Response and remission after first-line corticosteroid therapy in primary immune thrombocytopenia

D Mapimhidze, MB ChB, MMed (Int); **J Bailly,** MB ChB, FC (Path); **K Brown,** BSc (Med) Hons, MPH
J Bailey, BSc (Med) Hons, MPH; **E Verburgh,** MD, PhD

Division of Clinical Haematology, Department of Medicine, Faculty of Health Sciences, University of Cape Town and Groote Schuur Hospital, Cape Town, South Africa

Corresponding author: *E Verburgh (estelle.verburgh@uct.ac.za)*

Background. Primary immune thrombocytopenia (ITP) is an acquired autoimmune disease characterised by an isolated thrombocytopenia of <100 × 10^9/L in the absence of identifiable secondary causes. Treatment is indicated when the platelet count is <20 - 30 × 10^9/L, but may be commenced at higher platelet counts when the risk of bleeding is high. Corticosteroids are the backbone of initial treatment of ITP. There is a paucity of data in South Africa (SA) on the outcomes of newly diagnosed ITP patients treated with corticosteroids.
Objectives. To describe the response, remission and clinical outcomes of newly diagnosed primary ITP patients on first-line corticosteroids.
Methods. This was a retrospective cohort study of 68 patients with a new diagnosis of ITP, seen at the Clinical Haematology Unit at Groote Schuur Hospital, Cape Town, SA, over a 5-year period (2016 - 2020). Demographic and clinical data were obtained from paper and electronic record systems. All participants with secondary causes were excluded. The initial platelet responses to corticosteroids and the final outcomes at last follow-up were determined. Initial platelet responses were classified into no response (NR), partial response (PR) and complete response (CR) in accordance with consensus definitions. Remission was defined as maintenance of a CR after being off corticosteroids for ≤6 months. Categorical variables were described by frequencies and percentages, while numerical variables were described by medians and interquartile ranges (IQRs) as data were non-parametric.
Results. The majority of patients were female (88.2%) and the median (IQR) age at diagnosis was 36 (23.0 - 55.5) years. The female to male ratio was 7.5:1. Most (92.4%) patients responded to corticosteroids, with 74.2% achieving a CR and 18.2% achieving a PR. Only five patients failed to respond (7.6%). The median (IQR) time to achieve CR was 15 (8 - 25) days, and the median (IQR) time to achieve PR was 10.5 (8 - 22) days. Half of the patients went into remission. Following remission, two patients (6.1%) subsequently relapsed at day 344 and day 777, respectively. Hypertension and/or diabetes mellitus were newly diagnosed in 10.6% of patients.
Conclusion. Corticosteroids are effective first-line therapy for ITP, but are not remission-inducing in all patients. For those patients progressing to chronic ITP, there is a need to investigate cost-effective treatment. Some patients are at high risk of developing new hypertension and diabetes mellitus on corticosteroids, and should be monitored.

Keywords: ITP, immune thrombocytopenia, corticosteroids, first-line, treatment response

S Afr Med J 2025;115(2):e2191. https://doi.org/10.7196/SAMJ.2025.v115i2.2191

Primary immune thrombocytopenia (ITP) is an autoimmune disease defined by an isolated thrombocytopenia of <100 × 10^9/L in the absence of distinguishable secondary causes.[1,2] The worldwide incidence varies from 2 to 4 cases per 100 000 person-years, affecting more females and increasing with age.[3-5] The depleted platelet pool is a result of several incompletely understood pathophysiological processes, namely platelet autoantibodies, depressed megakaryocytopoiesis and T-cell mediated cytotoxicity.[6,7] Following new diagnosis, the clinical picture is diverse, but in the majority of patients the disease runs a mild course, with bleeding episodes mostly occurring with platelet counts <10 × 10^9/L.[8] In newly diagnosed adults with primary ITP, the indication of treatment is a platelet count <30 × 10^9/L, but treatment is individualised based on bleeding risk.[9] In the HIV endemic region of southern Africa, the main cause of secondary ITP is HIV, and the prevalence of thrombocytopenia among people living with untreated HIV is 30 - 40%.[10] Due to a perceived wider range of differential diagnoses in this environment, bone marrow examination (BME) for isolated thrombocytopenia is not uncommon, and was performed in 21% and 14.3% of HIV patients in two previous local studies, respectively.[11,12] Indications for BME in HIV-uninfected patients are age >60 years, the presence of clinically concerning systemic symptoms and signs suggesting primary or secondary bone marrow pathology, and in preparation for splenectomy.[1]

First-line treatment of ITP encompasses corticosteroids, which have been in use for ITP since the 1950s.[13] Intravenous immunoglobulins and anti-D immunoglobulins are useful as rescue therapy to achieve rapid haemostasis.[9] Corticosteroids have broad anti-inflammatory and immunosuppressive effects and modulate endothelial function, ultimately reducing bleeding risk.[14] The gold standard of treatment is a 4-day regimen of 40 mg dexamethasone intravenously daily, repeated monthly; or 0.5 - 2 mg/kg of prednisone orally, which is gradually weaned over 4 - 6 weeks and then withdrawn.[9] Initial response is classified into no response (NR), partial response (PR) and complete response (CR), and measured within the first 10 days for those receiving dexamethasone and the first 28 days for those receiving prednisone.[2] This initial response rate to corticosteroids ranges from 60 - 80%, but only 30 - 55% of patients remain in remission.[15-17] It is the responsibility of physicians to ensure that patients are sufficiently monitored for conceivable corticosteroid side-effects, the most immediate of which are hypertension and hyperglycaemia.[9] Other notable side-effects of corticosteroids are

weight gain, osteoporosis, peptic ulcers, impaired wound healing, psychosis and increased risk of infections.[18]

There is limited research in sub-Saharan Africa on the diagnosis and treatment of primary ITP.

Two South African (SA) centres previously reported favourably on the role of splenectomy in second-line treatment of ITP patients.[19,20] Two other local studies reported that intravenous immunoglobulins had no advantages over oral corticosteroids as primary therapy for ITP.[21,22] An unpublished dissertation retrospectively analysing 243 patients over a 25-year period at another SA hospital showed that 65% of patients with primary and secondary ITP achieved CR after corticosteroids.[23] What is not known in our local cohort is the response rate and remission rates of patients with primary ITP on first-line corticosteroid therapy. To this aim we reviewed all patients who attended our ITP clinic in the Clinical Haematology Unit at Groote Schuur Hospital (GSH) during the period 2016 - 2020, for clinical characteristics and treatment outcomes.

Methods

Study design and patient selection

This retrospective cohort study included patients with newly diagnosed ITP managed in the Clinical Haematology Unit at GSH, a tertiary and quaternary public healthcare facility in Cape Town, SA, from January 2016 to December 2020. Approval for the study was obtained from the Human Research Ethics Committee at the University of Cape Town (ref. no. HREC 197/2022). Patients treated at the Clinical Haematology Unit at GSH are included in the clinic's electronic patient registry. A waiver of written consent for retrospective data collection is in place for patients included prior to 2018, and informed consent is obtained for patients included from 2018 onwards.

Diagnostic criteria

ITP is defined as an isolated thrombocytopenia (platelet count $<100 \times 10^9$/L) in the absence of other conditions or causes associated with thrombocytopenia.[2] A diagnosis of primary ITP is made after secondary causes of ITP are excluded.[2] The diagnosis of ITP was confirmed by careful review of the clinical history (including drug list and known medical conditions) and clinical and laboratory examination to differentiate between primary ITP and secondary ITP. The full blood count, differential count, peripheral blood smear and the results of other laboratory tests, in particular HIV, hepatitis B and C virus, and antinuclear antibodies (ANA) were recorded and reviewed for significance (i.e. reported in the literature to be associated with ITP). Patients with proven HIV, hepatitis B and C and systemic lupus erythematosus (SLE) were categorised as secondary ITP. ANA positivity alone was not seen as an exclusionary criterion in the absence of characteristic clinical manifestations suggestive of SLE. [2,24,25] Other causes of secondary ITP were considered.

Demographic and clinical data

Patient demographic and clinical data were obtained from patient files and electronic record systems. Demographic data collected included age and gender. Clinical data collected at presentation included presenting symptoms, diagnosis setting, blood results (platelet count, haemoglobin level and ferritin level) and the presence or absence of iron deficiency anaemia (IDA), diabetes and hypertension. Presenting symptoms were categorised as critical bleeding, other bleeding, only bruising, asymptomatic and unclear. Critical bleeding was defined as haemorrhage into a critical anatomical site, including intracranial, intraocular, intraspinal, pericardial, retroperitoneal, or intramuscular with compartment syndrome; or continuous haemorrhage that resulted in haemodynamic or respiratory compromise.[26] IDA was defined as per the World Health Organization (WHO) definition for iron deficiency (a ferritin <30 ng/mL) and anaemia (low haemoglobin of <12 g/dL in non-pregnant females, <11 g/dL for pregnant females and <13 g/dL in males).[27] Hypertension and diabetes were diagnosed by clinicians in accordance with local guidelines, and recorded at presentation with ITP. BME at diagnosis was done at the clinician's discretion. The institutional policy mandated BME in patients >60 years of age.[1]

Patient outcomes on first-line therapy

For first-line corticosteroid therapy in the primary ITP cohort, outcome data were collected. These data included response to first-line corticosteroids, time to response to first-line corticosteroids, development of a new diagnosis of hypertension and diabetes, achievement of remission, relapse and death. For patients who died on first-line corticosteroids, the cause of death and timing from diagnosis were considered.

Types of corticosteroids administered were dexamethasone, prednisone or a combination of the two. Responses to corticosteroids were measured as per the International Working Group, where CR is defined as a platelet count of a minimum of 100×10^9/L; PR as a platelet count between 30 and 100×10^9/L and no less than doubling of the baseline platelet count; and NR as any platelet count $<30 \times 10^9$/L or lower than doubling of the baseline platelet count.[2] According to the American Society of Haematology (ASH) guidelines of 2019, remission is defined as a platelet count of $>100 \times 10^9$/L lasting at least 12 months.[9] In the GSH setting, first-line corticosteroid therapy was often continued beyond 6 months. Therefore, for the purposes of this study in the setting of first-line corticosteroid therapy, this criterion included the patient being off corticosteroid therapy for at least 6 months. Relapse was defined as a loss of CR or PR after stopping first-line treatment.[2] For non-responders or those with a loss of response, a BME was done at the discretion of the treating clinician. Follow-up time was defined as date of diagnosis to date of last follow-up, or date of relapse. The last follow-up date for this study was 30 June 2022.

Statistical analysis

Data were analysed using STATA V14 (Stata Corp., USA). Categorical variables were described by frequencies and percentages. Numerical variables were described by medians and interquartile ranges (IQRs) as data were non-parametric.

Results

A total of 101 patients were referred to our facility with newly diagnosed ITP from 2016 to 2020 (Fig. 1). Thirty-three patients were found to have a secondary cause of ITP and were excluded. The final cohort comprised 68 patients meeting the criteria for primary ITP. Baseline characteristics of the patients are presented in Table 1. The median (IQR) age of the cohort was 36 years (23.0 - 55.5), and the majority (88.2%) of patients were female. The female:male ratio was 7.5:1. The proportion of patients >60 years of age was 17.6%. The median platelet count at presentation was 5×10^9/L (IQR 1.0 - 16.5), and 3 patients had critical bleeding. Two patients survived intracerebral haemorrhage without residual neurology, and one had fatal gastrointestinal bleeding (an 84-year-old hypertensive woman with a platelet count of 0×10^9/L at diagnosis who died 6 days after diagnosis following appropriate dexamethasone therapy). Of the 68 patients, 53 (77.9%) were diagnosed as inpatients, with a median hospital admission duration of 7 days (IQR 4 - 10).

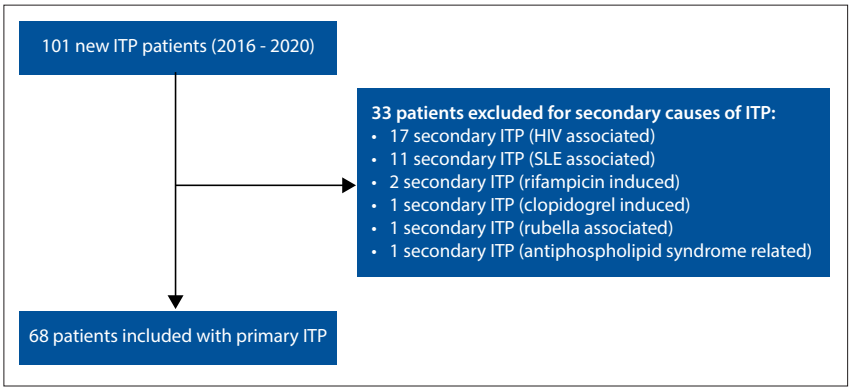

Fig. 1. Flow chart of patients included in the study. (ITP = immune thrombocytopenia; SLE = systemic lupus erythematosus.)

Table 1. Baseline characteristics of patients (*N*=68)

Characteristic	*n* (%)*
Age at diagnosis, years, median (IQR)	36 (23.0 - 55.5)
Gender	
Male	8 (11.8)
Female†	60 (88.2)
Female:male ratio	7.5:1
Presenting symptoms	
Critical bleeding	3 (4.4)
Other bleeding	45 (66.2)
Bruising only	6 (8.8)
Asymptomatic	11 (16.2)
Unclear	3 (4.4)
Blood results at diagnosis, median (IQR)	
Platelet count (× 10^9/L)	5.0 (1.0 - 16.5)
Haemoglobin (g/dL)	11.1 (8.5 - 13.1)
Ferritin (*n*=42)	26.0 (11.0 - 93.0)
Comorbidities at diagnosis	
Diabetes mellitus	10 (14.7)
Hypertension	28 (41.2)
Iron deficiency anaemia	16 (23.5)
Setting of diagnosis	
Inpatient	53 (77.9)
Outpatient	15 (22.1)
Duration of hospital admission in days, median (IQR)	7 (4 - 10)
Bone marrow examination	22 (32.4)

IQR = interquartile range.
*Unless otherwise indicated.
†5 patients were pregnant at the time of diagnosis.

A significant proportion of patients had comorbidities at diagnosis, namely hypertension in 41.2% and diabetes in 14.7%. Five patients were ANA positive with measured titres of <1:80, and they did not meet any other criteria for SLE. These ANA-positive patients were all young females with comparable baseline platelet counts and they did not progress to SLE during this retrospective study's time frame. Out of the ANA-positive group, only one patient went into remission after corticosteroids. Approximately one quarter (23.5%) of patients had IDA at the time of ITP diagnosis. A total of 22 patients had a BME performed, 8 of whom were >60 years old. The median age at time of BME was 44 years of age. All BMEs were diagnostic except for 5 (22.7%), which were done when patients had a poor response to therapy (Table 1). All BMEs supported a diagnosis of primary ITP. Treatment responses and clinical outcomes on corticosteroids and response times are shown in Table 2. Two patients were excluded from the treatment response analysis. The first exclusion was the elderly woman described above who died of gastrointestinal haemorrhage, and the second exclusion was a 44-year-old man with a platelet count of 45 ×10^9/L at diagnosis, who was managed with clinical observation only. The initial response rate was 92.4% (CR or PR), with 74.2% achieving a CR and 18.2% achieving a PR. Only five patients (7.6%) failed to respond to corticosteroids. The median (IQR) time to response (TTR) for those achieving CR was 15 (8 - 25) days, and for those achieving PR it was 10.5 (8 - 22) days. Half of the patients went into remission. The median time off steroids at date of last follow-up/date of relapse for those who went into remission after first-line treatment was 26.9 months.

Of the 34 patients who went into remission, 5 (14.7%) relapsed. The median follow-up time (from date of diagnosis to date of last follow-up/date of relapse) was 33 months for those who went into remission, and 37 months for those who did not.

Table 3 shows patients known and diagnosed with diabetes mellitus and hypertension on corticosteroid therapy according to remission status. Of the patients who did not achieve remission, 46.9% had hypertension at diagnosis, while 21.9% had diabetes mellitus at diagnosis. After corticosteroid therapy, five patients developed new-onset diabetes mellitus, one patient developed hypertension and one patient developed both diabetes mellitus and hypertension. There were no noteworthy differences between those who developed comorbidities, and remission status.

Discussion

There are limited published data on the epidemiology and treatment responses to corticosteroids among patients with primary ITP in sub-Saharan Africa. Over the 5-year period of our study, the median age of patients newly diagnosed with ITP was 36 years, with a strong female predominance. This is not in keeping with European data showing an older median age group of 55 - 60 years and a slight female preponderance.[28,29] Our findings are more comparable to those reported in an unpublished dissertation on ITP at another quaternary hospital in SA, which showed a median age of 32 years, and just over 80% females.[23] The younger age group in Africa can be explained by the generally younger population in developing countries. Our median platelet count of 5 × 10^9/L is slightly lower than 10 × 10^9/L reported in the local SA study above.[23] Published data in Europe show slightly higher median platelet counts of 12 - 20 × 10^9/L.[30,31] The lower platelet counts in Africa are likely a reflection of delayed presentation due to poor patient

Table 2. Treatment response, median time to platelet response and clinical outcomes of first-line corticosteroids in 66 patients*

Platelet response	*n* (%)	Time to response (days), median (IQR)	Remission achieved, *n*
No response	5 (7.6)	-	0
Partial response	12 (18.2)	10.5 (8 - 22)	0
Complete response	49 (74.2)	15 (8 - 25)	34 (51.5)

IQR = interquartile range.
*Two patients excluded from treatment response: 1 patient died within a week of diagnosis; 1 patient was only observed.

Table 3. Comorbidities at diagnosis and comorbidities developed during treatment by remission status, in patients receiving first-line corticosteroid treatment

Comorbidity	Remission achieved (*n*=34), *n* (%)	Remission not achieved (*n*=32), *n* (%)
At diagnosis		
Diabetes mellitus	2 (5.9)	7 (21.9)
Hypertension	11 (32.4)	15 (46.9)
Developed during treatment		
New onset diabetes mellitus	2 (6.1)	3 (9.1)
New onset hypertension	-	1 (3.0)
New onset diabetes mellitus and hypertension	1 (3.0)	-

access to healthcare. The median TTR to corticosteroids was shorter in the partial responders (10.5 days) than the complete responders (15 days). This is within the expected 4 - 28 days to reach peak response, but considerably longer than the TTR of 3 - 6 days found in a prospective multicentre randomised Asian study.[2,32] In our study, the response rate to corticosteroid therapy was 92.4%, and the remission rate was 50%. This is comparable to other studies, with response rates to corticosteroids of 60 - 80% and remission rates of 30 - 55%.[15-17]

BMEs were performed in 22 participants, of whom 8 were >60 years of age. According to the ASH guidelines at that time, BMEs were performed to exclude haematological malignancies that may mimic ITP, in particular myelodysplastic syndrome.[33] We performed diagnostic BMEs on 25.8% of the cohort, which is lower than the 37.8% of diagnostic BMEs reported in a Scandinavian review done from 2009 to 2017.[34] The higher percentage in Europe is multifactorial, and possibly due to a combination of the older population, guidelines recommending diagnostic BMEs for those >60 years old and improved patient access to healthcare.[1]

The percentage of patients (26%) diagnosed with IDA is higher than the published 10% prevalence in the 'healthy' SA adult population.[35,36] This is likely explained by delayed presentation of a population already at risk of IDA. IDA is often associated with reversible extremes of platelet count.[37] The typical picture of IDA is associated with a reactive thrombocytosis; however, IDA is rarely associated with a thrombocytopenia – a term called iron deficiency thrombocytopenia (IDT).[38,39] Platelet counts in both conditions respond rapidly to the correction of IDA. Platelet counts in ITP tend to be much lower (median $<10 \times 10^9$/L) than those in IDT (median $>30 \times 10^9$/L).[38] In our ITP patients with IDA, there was only one patient with a platelet count $>30 \times 10^9$/L, supporting the likelihood of ITP over IDT.

Prior to corticosteroid use, >50% of the patients had hypertension and diabetes mellitus. After corticosteroid exposure, another 10.6% of participants developed new diabetes mellitus and hypertension. Meta-analyses have demonstrated that the occurrence of diabetes is 1 - 50% in previously normoglycaemic people following ≥1 month of corticosteroid exposure.[40,41] The prevalence of corticosteroid-induced hypertension is unclear, but the risk increases with daily doses equivalent to 7.5 mg of prednisone or more.[41] ITP treatment consists of much higher doses of prednisone given for at least a month, and there is a need to monitor patients for these side-effects.

Our study has some limitations, including its retrospective design. It was impossible to measure the treatment outcomes of dexamethasone in comparison with prednisone. This is because most patients ended up receiving both regimens. This was likely done as a safety precaution, in absence of readily available second-line treatments. Additionally, patients who had slow or incomplete responses, may have been inappropriately kept on high doses of prednisone beyond recommended time periods. This created problems in classification of these patients into remission status.

Conclusion

There is a paucity of data to date on primary ITP in sub-Saharan Africa. In our cohort, we found that primary ITP is a disease of predominantly young women. Corticosteroids are justified frontline agents for ITP, owing to their availability and their impressive initial response rate in our setting. However, they are not remission-inducing in all patients, which is in accordance with the results obtained in Europe and the USA.[15-17] The high doses of corticosteroids used to treat ITP further expose patients to the risk of newly diagnosed hypertension and/or diabetes mellitus. In our setting, it is unclear whether dexamethasone is more efficient than prednisone, as has been shown in other studies.[17,32] This study had several limitations due to its retrospective nature and limited follow-up period. A prospective study evaluating the efficacy of oral corticosteroids in comparison to dexamethasone would be useful.

Data availability. The de-identified data used in this study are available from the authors on request.

Declaration. This study formed part of the thesis requirements for the MMed (Internal Medicine) degree conferred upon the first author, DM, by the University of Cape Town.

Acknowledgements. The authors would like to thank the Clinical Haematology Unit patients and staff for their contributions to this project.

Author contributions. DM and EV conceptualised the study. DM collected the data, and all authors collaborated on completing and reconciling data points. KB and JB analysed the data. DM wrote the article, and all authors edited and contributed to writing the final article.

Funding. Research reported in this publication was supported by the Fogarty International Center and the National Heart, Lung & Blood Institute of the National Institutes of Health under award number D43 TW010345.

Conflicts of interest. None.

1. Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood 2010;115(2):168-186. https://doi.org/10.1182/blood-2009-06-225565
2. Rodeghiero F, Stasi R, Gernsheimer T, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: Report from an international working group. Blood 2009;113(11):2386-2393. https://doi.org/10.1182/blood-2008-07-162503
3. Kurata Y, Fujimura K, Kuwana M, Tomiyama Y, Murata M. Epidemiology of primary immune thrombocytopenia in children and adults in Japan: A population-based study and literature review. Int J Hematol 2011;93(3):329-335. https://doi.org/10.1007/s12185-011-0791-1
4. Feudjo-Tepie MA, Hall S, Logie J, Bennett D. The incidence of idiopathic thrombocytopenic purpura (ITP) among adults in the United Kingdom's General Practice Research Database (GPRD), 1992 - 2005. Blood 2007;110(11):3209. https://doi.org/10.1182/blood.V110.11.3209.3209
5. Frederiksen H, Christianse CF, Nørgaard M. Risk and prognosis of adult primary immune thrombocytopenia. Exp Rev Hematol 2012;5(2):219-228. https://doi.org/10.1586/ehm.12.7
6. Zhou B, Zhao H, Yang RC, Han ZC. Multi-dysfunctional pathophysiology in ITP. Crit Rev Oncol/Hematol 2005;54(2):107-116. https://doi.org/10.1016/j.critrevonc.2004.12.004
7. Najean Y, Ardaillou N, Dresch C, Bernard J. The platelet destruction site in thrombocytopenic purpuras. Br J Haematol 1967;13(3):409-426. https://doi.org/10.1111/j.1365-2141.1967.tb08755.x
8. Piel-Julian M, Mahevas M, Germain J, et al. Risk factors for bleeding, including platelet count threshold, in newly diagnosed ITP patients. Blood 2017;130(Suppl 1):S1041. https://doi.org/10.1111/jth.14227
9. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv 2019;3(23):3829-3866. https://doi.org/10.1182/bloodadvances.2019000966
10. Woldeamanuel GG, Wondimu DH. Prevalence of thrombocytopenia before and after initiation of HAART among HIV infected patients at Black Lion Specialized Hospital, Addis Ababa, Ethiopia: Across sectional study. BMC Hematol 2018;18:9. https://doi.org/10.1186/s12878-018-0103-6
11. Opie J. Haematological complications of HIV infection. S Afr Med J 2012;102(6):465-468. https://doi.org/10.7196/samj.5595
12. Abdullah I, Subramony N, Musekwa E, et al. Indications and diagnostic value of bone marrow examination in HIV-positive individuals: A 3-year review at Tygerberg Hospital. S Afr J Infect Dis 2021;36(1):273. https://doi.org/10.4102%2Fsajid.v36i1.273
13. Stasi R, Newland AC. ITP: A historical perspective. Br J Haematol 2011;153(4):437-450. https://doi.org/10.1111/j.1365-2141.2010.08562.x
14. Salama A. Emerging drugs for immune thrombocytopenia. Exp Op Emerging Drugs 2017;22(1):27-38. https://doi.org/10.1080/14728214.2017.1294158
15. Vianelli N, Valdrè L, Vivo A, et al. Long-term follow-up of idiopathic thrombocytopenic purpura in 310 patients. Haematologica 2001;86(5):504-509.
16. Schiavotto C, Rodeghiero F. Twenty years experience with treatment of idiopathic thrombocytopenic purpura in a single department: Results in 490 cases. Haematologica 1993;78(6 Suppl 2):S22-S28.
17. Mithoowani S, Gregory-Miller K, Goy J, et al. High-dose dexamethasone compared with prednisone for previously untreated primary immune thrombocytopenia: A systematic review and meta-analysis. Lancet Haematol 2016;3(10):e489-e496. https://doi.org/10.1016/s2352-3026(16)30109-0
18. Stanbury RM, Graham EM. Systemic corticosteroid therapy – side effects and their management. Br J Ophthalmol 1998;82(6):704-708. https://doi.org/10.1136/bjo.82.6.704
19. Antel KR, Panieri E, Novitzky N. Role of splenectomy for immune thrombocytopenic purpura (ITP) in the era of new second-line therapies and in the setting of a high prevalence of HIV-associated ITP. S Afr Med J 2015;105(5):408-412. https://doi.org/10.7196/samj.8987
20. Abdulraheem TR. Impact of splenectomy on the management of immune thrombocytopenia in adults. MMed thesis. Johannesburg: University of the Witwatersrand, 2018:1-79.
21. Jacobs P, Wood L, Novitzky N. Intravenous gammaglobulin has no advantages over oral corticosteroids as primary therapy for adults with immune thrombocytopenia: A prospective randomized clinical trial. Am J Med1994;97(1):55-59. https://doi.org/10.1016/0002-9343(94)90048-5
22. Jacobs P, Wood L. The comparison of gammaglobulin to steroids in treating adult immune thrombocytopenia. An interim analysis. Blut 1989;59(1):92-95. https://doi.org/10.1007/bf00320256
23. Variava F. Immune thrombocytopenia at Chris Hani Baragwanath Hospital. MMed thesis. Johannesburg: University of the Witwatersrand, 2014:1-103.
24. Kurata Y, Miragawa S, Kosugi S, et al. Clinical significance of antinuclear antibody in patients with idiopathic thrombocytopenic purpura. Rinsho Ketsueki 1992;33(9):1178-1182.
25. Aringer M, Johnson SR. Systemic lupus erythematosus classification and diagnosis. Rheum Dis Clin North Am 2021;47(3):501-511. https://doi.org/10.1016/j.rdc.2021.04.011
26. Sirotich E, Guyat G, Gabe C, et al. Definition of a critical bleed in patients with immune thrombocytopenia: Communication from the ISTH SSC Subcommittee on Platelet Immunology. J Thromb Haemostasis 2021;19(8):2082-2088. https://doi.org/10.1111/jth.15368
27. Pavord S, Daru J, Prasannan N, et al. UK guidelines on the management of iron deficiency in pregnancy. Br J Haematol 2019;188(6):819-830. https://doi.org/10.1111/bjh.16221
28. Frederiksen H, Schmidt K. The incidence of idiopathic thrombocytopenic purpura in adults increases with age. Blood 1999;94(3):909-913. https://doi.org/10.1182/blood.V94.3.909.415k02_909_913
29. Neylon AJ, Saunders PW, Howard MR, et al. Clinically significant newly presenting autoimmune thrombocytopenic purpura in adults: A prospective study of a population-based cohort of 245 patients. Br J Haematol 2003;122(6):966-974. https://doi.org/10.1046/j.1365-2141.2003.04547.x
30. Steurer M, Quittet P, Papadaki H, et al. A large observational study of patients with primary immune thrombocytopenia receiving romiplostim in European clinical practice. Eur J Haematol 2017;98(2):112-120. https://doi.org/10.1111/ejh.12807
31. Palau J, Sancho E, Herrera M, et al. Characteristics and management of primary and other immune thrombocytopenias: Spanish registry study. Hematology 2017;22(8):484-492. https://doi.org/10.1080/10245332.2017.1311442
32. Wei Y, Ji X, Wang W, et al. High-dose dexamethasone vs prednisone for treatment of adult immune thrombocytopenia: A prospective multicenter randomized trial. Blood 2016;127(3):296-302. https://doi.org/10.1182/blood-2015-07-659656
33. Neunert C, Lim W, Crowther M, Cohen A, Solberg Jr L, Crowther MA. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood 2011;117(16):4190-4207. https://doi.org/10.1182/blood-2010-08-302984
34. Gotschalck MA, Norgaard M, Risbo N, et al. Predictors for and outcomes after bone marrow biopsy in Scandinavian patients with chronic immune thrombocytopenia. Eur J Haematol 2021;107(1):145-156. https://doi.org/10.1111/ejh.13635
35. Phatlhane DV, Zemlin AE, Matsha T, et al. The iron status of a healthy South African adult population. Clin Chim Acta 2016;460:240-245. https://doi.org/10.1016/j.cca.2016.06.019
36. Lawrie D, Coetzee LM, Glencross DK. Iron deficiency anaemia in healthy South African women despite iron fortification. S Afr Med J 2008;98(8):606-607.
37. Soto AF, Ford P, Mastoris J. Thrombocytosis in iron deficiency anemia: What the primary care physician needs to know. Blood 2006;108(11):3723.
38. Huscenot T, Darnige L, Wagner-Ballon O, et al. Iron deficiency, an unusual cause of thrombocytopenia: Results from a multicenter retrospective case-controlled study. Ann Hematol 2019;98(10):2299-2302. https://doi.org/10.1007/s00277-019-03757-0
39. Ayalew GD, Mittal J, Khillan R, Kim M, Braverman A, Sidhu G. Thrombocytopenia in severe anemia of iron deficiency. Blood 2010;116(21):5153. https://doi.org/10.1182/blood.V116.21.5153.5153
40. Alabbood M, Ling M, Ho K. Glucocorticoid-induced diabetes among people without diabetes: A literature review. Pract Diabetes 2018;35(2):63-67. https://doi.org/10.1002/pdi.2164
41. Costello RE, Yimer B, Roads P, Jani M, Dixon WG. Glucocorticoid use is associated with an increased risk of hypertension. Rheumatol 2020;60(1):132-139. https://doi.org/10.1093/rheumatology/keaa209

Received 22 October 2024; accepted 5 February 2025.