Experiences of Adolescents and Young Adults (AYAS) with Primary ITP
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Pediatric ITP is often described as a self-limiting disorder (meaning it usually resolves quickly) that causes a low platelet count (thrombocytopenia) usually following a viral infection and usually comes on suddenly (acute). In contrast, adult ITP is often described as a long-term (chronic) disease that does not resolve quickly and has more of a slow onset (insidious) with increased morbidity and mortality. Currently, ITP is defined in only two age categories (pediatric vs adult). Management principles for pediatric and adult ITP consist of different treatment protocols and practice guidelines. Since AYAS are by nature an active group of patients, going through unique hormonal, behavior, and social changes as they begin their transition to adulthood, understanding how ITP presents and evolves in this age group is the first step to better managing the disease.

In this study, data from patients were collected from three large ITP registries, including the PARC-ITP (international) registry, the CARMEN-France registry, and OBS'CEREVANCE (France) which is a national registry for the follow-up of children with severe autoimmune cytopenia. Patients with secondary or misdiagnosed ITP and pregnant women were excluded from participating.

For this study, the following definitions were used:

- Chronic disease was defined as having a platelet count below 100,000 μL or ongoing treatment at the one-year mark or relapse at later follow-up.
- Remission was defined as a platelet count greater than 100,000.
- Sustained remission was defined as a platelet count of 100,000 beyond the one-year mark without treatment for at least 6 months.
- Late remission was defined as achieving a platelet count above 100,000 anywhere between 12-36 months, while "very late" remission was defined as achieving a platelet count above 100,000 between 36-48 months.

Two separate parts of this study were conducted.

<u>Part one: The Newly Diagnosed AYAS Experience</u>

A total of 656 AYAS (61% female) with primary ITP were included into the first part of the study; and a total of 428 AYAS (64% female) who went on to develop chronic ITP were included in the study. The median age (middle of the age range) of AYAS was 15 years.

Platelet count at first presentation was very low (median 12, 000), however 109 patients presented without bleeding symptoms. Apart from gynecological bleeding, males and females had similar bleeding and half of all patients developed chronic ITP. Chance of remission was higher in patients if at diagnosis they had a very low platelet count (less than 20,000), especially, if these participants received corticosteroids and/or intravenous immunoglobulins (IVIG) compared to those who did not receive any treatment in the first 4 weeks following their diagnosis.

There were small differences in the subgroup of adolescents who were between the ages of 12-18 compared to young adults between the ages of 18-25 years. The 12–18-year group experienced more moderate thrombocytopenia at diagnosis, and less bleeding at all follow-ups compared to the 18–25-year-old group.

Part two: Long-Term Follow-up with AYAS who have Chronic ITP

A total of 428 AYAS with chronic primary ITP were included into the second part of the study. The initial median platelet count at the 24-month follow-up was 15,000. Follow-up information was available for 88% at 24 months, 77% at 36 months and 59% at 48 months. There were 74 patients (19%) who reported no bleeding at diagnosis. Overall, 7 patients (1.6%) reported intracranial hemorrhage; 3 at the time of diagnosis, 3 within the first 6 months, and 1 between 12-24 months.

Patients with sustained chronic disease had median platelet count of 55,000 at 24 months and 62,000 at 48 months follow-up. About half needed treatment during the follow-up. The number of patients who experienced a bleeding event and the location of such a bleeding event was similar across all in this subgroup during the follow-ups, with 70% suffering ‘wet bleeding’ (blood blisters in mucosal lining such as in the mouth). The proportion of patients receiving 2nd/3rd line therapies increased with time. However, IVIG and corticosteroids were still reported for about 40% and 30% of treated patients beyond 12 months.

Among those who maintained a sustained chronic disease, 23% showed "late or very late remission" and 15% had unknown remission status. They found no differences in symptoms experienced at the time of initial disease presentation between patients with "late/very late remission" vs patients with sustained chronic disease. However, over time, the AYAS who experienced a "late remission" displayed less bleeding, higher platelet counts and needed IVIG less often at 6 and 12-months compared to AYAS with sustained chronic disease.

In total, 11 patients were diagnosed with secondary ITP after 12 months, including: 2 with common variable immunodeficiency (CVID), 4 with Evans syndrome, and 5 patients with systemic lupus erythematosus (Lupus).

In summary, this study highlights the importance of adapting medical care for AYAS, rather than treating them simply as pediatric patients. Rate of chronic disease was 50% at the one-year mark, unlike what is typically seen in pediatric ITP, however remission thereafter was still achievable. Remission within 1 year appeared to be associated with earlier administration of treatment; this was not the case for patients with "late/very late remission". However, AYAS with "late remission" had a less severe disease course in the first year of disease (excluding initial presentation) compared to those with sustained chronic disease. This study also highlighted that AYAS are mainly treated with corticosteroids for the first year and also widely throughout the observation period.

This study could serve as a basis for designing future studies to establish better diagnostic and therapeutic strategies in AYAS with ITP. Future studies should focus on: (1) accepting ITP of AYAS as a distinct entity from pediatric and adult ITP; (2) adopting treatment endpoints that

reduce the rate of chronic disease; and (3) curbing the use of corticosteroids beyond the initial management.

PDSA has designed our research program to specifically focus on patient priorities and funds studies that will make a significant impact on ITP diagnosis, therapies, and quality of life. If you'd like to donate to our research fund, please visit https://www.pdsa.org/pdsa-donation.html.