Immune thrombocytopenia (ITP) is the most common cause of thrombocytopenia in children. This retrospective study was designed to analyze presenting features of ITP cases in Benha, evaluate outcomes in children and determine prognostic factors. 

Aim of the study. To analyze the details of ITP cases, evaluate the outcomes among children in Benha and determine the prognostic factors as guidelines for new cases at the time of diagnosis.
MATERIALS AND METHODS

Study subjects
This retrospective study was conducted in Al-Qalyubia Governorate at Haematology Clinics in Benha University Hospitals and Benha Children Hospital.

The data of patients with ITP (aged between 6 months and 17 years) admitted to Behna hospitals from May 2014 to January 2021 were collected.

Inclusion criteria:
- Patients diagnosed with ITP
- Age: from 6 months to ≤ 18 years

Exclusion criteria:
- Patients with significant lymphadenopathy, hepatomegaly, splenomegaly or systemic symptoms (e.g., bone or joint pain, or weight loss etc.) and atypical bone marrow findings.
- Cases diagnosed with ITP and associated with another chronic disease (e.g., chronic renal failure, chronic liver disease).
- Patients with other autoimmune diseases, such as hypothyroidism, celiac disease, etc.

Methods

Three hundred and eight children diagnosed with ITP and followed up in pediatric haematology clinics in Benha University Hospitals and Benha Children Hospital were included.

A specially designed sheet was used to collect socio-demographic, clinical, and laboratory data of the studied children. Such information as age, gender, residence, date of diagnosis, complaints at presentation, as well as data on previous infection or vaccination, type of bleeding, initial platelet count, LDH level, initial treatment and follow-up of the disease were recorded.

Ethical consideration

This research was accepted by Research Ethics Committee (REC) of Faculty of Medicine, Benha University (chairman: Prof. Nermeen Adly Mahmoud). Ethics committee reference number MS 40-3/2019.

Statistical analysis

The collected data were tabulated and analyzed using SPSS version 16 software (SpssInc, Chicago, ILL Company). Categorical data were presented as numbers and percentages, Chi squared ($\chi^2$) test and Fisher’s exact test were used to analyze them. Quantitative data were tested for normality using Kolmogorov–Smirnov test, assuming normality at $p > 0.05$. Normally distributed variables were expressed as mean ± standard deviation, while nonparametric data were presented as median, IQR, and range and analyzed by Mann–Whitney U test. $P \leq 0.05$ was considered significant.

RESULTS

Out of 308 patients, 164 (53.2%) were males, and 144 (46.8%) were females; the median age of patients at diagnosis was 5 ± 3.4 years, the majority of the children were in the age group from 2 to 10 years old (72.7%). The incidence was higher in rural areas (61.7%) than in urban areas. The incidence in summer was higher (39.6%) than in other seasons of the year. Our study showed that about 90.9% of the study group had no history of preceding vaccination, and about 17.5% of the patients had a previous infection (14.9% and 2.6% of the patients had a history of upper respiratory tract infection and acute gastroenteritis, respectively). A total of 4.2% of the patients had positive consanguinity and 3.9% of the children had a positive family history for ITP (table 1).

Table 1
Baseline characteristics of the children diagnosed with ITP

| Variable | Number of the patients ($n = 308$) | % |
|----------|-----------------------------------|---|
| Age (years) | Median ± SD | 5.0 ± 3.4 |
| Range | 0.5–17 |
| < 2 years | 40 | 13.0 |
| 2–10 years | 220 | 71.4 |
| > 10 years | 48 | 15.6 |
| Gender | | |
| Male | 164 | 53.2 |
| Female | 144 | 46.8 |
| Residence | | |
| Urban | 118 | 38.3 |
| Rural | 190 | 61.7 |
| Season | | |
| Winter | 70 | 22.7 |
| Spring | 78 | 25.3 |
| Summer | 122 | 39.6 |
| Autumn | 38 | 12.4 |
| Preceding infection | URTI | 46 | 14.9 |
| GE | 8 | 2.6 |
| No | 284 | 82.5 |
| Preceding vaccination | Yes | 28 | 9.1 |
| No | 280 | 90.9 |
| Family history | Positive | 12 | 3.9 |
| Negative | 296 | 96.1 |
| Consanguinity | Positive | 13 | 4.2 |
| Negative | 395 | 95.8 |

Also, about 97% of the study group had cutaneous manifestations, 18.5% of them had mucosal bleeding, and only 8 (2.6%) cases presented with other complaints, such as pallor, fatigue, and blurring of vision.

Our study showed that 220 (71.4%) cases had acute ITP, and 88 (23.6%) patients had chronic ITP. Older age was an important predictor of chronic disease with the median age of 8 ± 3.1 years in comparison to the median age of 3.8 ± 3.0 years in acute cases ($p < 0.001$). Patients aged ≥ 10 years developed chronic disease more often than younger ones ($p = 0.029$). Regarding gender distribution, our study showed that
females (58%) were more likely to develop chronic ITP than males (42%) (p = 0.013). According to the present study, the type of bleeding, the residency of patients, the season when a patient developed ITP, consanguinity and family history did not significantly modify the course of the disease (table 2). Also, the history of previous infection and preceding vaccination did not significantly affect the disease course.

**Table 2**
Demographic data outcome in ITP cases

| Variable          | Acute ITP (n = 220) | Chronic ITP (n = 88) | p value |
|-------------------|---------------------|----------------------|---------|
| Age (years)       | Median ± SD Range   |                      |         |
| < 2 years, n (%)  | 3.8 ± 3.0 0.5–17    | 8.0 ± 3.1 1.5–15     | < 0.001*|
| 2–10 years, n (%) | 34 (15.5) 185 (81.8)| 6 (6.8) 62 (70.5)   |         |
| > 10 years, n (%) | 28 (12.7)           | 20 (22.7)            |         |
| Gender            | Male                | Female               |         |
|                   | 127 (57.7) 93 (42.3)| 37 (42.0) 51 (58.0) | 0.013   |
| Residence         | Urban               | Rural                |         |
|                   | 86 (39.1) 134 (60.9)| 32 (36.4) 56 (63.6) | 0.656   |
| Season            | Winter              | Spring               |         |
|                   | 50 (22.7) 60 (27.3)| 18 (20.5) 34 (38.6) | 0.204   |
|                   | Autumn              | Summer               |         |
|                   | 12 (10.0)           | 16 (18.2)            |         |
| Preceding infection| URTI Yes            | No                   |         |
|                   | 36 (16.4) 178 (80.9)| 10 (11.4) 76 (86.4) | 0.516*  |
|                   | GE Yes              | No                   |         |
|                   | 6 (6.8) 202 (91.8)  | 2 (2.3) 78 (86.6)    | 0.38    |
|                   | Family history      | Positive             |         |
|                   | 214 (97.3)          | 82 (93.2)            | 0.108*  |
|                   | Negative            |                      |         |
|                   | 7 (3.2) 213 (96.8)  | 6 (6.8) 82 (93.2)    | 0.206*  |

*Note. † – p of Mann–Whitney U test; * – p of Fisher’s exact test was used.*

We found that 3.2% of the patients had no medication, 96.7% received steroid therapy, while 0.6% received IVIG therapy and 20% received combined therapy. Initial treatment was steroids or no treatment and statistically, there was no significant difference in the outcome (p = 0.119).

According to the present study, at the time of diagnosis, steroids were administered to 88% of the patients, IVIG to 5.2% of the patients and IVIG with steroids to 2.9% of the patients, while 3.9% of the patients did not receive any treatment (observation only group). Statistically there was no significant difference in the outcomes between initial lines of treatment (p = 0.105) (table 3).

**Table 3**
Initial lines of treatment in ITP cases

| Initial treatment | Acute ITP (n = 220) | Chronic ITP (n = 88) | p value |
|-------------------|---------------------|----------------------|---------|
| Steroids          | 190 (86.4)          | 81 (92.0)            | 0.105   |
| IVIG              | 12 (5.5)            | 4 (4.5)              |         |
| IVIG + steroids   | 6 (2.7)             | 3 (3.4)              |         |
| Observation       | 12 (5.5)            | 0 (0.0)              |         |

Our study showed a significant difference in initial platelet counts between acute and chronic ITP, the median platelet count was $13 \times 10^9$ (range 2–54) in acute cases. We found that the median platelet count at diagnosis and platelet count > $20 \times 10^9$ was significantly higher in patients who developed chronic ITP (the median platelet count was $18.5 \times 10^9$ (range 3–60) (p < 0.001)) (figure 1). Our study showed that LDH is an important predictor of chronic ITP (figure 2) as the median LDH level was significantly higher in chronic cases (746 U/L) compared to acute cases; the median was 714 U/L (p = 0.002) (table 4).

**DISCUSSION**

Our retrospective study was designed to determine the presenting features and the clinical characteristics of diagnosed immune thrombocytopenia cases (ITP) among studied children. It also aims to determine
the prognostic factors that could predict the disease course at diagnosis. The ages of the studied cases in the present study ranged between 6 months to 17 years, with a median age of 5 years. Makis et al. [8] similarly showed that the median age of incidence was 4.8 years in their retrospective study. Also, Yong et al. [9] agreed with this.

Our study showed a higher incidence in males than females (1.14:1) with no significance. This agrees with Saeidi et al. [10] and Nazari et al. [11] as they found a higher incidence in males.

Our results showed a higher incidence in rural areas compared to urban areas. Contrary to this result, AL-Zuhairy [12] found that about two-thirds of the patients diagnosed with ITP lived in Iraq’s urban areas. Our study showed a higher incidence in summer than in other seasons of the year. This disagrees with Yong et al. [9] as they found a higher incidence in winter than other seasons of the year.

Our study showed that about 9.1% of the patients had a history of preceding vaccination before diagnosis. This agreed with Yong et al. [9] who found that 8.6% of patients received vaccination shortly before the ITP diagnosis, and France et al. [13] who found that 3.2% of patients received MMR vaccine before the ITP diagnosis.

Our study showed that 17.5% of the patients had a history of previous infection: 85.2% of them had a history of upper respiratory tract infection, and 14.8% of them had a history of gastroenteritis. This agrees with Söğüt et al. [14] who found that 22.5% of patients had evidence of infection before ITP diagnosis: 85% of them had a history of upper respiratory tract infection, and 15% of them had a history of acute gastroenteritis (AGE). However, the number of patients with a history of previous infection in our study was less than in Makis et al. [8] study, where 65% of newly diagnosed patients had a previous infection.

Our study showed that most of the study group (97.1%) had cutaneous bleeding such as petechiae, ecchymosis or both, and 18.5% had mucosal bleeding. This agrees with AL-Zuhairy [12] who showed that petechiae and/or bruising were the most common (92%) clinical features among children diagnosed with ITP, but in Makis et al. [8] study, the number of patients with mucosal bleeding was less (70%). Our study showed that at the time of presentation, the patients had elevated LDH levels (242 of our cases had data on LDH levels available). This agrees with Al-Samkari and Kuter [15] who found a statistically significant inverse correlation between LDH level and platelet count, as LDH is present in numerous cell types including platelets.

In this study, 71.4% and 28.6% of the cases had acute and chronic ITP, respectively. Grimaldi-Bensouda et al. [16] also found that 24.2% of cases developed chronic ITP and Singh et al. [17] found that chronic ITP represents 15–20% of cases.

In the present study, there was a significant correlation between the age of the patients and the course of the disease. We found that the median age of chronic cases was 8 years and children aged ≥ 10 years had a significantly higher incidence of chronic ITP. This agrees with Gungor et al. [18] who found that age ≥ 10 years is a predictor of chronic ITP. This also agrees with Donato et al. [19] and Watts et al. [20] who revealed that older age was an important predictor of chronic disease.

There was no statistically significant difference between initial treatment and the course of the disease which is consistent with Bansal et al. [21]. Regarding gender distribution, our study revealed that females had a higher incidence to be chronic than males. This is consistent with Nazari et al. [11] who found that the female gender is an indicator for chronicity; this may be explained by the fact that, as in other immune disorders, sex hormones may play a role in the susceptibility to chronicity. In addition to impacting the immune system, sex hormones may also alter the clinical picture and response to therapy. In the present study, the residency of patients did not significantly modify the course of the disease. Also, there was no significant correlation between the season in which patients showed their first symptoms and the disease’s course; this is supported by Akbayram et al. [22]. Also, the type of bleeding did not significantly modify the disease’s course; this result was supported by Akbayram et al. [22].

Our study showed that there is a significant difference in initial platelet counts between the patients with acute ITP and chronic ITP as the median platelet count was 10 × 10^9/L in acute cases and 18.5 × 10^9/L in chronic cases, so we found a significantly higher median platelet count at diagnosis in patients who developed chronic ITP. This result agrees with Makis et al. [8] as the median platelet count at diagnosis was 14.6 × 10^9/L in acute ITP and 26.3 × 10^9/L in chronic cases. Also, our study showed that in chronic cases, the patients had a significantly higher platelet count (≥ 20 × 10^9/L) than in acute cases; this is consistent with Gungor et al. [18].

Our study showed that LDH was an important predictor of chronic ITP; it was elevated in all ITP cases but was higher in cases of chronic ITP with the median level of 752 U/L vs 686 U/L in acute cases.

CONCLUSIONS

- Age ≥ 10 years is an important predictor of chronic disease.
Females are more likely to develop chronic ITP than males.

There is a statistically significant difference in initial platelet counts between patients with different courses of the disease.

High LDH level is an important predictor of chronic ITP.

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