Evaluation of Prognostic Factors in Newly Diagnosed Childhood Primary Immune Thrombocytopenia (ITP): Two - Year Prospective Study at Al-Sadder Hospital, Missan Province

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Abstract

Background: Primary immune thrombocytopenia (ITP) is a common benign bleeding disorder in childhood. It generally presents with the sudden appearance of bruising, bleeding, or petechiae in an otherwise healthy child, often after a preceding viral illness.

Objective: Study the presenting socio demographic, clinical and laboratory features, and types of treatment of newly diagnosed children with ITP, and to determine their effects on the course, and outcome of the disease.

Materials and Methods: This is a prospective study. The presenting features and types of treatment for 25 children with newly diagnosed ITP admitted to the pediatric ward of AL-Sadder Hospital, Missan / Iraq, between 1st of December 2009 and 1st December 2011, were evaluated to determine their prognostic significance on the course of the disease. The patients were followed up for at least 6 months.

Rsultes: The presenting features of 25 children with newly diagnosed ITP were analyzed. At diagnosis ITP was more prevalent in males (64%) with male: female ratio 1.7: 1, 1-5-year group (60%), and urban residency (60%) children. It was commonly occurred in spring (44%), and nadir in autumn (12%), with preceding history of acute viral illness (76%). ITP was commonly presented as sudden onset of petechiae and/or bruising (92%), with initial platelet count less than 20 x 10^9/L (84%). Among studied children, (72%) had a favorable outcome and followed an acute course, while (28%) developed chronic ITP. Univariate analysis was demonstrated that, only onset of the disease and history of preceding acute viral illness were significantly affecting the course of ITP. Gradual onset of symptoms and absence of history of preceding acute viral illness correlated with a chronic course of ITP. Intravenous immunoglobulin (IVIG) was commonly used (60%), and mode of treatment had no significant effect on the clinical course of ITP.

Conclusion: Childhood ITP has a favorable outcome. Only a small number of children go on to develop chronic phase.Among initial presenting features, only gradual onset of symptoms and absence of history of preceding acute viral illness correlated with a chronic course of ITP. Future large prospective studies are recommended to confirm our results.

Key wards: Childhood immune thrombocytopenia, prognostic factors.

تقييم عوامل التكهُن في ندرة الأقراص الدموية المناعي الأولي: سنتان من الدراسة التقدمية في مستشفى الصدر / محافظة ميسان

الخلاصة

المقدمة: ندرة الأقراص الدموية المناعي الأولي من الاضطرابات ألنزفيه الحميدة الشائعة في الطفولة. هو عامة يتقدّم بظهور مفاجئ للكدمات ، نزف،أو نزف تحت الجلد في ما عدا ذلك الطفل صحي، وغالبا" بعد مرض فيروسي.

الهدف: دراسة الصفات الاجتماعية – السكانية ، ألسريريه والمختبرية، وأنواع العلاج للأطفال المشخَصين حديثا" بندرة الأقراص الدموية المناعي ، وتحديد تأثيرها على سياق المرض.

المواد والطرق: هذه دراسة تقدمية . العلامات التقدمية وأنواع العلاج ل 25 طفل مشخَص حديثا" بندرة الأقراص الدموية المناعي الداخلين لردهة الأطفال في مستشفى الصدر ، محافظة ميسان– العراق ، للفترة بين الأول من كانون الأول 2009 والأول من كانون الأول ٢٠١١، قيمت لتحديد أهميتها التكهُنية على سياق المرض. المرضى توبعوا لحد أدنى ٦ أشهر.

النتائج: العلامات ألتقدميه ل 25 طفل مشخص حديثا" بندرة الأقراص الدموية المناعي تم تحليلها. في وقت التشخيص ندرة الأقراص الدموية المناعي كانت أكثر شيوعا" في الذكور (64%) مع نسبة الذكور : الإناث1,7 :1، المجموعة العمرية 1–5 سنوات (60%)، والسكن الحضري (60%). المرض أكثر حدوثا" في فصل الربيع (44%) ونادرا في الخريف (12%) ، مع تاريخ مسبق لأمراض فيروسية حادة (76%). ندرة الأقراص الدموية المناعي يتقدم بصورة شائعة كظهور مفاجئ لنزف تحت الجلد، مع / أو كدمات (92%)، مع عدد ابتدائي للصفائح الدموية أقل من 20,000 ملم مكعب (٨٤%). بين الأطفال المدروسين (72%) لهم نتيجة مفضّلة واتبعًوا سياق حاد، بينما (28%) تطوّروا إلى ندرة الأقراص الدموية المناعي المزمن.

التحليل ألآحادي بينً أنً فقط بداية المرض، وتاريخ مسبق لمرض فيروسي حاد لهما تأثير هام على سياق المرض .البداية التدريجية للأعراض، وغياب التاريخ المسبق لمرض فيروسي حاد يترافقان مع سياق مزمن لندرة الأقراص الدموية المناعي. الامينوكلوبيولين الوريدي كان المستخدم شيوعا"(60%)، ونمط العلاج ليس له تأثير هام على السياق ألسريري لندرة الأقراص الدموية المناعي .

الاستنتاج: ندرة الأقراص الدموية المناعي الطفولي يمتلك نتيجة مشجعة. في عدد قليل فقط من الأطفال يستمر إلى الطور المزمن. ما بين الصفات المتقدمة الأولية ، البداية التدريجية للإعراض وغياب التاريخ المسبق لمرض فيروسي حاد يترافقان مع سياق مزمن لندرة الأقراص الدموية المناعي. نوصي بدراسات تقدمية كبيرة مستقبلية لدعم نتائجنا.

Introduction

Primary immune thrombocytopenia commonly encountered in clinical practice characterized by isolated thrombocytopenia in the absence of any obvious initiating or underlying cause[1-3]. Childhood ITP generally presents with the sudden appearance of bruising, bleeding, or petechiae in an otherwise healthy child, often after a preceding viral illness.[4]

Immune thrombocytopenia and its most widely accepted abbreviation, ITP, has variably been defined as ‘‘immune thrombocytopenic purpura,’’ ‘‘idiopathic thrombocytopenic purpura,’’ and, most recently, ‘‘immune thrombocytopenia.’’[5]The new terminology reflects the current understanding of the immune mediated nature of the disease and the absence or minimal signs of bleeding in most cases [2-4]

Immune thrombocytopenia was believed to be caused by increased platelet destruction at a rate that exceeded production by a compensating bone marrow. New knowledge has questioned this model, providing evidence that platelet production is also decreased in many patients with ITP.[6] ITP may occur in isolation (primary) or in association with other disorders (secondary). The term secondary ITP refers to immune-mediated thrombocytopenia that are due to an underlying disease or to drug exposure.[2, 3]

Unfortunately, definitions and clinical criteria for ITP have varied

among studies. Nevertheless, most ITP patients could easily be classified using the 2009 international working group (IWG) criteria.[7]The platelet count now used to define cases of ITP is less than $100x10^9$/L.This threshold preferred to the more commonly used level of less than $150x10^9$/L,rendering patients with platelet counts between 100,000 and $150x10^9$/L as ‘‘normal’’ or without a diagnosis.[2,7]The IWG also defines ITP as newly diagnosed (within 3 months from diagnosis), persistent (3 to 12 months from diagnosis), or chronic (lasting for more than 12 months).[2] It is important to note that these definitions have not been formally validated, and that they may not apply to patients with secondary forms of ITP, and the utility of using IWG criteria within prospective trials remains to be determined.[1,7]

The diagnosis of ITP can be made based on two criteria: 1) isolated thrombocytopenia with otherwise normal blood counts and peripheral blood smear and 2) no clinically apparent associated conditions that may cause thrombocytopenia.[4] There is no “gold standard” test that can reliably establish the diagnosis.[3] Traditionally a bone-marrow aspirate (BMA) was routinely performed. [8] Evidence has now confirmed that BMA is rarely needed at presentation but must be reconsidered in the presence of excessive or persistent bleeding despite a platelet count $>20\times10^9$ /L, failure to respond to treatment or persistent disease.[1,3,4,8,9]Testing for antinuclear antibodies is not necessary in the evaluation of children with suspected ITP.[1,4,10]

For children with an established diagnosis of ITP, hospital admission should be reserved for those who have clinically significant bleeding.[3] The goal of all treatment strategies for ITP in children, or in adults, is to achieve a platelet count that is associated with adequate hemostasis, rather than a “normal” platelet count.[1, 2, 4, 8, 11]

The majority of children with newly diagnosed ITP lack significant bleeding symptoms and may be managed with observation alone regardless of platelet count.The decision to manage with observation alone requires a detailed discussion with the family about health-related quality of life, medication side effects and efficacy, and anticipatory guidance about preventing and monitoring for bleeding.It is necessary to treat all children with severe bleeding symptoms and treatment should also be considered in children with moderate bleeding or those at increased risk of bleeding.For pediatric patients requiring treatment, a single dose of intravenous immunoglobulin (IVIG) or a short course of corticosteroids or intravenous anti-D immunoglobulin in Rh-positive, non splenectomized children be used as first-line treatment.[1,3] When moderate-to-severe thrombocytopenia is recognized, implementing reasonable precautions to minimize bleeding risk is recommended. These steps include trauma precautions and avoidance of

medications that have antiplatelet or anticoagulant activity.[3, 4]

Intracranial hemorrhage (ICH) is the most devastating complication of childhood ITP and the primary cause of death, [12 – 14] and prevention of ICH is the primary goal of ITP treatment. However, the great majority of patients with ITP, even those with very low platelet counts, do not experience severe bleeding, [13]and ICH occurs in less than 1 in 100 children with ITP.[4,14–18] Risk factors for ICH in children with severe thrombocytopenia include head trauma and concomitant use of medications that adversely affect platelet function.[3]

Aim of the study

This study is designed to:

1. Determine the presenting features, clinical characteristics, and pattern (acute / chronic) of immune thrombocytopenia (ITP) among studied children.
2. Determine prognostic factors that could predict the disease course at diagnosis.
3. Evaluate treatment types and outcome in childhood ITP.

Material and Methods

This prospective study was conducted from first of December 2009 to first of December 2011. All 25 children below 15 years of age, with newly diagnosed immune thrombocytopenia (ITP), admitted to the pediatric ward in Al-Saader Hospital, Missan Province, were included. The patients were diagnosed, treated and followed up closely.The patients have followed up period for at least 6 months and median duration of follow- up was 10 months (range 6 – 24 months).

An especially designed questionnaire was used to collect initial socio demographic, clinical and laboratory data of the studied children at diagnosis. The initial data of patients like, gender, age, residence,season of occurrence, onset of symptoms, preceding acute viral illness within 6 week before presentation, platelets count, site of the bleeding, and types of treatment were recorded. The medical records of studied patients were reviewed to determine the disease course.

The diagnosis of ITP was determined based on detailed history, physical examination; a complete blood count revealing isolated thrombocytopenia (platelet count < 100×10^9/L), normal hemoglobin concentration, white blood cell count and peripheral blood smear, and absence of underlying conditions and malignancy cases were also considered as inclusion criteria. Blood counts were done by a Coulter Analyzer. Bone marrow aspiration was performed in all children presenting with typical features of acute ITP, mainly to rule out other causes of thrombocytopenia.Chronic ITP was defined as thrombocytopenia (platelet count < 100×10^9/L) persisting for longer than 6 months after diagnosis of acute ITP.We investigated possible correlation between the initial clinical and laboratory features, and types of treatment with event of chronicity of the

disease. Fisher's exact test was used for analysis of the effect of variables on this disease, P value less than 0.05 regarded to be significant. The statistical analysis had been done by using SPSS version 16.

Results

There were a total of 25 pediatric patients who met the criteria of acute primary ITP during the study period. Their socio demographic, clinical and laboratory data, and types of treatment are described in Table 1.

Immune thrombocytopenia was more common among males (64%, 16 patients) than females (36%, 9 patients), with male to female ratio was 1.7:1.

The patients age range was between 1 – 15 years, with median age = 4.8 years, and mean age at diagnosis of 5.9 years (SD = 3.6). ITP was more prevalent among children in the 1-5-year group. About two thirds of the patients (60%, 15 patients) were in this age group, followed by children in the 6-10-year group (24%, 6 patients).

About two thirds of patients (60%, 15 patients) that diagnosed with ITP were lived in urban area. Higher number of newly diagnosed ITP occurred in spring (44%, 11 patients), followed by winter (24%, 6 patients), and lowest occurrence was reported in autumn (12%, 3 patients). About three quarters of patients (72%, 18 patients) were presented initially as abrupt onset. A total of 19 (76%) of the cases had an acute viral illness within 6 weeks of ITP onset. These illness included mainly (72%, 18 patients) upper respiratory tract infections, and only one case (4%) chicken pox.

The mean platelet count at diagnosis was 13.200 $x10^9$/L (range 5 – $50x10^9$/L) and the median value was 10 $x10^9$/L. At initial presentation, the majority of patients (84%, 21 patients) presented with platelet count below $20x10^9$/L, and only (4%, 1 patient) presented with count 50 $x10^9$/L.Clinical features of bleeding were assessed by location (skin, nose, oral cavity, gastrointestinal tract, and urinary tract).Petechiae and/or bruising were the most common (92%, 23 patients) clinical features among children diagnosed with ITP followed by epistaxis (44%, 11 patients) and oral bleeding (32%, 8 patients). Other bleeding sites such as from gastrointestinal tract (20%, 5 patients) and urinary tract (4%, 1 patient) are less common.None of the patients developed intracranial hemorrhage (ICH) at diagnosis or during follow – up period. (Figure 1).

All of newly diagnosed ITP children were admitted to the hospital, and majority of patients (96%, 24 patients) were received at least 1 medication for their ITP. Of those who received medication, 15 patients (60%) were treated with intravenous immunoglobulin (IVIG), 6 patients (24%) were treated with oral steroid, and 3 patients (12%) received both medications. One patient (4%) was treated conservatively by observation alone after discussion with the family because he had mild bruising with

platelet count 50 x109/L at presentation. Supportive care was provided in the form of tranexamic acid to 16% (4 patients) of all the children, including 2(8%) patients with epistaxis in addition to nasal package, and 2(8%) patients with gingival bleeding. None of the patients underwent splenectomy at diagnosis or during follow – up period.

Table 1 Socio demographic, clinical and laboratory characteristics of children with ITP

Variables	Acute ITP No. (%)	Chronic ITP No. (%)	Total No. (%)	P value
Gender				0.49
Male	12 (75)	4 (25)	16 (64)	
Female	6 (66.67)	3 (33.33)	9 (36)	
Age/ Years				0.48
1-5	12 (80)	3 (20)	15 (60)	
6-10	4 (66.67)	2 (33.33)	6 (24)	
11-15	2 (50)	2 (50)	4 (16)	
Residence				0.6
Urban	11 (73.33)	4 (26.67)	15 (60)	
Rural	7 (70)	3 (30)	10 (40)	
Season				0.92
Winter	5 (83.33)	1 (16.67)	6 (24)	
Spring	8 (72.73)	3 (27.27)	11 (44)	
Summer	3 (60)	2 (40)	5 (20)	
Autumn	2 (66.67)	1 (33.33)	3 (12)	
Onset				0.006
Abrupt < 1 week	16 (88.89)	2 (11.11)	18 (72)	
Gradual >2 weeks	2 (28.57)	5 (71.43)	7 (28)	
Acute viral illness within 6 weeks				0.032
Yes	16 (84.21)	3 (15.79)	19 (76)	
No	2 (33.33)	4 (66.67)	6 (24)	
Platelet count(x10^9/L)				0.5
< 10	6 (66.67)	3 (33.33)	9 (36)	
10 – 19	10 (83.33)	2 (16.67)	12 (48)	
20 – 49	2 (66.67)	1 (33.33)	3 (12)	
50 – 100	0 (0)	1 (100)	1 (4)	
***Site of bleeding**				0.348
Cutaneous(Petechiae and/or bruising)	17 (94.44)	6 (85.71)	23 (92)	
Oral	3 (16.67)	5 (71.43)	8 (32)	
Nasal	7 (38.89)	4 (57.14)	11 (44)	
Gastrointestinal tract (GIT)	3 (16.67)	2 (28.57)	5 (20)	
Urinary tract	1 (5.56)	0 (0)	1 (4)	
Treatment				0.99
Steroid	4 (66.67)	2 (33.33)	6 (٢٤)	
1VIG	11 (73.33)	4 (26.67)	15 (60)	
Steroid + IVIG	2 (66.67)	1 (33.33)	3 (12)	
Observation	1 (100)	0 (0)	1 (4)	
Total	**18 (72)**	**7 (28)**	**25 (100)**	

ITP = Immune thrombocytopenia; IVIG = Intravenous immunoglobulin.
*Percentage do not added to 100% because some children presented with ≥ 1 bleeding site.

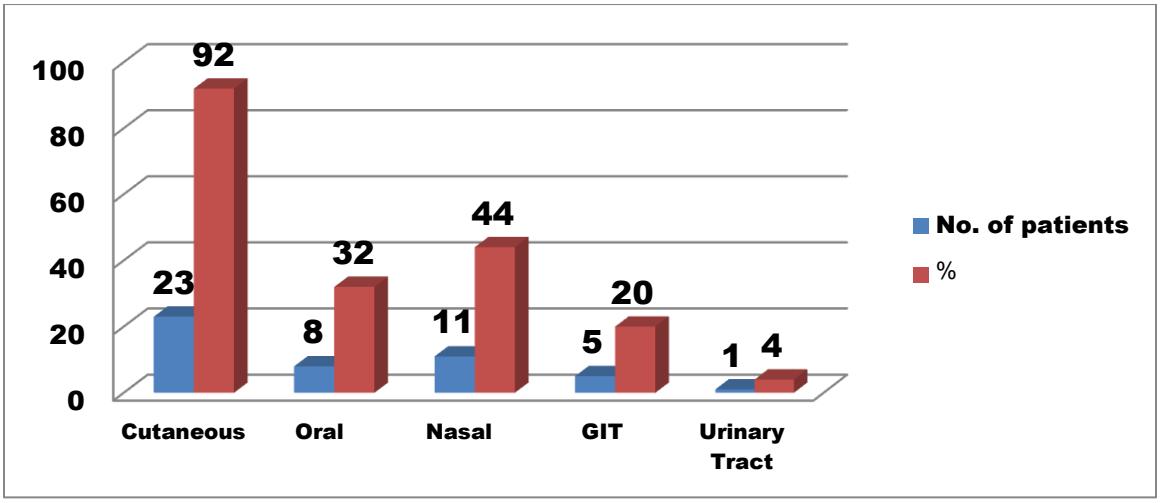

Figure 1 Distribution of patients with ITP according to site of bleeding at presentation.

Follow- up

Among the 25 patients admitted with newly diagnosed ITP, 7(28%) developed chronic ITP during follow – up period. On univariate analysis, onset of symptoms at diagnosis, and prodromal viral illness within six weeks of presentation were associated with disease outcome.

Three quarters (75%, 12 patients) of male patients have acute ITP, while one third (33.33%, 3 patients) of female patients had developed chronic ITP, so gender of patients was not significantly affecting the course of ITP (p=0.49).

Age of the patient had no significant affect for the development of chronicity in ITP. As greater proportion of children with acute ITP was occurred in the 1-5-year group (80%, 12 patients) and in the 6-10-year group (66.67%, 4 patient), while half of cases in the 11-15-year group was developed chronic ITP, so this result was not significant (P=0.48). Chronic ITP occurred nearly an equal distribution among patients lived in rural (30%, 3 patients) and urban areas (26.67%, 4 patients), so residency of patients was not significantly associated with high risk for progression into chronic ITP (P= 0.6).

The seasonal occurrence of newly diagnosed ITP was not significantly affecting the course of the disease. As highest number of cases that registered in winter (83.33%, 5 patients) and in spring (72.73%, 8 patients) were followed an acute course, and one third of cases (33.33%, 1 patient) that reported in autumn was progressed into chronic disease (P=0.92).

As greater proportion of patients (71.43%, 5 patient) that developed chronic ITP had gradual onset of symptoms at diagnosis, in comparison to acute ITP group most of them (88.89%, 16 patients) had sudden onset, we found that onset of bleeding symptoms at initial diagnosis significantly affect the course of ITP (P=0.006).

The history of preceding an acute viral illness was highly affect the course

of disease, among chronic ITP two thirds of patients (66.67%, 16 patients) have no history of preceding an acute viral illness within 6 weeks before the diagnosis, while higher number (84.21%, 16 patients) of acute ITP children had such history, and this result was significant (P=0.032).

There was no significant relationship between platelet count at presentation and disease progression toward the chronic phase, about one third of patients in both groups of platelet count < 10 x109/L (33.33%, 3 patients), and platelet count between 20 - 49 x109/L (33.33%, 1 patient) developed chronic ITP (P=0.5).

The cutaneous bleedings either in the form of petechiae and /or bruising were the most common bleeding site in both acute and chronic ITP, (94.44%, 17 patients) and (85.71%, 6 patients) respectively, while the oral (71.43%,5 patients), nasal (57.14%, 4 patients), and gastrointestinal tract (28.57%, 2 patients) bleedings were most common in chronic ITP than the acute form(16.67%, 3 patients; 38.89%, 7 patients; and 16.67%,3 patients respectively) and this result reflected that the location of bleeding at initial presentation of ITP was not affect the course of disease (P = 0.348).

Highest number (73.33%, 11 patients) of IVIG treated group, and two thirds in each steroid (66.67%, 4 patients) and IVIG with steroid (66.67%, 2 patients) treated groups were have followed an acute course, so initial treatments was not significantly influence the course or phase of the disease (P =0.99).

Discussion

This prospective study allowed to evaluate the presenting socio demographic, clinical and laboratory features, and types of treatment of newly diagnosed children with immune thrombocytopenia (ITP) ,who were admitted to and treated in the pediatric ward of AL-Sadder Hospital, Missan Province , and to assess their effects on the course of disease.

Of 25 children with newly diagnosed ITP followed- up closely, 7(28%) have persistent platelet count < 100 $x10^9$/L, and regarded as chronic ITP.The rate of chronic ITP found in this study is similar to the rate expected for children below 15 years of age (20 – 30%),[3, 4, 15, 19 -26] but it is higher than the rate reported in Turkey by Koçak et al (16%),27and lower than that observed in UK by Grainger et al (32%),[8] Qatar by Al-Mulla et al (38%),[28]and Kuwait by Zaki et al (31.66%).[29]

Among newly diagnosed children with ITP, there was slight males predominance with male / female ratio 1.7/1, which is similar to that reported in literatures, [28, 30-34] while Grainger et al found that, there was a predominance of boys in the children up to 5 years old and a predominance of girls over 5 years.[8] Zeller et al,[15]and Kühne et al,[35] mentioned that the male /female ratio decreasing from infancy into adolescence, but some studies reported

that the gender distribution was equal among children with ITP.[19, 20, 27] However Zeller et al, found slight female predominance in children with female/ male ratio 1.2/1.[36] Reasons for the observed high proportion of males in childhood ITP remain unknown.[37,38] In present study there was no significant relationship between the gender of patient and disease progression towards chronic phase. Our data supported and confirmed by some previously reported observations,[4,19,20,34,39,40] but other studies have been suggested that girls are at increased risk for developing chronic ITP.[21,25,31,41- 43]

In our study, the patients age range was between 1 – 15 years, with median age = 4.8 years, and mean age at diagnosis of 5.9 years. ITP was more prevalent among children in the 1-5-year group (60%) which is similar to that reported by others. [4, 8, 21, 22, 27, 28,31] Age of the patient at presentation had no effect on the course of ITP, as greater proportion of children with acute ITP occurred in the 1-5-year group (80%), while half of cases in the 11-15-year group was developed chronic ITP, so this result was not significant, and it is similar to that mentioned by some studies. 20,28,39 Other studies reported larger proportion of pediatric ITP patients with persistent or chronic disease in older age group.[3,4,19, 22, 23, 25,27, 31,35,37,38, 43]

In present study, residency of patients was not significantly modified the course of the disease, and this result is not documented in the reviewed literatures.

There was a seasonal variation noticed in this study, higher number of newly diagnosed ITP registered in spring (44%) and lowest occurrence was reported in autumn (12%), this result is similar to that reported by Kühne et al.[37] In Egyptian study by Kalifa et al, reported that most case of ITP presented in winter and spring,[23] while in Qatar study by Al-Mulla et al, reported higher number in winter and summer with equal frequency.[28] No significant seasonal occurrence was observed in this study, as most cases that registered in winter (83.33%) and in spring (72.73%), were followed an acute course, and one third of cases (33.33%) that reported in autumn was progressed into chronic disease (P=0.92), and this result is confirmed by other studies.[19,22, 28,29, 44] In contrast, Kühne et al, reported a peak in occurrence of childhood ITP during spring and a nadir in autumn.[37] While Zellar et al, showed that there were seasonal variations with sudden onset ITP and little seasonal variation in the insidious onset ITP which ran a chronic course in more than half the cases.[15]

Most of newly diagnosed ITP children presented as sudden onset of symptoms (72%), and although the sudden onset of bleeding is alarming to parents and primary physicians,but sudden acute bleeding symptoms are more likely to bring the child to diagnosis, in present study, abrupt onset had a favorable outcome, and it was

more significantly associated with acute ITP (88.89%) than with chronic ITP (28.57%), this result support findings that insidious onset of symptoms was predictor of chronic ITP, [3,4,15,19,28, 37, 43,45,46] but, it is not comparable to that reported in Saudi Arabia by Al Fawaz, who reported that no correlation in Saudi patients with ITP between duration of symptoms prior to presentation and outcome of the disease.[34]

The majority of patients (76%) with newly diagnosed ITP in present study had history of recent acute viral illness within 6 weeks prior to presentation, and preceding viral infection was common in acute ITP. The most common type of infections was upper respiratory infection, as it is generally thought that most childhood ITP diagnosed with acute ITP were previously in good health and that the disease develops following an acute nonspecific viral infection in 45-75% of acute childhood ITP or immunization.[4, 8, 10, 15, 19, 20, 21, 23, 24, 27, 28, 32, 38,44, 46 – 48] However, Yong M et al, reported lower proportion of ITP patients with preceding infection (20.2%), but the most common type of infection was upper respiratory infection.[31]This high incidence of preceding infection in present study mostly because of the majority of cases who had an ITP diagnosis following an infection was diagnosed in winter and spring. One patient (4%) with newly diagnosed ITP had history of chickenpox within 6 week before the diagnosis, and followed an acute course with good response to treatment, as the study by Hashemi et al, who reported that 2/66 infants (3%) have a history of chickenpox in recent month.[48]An infectious prodrome within 6 weeks of diagnosis was important favorable prognostic variable in this study and this result is in agreement with previous observations, [19,20,23,27] but studies in Kuwait by Hijazi et al,[24] and Qatar by Al- Mulla et al,[28] found no significant association between the preceding viral illness and the course of the disease.

At initial diagnosis, the mean platelet count was 13.200 $x10^9$/L, and the majority of patients (84%) presented initially with platelet count below 20 $x10^9$/L, this value is probably due to patients who have platelet count less than 20 $x10^9$/L are much more likely to bleeding, and bringing a child to medical attention, this finding is similar to that reported in literatures.[4,8,13,15, 19, 20,27,28, 30,37, 38,41,46] Initial platelet countin this study was not significant factor for prediction of disease outcome, which is in accordance to AL-Mulla et al study,[28] but is not similar to the results observed by Shahid et al,[20] and Watts.[22] However, Glanz et al, reported that no significant association between the mean presenting platelet count and the course of the disease, but demonstrated that both age and presenting platelet count modified the risk for progression to chronic illness. Patients who received the diagnosis after 10 years of age and had platelet counts

>20 x 10^9 /L were at particularly high risk for developing chronic ITP, and the risk continued to increase with progressively higher platelet counts.[19] Al Fawaz reported that, the platelet counts at four weeks and three months after diagnosis were found to be a significant factor for prediction of chronicity of ITP. If the platelet counts are less than $100x10^9$/L during these periods, the risk of chronic ITP is increased and vice versa.[34]

Bleeding manifestations (any site) were observed more frequently in children than in adults.[30]In present study, skin hemorrhagic symptoms were the most common initial clinical features among children diagnosed with ITP followed by epistaxis and this result is similar to that observed in other studies. [8, 10, 19, 21, 27, 28, 30 ,43, 48] Although most patients presented initially with petichiae, bruises and some mucosal bleeding from nose, mouth, gastrointestinal and urinary tracts, the site of hemorrhagic manifestation was not significantly predict the course of disease, and this result is confirmed by observation in Qatar by Al-Mulla et al,[28] but Glanz et al reported that, the presence of mucosal bleeding symptoms at diagnosis were inversely related to the risk for development of chronic ITP.[19] Grainger et al found that, the number of bleeding sites at presentation correlates with bleeding severity; increasing from a mean of 1.9 bleeding sites for children with mild bleeding severity, to 2.5 with moderate bleeding and 3.6 with severe bleeding[8]

Immune thrombocytopenia treatment differs worldwide in terms of when to initiate the therapy, what treatment to use and whether hospitalization is needed,[11] in addition to that, initial treatment of children with typical acute ITP remains controversial, in part because the outcome is so favorable without treatment .[25, 49, 50]Although there are many reasons why physicians prescribe drug treatment to newly diagnosed patients with ITP, [51] the main goal of all treatment strategies for ITP in children, or in adults, is to achieve a platelet count that is associated with adequate hemostasis, rather than a "normal" platelet count.[1] The United Kingdom 2009 registry data had shown a continued reduction in treatment to 16% of all the children with ITP. In contrast, historical international data reported 69% of children received interventional therapy.[8]

For childhood ITP, pharmacologic intervention, including corticosteroids, intravenous immunoglobulin (IGIV), and anti-Rho(D) immune globulin, has been shown to raise the platelet count more quickly than no therapy and is recommended for children who have or at risk for severe or life-threatening bleeding, based on strong evidence.[1, 3,4,25] In the present study all children with newly diagnosed ITP were admitted to the hospital to confirm the diagnosis and to start the treatment.Intravenous immunoglobulin (IVIG) was the treatment most commonly used in children with acute and chronic ITP, and

initial treatment had no significant effect onthe clinical course of the disease, which is in agreement with that reported in literatures. [4, 19, 20, 27, 28, 51, 52] Study from Turkey by Özsoylu mentioned that, probably chronicity of acute ITP would be less with oral megadose methylprednisolone (MDMP) treatment[53]

Conclusion

Immune thrombocytopenia in children has a favorable outcome. Only a small number of children go on to develop chronic phase. However at time of presentation, it is difficult to predict the course of the disease. ITP at diagnosis was more prevalent amongmale gender, 1-5-year group, and urban residency children. It commonly occurred in spring and winter, with history of preceding viral illness. Majority of children with ITP, were presented as sudden onset of petechiae and/or bruising, with initial platelet count less than 20 x 10^9/L. Most of children were treated with intravenous immunoglobulin and mode of treatment had no effect on the clinical course and prognosis of ITP. In univariate analysis, among initial socio demographic, clinical and laboratory features, only onset of the disease and preceding history of acute viral illness were significantly affecting the course of ITP. Gradual onset and absence of preceding viral illness correlated with a chronic course of ITP. Future large prospective studies are recommended to confirm our results.

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