	5 (17.9)	
Chronic malaria	0	0	1 (4)	0	
Liver disease	0	0	2 (8)	4 (14.3)	6 (6.5)
ITP	0	0	5 (20)	4 (14.3)	9 (9.8)
Acute leukemia	0	0	2 (8)	2 (7.1)	4 (4.3)
HDN	3 (17.6)	3 (13.6)	0	0	6 (6.5)
Coagulation disorders	0	3 (13.6)	6 (24)	2 (7.1)	11 (12)

HSP: Henoch–Schonlein purpura, DIC: Disseminated intravascular coagulation, TB: Tuberculosis, HSU: Hemolytic-uremic syndrome, ITP: Immune thrombocytopenic purpura, HDN: Hemorrhagic disease of newborn

7 cases (25%) followed by liver disease and ITP in 4 cases each and 2 (7.1%) cases each of hypoplastic anemia and leukemia.

DISCUSSION

Bleeding complications in children may be caused by disorders of secondary hemostasis or fibrinolysis [1-3]. A child who presents with bleeding warrants evaluation for a significant bleeding problem. The child's age, gender, and family history provide important clues in decision-making. Exaggerated bleeding responses to the commonly encountered events are suggestive of an underlying bleeding disorder. There is a paucity of the literature regarding the incidence of various causes of bleeding. Studies have mainly directed to a subgroup such as coagulation disorder, immune thrombocytopenia, and HSP [13-17,19]. We did not come across any study which covers all the causes of bleeding in children and its presentation in different age groups. Hence, this study was planned to give an overview of various causes of bleeding in children and its manifestation in different age groups.

In our study, 92 children presented with bleeding at the time of admission out of which, 73 patients presented with skin, subcutaneous, and joint bleeds. In a study by Naseem et al. among 571 children with pancytopenia or bicytopenia, bleeding was the presenting symptom in 26.6% patient with pancytopenia and 12.1% patients with bicytopenia [20].

Among 9 cases of ITP, 4 presented between 1 and 7 years of age and 5 cases presented after 7 years of age. The most common clinical manifestations were bruises in 6 cases (66.6%), epistaxis in 3 (33.3%), and petechial rashes in 5 cases (55.5%). Similarly, in a study by Alam, records of 95 children between 0 and 15 years suffering from ITP over 10 years period were reviewed. This study found that the mean age at the time of presentation was 6.1±3.8 years and bruises 81 (85.3%), petechial rash 75 (79%), and epistaxis 23 (24%) were the common clinical presentations [19].

Among the coagulation disorders, hemophilia A (81.8%) was the most common coagulation disorder followed by two cases of hemophilia B. The family history was positive in 7 cases (77.78%) of hemophilia A. The incidence of the disease may be high because of our institution is the premier referral center in Haryana. The most common manifestations were epistaxis, gingival bleed, hemarthrosis, and ecchymotic spots. Similarly, in a study by Lakshmi et al. in Andhra Pradesh, 66 diagnosed cases of hemophilia <15 years of age were analyzed. Hemophilia A was seen in 51 (77%) cases and 15 (23%) cases were identified as hemophilia B. Only 49% cases had a family history of bleeding. Hemarthrosis (68%) was the most common problem with which the patients presented. Gum bleeding was the second most common presentation followed by prolonged bleeding after tooth extraction, bruises, and ecchymosis [17].

In our study, among nine cases of HSP, 77.8% of cases presented after 7 years of age. The most common clinical presentation was purpuric rash (8 cases, 88.8%), arthralgia (5 cases, 55.6%), and abdominal pain (3 cases, 33.3%). This is comparable to a study by Lewis, which also showed that this condition is uncommon in children younger than 2 years of age [21]. In a study by Bagga et al., 47 patients were diagnosed to have HSP and the mean age of presentation was 8.5±2.8 years (3-12 years). The presenting manifestations were skin rash (29 cases, 62%), joint pain (10 cases, 21%), and abdominal pain (8 cases, 17%) [15]. In a study by Shahzad et al. in Kashmir, 27 patients (17 males and 10 females) were diagnosed to have HSP. The common clinical features were purpuric rash in 17 (100%), abdominal pain in 18 (66.6%), and arthritis/arthralgias in 16 (59.26%) cases [22].

Vitamin K deficiency is one of the common causes of bleeding in neonatal period [23]. In our study, we found 6 cases of HDN and among them, 3 had classical and 3 had late-onset disease. In a retrospective study by Choo et al., 42 neonates diagnosed to have HDN, and the classical HDN was the most common presentation (48%), followed by early-onset (29%) and late-onset (24%) disease [24].

In our study, the maximum incidence of bleeding in 0-1 month age group was due to infective causes in 10 cases (58.8%), out of which, maximum cases were associated with thrombocytopenia and rest of neonates (17.6%) had HDN. It has been known that the overall prevalence of thrombocytopenia in neonates ranges from 1% to 5% and is reported to be much higher in neonates admitted to NICUs, ranging from 22% to 35% [16,25]. In our study, 47.05% of the neonates had infections thrombocytopenia. Gram-negative bacterial infections were the cause in most of our cases. Out of I7 neonates with bleeding, 7 had septicemia with thrombocytopenia (41.2%) and 2 had thrombocytopenia associated with severe birth asphyxia. This is similar to findings by Oren et al. where they found sepsis as a major factor (43.0%) in neonatal thrombocytopenia [26]. In a prospective study in 200 neonates with thrombocytopenia, the most common neonatal risk factors were sepsis in 48.5% of babies and birth asphyxia in 20% of babies [27]. Hypoxia is common insult in the newborn period and it has been shown that hypoxia can induce neonatal thrombocytopenia [28,29]. Out of three asphyxiated at birth, two had thrombocytopenia and both of them expired. In our study, neonatal thrombocytopenia occurred by day 2 and resolved by day 8. These findings are similar to study by Oren et al. where they found that the thrombocytopenia occurred by day 2 in 43% of neonates and resolved by the day 8 in 61% [26]. Thus, in concordance with other studies, our study thus demonstrated that sepsis, hypoxia, and DIC play an important role in the etiology of neonatal thrombocytopenia [16,30,31].

Our study has few limitations such as we did not evaluate the patients for Von Willebrand disease, platelet function disorders, and rare coagulation disorders, doing this may have altered the results and also this being a single-center study; we should be cautious while extrapolating the results to a large population.

CONCLUSION

Our study found that the gastrointestinal tract is the most common site of bleeding in children presenting with non-traumatic spontaneous bleed, and thrombocytopenia was present in 50% of cases in each age group. We also found that infections are the most common cause of bleeding in younger children while immunological causes and coagulation disorders predominate in older children. Hence, while evaluating any child with bleeding, age at presentation is also an important parameter to find the etiological diagnosis.

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