Original Article

An Experience of Thrombocytopenia in Children at Tertiary Care Hospitals Sukkur and Larkana

1. Bahwaluddin Jamro 2. Aftab Ahmed Soomro 3. Saleh Muhammad Channa 4. Shankar Lal 5. Saifullah Jamro

1. Asstt. Prof. of Paediatrics, GMMMC, Sukkur 2. Asstt. Prof. of Haematology, GMMMC, Sukkur 3. Asstt. Prof. of Medicine, GMMMC, Sukkur 4. Sen. Registrar Paediatric, CMC, Larkana 5. Prof. and Chairman of Paediatric, CMC, SMBBM University Larkana,

ABSTRACT

Background: Thrombocytopenia is the most common cause of bleeding in children. Patients with thrombocytopenia may experience petechiae, epistaxis, gum bleeding, hematuria or gastrointestinal hemorrhage or intracranial bleeding, seizures and unconsciousness.

Objective: To determine the various causes, and clinical features of thrombocytopenia in children.

Study design: Prospective descriptive study.

Place and Duration of Study: This study was conducted at the Paediatric Departments of Shaheed Mohtrama Benazir Bhutto Medical University at Ghulam Muhammad Mahar Medical College Hospital Sukkur and Chandka Medical College Hospital Larkana, from July 2009 to July 2011.

Patients and Methods: This was a prospective descriptive study, include 200 patients1 to 12 year of age, presenting with fever, mucocutaneous bleeding and thrombocytopenia on peripheral smear at both departments. After consent a separate pro-forma was filled for each patient to record demography and data about various causes, clinical presentation and laboratory investigations.

Results: Out of 200 thrombocytopenic patients 128 (64%) were males and 72 (36%) females, majority in age group of under 10 years 154 (77%). The most common cause was the malaria in 50% of cases, followed by ITP 20 (10%), aplastic anemia and thalassemia (hypersplenism) in 7.5% respectively. Dengue fever and Typhoid fever was (5%) of cases. The other minor causes were severe malnutrition, acute leukemia, hemolytic uraemic syndrome 2.5% each. The most common clinical presentation was petechiae and echymosis in 92 (46%), followed by epistaxis and gum bleeding 68 (34%) of cases, subconjuctival hemorrhage in (14%) and hematuria in (08%) of cases. Unconsciousness was present in (9%) of cases. Anemia was found in most of patients (71%). Splenomegaly was present in 79 (39.5%) and hepatomegaly in 59 (29.5%) of patients. Platelets were less than 50,000/cmm in majority (60%) of patients.

Conclusion: The common cause of thrombocytopenia in febrile children was malaria, followed by ITP, Aplastic anemia and thalassemia (hypersplenism), Dengue hemorrhagic fever and enteric fever was less common. The other minor causes were severe malnutrition, acute leukemia, hemolytic uremic syndrome and lymphoma.

Key Words: Thrombocytopenia, mucocutaneous bleeding, Malaria, ITP, Aplastic anemia..

INTRODUCTION

Thrombocytopenia refers to a reduction in platelet count to <150x 10/ L in children. It is the most common cause of bleeding in children[1]. Patients with thrombocytopenia may experience petechiae, epistaxis, gum bleeding, hematuria or gastrointestinal hemorrhage or intracranial bleeding, seizures, unconsciousness. In patients with normal physical examination other than mucocutaneous bleedings the diagnosis of acute idiopathic thrombocytopenia can be made. Immune thrombocytopenia (ITP), formerly known as idiopathic thrombocytopenic purpura, is an acquired bleeding diathesis resulting from premature platelet destruction, reduced platelet production or a combination[2] Primary ITP is defined as isolated thrombocytopenia in the absence of an identified etiology or illness. Secondary ITP assumes the presence of a concurrent underlying disorder responsible for disturbed immune function leading to thrombocytopenia. The estimated incidence of ITP in children is approximately 1.9 to 6.4 cases per 100,000 per year [3] Patient with fever, anemia, splenomegaly or hepatomegaly , lymphadenopathy and thrombocytopenia may have malaria or other systemic infections or/ systemic lupus erythematosus, and malignancy[4]

Thrombocytopenia has been reported to be associated with malaria, with incidence ranging from 40.5%-85% [5, 6] with some studies reporting g a lower incidence in vivax malaria as compared to falciparum[7].A local study from Karachi reports thrombocytopenia in 72% of plasmodium vivax malaria cases [8]. Pancytopenia is a frequently occurring condition in children. It may be a transient event secondary to viral infection like parvovirus B19 or very serious condition like congenital bone marrow aplasia [9] Pancytopenia can also

result from either a failure of production of hematopoietic progenitor cells called aplastic anemia or peripheral destruction of cellular elements either due to infection, immune mediated damage or hyperslenism[10,11.12,13] Dengue hemorrhagic fever is one of the important cause of thrombocytopenia in children occurring in epidemics[14,15].As the list of causes of thrombocytopenia in children is long with varying degree of severity and out come is unpredictable in most of cases and sometimes serious complication can occur without proper management. Therefore this study was planned to find out various causes, and clinical presentation of thrombocytopenia in children.

PATIENTS AND METHODS

All 200 patients 1 to 12 years of age, presenting with fever, mucocutaneous bleeding and thrombocytopenia on peripheral smear at both departments were included. After consent a separate pro-forma was filled for each patient to record demography and data about various causes, clinical presentation and laboratory investigations, including complete blood counts, peripheral smear for malarial parasites by standard thick and thin films, and immunochromatography was used for confirmation of malaria cases .Other investigations to evaluate other causes of fever and thrombocytopenia including blood culture, bone marrow aspiration, antibody titers for dengue virus, prothrombin time, activated partial thromboplastin time, anti-nuclear antibody and anti-double stranded DNA, blood urea nitrogen and serum creatinine and cerebrospinal fluid, X-rays as needed in selected cases. Data was recorded on tabulated sheets and analyzed to find out the percentages of the causes and clinical features and platelets. The patients were managed according to the underlying causes.

RESULTS

Out of 200 cases of thrombocytopenia, 128 (64%) were males and 72 (36%) females, most of patients were in age group under 10 years 154 (77%) in table 5. The most common cause was malaria in 100 (50%) cases, followed by idiopathic thrombocytopenia 20 (10%) cases, aplastic anemia and thalassemia (hypersplenism) 15 (7.5%) respectively. Dengue hemorrhagic fever and enteric fever was 10 (5%) of cases. The other minor causes were severe malnutrition (2.5%), acute leukemia (2.5%), hemolytic uremic syndrome (2.5%) and lymphoma (1.5%), osteopetrosis (1%), DIC (1%), type 11 Von Willebrand disease (1%) as shown in table 1.

Among the malaria cases, the P. Falciparum was the most common species (45%), followed by mixed infection of P. Falciparum and P. Vivax (30%) and P. Vivax (25%) of cases as shown in table 2. The common clinical presentation was petechiae and echymosis in 92 (46%) of cases, followed by epistaxis and gum bleeding 68 (34%) of cases, subconjuctival hemorrahage in 28 (14%), hematuria in 16 (08%), and vaginal bleeding 3 (1.5%) of cases. Unconsciousness was present in 18 (09%) of cases.

Table No.1: Show the underlying causes in cases of febrile illness with thrombocytopenia

Cases	No of cases	%age
Malaria	100	50%
Idiopathic thrombocytopenia	20	10%
Aplastic anemia	15	7.5%
Thalassemia (hypersplenism)	15	7.5%
Dengue fever	10	5%
Enteric fever	10	5%
Severe malnutrition	05	2.5%
Acute leukemia	05	2.5%
Hemolytic uremic syndrome (HUS)	05	2.5%
Systemic lupus erythematosus (SLE)	05	2.5%
Lymphoma	03	1.5%
Osteopetrosis	02	01%
DIC	02	01%
Type 11Von Willebrand disease	02	01%
Meningitis	01	0.5%
Total	200	100%

Table No.2: Type of Plasmodium in Malaria cases with thrombocytopenia.

Plasmodium species	No of cases	%age
Plasmodium falciparum	45	45%
Plasmodium vivax	25	25%
Mixed (P . falciparum + vivax)	30	30%

Table No.3: Clinical features of 200 patients with thrombocytopenia

Clinical feature	No of patients	%age
Petechiae and echymosis	92	46%
Epistaxis and gum bleeding	86	34%
Haematuria	16	08%
Vaginal bleeding	03	1.5%
Subconjuctival hemorrhage	28	14%
Unconsciousness	18	09%
Slenomegaly	79	39.5%
Hepatomegaly	59	29.5%

Table No.4: Platelets count in patients with febrile illness.

Platelet counts (/dl)	No of patients	%age
<10,000	60	30%
>10,000-<20,000	30	15%
>20,000- <50,000	30	15%
>50,000-<100,000	40	20%
>100,000-<150,000	40	20%
Total number	200	100%

The anemia was found in most of patients 142 (71%). Splenomegaly was found in 79 (39.5%) of cases, where as hepatomegaly was found in 59 (29.5%) of patients as shown in table 3. The lymphadenopathy was found in 10 (05%) of patients. The complete blood picture reveal Hb in the range of 4g/dl to 11g/dl, majority of patients had hemoglobin lower than 8g/dl and thrombocytopenia in all cases, but most of patients platelets were less than 50,000 in (60%) of cases as shown in table 4.

Table No.5: Shows age and sex of 200 patients

Age in years	No of patients	%age
1-5 y	82	41%
6-10 y	72	36%
11-12 y	46	23%
Male	128	64%
Female	072	36%

DISCUSSION

Thrombocytopenia is one of the most common hematological disorder in children and had many causes. In our study of 200 cases of thrombocytopenia 128 (64%) were males and 72 (36%) females, similar to the local and international studies[16, 17, 18] Most of patients were in age group under 10 years 154 (77%).The most common cause was malaria in 100 (50%) cases followed by ITP 20 (10%) cases, aplastic anemia and thalassemia (hyperslpenism) 15 (7.5%) respectively. Finding of thrombocytopenia with anemia is an important clue to the diagnosis of malaria in patients with acute febrile illness[19] The thrombocytopenia with malaria was reported (69.18%) higher than our results by Ansari S et at[16], 72% by Jamal A et al [9], 85% by Beale P et al [6, 7].The second common cause was ITP 20 (10%) in our cases while 6.21% was reported by Kibria SG [18] and 15.7% was reported by Khan A et al[20] in his series of hematological diseases. The higher results was reported 32% by Jan MA[21]this is most probably due to selection of patients without fever. Aplastic anemia was the 3rd common cause in our cases 7.5% near to the (10.74%) reported by Kibria SG[18], in contrast to our results others had reported much cases 24% ,20.2%, 20%,14.5% [21, 20, 22, 24] respectively. It is more common in developing countries as compared to the industrialized world [23]. Hypersplenism was found in 7.5% of our cases near to the reported in other local study[21]. Dengue hemorrhagic fever was present in 10 (5%) cases but in contrast to our results 11.11%, and 17.6 % cases reported by Jamal A, et al[9] and Mahmood K et al[14].The other minor causes were severe malnutrition 2.5%, acute leukemia 2.5% hemolytic uremic syndrome 2.5% and lymphoma 1.5% of cases. Jan MA reported in his study acute leukemia 22%, lymphoma 4%, hemolytic uremic syndrome 4% respectively [21]. Among the malaria cases, P. Falciparum was the most common species responsible for thrombocytopenia 45% followed by mixed infection of P. Falciparum and P. Vivax 30% and P. Vivax 25% of cases. Similar to our experience P .falciprum was found most common 69.18% cases of malaria,[16] in contrast to our results Jamal A et al[9] reported 72% thrombocytopenia in cases of P vivax and 11% with P. Falciparum species An other study conducted by Patel U et al reported P. falciparum 47.5% and Pvivax 52.5% of species associated with thrombocytopenia cases respectively[19].

The common clinical presentation was petechiae and echyomosis in 92 (46%) of cases, followed by epistaxis and gum bleeding 68 (34%) of cases, subconjuctival hemorrhage in 28 (14%) of cases, hematuria 16 (08%) and vaginal bleeding in 3 (1.5%) of cases. Signs of bleeding were reported in 24% children and in 23% adults by Kuhne T et at[17]. Jan MA reported in his study that all patients presented with petechiae and ecchymosis, 11(34%) patients came with mild to moderate epistaxis, 9 (28%) with gingival bleeding, 3 (9%) with hematuria, 2(6%) with melaena and one girl came with bleeding per vagina[21].The anemia was found in most of patients 142 (71%) of cases in our series but in 38% patients with acute ITP by Jan MA[21], while Ayub T et al[22] in his study reported anemia in100% of cases aplastic anemia in children. Splenomegaly, hepatomegaly and lymphadenopathy were found 79 (39.5%), 59(29.5%) and in 10 (5%) of patients respectively in our series. Khan A et al[20] in his series of patients with malignancy reported various degrees of splenomegaly (79.2%), hepatomegaly (60.9%) and lymphadenopathy (39.1%) as well. The hemoglobin levels ranges from 4 gram/dl to 11gram / dl, in majority of patients hemoglobin was lower than 8g/dl (71%) and thrombocytopenia in all cases as reported in local literature[21], but most of patients platelets were less than 50,000 in (60%) of cases in our study consistent with the previous observations [16,21]

CONCLUSION

The common cause of thrombocytopenia in febrile children was malaria, followed by ITP, aplastic anemia and thalassemia (hyperslenism), dengue hemorrhagic fever and enteric fever in less common causes. The other minor causes were severe malnutrition, acute leukemia, hemolytic uremic syndrome and lymphoma.

REFERENCES

1. Ambruso DR, Hays T, Goldenberg N. Hematologic disorders in current Pediatric diagnosis and treatment. 18th ed. A Lange medical books. McGraw-Hill;2007.p.860-862.
2. Cines DB, McMillan R. Pathogenesis of chronic immune thrombocytopenic purpura. Curr Op Hematol 2007;14(5): 511-4.
3. Terrell DR, Beebe LA, Vesely SK, Neas BR, Segal JB, George JN. The incidence of immune

thrombocytopenic purpura in children and adults; A critical review of published reports. Am J Hematol 2009; 85(3):174-80.
4. Scott JP, Montgomery RR. Hemorrhagic and Thrombotic diseases. Nelson textbook of Pediatrics. 18th ed. 2007.p.2082-2085.
5. Murthy GL, Sahay RK, Srinivasan VR, et al. Clinical profile of Falciparum Malaria in a Tertiary Care Hospital. JIMA 2000; 98:158-160.
6. Beale P, Cormack J, Oldrey T. Thrombocytopenia in malaria with immunoglobulin (IgM) changes. Br Med J 1972; 1:345-349.
7. Kueh Y, Yoe K. Haematologic alteration in acute malaria .Scand J Hemato 1982;29 :147-152.
8. Srichaikul T, Pulket C, Sirisatepisarn T, et al, Platelet dysfunction in malaria. Southeast Asian J Trop Med Pub Helth1988; 19: 225-233.
9. Jamal A, Memon IA, Lateef F. The association of plasmodium vivax malaria with thrombocytopenia in febrile children. Pak Paed J 2007;31(2) : 85-89.
10. Miron D, Luder A, Horovitz Y, Izkovitz A, Shizgreen I, David EB, et al. Acute human parvovirus B19 infection in hospitalized children. A serologic and molecular survey Pediatr Infect Disease J 2006; 25 :898-901.
11. Lanzkowsky P. Manual of pediatric hematology and oncology. 2nd ed. New York: Churchill Livingstone; 1995.p.77-95.
12. Freedman HM, Hord JD.The pancytopenia. Nelson textbook of Paediatrics 18th ed. 2007.p.2047-2058.
13. Klein-Gitelman MS, Miller ML Systemic Lupus Erythematous. Nelson textbook of Pediatrics. 18th ed. 2007.p.1015-1019.
14. Mahmood K, Jameel T, Aslam HF, Tahir M. Incidence of dengue haemorrhagic fever in local population of Lahore, Pakistan. Biomedica 2009; 23:93-96.
15. Ahmed S, Arif F, Yahya Y, et al. Dengue fever outbreak in Karachi 2006 a study of profile and outcome of children under 15 years of age. J Pak Med Assoc 2008; 58 (1): 4-8.
16. Ansari S, Khoharo HK, Abro A, Akhund IA, Qureshi F. Thrombocytopenia in plasmodium malaria. J Ayub Med Coll Abbottabad 2009; 21(2): 145-147.
17. Kuhne T, Berchtold W, Michaels LA, Wu R, Donato H, et al. Newly diagnosed immune thrombocytopenia in children and adults: a comparative prospective observational registry of the International Cooperative Immune Thrombocytopenia Study group. Haematologica J 2011;96(12):1831-1837.
18. Kibria SG, Islam MDU, Chowdhury AJ, Ali MY, Haque MR, Mustanzid SM, et al. Prevalence of hematological disorder; A bone marrow study of 177 cases in a private hospital at Faridpur. Faridpur Med Coll J 2010;5(1): 11-13.
19. Patel U, Gandhi G, Friedman S, Niranjan S. Thrombocytopenia in malaria. J National Medical Association 2004;96: 1212-1214.
20. Khan A, Aqeel M, Khan TA, Munir A. Pattern of hematological diseases in hospitalized paediatric patients based on bone marrow examination. JPMI 2008; 22(3): 196-200.
21. Jan MA Thrombocytopenia in children. JPMI 2004;18 (3): 353-358.
22. Ayub T, Khan FUR, Mahsud MAJ. Frequency of aplastic anemia in children. G J Med Sciences 2011; 9(1): 62-64.
23. Neal S, Young JL, Abkowitz, Luzzatto L. New Insight into the pathophysiology of Acquired Cytopenias. Hematology 2000: 18-38.
24. Rahim F, Ahmed I, Islam S, Hussain M, Khattak TAK, Bano Q. Spectrum of hematological disorders in children observed in 424 consecutive bone marrow aspirations/ biopsies. Pakistan J of Medical Sciences 2005;21(4):433-436.

Address for Corresponding Author:
Dr. Bahawaluddin Jamro
Assistant Professor of Paediatrics,
Ghulam Muhammad Mahar Medical College Sukkur.
Email Address: drbahawaljamro@gamil.com
Cell no: 03363861772
Fax no: 0719310117