OUTCOME OF IMMUNE THROMBOCYTOPENIC PURPURA IN A TERTIARY CARE CENTRE

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Abstract

Background : The study aimed to demonstrate the pattern of clinical presentations and outcome of Immune Thrombocytopenic Purpura (ITP) in Bangabandhu Sheikh Mujib Medical University (BSMMU) Dhaka.

Materials and methods: A retrospective study was conducted by record reviewing and analyzing the data of 103 patients of acute ITP, ageing between 1-16 years, at the Department of Paediatric Haematology and Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU) Dhaka from June 2017 to December 2019. We reviewed the data regarding age, sex, clinical presentations, history of preceding viral infections, vaccination history, laboratory values, different treatment options used and response to the treatment concerning complete response, partial response and poor responders. Statistical analysis performed by using IBM SPSS statistics version 20.

Results: We retrospectively reviewed a total of 103 patients. The median age, at the time of presentation, was 5±3.4 years while the mean age was 4.5±2.9 years. The male to female ratio was 1.28:1. Mean platelet count on presentation was 7 x 10^9/L (Range: 0-24). Twenty three (22.3%) patients had the history of preceding febrile illness. Bruises, petechiae, epistaxis and hematemesis remained the common presentations. Six (5.8%) patients showed spontaneous recovery while 97 (94%) patients received treatment for ITP. Overall, 71 (68.9%) showed a response after treatment. Sixty-two patients (59.22%) showed loss of response and received treatment again. Among these patients, thirty-four patients (33%) developed chronic disease.

Conclusion: Majority of patients presenting to our tertiary care centre had severe acute ITP on presentation.After management and follow-up, almost one third of the patients develop chronic disease hence the incidence of developing chronic disease remained high as compared to the other centers.

Key words
Immune thrombocytopenic purpura; Treatment outcome; Tertiary care centre.

Introduction

Immune Thrombocytopenic Purpura (ITP) is a common cause of thrombocytopenia in pediatric patients. The typical clinical presentation is of sudden isolated thrombocytopenia and the diagnosis is one of exclusion. ITP in children is in most cases an acute and self-limiting condition that resolves in a matter of weeks or months. Approximately 20% of children continue to exhibit thrombocytopenia beyond 12 months, defining chronic ITP[1-6]. The history of ITP management resonates with controversy. Even in the days of Worloff in the late 18th century, the discussion of whether or not to institute treatment for non febrile purpura was actively debated. Treatment options then included the use of purgatives or venesection, although Worloff himself questioned whether it was necessary[7-10].

Given the variation in the course of untreated cases, side effects, and economic impact, the introduction of each modern-day therapy for acute ITP

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Submitted on : 23.01.2020
Accepted on : 07.02.2020

has been met with mixed sentiment by patients and physicians, as well as health care insurers. Since the condition is often self-limiting, and the threat of life-threatening hemorrhage is rare, the physician may choose between numerous therapeutic options. The principal decision for the treating physician is whether to manage the patient with clinical observation only, or to actively treat the condition. Although ITP is usually a brief and self-limiting illness, there are circumstances where observation with the anticipation of possible hemorrhage is unacceptable to the patient or the physician. The goal of immunomodulatory treatments (To include corticosteroids, IVIG or anti-D) is to temporarily increase the platelet concentration until the autoimmune reaction subsides[4].

Materials and methods

A retrospective study was conducted at the Department of Paediatric Haematology and Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU) Dhaka, Bangladesh from June 2017 to December 2019. We reviewed the record of total 103 patients meeting the inclusion criteria, i.e age between 1-16 years, presented with the diagnosis of acute ITP, did not take any previous treatment and remained on regular follow up over a period of one year. Patients < 1 year old, having chronic ITP on presentation or showing incomplete data were excluded from the study. The institutional review board approved the study. We reviewed the data, keeping in accordance of age, sex, clinical presentations, history of preceding viral infections, vaccination history within 8-12 weeks, seasonal variations, laboratory values, different treatment options used, and response to the treatment in terms of complete response, response and poor responders. Response after initial treatment was measured by platelet count at 48 hours of therapy in case of IVIG, I/V steroids and I/V anti-D, and at two weeks in case of oral steroids. All patients were followed for one year from the time of presentation to find out the number of patients developing chronic disease. Before defining a patient as a chronic disease bone marrow study was done to exclude other bone marrow disease. Statistical analysis performed by IBM SPSS statistics version 20.

Results

The record of 103 patients was reviewed retrospectively during the study period, diagnosed as acute Immune Thrombocytopenic Purpura. The median age, at the time of presentation, was 5±3.4 years while mean age was 4.5±2.9 years. Amongst 103 patients, 58 (56.31%) patients were male while 45 (43.6%) patients were females. The male to female ratio was 1.28:1 (Table I). Mean platelet count on presentation was $7x10^9$/L (Range: 0-24). At the time of presentation, the platelet count did not vary between two sexes ($p>0.05$). Regarding age, the children above 10 years presented with least platelet count (Table-III).

Furthermore, 23 (22.3%) patients had the history of preceding illness, 13 (12.6%) with upper respiratory infections, 9 (8.7%) with acute gastroenteritis and 1 (1.0%) with varicella zoster infection. None of the patients had received vaccinations, prior to developing symptoms of ITP within 8-12 weeks. Bruises, petechiae, epistaxis and hematemesis remained the common presentations. On clinical examination, 92 (89.3%) patients were reported to have bruises, 81 (78.6%) patients with petechiae, 33 (32.0%) with epistaxis, 13 (12.6%) with hematemesis, and five (4.9%) patients with menorrhagia (Table-II). Sixty-two (60.2%) patients were diagnosed by clinical presentations, thirty-two (31.0%) patients after bone marrow examination and nine (8.7%) patients by Immature Platelet Fraction (IPF). Six (5.8%) patients showed spontaneous recovery while the rest of the patients were treated with one or more of the options mentioned above, at one time or more. Overall, 97 (94%) patients received treatment for ITP. Treatment was given only to symptomatic patients with significant bleeding diathesis. Treatment type was based on the severity of symptoms. Patients with severe life threatening active bleed were given combination treatment with IV methylprednisolone, IVIG and platelet transfusion. Oral steroids was 1st line of treatment in stable patients, while IVIG and Anti-D (For rhesus positive patients) was a 1st line treatment for patients with active bleed admitted through emergency. A total of 32 (31.1%) patients received IVIG, 30 (29.1%) received oral steroids while 22 (22,3%) I/V steroids, 5 (4.9%) received both I/V steroids and IVIG, and 8 (7.8%) received anti D (Table- IV).

Table I : Distribution of age and mean platelet count at presentation (n=103).

Age group	Male	Female	Mean platelet count(109/L)
12 month – 5years	30 (29.1%)	22 (21.3%)	09
>5 years – 10 years	21 (20.3%)	17 (16.5%)	13
>10 years – 16 years	07 (6.7%)	06 (5.8%)	07
Total	58 (56.3%)	45 (43.6%)	

Table II : Clinical features of patients at presentation.

Clinical features	No. of patients n (%)
Bruises	92(89.3%)
Petechiae	81(78.6%)
Epistaxis	32(33%)
Hematuria	13(12.6%)
Melena	3(2.9%)
Menorrhagia	5(4.9%)
ICB	1(1%)

Table III : Platelet counts on presentation (n=103).

Platelet counts(10^9/L)	No. of patients n (%)
<10000	43(41.7%)
10000-20000	42(40.8%)
>20000	18(17.5%)

ICB= Intracranial Bleeding.

Table IV : Treatment given to ITP patients and Response (n=103).

Treatment	Patient received treatment n (%)	Patient response shownn (%)
IVIG	32(31%)	24(75%)
Methylprednisolone	22(21.4%)	16(72.7%)
Oral steroid	30(29.1%)	23(76.7%)
Anti-D	8(7.8%)	3(37.5%)
Combination therapy	5(4.9%	5(100%)
No treatment	6(5.8%)	

Overall, 71(68.9%) showed a response after treatment where all patients followed up clinically and with their platelet counts for a total of 12 months. Follow up was initially weekly after an acute episode to document response/no response and later on monthly basis for loss of response. Sixty-two patients (59.2%) showed relapse of thrombocytopenia and received treatment again. Among these patients, 34(33%) patients developed chronic disease. Most of the patients (n=9, 70%) from the age group 10-14 years did not achieve remission at the end of one years. Interestingly, age above 10 years was observed to play a significant role in developing chronicity of the disease ($p<0.05$). Besides, female patients above 10 years showed higher risk of developing chronic ITP than male patients ($p<0.05$). However, after exclusion of patients above 10 years, the incidence of developing chronic disease was found to be similar between two genders ($p>0.05$).

Discussion

Regarding the epidemiological data of acute ITP, the results varied from previous studies. In our study, the boys out numbered the girls where another two study observed female predominance in patients with acute ITP[12,13]. Vast majority of our patients presented had a clinically significant bleeding that warranted medical treatment while a large study group reported that more than half of the patients had no or only mild bleed[14]. A reason might be that acute ITP is also treated by general pediatricians and only complicated cases are referred to Pediatric hematologist/oncologists. Our data was collected at a tertiary care center and thus shows complicated initial presentation for this cohort.

In our study, preceding viral illness found in only 22% patients while a study in China demonstrated the history of viral illness in 74% patients[15]. This marked difference can probably be due to poor historians or the fact that people in low-income countries like Bangladesh do not register minor viral illnesses and frequently overlook them.

We observed that more than half of our patients (60.2%) were diagnosed by clinical features only (Bone marrow aspiration, biopsy or immature platelet fraction not done) and follow up of those patients over a period of one year showed no change in the diagnosis. Bone marrow biopsy does not seem to be mandatory for the diagnosis of acute ITP and this matches with the general British and American guidelines and conclusions of other studies[16,17].

In our study, children above 10 years presented with severe thrombocytopenia. Five such patients received combination therapy (I/V Methylprednisolone and IVIG). A combination therapy given to 11.6% of the patients in a study (I/V Methylprednisolone and IVIG) recommended it for older

children of acute ITP. While in our study, only 5 (4.9%) patients received both the drugs simultaneously. All these patients, who received combination therapy showed a response after initial treatment but 12 months follow up revealed that only 40% achieved complete remission. We observed two factors; age above 10 years and female gender which play significant role in developing chronic ITP, which is similar to the results of other study[18]. In our study, among 103 patients, 34 (33%) patients developed chronic disease and all patients undergo bone marrow study before defining as a chronic disease, while in another study, 36 (14%) patients showed chronic disease[19]. Similarly in another study, out of 95 children, only 5 (5.3%) patients developed chronic ITP[12]. The high rate of chronicity might be due to complicated initial presentation, as suggested by another study, female gender, older age at presentation absence of preceding infection or vaccination were identified as risk factors for developing chronic ITP[20]. However this warrants further investigation.

Some studies published in literature show significant association of Acute ITP with MMR vaccination[21]. In our study, none of the patients had a history of receiving vaccines in last 8 to 12 weeks. Studies conducted in five health care systems, on 197 cases of ITP also reported that there is no significant increase in the risk of developing ITP after early childhood vaccines. While a systematic review of 12 studies showed that post MMR vaccines ITP is a rare phenomenon, reporting only 2.6 cases per 100,000 vaccines doses[22]. Besides, all these cases presented in a milder form showing a self-limiting pattern. Having discussed these results and keeping in view the high risk of developing infections, which are preventable with these vaccines, association of ITP with the childhood vaccines should not be used as a reason for limiting the use of vaccines in a developing country like Bangladesh, thus supported by the conclusion of other study[22].

Our study shows varied presentation, male predominance without significant preceding history of viral infection or vaccination. However this is a single center study carried out in a tertiary care referral center. Collaborative groups and national guidelines do not exist in Bangladesh to manage ITP in children, which are much needed. Multicenter, prospective randomized control trials are needed, using standardized management protocols, involving large cohort of patients to evaluate exact disease behavior in our country.

Conclusion

Majority of patients presenting to our tertiary care centre had severe acute ITP on presentation. After management and follow-up, almost one third of the patients develop chronic disease hence the incidence of developing chronic disease remained high as compared to the other centers. Pediatric ITP diagnosis is mainly clinical and initially does not require bone marrow aspiration or biopsy for confirmation. Further prospective studies are required to identify different risk factors and to compare the results of different treatment options in use.

Limitations

Some limitations of our study included retrospective study in nature and small sample size, a large-scale cohort prospective study is required to confirm our findings.

Recommendation

A significant number of patients may develop chronic disease in spite of getting 1st line treatment. Bone marrow study is recommended before defining a patient as a chronic disease for exclusion of other bone marrow disease.

Acknowledgment

To patients, patients guardians, doctors and OPD staff of Department of Paediatric Haematology and Oncology, BSMMU, Dhaka.

Contribution of authors

ATMAR-Conception, design, drafting & final approval.

AKMRK-Acquisition of data, critical revision & final approval.

MB-Acquisition of data, drafting & final approval.

TC-Acquisition of data, interpritation of data & final approval.

CHK-Data analysis, drafting & final approval.

MHI-Acquisition of data, interpritation of data & final approval.

KAS-Data analysis, critical revision & final approval.

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Disclosure

All the authors declared no competing interest.

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