Treatment outcomes, adherence, and health-related quality of life of patients with immune thrombocytopenia in two teaching hospitals, Addis Ababa, Ethiopia: A retrospective cohort study

Dessale Abate Beyene (BPharm)

A thesis submitted to the Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University in Partial Fulfilment for the Requirements of Master's degree in Pharmacy Practice.

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Addis Ababa, Ethiopia

Addis Ababa University

College of Health Sciences

School of Pharmacy

Department of Pharmacology and Clinical Pharmacy

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By: Dessale Abate Beyene (BPharm)

Email: dessale2010@gmail.com

Adviser:

Eskindir Ayalew Sisay (BPharm, MSc, Assistant Professor of Clinical Pharmacy)

Co-adviser:

Amha Gebremedhin (MD, Associate professor in medicine)

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This is to certify that the thesis prepared by Dessale Abate Beyene, entitled "***Treatment outcomes, adherence, and health-related quality of life of patients with immune thrombocytopenia in two teaching hospitals, Addis Ababa, Ethiopia***" and submitted in partial fulfillment of the requirements for Degree of Master of Sciences in Pharmacy Practice complies with the regulation of the university and meets the accepted standards concerning originality and quality.

Principal investigator: Dessale Abate Beyene (BPharm)

Signed by the examining committee:

External Examiner: Kabaye Kumela (B. Pharm; MSc, Assistant Professor Clinical Pharmacy)

Date June 21, 2023 Signature 

Internal Examiner: Tamrat Assefa (BPharm, MSc, Assistant Professor of Clinical Pharmacy)

Date June 22, 2023 Signature 

Advisor: Eskindir Ayalew (BPharm, MSc, Assistant Professor of Clinical Pharmacy)

Date June 22, 2023 Signature 

Amha Gebremedhin (MD, Associate professor in medicine)

Co-advisor

Date June 22, 2023 Signature 

Abstract

Background: Treatment of immune thrombocytopenia (ITP) is challenging, and treatment outcomes depend on a variety of factors, most of which are unknown and specific to each patient. The severity and treatment outcomes of ITP are assessed clinically by platelet count, bleeding risk, and response to treatment. Corticosteroids are the cornerstone of ITP treatment but have many side effects, and long-term response is observed in only 25% of patients. More than 80% of ITP patients responded to corticosteroid treatment, but relapses were common after treatment was discontinued. ITP also affects the health-related quality of life (HRQoL) of affected patients. Treatment outcomes, treatment adherence, and HRQoL have not been studied in Ethiopian ITP patients.

Objective: To assess treatment outcomes, treatment adherence, and HRQoL in patients with ITP at Tikur Anbessa Specialized Hospital (TASH) and St. Paul's Hospital Millennium Medical College (SPHMMC).

Methods: The retrospective hospital-based cohort study design was conducted from September 15/2022 to January 15/2023. Convenient sampling was used to recruit 214 study participants. Ethical clearance and approval of the study protocol were obtained from the institutional ethics review board of the School of Pharmacy, and permission was obtained from the respective study sites. Descriptive statistics were used to summarize the sociodemographic data and clinical and treatment characteristics. Multinomial regression analysis models were used to identify Predictive factors for treatment outcomes and linear regression analysis models were also used to identify Predictive factors for HRQoL. A p-value of less than 0.05 was generally considered statistically significant.

Results: Most of the study participants 161(75.5%) were female patients. During diagnosis, 166(77.6%) had epistaxis and wet purpura (mucosal bleeding). Regarding the treatment, the majority 172(80.4%) of study participants took prednisolone alone, and 143(66.8%) of the study participant have experienced at least one side effect of corticosteroids throughout the treatment period. Regarding medication adherence 178(83.2%) of study participants had good adherence to their ITP medications. The complete response rate at 3 months was 139 (65.0%) and the overall impact of ITP on HRQoL was 35.41±9.27. Predictive factors for partial response to treatment were increased impact of ITP on HRQoL (AOR =1.221, 95% CI: 1.096-1.360), study site TASH (AOR =0.431, 95% CI: 0.197-0.941), and presence of heavy

menstrual bleeding (AOR =2.255, 95% CI: 0.925-5.497) compared with complete response. Hepatitis B virus-infected ITP patients (AOR = 0.052, 95% CI: 0.004-0.621) was also a predictive factor for no response compared with complete response. Furthermore, predictive factors for an increasingly higher impact of ITP on HRQoL were the development of emotionally related corticosteroid side effects (β= 0.392, 95% CI: 5.160-9.961, P< 0.001), the presence of fatigue during the assessment (β= 0.326, 95% CI: 4.394-9.475, P< 0.001), patients not taking cotrimoxazole prophylaxis treatment (β= 0.236, 95% CI: 2.236-6.570, P< 0.001), living far from the hematology clinic (outside Addis Ababa) (β= 0166, 95% CI: 1.107-5.114 P=0.003), having epistaxis and wet purpura (mucosal bleeding) (β= 0.191, 95% CI: 0.091-4.259, P=0.001), and skin symptoms (petechiae and ecchymosis) (β= 0.041, 95% CI: 0.091-4.259 P=0.041) during diagnosis.

Conclusion: The highest complete response rate was achieved at 12 months and the impact of ITP on HRQoL was high in terms of daily energy level and work capacity. The patients had good adherence to their ITP medications, and more than half of the study participants experienced at least one side effect of corticosteroids throughout the treatment period.

Keywords: Immune thrombocytopenia, treatment outcomes, health-related quality of life, Platelet count, Immune thrombocytopenia life quality index, corticosteroids, Ethiopia.

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Table of Contents

Abbreviations

ASH	American Society of Hematology
CLL	Chronic lymphocytic leukemia
COVID-19	Coronavirus Disease
H. pylori	Helicobacter pylori
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HMIS	Health Management Information System
HRQoL	Health-Related Quality of Life
ILQI	ITP Life Quality Index
ITP	Immune Thrombocytopenia
ITP-PAQ	ITP-Patient Assessment Questionnaire
IVIgs	Intravenous Immunoglobulin's
LS	Laparoscopic splenectomy
MGL	Morisky Green Levine scale
SPHMMC	St Poulos Hospital Millennium Medical College
TASH	Tikur Anbessa Specialized Hospital
TPO-RAs	Thrombopoietin-Receptor Agonists
SLE	Systemic Lupus Erythematous

List of Tables

List of Figures

1. Introduction

1.1. Background

Immune thrombocytopenia (ITP) is an acquired form of thrombocytopenia and bleeding disorder caused by autoantibody-mediated and cell-mediated destruction of platelets, resulting in accelerated platelet clearance and impaired thrombopoiesis [1-3]. It is described by a transient or persistent reduction in platelet count <100 $x10^9$/L and an increased risk of bleeding depending on the degree of thrombocytopenia [4, 5]. Autoantibodies are considered the main cause of thrombocytopenia and binding of anti-platelet autoantibodies to their antigenic glycoprotein leads to elimination/phagocytosis of platelets in the reticuloendothelial system by monocytes/macrophages, primarily in the spleen [6, 7].

The incidence of ITP varies and is most common in young adults, particularly women of childbearing age, with a female-to-male ratio of 2 to 1 and an estimated 1.6-4.4 per 100,000 person-years [8-10]. The age-adjusted prevalence of ITP in the United States is estimated to be 9.5 per 100,000 persons [11]. In the adult population, more than 20% of ITP patients have secondary etiology with infectious, autoimmune diseases, malignancies, and certain medications such as heparin, carbamazepine, linezolid, rifampicin, and vancomycin [12-16]. The Coronavirus disease (COVID-19) virus has also caused moderate ITP after one week of presentation and diagnosis [17].

According to the guidelines of the American Society of Hematology (ASH) of 2019, ITP is classified into a primary and a secondary form depending on the cause [18]. Primary ITP is an autoimmune disease characterized by isolated thrombocytopenia with a platelet count of <100 $x10^9$/L in the peripheral blood without other causes or diseases that may be associated with thrombocytopenia. Secondary ITP includes all forms of ITP due to underlying disease or drug exposure, with the exceptions of primary ITP. Based on the phases of the disease, ITP can be classified as newly diagnosed persistent, chronic, and severe ITP [4, 5, 19]. The diagnostic modality of ITP is based on clinical evaluation of isolated bleeding symptoms consistent with thrombocytopenia and exclusion of other causes of isolated thrombocytopenia based on history, physical examination, blood count, and evaluation of peripheral blood count in the absence of hepatosplenomegaly or lymphadenopathy [19-21]**.** A platelet count <100 $x10^9$/L has been established as a threshold for the diagnosis of ITP [4, 19]. Autoantibodies to platelet antigens are considered a diagnostic feature of ITP, but only about 60% of patients

have platelet antibodies detected [13]. At our institution, due to the unavailability of local guidelines for the treatment and diagnosis of ITP, the ASH guidelines and the international consensus report were used.

The goal of ITP therapy is to reduce the risk of clinically important bleeding and increase platelet count [22]. Treatment outcomes of ITP are mainly evaluated by the clinical response rate to treatment, relapse rate after the treatment, platelet count before and after the treatment, health-related quality of life (HRQoL), and adverse events of the treatment/procedure [4, 18, 23-27]. Currently, there are mainly three approaches in ITP treatment, namely suppression or modification of abnormal immune responses (corticosteroids or rituximab), suppression of platelet clearance (splenectomy), and stimulation of platelet production (thrombopoietin receptor agonists (TPO-RAs)) [28]. Corticosteroids are the standard first-line treatment for adults with ITP who require treatment, and there is no relative contradiction with the addition of intravenous immunoglobulin (IVIg) in patients with active bleeding or those who prefer a rapid increase in platelet count [21]. Due to the unavailability of IVIg and TPO-RAs, our institution mainly used corticosteroids as first-line treatment and rituximab, azathioprine, splenectomy, and Prednisolone as second-line treatment.

Clinicians and researchers increasingly recognize the HRQoL as an important tool for assessing the effectiveness of the medical intervention as a treatment outcome. Actual bleeding, fatigue, decreased energy, depression, and treatment side effects all contribute to HRQoL impairment in ITP patients, which can lead to lifestyle restrictions [21, 29]**.** An assessment of patient-reported outcomes in ITP is valuable to understanding and guiding treatment by modifying specific treatment elements such as medications, consultant care, patient education, or support services hence improving patient outcomes [30]. Patient-reported outcomes are direct responses from patients about how they feel or function to a health condition without interpretation by healthcare professionals and one of the valid and reliable instruments that exist to capture ITP disease-specific outcomes was the ITP Life Quality Index (ILQI) tool [31].

1.2. Statements of problem

In recent years, the basic understanding of the pathophysiology of ITP has improved significantly, but the epidemiology, patient-reported outcomes, and clinical course of ITP have not been well studied in the general population [32], particularly in African populations. ITP treatment is challenging, and treatment outcomes are dependent on a variety of factors, the majority of which are unknown and specific to each patient. Due to this, treatment should be tailored to the individual patient, considering factors such as age, lifestyle, comorbidities, compliance, patient preferences, the presence and severity of bleeding, and the potential treatment side effects [33]. Only about one-third of treated patients can expect a long-term response due to this 60–70% of adult patients require additional treatment owing to intolerability to steroids or relapse and 98% of ITP patients who are taking steroids was reporting at least one side effect [34]. Immune thrombocytopenia becomes persistent or chronic in approximately 70% of adult cases, indicating assessment of patient-reported outcomes in ITP is valuable to understanding and guiding treatment, these measures are not routinely measured in the clinical setting [4, 24]. With this variation in disease progression and management, assessing treatment outcomes of ITP patients is critical and helps optimize treatment strategies.

Corticosteroid therapy is one of the cornerstones of treatments for acute ITP, but steroids have several side effects and long-term responses are seen in only 25% of patients that affect the treatment outcome [35]. More than 80% of ITP patients responded to corticosteroid treatment, but relapses were common after treatment discontinuation [36]. Immunosuppressive therapy, especially high-dose corticosteroids, predisposes patients to infections and reduces response rates significantly [37]. Close evaluations of ITP treatment and associated outcomes are important to improve outcomes. This is critical for ITP patients because the prolonged duration of corticosteroid treatment is associated with various steroid-induced toxicities to reduce toxicity ASH Guidelines and an international consensus report recommended that the use of steroids should be limited to a short period [4, 18].

Current ITP treatments, particularly corticosteroids, are associated with multiple bothersome side effects that may lead to patients stopping or reducing therapy. Due to this more than 90% of patients who had to discontinue or reduce treatment due to corticosteroid side effects was roughly double (37.8%) of patients treated with other therapy types (IVIg, 18.0%; anti-D, 20.6%; Rituximab, 16.4%) [34]. Clinical practice varies greatly not only between countries

but also between centers within the same country, and there is insufficient data in the literature to estimate treatment adherence in ITP patients [38]. In Ethiopia, no study assesses the treatment adherence of the ITP patient to the recommended therapy by health care providers.

Treating physicians prioritize addressing low platelet counts and avoiding life-threatening bleeds over HRQoL. Patients, on the other hand, are concerned with how ITP affects their lives, specifically how they feel and function [39]. Fatigue, along with anxiety, fear, and frustration, was one of the most debilitating aspects of ITP patients' HRQoL on their condition [40]. The assessment is required in Ethiopia because the majority of chronic ITP patients have poor HRQoL in emotional well-being, fatigue, functional, reproductive, and health domains, affecting daily life and, as a result, mental health. Prolonged use of corticosteroids in adults may have a negative impact on HRQoL due to the effects on sleep disturbances, weight gain, and mental health [41]. Furthermore, while on corticosteroids, these patients may develop gastrointestinal ulcers, osteoporosis, increased blood pressure, and blood glucose, necessitating the administration of additional medications [39].

As far as our knowledge, still there is no published evidence-based literature done in Ethiopia and as well as in Africa that assesses the treatment outcomes, HRQoL, and treatment adherence of ITP patients. The cornerstone of most ITP treatments was corticosteroid common side effects and impact on HRQoL and treatment outcome was not assessed. Hence, this study aimed to investigate the treatment outcomes treatment adherence, and HRQoL of ITP patients and to determine the factors associated with treatment outcomes, treatment adherence, and HRQoL of ITP patients in Tikur Anbessa Specialized Hospital (TASH) and St. Paul's Hospital Millennium Medical College (SPHMMC) in Addis Ababa, Ethiopia.

1.3. Significance of the study

Evaluation of clinical outcomes, treatment adherence, complications of corticosteroid treatment, and HRQoL of ITP patients in Ethiopia may provide new insights into ITP treatment practices by allowing quantification of disease outcomes according to patient perceptions. It also allows medical decisions for health professionals to be adapted from the physical, emotional, and social needs of the patient. It also improves adherence to the treatment plan, quality of medical care, caregiver skills, and patient survival.

The information of the current study finding will help the respective institutions and other relevant stakeholders to develop a local guideline by including the patients' perspectives on HRQoL, side effects of corticosteroid treatments, and treatment adherence. The study can also serve as a basis for future evaluations of clinical outcomes, treatment complications of corticosteroids, treatment adherence, and HRQoL of ITP patients. Further, it might serve as a reference for future public health and clinical research.

2. Literature review

Immune thrombocytopenia is a heterogeneous disorder due to variability in the natural history of the disorder and treatment response leading to platelet autoantibody production [13, 21]. Furthermore, environmental factors may have an impact on platelet turnover, bleeding propensity, and response to ITP-targeted therapy [13]. Initial treatment decisions are based on the extent of bleeding, the patient's age, complications or tolerance of side effects of certain therapies, concomitant diseases that may promote bleeding propensity, physical activity, and patient lifestyle [21].

2.1. Secondary causes of immune thrombocytopenia

Secondary ITP is all forms of ITP due to an underlying disease or due to drug exposure except primary ITP [4]. The occurrence of ITP following infections that result in the production of cross-reactive antibodies and the co-occurrence of specific autoantibodies suggests that the predisposition to form platelet autoantibodies is caused by several mechanisms [13]. From the infection disease cause; human immunodeficiency virus (HIV), hepatitis B virus (HBV), *H- Pylori*, and hepatitis C virus (HCV) were the most common Couse of secondary ITP but the patients are relatively asymptomatic [42]. The Hepatitis C virus is the most common infection associated with ITP, which is present in up to 20% of ITP cases [15]. In addition that the incidence of ITP in patients with HCV infection is about twice as high as in the uninfected population [12]. About 5-10% of HIV-infected patients develop ITP during the disease [16]. Drug-induced thrombocytopenia is typically severe and occurs suddenly. Drugs that have definite clinical evidence for causing ITP were quinine, carbamazepine, heparin, vaccines, linezolid, rifampicin, sulfonamides, vancomycin, cotrimoxazole, oxaliplatin, and Exenatide extended-release were the common drugs that cause ITP [14, 43]. From hematologic malignancy, chronic lymphocytic leukemia (CLL) is the most common malignancy that has an association with ITP and 1% to 5% of patients with CLL can develop ITP [13, 44, 45].

Screening tests for HIV and HCV patients are appropriate for secondary causes of ITP and recent studies have demonstrated the association between ITP and *H-pylori* infection with the significant rise in platelet count following *H-pylori* eradication therapy [15, 16, 42]. About 50% of ITP symptoms spontaneously resolved after empirical treatment of *H. pylori* infection [46, 47]. The guidelines suggest that the initial treatment of most viral infections

consisted of observation and then treatment with corticosteroids, IVIg, or anti-D immunoglobulin [42]. In a study conducted in Syria out of 50 patients diagnosed with cases of chronic ITP 36 were diagnosed with *H-pylori* infection [48]. In another study done in Japan Out of 61 diagnosed cases of ITP, 50 of them were *H-pylori*-positive patients, only 29 patients received *H-pylori* eradication therapy, and 27 patients with a response rate of 93% showed a rise in platelet count [49]. In addition to that a bone marrow biopsy confirmed ITP in 14% of HIV-positive adult patients with thrombocytopenia (67% with less than 100 $x10^9$/L) [50]. In a cohort study done in the United States of America, individuals indicate that those infected with HCV were at high risk for ITP with an overall incidence of 30.2 per 100,000 person-years and HCV-associated risks for ITP [12].

2.2. Treatment outcomes of immune thrombocytopenia

ITP treatment should be personalized for each patient, but this is not always possible. Treatment decisions in ITP are based on the extent of bleeding, age, comorbid diseases that promote bleeding, complications of specific therapies, activity, lifestyle, fatigue, tolerance to side effects, need for interventions with bleeding risk, and accessibility of care. Female sex, a platelet count of less than 20 $x10^9$/L, and the use of anticoagulants were all associated with bleeding at diagnosis [21, 51]. Corticosteroids, IVIg, and anti-D immunoglobulin are standard first-line treatment options for patients with newly-diagnosed primary ITP [21, 40]. More than 80% of ITP patients responded to corticosteroid treatment, but relapsing was common after stopping treatments and also maintenance of low-dose prednisolone (7.5mg/day) for 6 months was not preventing relapse of ITP [36, 52]. In a study done in Malaysia about 36.5%, 22.6% and 14.9% of study participants had Complete response, partial response, and no response at 3 months of starting treatment respectively; in addition to that at 12 months of starting treatment 26.1%, 18.6%, and 13.4% have a complete response, partial response, and no response respectively [32]. In a multicenter pilot study done in Italy, a patient treated with four to six cycles of dexamethasone showed that 80-90% of response rate at 15 months [53]. Another study compared daily prednisone to pulsed dexamethasone in treatment-naive adults in patients with ITP in Germany, the initial response rates (platelet count > 50 $x10^9$/L) were similar between prednisone and dexamethasone, but long-term remission was significantly higher in dexamethasone 77% than prednisone 22% [54]. In a prospective cohort study done in the United States of America about 50% of patients have been prescribed an oral corticosteroid, with the majority being prescribed immediately

following diagnosis [55]. Chronic lymphocytic leukemia-related IPT is less responsive to IVIg and prednisone, but rituximab and cyclosporine treatments have shown promising results [13, 56].

There are numerous second-line treatment options available, but there is no clear consensus on the optimal order of use due to the marked variability of ITP treatment options [40]. The 2019 ASH guidelines recommend splenectomy or TPO-RA in adults with ITP lasting 3 months who are corticosteroid-dependent or have no response to corticosteroids [18]. A splenectomy is a second-line treatment option for adults who have had ITP for more than 12 months [18]. In a study conducted in the United States of America, rituximab (16%) was the most commonly used second-line treatment option for ITP, followed by romiplostim (9%) and eltrombopag (5%) [55]. Another study conducted in Korea found that 47.5% of patients had a complete response, 40.7% had a partial response, and 11.9% had no response to Laparoscopic splenectomy (LS). During the follow-up period, the relapse rate was 15.2%, and infections were the most common morbidities [57]. In emergencies where the platelet count must be increased within 24 hours, a combination of initial treatments, including IV corticosteroids and, in most cases, IVIg, should be used. Platelet transfusions can be beneficial and should not be delayed in cases of life-threatening bleeding, particularly intracranial hemorrhage [21].

2.3. Side effects of treatment and its adherence to treatment plan.

The most important complication in ITP patients is life-threatening hemorrhage, especially intracranial hemorrhage and gastrointestinal hemorrhage [46]. Current ITP treatments, particularly corticosteroids, are associated with several unpleasant side effects that may lead to patients discontinuing or reducing treatment [41]. In one survey, the overall burden of steroids in chronic ITP was (37.8%) and in more than 90% of patients who had to discontinue or reduce treatment because of corticosteroid side effects compared with patients treated with other forms of therapy (IVIg, 18.0%; anti-D, 20.6%; rituximab, 16.4%); and it was found that patients who reported one or more side effects were more likely to discontinue or reduce treatment if they also reported a higher level of discomfort for that specific treatment. For patients who had taken steroids, there was a significant association between the need to discontinue/reduce treatment based on the number of side effects and gender, as female patients reported a higher level of discomfort than males [34]. For patients who tolerate

steroids and IVIg less well, as expected, rituximab or romiplostim may be better choices, as these agents require less self-management in daily life. Regarding ITP treatment adherence, there is insufficient data in the literature to estimate treatment adherence in ITP patients to the recommended therapy by health care providers [38]. Health-related quality of lifeThe impact of ITP, particularly chronic ITP, on patients' HRQoL is significant [58]. Severe fatigue, which occurs in 39% to 59% of adult ITP patients and is underdiagnosed by physicians, is the most difficult ITP symptom to treat [59]. Studies have shown that patients with ITP suffer from fatigue, impaired HRQoL, and frequently withdraw from social activities, which can lead to depression [39]. Immune thrombocytopenia impairs HRQoL in all emotional, functional, reproductive, and health domains, as well as daily living, affecting mental health [21]. According to the ITP World Impact Survey data, petechiae (64%) and bruising of unknown origin (65%) were among the most frequently cited signs and symptoms by patients at diagnosis. In addition to that anxiety about maintaining a stable platelet count (34%) and fatigue were also common signs and symptoms that patients most desired to be resolved [40]. These signs and symptoms, such as fatigue, depression, anxiety, and fear of bleeding, affected HRQoL [58]. While many physicians focus on treating low platelet counts as the best approach to treat their patients and prevent life-threatening bleeding, for many patients, focusing on platelet counts alone does not truly assess the HRQoL of ITP patients [39].

A systematic review shows that treatment of ITP generally had no effect on the HRQoL of adult patients with chronic ITP. On the other hand, the burdens associated with treatment, such as hospitalization and side effects, have a negative impact on HRQoL [26, 58]. A study conducted on patients from 85 investigational sites in Germany, Belgium, Austria, Italy, France, Spain, the Netherlands, the United Kingdom, the Czech Republic, Poland, Switzerland, the United States, Canada, and Australia showed that patients receiving romiplostim had significant improvements in symptoms, mental health, and overall quality of life compared with standard treatment, but there was no significant difference in fatigue [60]. In randomized clinical trials in the United States, United Kingdom, France, the Netherlands, and Spain, patients who underwent splenectomy and received romiplostim showed significantly greater improvements in HRQoL compared with placebo [61].

Several studies have assessed the HRQoL of ITP patients using different instruments such as the 36-item Short-Form Health Survey, the EuroQol Questionnaire with five dimensions, the ITP Patient Assessment Questionnaire (ITP-PAQ), and the ILQI [29, 61-64]. In a systematic

review of HRQoL in ITP patients, the ITP-PAQ instrument was used to assess the impact on physiological measures as well as patient functioning and well-being [26]. The more recently accepted instrument for assessing HRQoL in ITP patients was the ILQI. The content and psychometric validity of the ILQI were established in 13 countries (the United States, China, the United Kingdom, France, Germany, Italy, India, Canada, Turkey, Japan, Colombia, Spain, and Egypt) [31].

2.4. Conceptual Frameworks

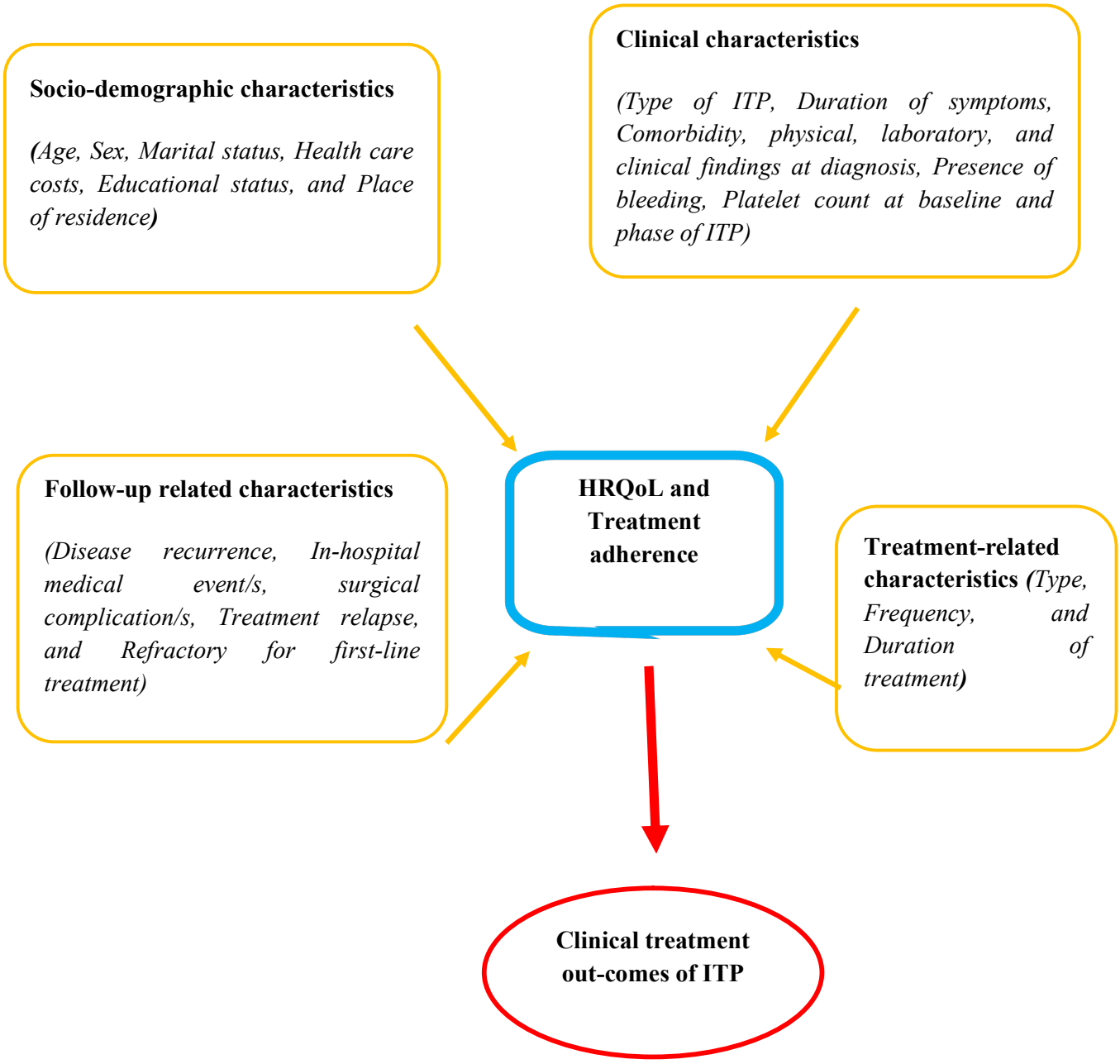

Figure 1: Conceptual framework which shows the association between the treatment outcomes, health-related quality of life, and treatment adherence of immune thrombocytopenia patients with different factors adopted from different kinds of literature.

3. Objective

To assess the treatment outcomes, treatment adherence, and HRQoL in patients with ITP at TASH and SPHMMC, in Addis Ababa, Ethiopia

3.1. Specific objective

- ✓ To assess treatment outcomes in patients treated for ITP
- ✓ To determine predictive factors for clinical treatment outcomes of ITP
- ✓ To assess treatment adherence in patients treated for ITP
- ✓ To describe the HRQoL of patients with ITP
- ✓ To determine factors associated with the HRQoL of a patient with ITP

4. Materials and Methods

4.1. Study setting

This study was conducted at TASH and SPHMMC. TASH is the largest teaching hospital affiliated with the College of Health Sciences at Addis Ababa University and serves as a training center for medical, pharmacy, and other health sciences students. It is also a facility where specialized comprehensive and clinical services are provided. According to the hospital's Health Management Information System (HMIS) data, an average of 50 ITP patients visited the hematology clinic per month. SPHMMC provides services in the emergency department, inpatient department, and outpatient department. The outpatient departments have many specialty clinics and hematology is one of them that serves patients with many hematologic disorders. According to the hospital's HMIS data, SPHMMC's hematology clinic was visited by an average of 20 ITP patients per month.

4.2. Study design and period

A retrospective, hospital-based cohort study was conducted to assess treatment response in ITP patients who were followed up in the hematology clinic of TASH and SPHMMC during the study period, which lasted from September 15, 2022, to January 15, 2023. Data on HRQoL, treatment adherence, and corticosteroid side effects were collected directly from patients.

4.3. Population

4.3.1. Source of population

All patients treated for ITP at the hematology clinics of TASH and SPHMMC were considered the source population.

4.3.2. Study population

The study population was all adult patients treated for ITP at the adult hematology clinics of TASH and SPHMMC who met the eligibility criteria during the study period.

4.4. Eligibility criteria

4.4.1. Inclusion criteria

I. All adult patients attending a hospital during the study period who have a confirmed diagnosis of ITP according to the guidelines of ASH of 2019 and the standardization of terminology, definitions, and outcome criteria in ITP of adults and children (primary, secondary, newly diagnosed, persistent, chronic and severe ITP) [4, 21]
II. Patients who have been taking treatment for at least three months
III. Aged ≥14 years and
IV. Patients willing to participate in the study were included.

4.4.2. Exclusion criteria

I. Patients in whom no medical treatment was started and
II. Incomplete medical recodes were excluded.

4.5. Sample size determination and sampling technique

4.5.1. Sample size determination

All adult ITP patients attending TASH and SPHMMC during the study period (4 months) were recruited. While the event is rare, the sample includes all patients who received ITP treatment and met the eligibility criteria during the study period. The study period was 4 months. This is because most patients were appointed after 3 or 4 months. If the study period were extended beyond 4 months, most of the data would be redundant and the chance of getting new patients would be very low.

4.5.2. Sampling technique

The study participants were recruited from TASH and SPHMMC using a consecutive sampling technique. Patients treated at both hospitals' outpatient hematology clinics during the study period who met the eligibility criteria and volunteered to participate in this study were enrolled.

4.6. Study variables

4.6.1. Dependent variables

- ✓ Treatment outcomes of ITP patients
- ✓ HRQoL of ITP patients
- ✓ Treatment adherence

4.6.2. Independent variable

- ✓ Socio-demographic and lifestyle characteristics (age, sex, educational status, place of residence, marital status, and health care costs).
- ✓ Clinical and pathological characteristics (type of ITP, duration of symptoms, comorbidity, physical, laboratory, and clinical findings at diagnosis, presence of bleeding, platelet count at baseline and during data collection and phase of ITP).
- ✓ Treatment-related characteristics (type, frequency, and duration of treatment)
- ✓ Follow-up related characteristics (disease recurrence, in-hospital medical event/s, surgical complication/s, treatment relapse, and refractory for first-line treatment).

4.7. Data collection and management

4.7.1. Data collection instruments:

A structured questionnaire was used to collect data from study participants on socio-demographic characteristics such as age, sex, educational status, place of residence, marital status, and health care costs. In addition, a data abstraction form was created by reviewing the medical chart and relevant published articles to capture relevant clinical and treatment characteristics. Data on treatment adherence and HRQoL was collected using the Morisky Green Levine scale (MGL), and the ITP Life Quality Index (ILQI) tool, respectively.

I. Data abstraction form

The data abstraction format is designed to extract information from the medical record or directly from the patient, such as clinical and pathologic characteristics (type of ITP, duration of symptoms, comorbidity, physical, laboratory, and clinical findings at diagnosis, presence of bleeding, platelet count at baseline and during data collection, and phase of ITP), treatment-related characteristics (type, frequency, and duration of treatment), follow-up-

related characteristics (disease recurrence, in-hospital medical events, surgical complications, treatment relapse, and refractoriness).

II. Treatment outcome tools

After an extensive review of the literature [32, 65-67]; and with the help of experts, structured questionnaires were designed to evaluate the treatment outcomes of ITP and the side effects of corticosteroid treatment in ITP patients.

III. Morisky Green Levine scale (MGL)

The MGL is in the public domain and is widely cited in peer-reviewed journals. It was originally developed and validated for patients with hypertension to assess self-reported medication-taking behavior [68]. Later, the scale was used to assess medication adherence in patients with various chronic conditions [69, 70]. The scale contains four items with a score of ***"Yes" = 1 and "No" = 0***. The items are summed to obtain a score range of 0 to 4. The scores were rated as follows: good adherence (MGL = 0), and poor adherence (MGL ≥1).

IV. ITP Life Quality Index (ILQI)

The ILQI was created by clinical experts in the field of ITP and was initially considered unidimensional, yielding a single score. It is a 10-item patient questionnaire with a 'last month' recall period. The responses range from 'never' to 'always'. For three questions (questions 1, 2, and 5), there are additional response options that allow the patient to indicate that the question is irrelevant to them or that they do not wish to answer. For these additional responses, 'I am not currently working/studying due to ITP' the value 4 applies and for responses 'I am not currently working/studying due to other reasons or does not apply/would rather not say" the value 0 applies. A total sum score between 7 and 40 was originally proposed. Content and psychometric validity were assessed in 13 countries [31].

In Ethiopia, the instrument was not validated. Therefore, the acceptability, reliability, and validity of the psychometric properties of the Amharic version of the IQLI were tested before conducting the main study on a patient with ITP at TASH. The Amharic version of the ILQI instrument is an acceptable, valid, and reliable instrument for assessing the HRQoL of patients with ITP in the Ethiopian population. Acceptability was tested in terms of overall adherence to each item of the ILQI instrument. A total of 100 patients participated, and all ten

items of the questionnaire were completed within 5 to 10 minutes. The instrument was reliable with a Cronbach's alpha based on the standardized items of 0.953 and inter-item correlation coefficient between items of 0.147 to 0.956 (average 0.552). Furthermore, the instrument proved to be construct-valid. Factor analysis between components revealed that Item-1 had an eigenvalue greater than one and explained 72.532% of the total variance of all ten ILQI domains. To test construct validity, factor loading was conducted. The results of factor loading showed that the influence of ITP on the completion of daily tasks (0.928), the influence of ITP on the ability to help others (0.903), and the influence of ITP on the ability to focus on daily tasks (0.901) had high positive loading. To examine the relationship between the ILQI total score (alternative score) and each ILQI item, as well as the relationship between individual ILQI items, convergent validity was used. The ILQI total score (alternative score) had a strong (r=0.9) correlation with item-8 (impact of ITP on the ability to support people close to you) and a moderate (r=0.317) correlation with item-5 (impact of ITP on their sex life).

4.9. Data quality assurance

This questionnaire was first translated from the original English version into Amharic by a bilingual person fluent in Amharic and English. A second bilingual translator, who did not know the original English version, back-translated the instrument from the Amharic version into English. The two English translation versions were then compared for equivalence. Any discrepancies in the translation were resolved in a discussion. A pretest was then administered to 5% of ITP patients at SPHMMC. The purpose of the pre-test was to ensure that respondents understand the questions and can review the wording, logic, and skip order in a way that makes sense to respondents. Based on the result of the pre-test, appropriate corrections were made before the actual study is conducted. Data collectors were recruited by two clinical pharmacists and one nurse and a half-day training was given by the principal investigator about the objectives of the study and how to use the tool to collect data directly from the patient and medical records/charts. To ensure the completeness and consistency of the data, all data were reviewed daily by the study director to ensure the quality of the data.

4.10. Data Analysis

Data was entered and analyzed using SPSS version 26. Descriptive statistics such as frequency, median, and range were used to summarize the sociodemographic data, and

clinical and treatment characteristics, and to assess the distribution of responses. After checking the assumptions, the univariate analysis was performed to obtain candidate variables for the multivariate regression model to determine possible predictors of the treatment outcome and HRQoL variables. In the bivariate analysis, factors associated with treatment outcomes and HRQoL that have a p-value of < 0.2 were considered as candidates for the multinomial regression model and multivariate linear regression model to identify strong factors associated with treatment outcomes and HRQoL, respectively. A p-value < 0.05 was considered statistically significant.

4.11. Operational definition

Treatment outcome: The treatment outcome was primarily explained by the platelet number increase; in addition to that it is affected by treatment adherence, bleeding, side effects of the medication, and HRQoL of ITP patients after the treatment. Treatment outcome is classified as complete response, partial response, and no response.

Complete response (CR): A platelet count after treatment ≥100 $x10^9$/L measured on two occasions > 7 days apart and absence of clinically relevant bleeding.

Partial response (PR): Platelet count ≥30 $x10^9$/L and a greater than 2-fold increase in platelet count from baseline measured on 2 occasions > 7 days apart and the absence of bleeding.

No response (NR): Platelet count <30 $x10^9$/L or a less than 2-fold increase in platelet count from baseline measured on 2 occasions > 7 days apart or the presence of bleeding.

Health-related quality of life (HRQoL): is a measure of how much ITP has affected patients' life over the past months and it is scored as ranging between 7 and 40; where the lower score indicates low impact and a higher score indicates that a higher impact of ITP on HRQoL.

Adherence: The extent to which a person's behavior corresponds with recommendations from health care providers.

- ✓ **Good adherence:** was determined when those study participants' Morisky Green Levine scale scored= 0.

- ✓ **Poor adherence:** was determined when those study participants on the Morisky Green Levine scales scored ≥1.

Primary ITP: Characterized by isolated thrombocytopenia with peripheral blood platelet count <100 $x10^9$/L in the absence of other causes or disorders that may be associated with thrombocytopenia.

Secondary ITP: All forms of ITP due to an underlying disease or due to drug exposure except primary ITP.

Newly diagnosed ITP: Within 3 months from diagnosis.

Persistent ITP: Between 3 to 12 months from diagnosis.

Chronic ITP: Lasting for more than 12 months from diagnosis.

Corticosteroid dependent ITP: The need for ongoing or repeated doses administration of corticosteroids for at least 2 months to maintain a platelet count at or above 30 $x10^9$/L and/or to avoid bleeding (patients with corticosteroid dependence are considered nonresponses).

4.12. Ethical consideration

Ethical Approval of the study and study protocol was obtained from AAU, CHS, School of pharmacy ethical review board (approval number: ERB/SOP/487/14/2022). Before data collection, a written permission letter was obtained from the hematology/oncology unit of TASH and SPHMMC. The aims of the study were clearly explained to the study participants. The information was collected after obtaining written informed consent from each participant and taken from participants' family/legal guardian for participants whose age was between 14-18 years. The right was given to the study participants to refuse or discontinue participation at any time they want and the chance to ask anything about the study. For obscurity, the participant's name was not used at the time of data collection and all other personnel information was kept entirely obscure and confidentiality was assured throughout the study period.

5. Results

5.1. Socio-demographic characteristics of study participants

A total of 214 study participants took part in this study; the majority 153(71.5%) of them were from TASH. Most 161(75.5%) were female patients with a female-to-male ratio of 3 to 1. Regarding the age distribution, the median age of the study participants was 30 years and ranged from 15 to 88 years, and most 78(36.4%) participants were in the 25-34 years age group. Married 149(69.6%) made up the largest proportion. One-third of the study participants had a university degree or more 76(35.5%) and were also self-employed 59(27.6%). Most participants 197(92.1%) live with their family and half of them 109(50.9%) live far from the hematology clinic (outside Addis Ababa). In addition, more than half of the health care costs of the study participants 133(62.1%) were borne by the patients themselves or by their relatives (Table 1).

Table 1: Sociodemographic data of ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

Variables		**Frequency**	**Percentage**
Study site	TASH	153	71.5
	SPHMMC	61	28.5
Sex	Female	161	75.2
	Male	53	24.8
Age	14-24	58	27.1
	25-34	78	36.5
	35-44	40	18.7
	45-54	20	9.3
	55 and above	18	8.4
Marital status	Married	149	69.6
	Never married	58	27.1
	Widowed	4	1.9
	Divorced	3	1.4
Educational level	Unable to read and write	7	3.3
	Enable read and Write	12	5.6

	Primary education (grades 1-8)	33	15.4
	Secondary Education (grades 9-12)	54	25.2
	Diploma/Certificate	32	15.0
	Degree and Above	76	35.5
Occupational status	Employed	59	27.6
	Housewife	47	22.0
	Self-Employed	45	21.0
	Student	41	19.2
	Unemployed	20	9.3
	Retired	2	0.9
Residence	Outside Addis Ababa	109	50.9
	Addis Ababa	105	49.1
Health service charge	With cash	133	62.1
	With health insurance	56	26.2
	With free	25	11.7
With whom do you live?	With family	197	92.1
	Alone	17	7.9

Note: TASH: Tikur Anbessa Specialized Hospital, SPHMMC: St. Paul's Hospital Millennium Medical College

5.2. Clinical characteristics of ITP patients during diagnosis

The clinical characteristics of study participants are shown in Table 2. Of the 214 study participants, only 91(42.5%) had comorbidities. During the assessment, the most common symptoms of ITP were fatigue 53(25.2%), followed by headache 14(6.5%). Common physical findings during diagnosis include epistaxis and wet purpura (mucosal bleeding) 166(77.6%), followed by fatigue 157(73.4%), and skin manifestations (petechiae and ecchymosis) 120(56.1%).

Table 2: Clinical characteristics of ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

Variables		**Frequency**	**Percentage**
Comorbidity	Yes	91	42.5
	No	123	57.5
Current symptoms of ITP	Fatigue	54	25.2
	Headache	14	6.5
	Depression	8	3.7
	Weight loss	3	1.4
	Bleeding	1	0.5
Physical findings during diagnosis	Epistaxis and wet purpura	166	77.6
	Fatigue	157	73.4
	Skin manifestation	120	56.1
	Heavy menstrual bleeding	59	27.6
	Signs of anemia (pallor)	54	25.2
	Severe bleeding*	12	5.6

Severe bleeding* gastrointestinal bleeding, Intracranial bleeding, rectal bleeding, retinal hemorrhage.

Of the total study participants, 91 (42.5%) patients had comorbidities and Iron deficiency anemia 20(22.0%), followed by HIV 15(16.5%), HBV 7(7.7%), and Systemic Lupus Erythematous (SLE) 7(7.7%) accounted for the highest proportion of comorbidities in ITP patients attending TASH and SPHMMC during the study period (Figure 2).

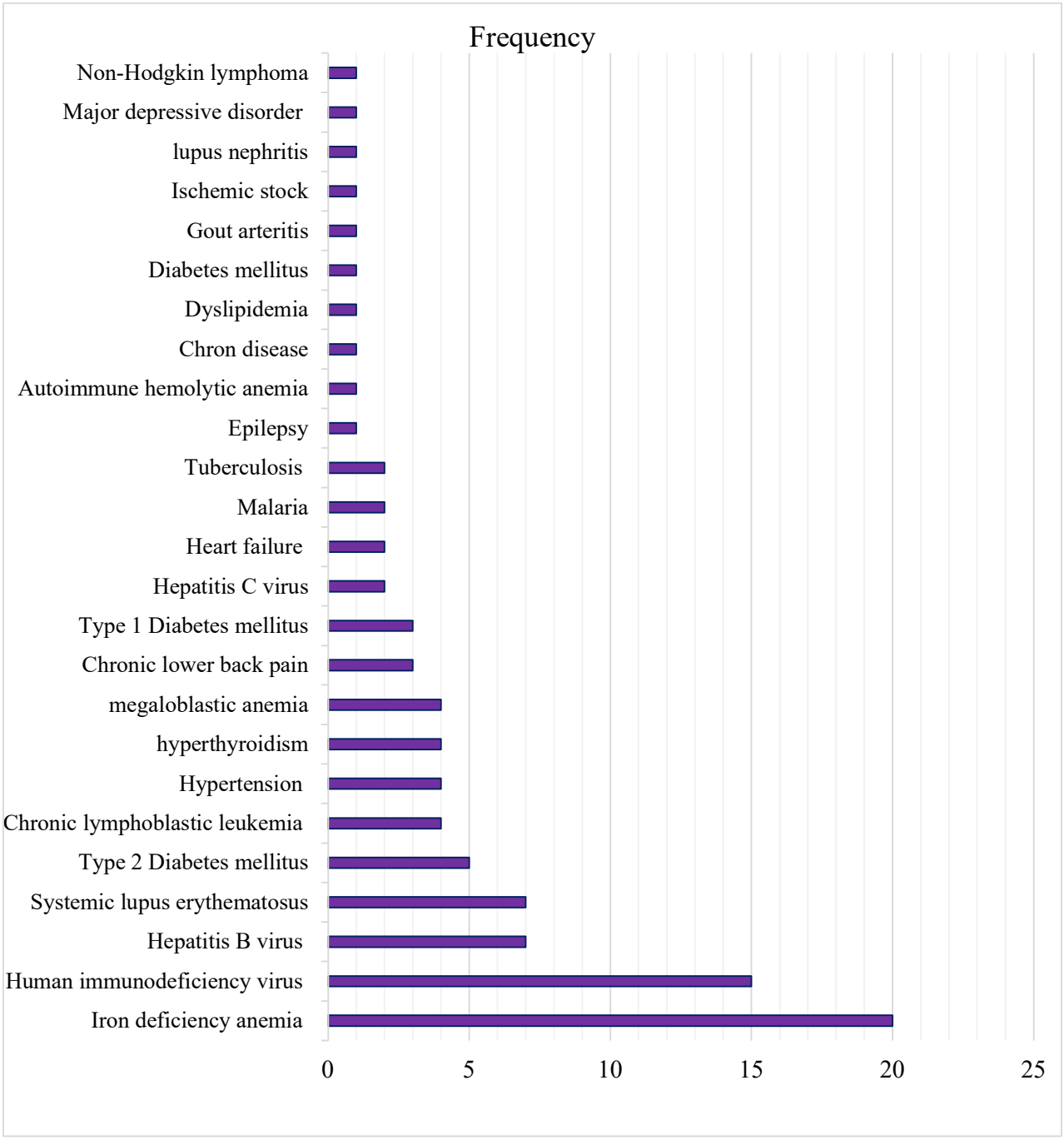

Figure 2: Comorbidities in ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

The median value of primary clinical/laboratory findings at diagnoses, such as platelet count were15 x10^9/L (ranging from 0 x10^9/L to 64 x10^9/L), hemoglobin was 13 g/dL (ranging from 2 g/dL to 17.7 g/dL), and white blood cell count was 7.1 x10^9/L (ranging from 1.62 x10^9/L to 76.3 x10^9/L). The median age of study participants at diagnosis of ITP was 27 years (ranged from 9 to 86 years), the median duration of ITP since diagnosis was 24 months (ranged from 3 to 240 months), and among study participants who experienced a relapse of ITP, the median duration of relapse was 12 months (ranged from 3 to 84 months) (Table 3).

Table 3: The medians of clinical characteristics in ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

Variables		**Median (range)**
Age at Diagnosis in a year		27(9-86) years
Duration since ITP diagnosis in a month		24 (3-240) months
Time of ITP relapse in months		12(3-84) months
Primary clinical/laboratory findings during diagnosis	Baseline platelet count(x10^9/L)	15(0-64)
	Baseline hemoglobin count (g/dl)	13(2-17.7)
	Baseline white blood cell count (x10^9/L)	7.1(1.62-76.3)
	Most recent platelet count(x10^9/L)	146(4-613)

Platelet counts (x10^9/L were obtained in patients who participated in the study, and the mean platelet count at diagnosis/baseline was 17.59±12.74. The median platelet count was also 15 x10^9/L (range 0 -64 x10^9/L) with 25th, 50th, and 75th percentiles of 8 x 10^9/L, 15 x10^9/L, and 24.25 x10^9/L, respectively (Figure 3).

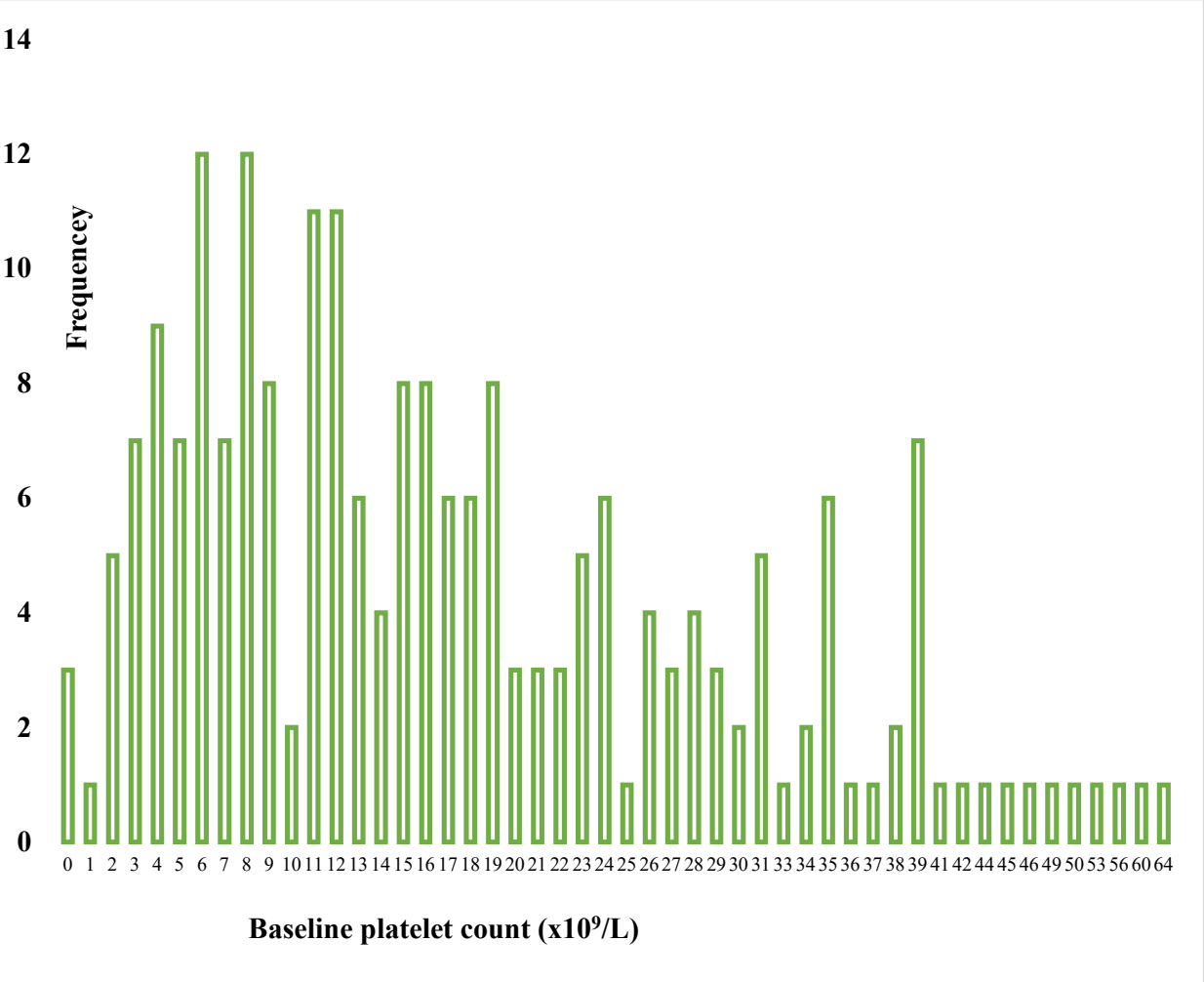

Figure 3: Baseline platelet count of ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

After the baseline platelet count was determined, platelet counts were determined at 2 weeks, 1 month, 3 months, 6 months, 12 months, and the most recent platelet count. The most recent mean platelet count of the study participant was also 146.93±108.23. The median value of the most recent platelet count was 146 x10^9/L (range 4 to 613 x10^9/L) with 25th, 50th, and 75th percentiles of 59.5 x10^9/L, 146 x10^9/L, and 202.5 x10^9/L, respectively (Figure4).

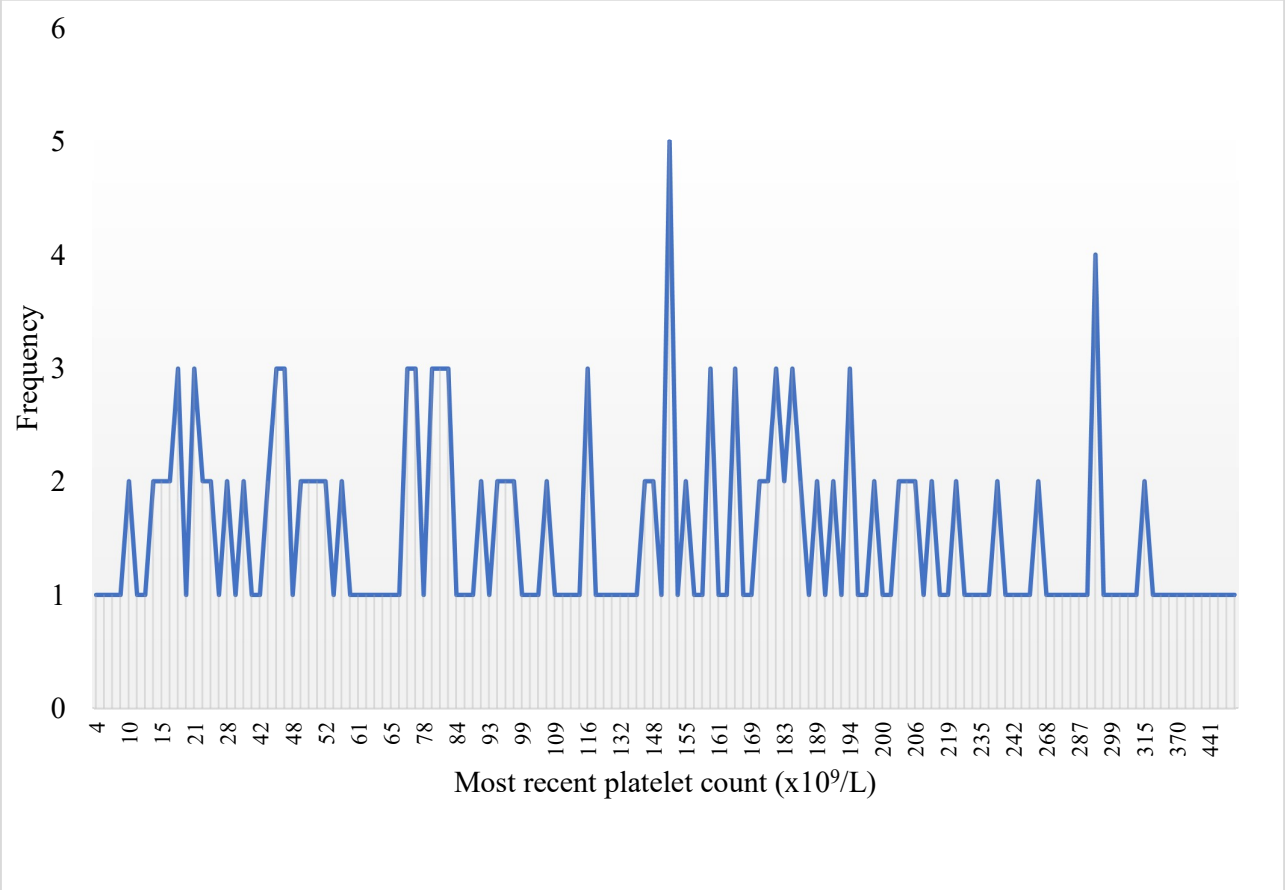

Figure 4: Most recent platelet count of ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

The majority 173(80.8) of study participants had primary ITP and for the phase of ITP, two-thirds 153(71.5) of study participants had chronic ITP; in addition, 24(11.2%) and 15(7.0%) of study participants had corticosteroid -dependent and corticosteroid -resistant, respectively. After completing the first-line treatment of ITP 55(25.7%) of patients relapsed within a median time of 12 months (Figure 5).

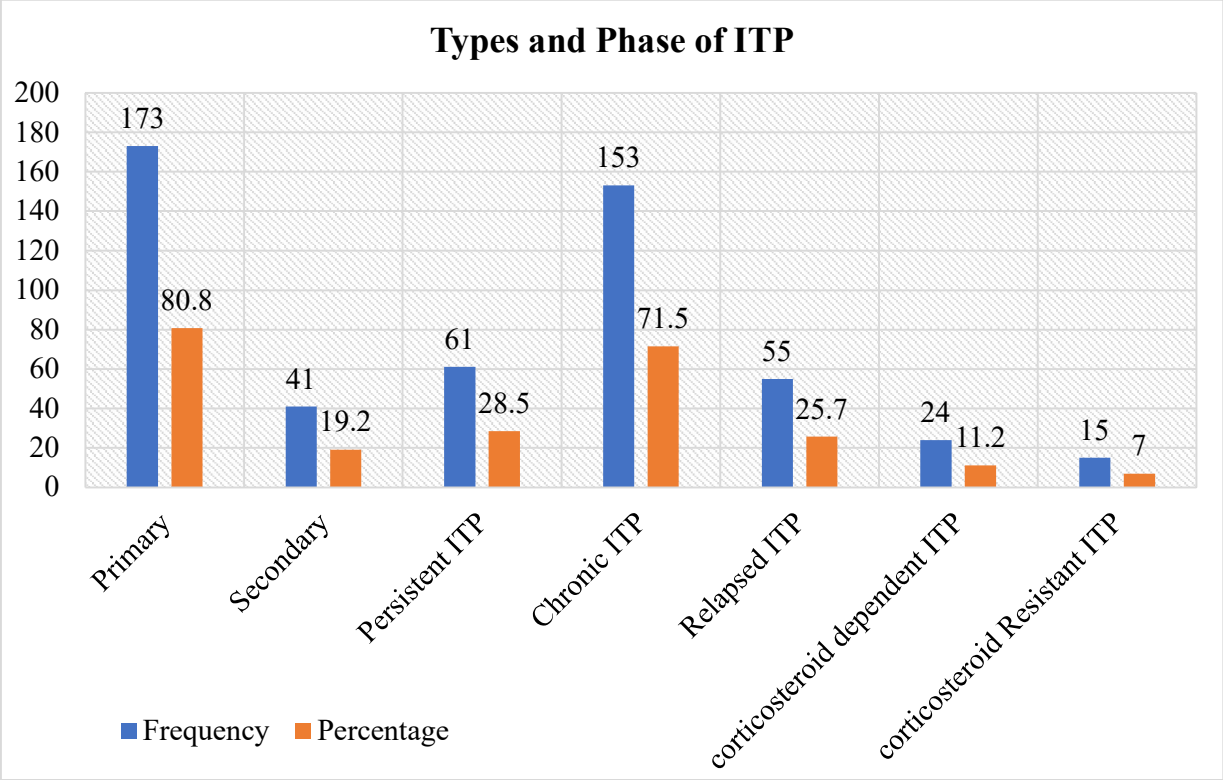

Figure 5: Classification of ITP according to the 2019 ASH guidelines of ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

Treatment-related characteristics of ITP

For the treatment of ITP, the majority 172(80.4%) of study participants took prednisolone alone, followed by combinations of prednisolone and dexamethasone 31(14.5%) for first-line treatment in this study setting. [Azathioprine or Rituximab] + Prednisolone 20(36.4%) were used as second-line treatment options for ITP.

About 63(29.4%) of the study participants received platelet transfusions to prevent bleeding and 27 (12.6%) took tranexamic acid to stop bleeding. In addition, about 121 (56.5%), 100 (46.7%), and 45 (21.0%) study participants took cotrimoxazole prophylaxis (CPT), proton pump inhibitors (PPI), and calcium with vitamin D3 supplement as prophylaxis to prevent immunosuppression-related infections, peptic ulcers, and osteoporosis, respectively (Table 4).

Table 4: Treatment-related characteristics of ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

Variables		Frequency	Percentage
First-line treatment of ITP			
	Prednisolone alone	172	80.4
	Prednisolone + Dexamethasone	31	14.5
	Dexamethasone alone	6	2.8
	Prednisolone + Methylprednisolone	5	2.3
Second-line treatments of ITP			
	[Azathioprine or Rituximab] + Prednisolone	20	36.4
	[Rituximab alone] or [Prednisolone alone] or [Azathioprine alone]	10	18.2
	Rituximab + Splenectomy + [Azathioprine or Prednisolone]	8	14.5
	[Rituximab + Azathioprine] ± Prednisolone	7	12.7
	[Splenectomy + Prednisolone] or [Splenectomy + Rituximab]	6	10.9
	[Splenectomy + Azathioprine+ Prednisolone] ± Rituximab	4	7.3
Other medications to stop bleeding			
	Platelet transfusion	63	29.4
	tranexamic acid	27	12.6
For prophylaxis of corticosteroid Complications			
	Cotrimoxazole prophylaxis treatment	121	56.5
	Proton pump inhibitors	100	46.7
	Calcium with Vitamin D3 supplementation	45	21.0

5.3. Secondary cause of ITP

Of the total study participants, only 41 patients (41, 19.2%) had secondary ITP. Of these 41 patients with secondary ITP HIV 15(36.6%) account for the largest proportion of causes,

followed by systemic lupus erythematous (SLE) 7(17.1%) and H. pylori infection 7(17.1%) (Figure-6).

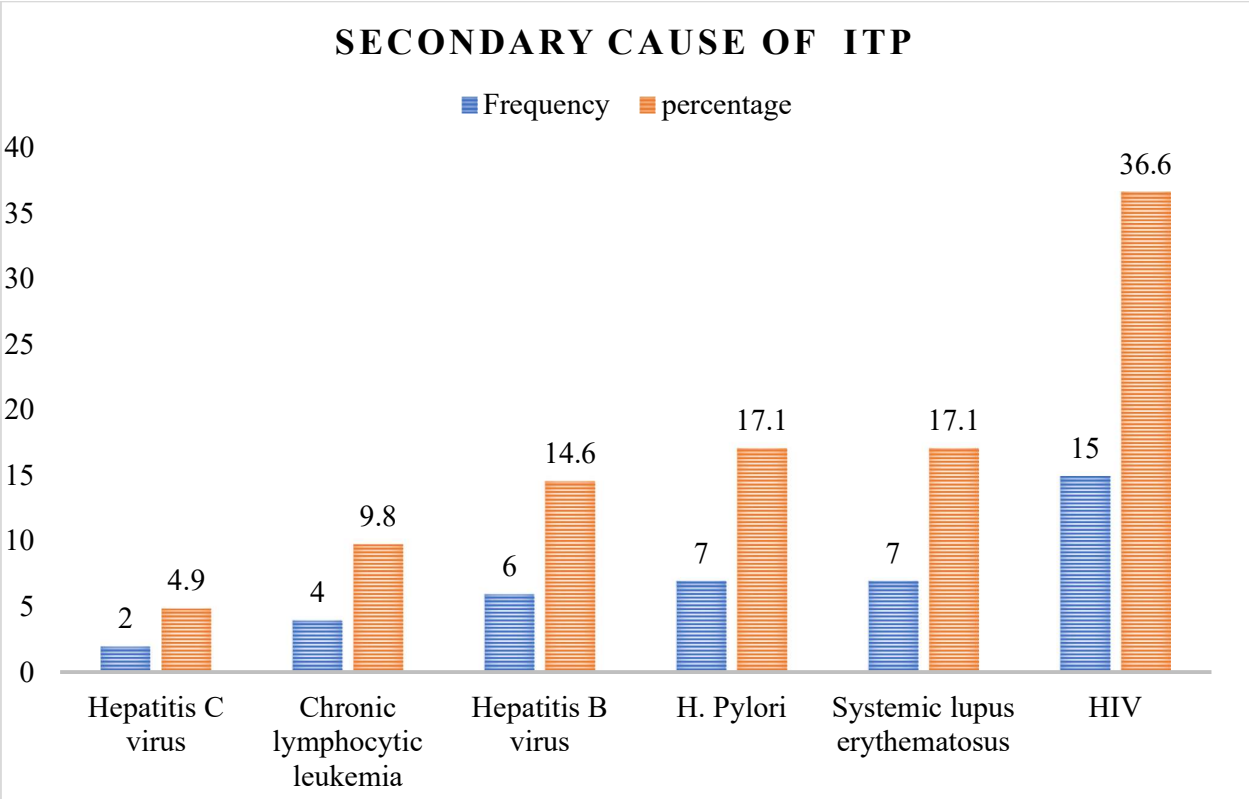

Figure 6: Secondary causes of ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

5.4. Corticosteroid side effects in ITP Patients

Regarding the side effects of corticosteroids 143(66.8%) of the study participant experienced at least one side effect from corticosteroids throughout their treatment period. Of the physical appearance-related, weight gain/increased appetite 86(40.2%) followed by a moon face, bloating, and swelling 72(33.6%) account for the highest proportion. Among emotional corticosteroid side effects, insomnia, restlessness, and/or sleep disturbances (70, 32.7%) and physical symptoms related to corticosteroid side effects, general weakness/fatigue 102(47.7%) and muscle weakness 30(14.0%) accounted for the largest proportion. On the other hand, corticosteroid-related complications such as increased blood glucose 19(8.9%), increased blood pressure 15(7.0%), develop iatrogenic Cushing's syndrome 9(4.2%), and osteoporosis 5(2.3%) occurred in the study participants (Table 5).

Table 5: Corticosteroid side effects in ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

Variables		Frequency	Percentage
At least one Side effect of corticosteroid			
	Yes	143	66.8
	No	71	33.2
Physical appearance-related corticosteroid side effects			
	Weight gain/increased appetite	86	40.2
	Moon face, bloating, swelling	72	33.6
	Stretch mark	11	5.1
	Acne	7	3.3
	Hair loss	6	2.8
Emotional-related corticosteroid side effects			
	Insomnia, restlessness, and/or trouble sleeping	70	32.7
	Depression and/or stress	17	7.9
	Anxiety and/or nervousness	12	5.6
	Anger and/or irritability	8	3.7
Physical symptoms related to corticosteroid side effects			
	Generalized weakness, fatigue	102	47.7
	Muscle weakness	30	14.0
	Visual problems (light sensitivity/ decreased visual acuity)	12	5.6
	Dizziness, headaches	34	15.9

	Nausea, upset stomach, vomiting, diarrhea	10	4.7
Other corticosteroid-related complications/Side effects			
	Increase blood glucose	19	8.9
	Increase blood pressure	15	7.0
	Iatrogenic Cushing's syndrome	9	4.2
	Osteoporosis	5	2.3

5.5. Medication adherence of ITP patients by using the Morisky Green Levine scale

According to the Morisky Green Levine scale, 178(83.2%) of study participants had good adherence to their ITP medications (Figure 7)

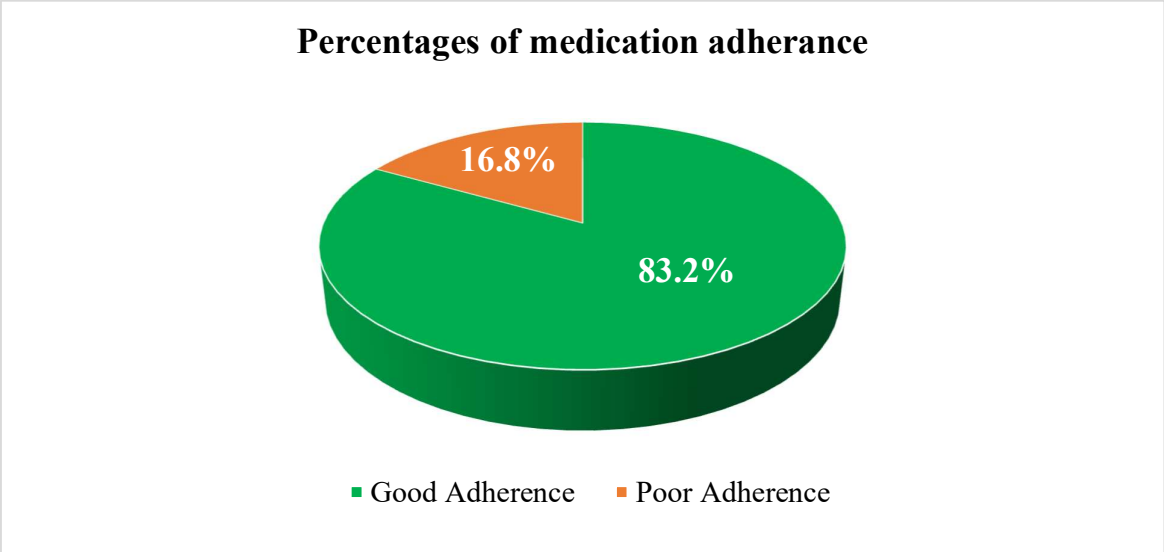

Figure 7: Medication adherence by using the Morisky Green Levine scale in ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

Treatment response of ITP patients

Response to treatment was assessed at 3, 6, and 12 months after treatment initiation. Of the included participants assessed at a different time point, 139(65.0%), 127(69.8%), and

109(76.2%) had complete responses at 3 months, 6 months, and 12 months, respectively (Table 6).

Table 6: Treatment response of ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

First line drugs		**Treatment responses of ITP at 3 months (n=214)**			
		Complete response (CR), N (%)	**Partial response (PR), N (%)**	**No response (NR), N (%)**	**Total N (%)**
	Prednisolone alone	117(68.0%)	43(25.0%)	12 (7.0%)	**172**
	Prednisolone + Dexamethasone	15(48.4%)	8 (25.8%)	8(25.8%)	**31**
	Prednisolone + methylprednisolone	4(80.0%)	1(20.0%)	0	**5**
	Dexamethasone alone	3(50.0%)	2(33.3%)	1(16.7%)	**6**
Total response at 3 months of treatment(n=214)		**139(65.0%)**	**54(25.2%)**	**21 (9.8%)**	**214**
Treatment responses of ITP at 6 months (n=182)					
	Prednisolone alone	109(72.7%)	33(22.0%)	8(5.3%)	**150**
	Prednisolone + Dexamethasone	12(50.0%)	8(33.3%)	4(16.7%)	**24**
	Prednisolone + Methylprednisolone	4(80.0%)	1(20.0%)	0	**5**
	Dexamethasone alone	2(66.7%)	1(33.3%)	0	**3**
	Total response at 6 months of treatment(n=182)	**127(69.8%)**	**43(23.6%)**	**12(6.6%)**	**182**
Treatment responses of ITP at 12 months (n=143)					
	prednisolone alone	91(75.8%)	21(17.5%)	8(6.7%)	**120**
	Prednisolone + Dexamethasone	13(76.5%)	3(17.6)	1(5.9%)	**17**
	prednisolone +	4 (80.0%)	0	1(20.0%)	**5**

	methylprednisolone				
	dexamethasone alone	1(100%)	0	0	**1**
Total responses at 12 months of treatment (n=143)		**109(76.2%)**	**24(16.8%)**	**10(7.0%)**	**143**

5.6. Mean scores for the impact of ITP on health-related quality of life

The impact of ITP on their energy levels accounts for the highest mean value (2.53±1.17) followed by the impact of ITP on their working lives or studies (2.51±1.10). On the other hand, the impact of ITP on their sex life (1.04±0.71) was lower than other parameters in the IQLI tool (Table 7).

Table 7: Mean scores for the impact of ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

Item	ITP life quality index tool	Mean ± SD
Item-1	How often has your ITP impacted your working life or studies?	2.51±1.10
Item-2	How often have you taken me off work or education because of your ITP?	2.49±1.11
Item-3	How often has your ITP impacted your ability to concentrate on everyday tasks?	2.00±1.10
Item-4	How often has your ITP impacted your social life?	1.86±1.08
Item-5	How often have your ITP impacted your sex life?	1.04±0.71
Item-6	How often have your ITP impacted your energy levels?	2.53±1.17
Item-7	How often has your ITP impacted your undertaking of daily tasks?	2.00±1.27
Item-8	How often has your ITP impacted your ability to support people close to you?	1.88±1.14
Item-9	How often has your ITP negatively impacted your hobbies?	1.87±1.12
Item-10	How often has your ITP negatively impacted your normal capacity to exercise?	2.48±1.15

The overall mean score for the impact of ITP on HRQoL according to the IQLI tool was 35.41±9.27. The mean score for the impact of ITP on their work or study was 50.01±2.17 and the impact of ITP on daily live was 31.69±7.38 (Table 8).

Table 8: The Domain transformed mean score of ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

Variables	**Likert scale Mean ± SD**	**The formula for domain mean***	**Domain mean of 100**
Impact of ITP on work or study (Items 1 and 2)	2.50±1.09	100/ (8-2) x (5.00-2)	50.01±2.17
Impact of ITP on daily live (Item 3 to Item 10)	1.95±0.92	100/ (32-8) x (15.6-8)	31.69±7.38
The overall mean score	2.06±0.93	100/ (40-10) x (20.64-10)	35.41±9.27

*Domain mean transformed to 100 = 100/ (maximum score – no of items) x (sum of means – no of items).

5.9. Predicting factors for ITP treatment response

To assess possible predictive factors for response to ITP treatment, all clinically relevant variables and other variables showing a marginal association at p< 0.2 after univariate analysis were included in the multinomial logistic regression analysis. Of the seven variables that met the inclusion criteria for multinomial logistic regression analysis, only four were significantly associated with response to ITP treatment. As the impact of ITP on HRQoL increases by one unit the odds of having partial response were increased by 1.22 (AOR =1.221, 95% CI: 1.096-1.360, p < 0001) as compared to complete response. The odds ratio for partial response in relation to complete response in patients having heavy menstrual bleeding during diagnosis was 2.255 (AOR =2.255, 95% CI: 0.925-5.497, P=0.025) times more likely compared to those not having heavy menstrual bleeding. ITP patients who visited TASH were less likely to have a partial response (AOR =0.431, 95% CI: 0.197-0.941, p=0.035) than patients who visited SPHMMC as compared to a complete response. Furthermore, HBV-positive ITP patients were less likely to be no response (AOR = 0.052, 95% CI: 0.004-0.621, p=0.02) than HBV-negative ITP patients as compared to complete response (Table 9). The model containing the full set of predictors represents a significant

improvement in fit relative to a null model (model x^2=228.505, P<0.001). In addition, Pearson and deviance statistics were also much higher with a respective p-value of (p = 0.98) and (p =1.0); which means the model is a good fit for the data. Besides overdispersion is not the problem for the model since p = 0.98 and p = 1.0 are much higher than 0.05.

Table 9: Predictive factors for treatment response of ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

Variables	Category	B(SE)	COR of 95% CI	B(SE)	AOR of 95% CI	P-Value
Partial response Vs Complete response						
HRQoL		0.022(0.018)	1.022(0.988-1.058)	0.200(0.055)	1.221(1.096-1.360)	0.000*
Study site	SPHMMC		1		1	
	TASH	-0.411(0.339)	0.663(0.341-1.289)	-0.842(0.399)	0.431(0.197-0.941)	0.035*
Heavy menstrual bleeding	No		1		1	
	Yes	0.540(0.398)	1.716(0.787-3.743)	0.813(0.455)	2.255(0.925-5.497)	0.025*
Helicobacter pylori	Negative		1		1	
	Positive	-0.556(0.927)	0.574(0.093-3.531)	-0.582(1.148)	0.559(0.059-5.298)	0.612
HBV	Negative		1		1	
	Positive	0.451(1.130)	1.570(0.172-14.376)	-0.418(1.191)	0.658(0.064-6.790)	0.725
Signs of anemia at presentations	No		1		1	
	Yes	-0.335(0.367)	0.716(0.348-1.470)	-0.601(0.435)	0.548(0.234-1.286)	0.167
Treatment adherence	Poor Adherence		1		1	
	Good Adherence	0.527(0.457)	1.694(0.692-4.148)	0.341(0.515)	1.406(0.512-3.862)	0.508
No response Vs Complete response						
HBV	Negative		1		1	
	Positive	-1.727(0.804)	0.178(0.037-0.859)	-2.957(1.266)	0.052(0.004-0.621)	0.02*

HRQoL		0.075(0.025)	1.078(1.027-1.131)	0.117(0.067)	1.125(0.985-1.283)	0.081
Study site	SPHMMC		1		1	
	TASH	-2.970(0.725)	3.705(0.824-16.659)	1.969(1.044)	7.166(0.927-55.40)	0.059
Heavy menstrual bleeding	No		1		1	
	Yes	-0.846(0.476)	0.429(0.169-1.090)	0.021(0.664)	1.021(0.278-3.750)	0.975
Signs of anemia at presentations	No		1		1	
	Yes	-1.002(0.487)	0.367(0.141-0.953)	-0.703(0.673)	0.495(0.132-1.853)	0.297
Treatment adherence	Poor Adherence		1		1	
	Good Adherence	1.618(1.046)	5.045(0.649-39.217)	2.478(1.736)	11.91(0.397-357.91)	0.153
Helicobacter pylori	Negative		1		1	
	Positive	-2.022(0.854)	0.132(0.025-0.706)	-2.106(1.192)	0.122(0.012-1.259)	0.077

Note: R^2= 0.694 (Cox and Snell), 0.847(Nagelkerke), 0.691 (McFadden), Model x^2=228.505, Pearson (p = 0.98) and deviance (p =1.0), *= P<0.05.

Abbreviations: SE; standard error, HRQoL; health-related quality of life, TASH; Tikur Anbessa Specialized Hospital, SHMMC; St. Paulo's Hospital Millennium Medical College, HBV; hepatitis B virus.

5.10. Association between health-related quality of life of ITP patients and explanatory variables

A one-way ANOVA was performed to compare the effects of sociodemographic and clinical characteristics and the corticosteroid side effect variables on HRQoL and the results of the comparative statistical analysis of the mean values of the HRQoL IQLI domains as a function of the categorical sociodemographic and clinical characteristics and the corticosteroid side effect variables are shown in Table 10. Patients who have skin manifestation (petechiae and ecchymosis) and epistaxis and wet purpura (mucous membrane bleeding) during diagnosis ($P < 0.0001$), patients not taking CPT ($P < 0.0001$), PPI ($P=0.007$) and calcium with vitamin D3 supplementation ($p= 0.034$), patients develop iatrogenic Cushing's syndrome ($p=0.02$), physical appearance, emotional symptoms, and physical symptoms related to corticosteroid side effects ($P < 0.0001$), patients had fatigue during the assessment ($P < 0.0001$) and living far from the hematology clinic (outside Addis Ababa) ($P=0.038$) were statistically significant associations with the higher impact of ITP on HRQoL.

Table 10: Comparative statistical analysis of IQLI domain mean scores among patients treated for ITP at TASH and SPHMMC, according to the Categorical Socio-demographic, Clinical Characteristics, treatment-related and corticosteroid-related side effects

	Variables, Mean ± SD		**HRQoL**	**Work**	**Daily live**
1	Place of residence	Addis Ababa	19.3±8.9	4.7±2.2	14.6±7.1
		Out of Addis Ababa	21.9±9.5	5.3±2.2	16.7±7.5
		P-value	0.038	0.083	0.036
2	Fatigue during assessment	No	18.5±8.2	4.7±2.0	13.9±6.4
		Yes	26.8±9.6	6.0±2.4	20.9±7.6
		P-value	<0.0001	<0.0001	<0.0001
3	Headache during assessment	No	20.1±9.1	4.9±2.1	15.2±7.2
		Yes	29.0±7.9	6.5±2.3	22.5±6.0
		P-value	<0.0001	0.007	<0.0001
4	Skin manifestation (petechiae and Ecchymosis)	No	17.9±8.3	4.4±2.1	13.5±6.5
		Yes	22.8±9.5	5.5±2.1	17.3±7.6
		P-value	<0.0001	<0.0001	<0.0001
5	Epistaxis and wet purpura (mucous membrane bleeding)	No	16.1±6.8	4.0±2.0	12.1±5.1
		Yes	21.9±9.5	5.3±2.1	16.7±7.6
		P-value	<0.0001	<0.0001	<0.0001
6	Cotrimoxazole prophylaxis treatment (CPT)	No	22.9±9.3	5.6±2.0	17.3±7.5
		Yes	17.8±8.4	4.2±2.1	13.5±6.7

		P-value	<0.0001	<0.0001	<0.0001
7	Proton pump inhibitors (PPI)	No	22.5±9.7	5.5±2.0	16.9±7.9
		Yes	19.0±8.6	4.6±2.2	14.5±6.7
		P-value	0.007	0.002	0.013
8	Calcium with Vitamin D3 supplementation	No	19.9±9.1	4.8±2.1	15.1±7.2
		Yes	23.2±9.6	5.8±2.1	17.5±7.8
		P-value	0.034	0.009	0.058
9	Iatrogenic Cushing's syndrome	No	20.33±9.1	4.9±2.2	15.4±7.3
		Yes	27.67±9.3	6.4±2.2	21.2±7.9
		P-value	0.02	0.042	0.02
10	Physical appearance-related corticosteroid side effects	No	17.5±7.5	4.4±2.0	13.2±5.8
		Yes	23.6±9.9	5.6±2.1	18.0±8.0
		P-value	<0.0001	<0.0001	<0.0001
11	Emotional-related corticosteroid side effects	No	17.9±8.3	4.4±2.1	13.6±6.6
		Yes	25.5±8.9	6.2±1.8	19.3±7.3
		P-value	<0.0001	<0.0001	<0.0001
12	Physical symptoms related to corticosteroid side effects	No	17.2±7.8	4.2±2.0	12.9±61
		Yes	23.3±9.5	5.6±2.1	17.7±7.6
		P-value	<0.0001	<0.0001	<0.0001

Abbreviations: HRQoL: health-related quality of life, SD: standard deviation

5.11. Factors affecting health-related quality of life in ITP patients: result from linear regression analysis.

Univariate analysis

In the univariate analysis, 13 of the variables examined showed an association with HRQoL measured by the ILQI. Of these candidate variables, all were categorical variables, 12 of which were binary variables (place of residence, fatigue during the assessment, headache during the assessment, epistaxis and wet purpura (mucosal bleeding), skin manifestations (petechiae and ecchymosis), CPT, PPI, Calcium with vitamin D3 supplementation, iatrogenic Cushing's syndrome, Physical appearance-related corticosteroid side effects, emotional-related corticosteroid side effects, and Physical symptoms related to corticosteroid side effects); and the rest are multi-categorical variable (education level).

Multivariate linear regression analysis

Of the 13 variables used for multivariate linear regression analysis, six variables were identified as correlated with HRQoL by stepwise and forward multivariate linear regression methods and cross-validated by the hierarchical regression method. When the number of patients experiencing emotional-related corticosteroid side effects increased by one, the impact of ITP on patients' HRQoL increased by 0.392 (β= 0.392, 95% CI: 5.160-9.961, P<0.001). The number of patients with fatigue during assessment increased by one, and the impact of ITP on patients' HRQoL increased by 0.236 (β= 0.326, 95% CI: 4.394-9.475, P<0.001). In patients who did not take CPT increased by one, the impact of ITP on patients' HRQoL increased by 0.236 (β= 0.236, 95% CI: 2.236-6.570, P<0.001). In addition, the number of patients with epistaxis and wet purpura (mucosal bleeding) increased by one during diagnosis, and the impact of ITP on patients' HRQoL increased by 0.191 (β= 0.191, 95% CI: 0.091-4.259, P=0.001). The number of patients living far from the hematology clinic (outside Addis Ababa) increased by one, and the impact of ITP on patients' HRQoL increased by 0.166 (β= 0166, 95% CI: 1.107-5.114 P=0.003), and the number of patients with clinical presentations of skin symptoms (petechiae and ecchymosis) of ITP patients increased by 0.041 (β= 0.041, 95% CI: 0.091-4.259 P=0.041).

All correlated variables explained 36.5% (adjusted R-squared=0.365, $P < 0.0001$) of the variance and had a moderate influence on the dependent variable (HRQoL). Of these, 15.4% of the variance (adjusted R-squared=0.154, $\beta = 0.392$, $P < 0.0001$) was accounted for by emotion-related corticosteroid side effects (Table 11). The tolerance of all independent variables ranged from 0.848 to 1. Thus, there were no multicollinearity problems in the models because all were above 0.2. All standardized residuals in the models were normally distributed ($P<0.05$) meeting the assumptions of the linear regression model.

Table 11: Factors Associated with the HRQoL of ITP patients attending the TASH and SPHMMC hematology clinics in Addis Ababa, Ethiopia, 2022 (n=214).

Model	Predictor variables	R-square	Adjusted R square	R square change	Change statistics			P-value	Predictor variables	**β (95% CI)**	SE
					F-change	Df1	Df2				
1	Emotional-related corticosteroid side effects	0.154	0.154	0.154	38.549	1	212	0.000	Emotional-related corticosteroid (ref: No)	0.392 (5.160-9.961)	1.218
2	Fatigue during assessment	0.256	0.249	0.102	28.949	1	211	0.000	Fatigue during assessment(ref:No)	0.326 (4.394-9.475)	1.289
3	CPT	0.309	0.299	0.053	16.038	1	210	0.000	CPT (ref: No)	0.236 (2.236-6.570)	1.099
4	Epistaxis and wet purpura	0.343	0.331	0.034	10.951	1	209	0.001	Epistaxis and wet purpura (ref: No)	0.191 (0.091-4.259)	1.281
5	Residence	0.370	0.355	0.027	9.027	1	208	0.003	Residence (ref: Addis Ababa)	0.166 (1.107-5.114)	1.024
6	Skin manifestation	0.383	0.365	0.013	4.236	1	207	0.041	Skin manifestation (ref: No)	0.041(0.091-4.259)	1.057

Note: CPT; Cotrimoxazole prophylaxis treatment, β; Beta coefficient, SE; standard error, DF; degree of freedom, CI; confidence interval

6. Discussion

The present study aimed to investigate the clinical outcomes of different ITP treatment regimens, treatment adherence, and HRQoL of patients with ITP, as well as factors related to treatment outcomes and HRQoL. The updated international consensus report indicates that there are differences in ITP clinical presentations, clinical outcomes, and treatment responses [21]. Therefore, the evaluation of clinical outcomes, treatment adherence, complications of corticosteroid treatment, and HRQoL of ITP patients plays an important role in the quality of outcomes and measuring the success of the disease management and service delivery system. In addition, steroids are currently the standard first-line treatment for adults diagnosed with ITP [18]. Steroids are also associated with numerous bothersome side effects that may cause patients to discontinue or reduce therapy [34].

Most epidemiologic data suggest that women are more commonly affected by ITP during their childbearing age and that the prevalence after menopause is similar to that of men [8-11, 71], and also in this study, 75.5% of the study participants were female, which is consistent with other studies from the United States of America (76%) [64], Turkey (71.3%) [72], and Malaysia (71.8%) [32]. In our study, the proportion of females was higher than in studies conducted in the United Kingdom (56.9%) [10], Germany (57 %) [73], China (63.6%) [62], and in the ITP World Impact Survey data (65%) [40]; but lower than compared to studies conducted in Mexico(81.8%) [74] and in Egypt (84%) [2]. The median age of ITP patients was 30 years, ranging from 15 to 88 years. It is comparable to other studies of 27 years in China [62], 34 years in Turkey [72], 34.2 in the United Kingdom [75], 34.3 years in Iran [76], and 37 years in Mexico[77]. The median age of ITP patients in this study was also relatively lower than in studies of 45.5 years in Twain [78], 50 years in the United States of America [79], 58 years in Spain [65], and 55 years in Germany [73].

The most common clinical presentation at diagnosis of ITP was epistaxis and wet purpura (mucosal bleeding) (77.6%), followed by fatigue (73.4%), skin manifestations (petechiae and ecchymosis) (56.1%), and heavy menstrual bleeding (27.6%). This was similar to studies conducted in Mexico Petechiae (39%), Ecchymosis (50.4%) [67], and the ITP impact world survey examined that petechiae (64%), bruising of unknown origin (65%), and fatigue (58%) were among the most common signs and symptoms reported by patients at diagnosis [40]. In the study conducted in Spain, skin manifestation (63%), bleeding from the oral cavity (24%), and epistaxis (24%) were the most common clinical symptoms at diagnosis [80]. Another

study conducted in France found skin bleeding (28%), bleeding from the oral cavity (epistaxis and/or mucous membranes), and visceral bleeding (gastrointestinal, cerebral, and gynecological) (55.9%) [81]. In the study conducted in Turkey the most common signs and symptoms of ITP also skin and mucosal bleeding (31.5%), spontaneous skin bleeding (22.1%), and mucosal bleeding (11.5%) [72].

In this study, 19.2% of study participants had secondary ITP, which is comparable with studies conducted in Malaysia 23% [32], and higher than studies conducted in Germany (9%) [73]. From the causes of secondary ITP; HIV (36.6%), followed by SLE (17.1%) and H. pylori infection (17.1%) account for the highest underlying disease conditions. On the other hand, studies conducted in Spain [80]; SLE 17.6% followed by lymphoproliferative syndromes 17.6%; in Mexico SLE (34.8%), infection (26.1%), and thyroid disease (17.3%) [77]; in Taiwan [78]; Evans' syndrome (33.3%), HCV (28.6%) and SLE 28.6%, and in Malaysia autoimmune disease (15.8%), and viral infections (4.4%) were the most common underlying diseases [32].

Corticosteroids remain the most commonly used first-line treatment, followed by IVIg for the management of ITP [18]. In this study, all ITP patients (100%) received corticosteroids, either prednisolone alone or dexamethasone and methylprednisolone, followed by prednisolone because IVIg was not available in our setup. A similar study was conducted in Malaysia where 98.8% of the study participants were taking steroids and the remaining 1.2% were taking IVIg [32]. On the other hand, in a study conducted in China, 78.5% of ITP patients received corticosteroids and 8.0% of ITP patients received IVIg as first-line treatment [82]. Two studies conducted in Spain showed that 40.6% and 64.3% of ITP patients also received corticosteroid monotherapy, respectively [65, 80]. In a study conducted in Mexico, only 33.3% were treated with steroids alone; the remaining 28.4% received low-dose rituximab plus steroids, 13.8% danazol plus steroids, and 8.9% eltrombopag plus corticosteroid [67].

Corticosteroid side effects may affect HRQoL or treatment response and in this study population, 71.5% of study participants had chronic ITP. There is a significant association between the duration of corticosteroid treatment and the average number of adverse events experienced [41]. The emotional corticosteroid side effects like insomnia, restlessness, and/or sleep disturbances (32.7%), physical symptoms including general weakness/fatigue (47.7%), and muscle weakness (14.0%) accounted for the largest proportion. On the other hand, steroid-related complications such as increased blood glucose (8.9%), increased blood pressure (7.0%), developing iatrogenic Cushing's syndrome (4.2%), and osteoporosis (2.3%)

occurred in the study participants. In a study conducted in the United States, patients treated with corticosteroids reported an average of 8.5 adverse events for a treatment duration of 3 months or less, an average of 11.3 adverse events for a treatment duration of 4-6 months, an average of 12.4 adverse events for a treatment duration of 7-12 months, and an average of 13.8 adverse events for a treatment duration of more than 12 months. In addition, the average severity of corticosteroid side effects was 25 in patients treated for 3 months, 37 in those treated within 4-6 months, 41 in those treated within 7-12 months, and 49 in those treated for more than 12 months [41]. According to the ITP World Impact Survey, approximately 50% of study participants suffer from fatigue during the survey [40], and in this study general weakness/fatigue (47.7%) was also the most common corticosteroid side effect in ITP patients. In addition, weight gain/increased appetite (40.2%), moon face (33.6%), and insomnia are also the most common corticosteroid side effects in ITP patients. This can severely affect HRQoL domains, such as energy levels to perform activities. On the other hand, 56.5%, 46.7%, and 21.0% of the study participants took CPT, PPI, and calcium with vitamin D3, respectively. This supportive treatment reduced the immunosuppression and gastrointestinal side effects of corticosteroids as well as the extent of osteoporosis. In general, to decrease corticosteroid-related side effects, prednisone should be rapidly tapered and usually stopped in responders, and non-responders stop the medications after 4 weeks of initiation [19].

In this study, the response rate to treatment at three months after treatment initiation was (65.0%) complete response, (25.2%) partial response, and (9.8%) no response, and there was a lower response rate compared with the study conducted in Iran (80.0%) complete response, (16.7%) partial response and (6.6%) no response [83]. This may be because, in the Iran study, all participants received high-dose dexamethasone, which is more effective than conventional corticosteroid therapy as initial treatment in newly diagnosed ITP and has fewer relapses and toxicities [84]. On the other hand, the response rate was higher compared to the study conducted in Malaysia with 36.5% complete response, 22.6% partial response, and 26.1% no response [32].

In this study, treatment response rates at six months after treatment initiation were also (69.8) complete response, (23.6%) partial response, and (6.6%) no response, which was lower than studies conducted in Iran (73.3%) complete response, (16.7%) partial response and (6.6%) no response [83]. In addition to that, response rates at 12 months after treatment initiation were (76.2%) complete response, (16.8%) partial response, and (7.0%) no response, which is

comparable to the study conducted in Spain with (72.3%) complete response, (19.8%) partial response and (7.8%) no response [80]. On the other hand, it is a higher response rate than the study conducted in Malaysia (26.1%) complete response, (18.6%) partial response, and (13.4%) no response [32]. This may be due to the fact that in Malaysia, 169 (41.9%) of study participants had lost follow-up 12 months after treatment initiation. The median time to relapse in this study after first-line treatment was 12 months, which is higher than studies conducted in Taiwan [78] and Mexico [77] the median time to relapse was 9.5 months and 2 months respectively. On the other hand, the median time to relapse is lower than in the Norway study where the median relapse was 17 months [85].

In this study, the total impact of ITP on HRQoL is 35.41±9.27, and the impact of ITP on work or study is 50.01±2.17; which is greater than the impact of ITP on daily live (31.69±7.38). The impact of ITP on patients' energy levels accounted for the highest mean value (2.53±1.17), followed by the impact of ITP on their working lives or studies (2.51±1.10); this is consistent with the ITP World Impact Survey data [40, 86] and a survey data reported from Switzerland, Austria, and Belgium [75]. Our study is also similar to the studies conducted in China [87], the United States of America [63], and Serbia [58], in which physical function was more impaired than in the other domains of HRQoL. On the other hand, an Indian study showed that the impact of ITP on patients' work/study was less than the impact of ITP on their daily lives [88]. A systematic review conducted in 2018 suggests that patients with ITP experience negative effects on their sexual activities, including decreased libido and bruising and bleeding during intercourse [26]. In this study, the mean impact of ITP on patients' sex life is rated as 1.04±0.71; which is lower than all other IQLI domains, and the result is similar to a qualitative study in the United Kingdom, which found that the impact of ITP on sex life was less relevant [89].

In this study, the multinomial logistic regression analysis indicated that the odds of response in patients having heavy menstrual bleeding during diagnosis is 2.255 more likely to be a partial response (AOR =2.255, 95% CI: 0.925-5.497, P=0.025) than those not having heavy menstrual bleeding as compared to complete response. When the impact of ITP on HRQoL increased by one (AOR =1.221, 95% CI: 1.096-1.360, p < 0001), the odds of response is 1.221 more likely to be partial response than complete response. Patients who had visited TASH were 56.9% less likely to have a partial response than Patients who visited SPHMMC (AOR =0.431, 95% CI: 0.197-0.941, p=0.035) as compared to a complete response. Furthermore, ITP patients who had HBV-positive were 94.8% less likely to have no response

(AOR = 0.052, 95% CI: 0.004-0.621, p=0.02) than HBV-negative ITP patients as compared to complete response.

In this study, the impact of ITP on HRQoL using the IQLI domain; which includes work/study and daily life is assessed. Patients with fatigue and headache during assessment (P < 0.0001), were associated with a higher impact of ITP on HRQoL. This may be because fatigue deprives ITP patients of energy for daily activities, and fear of bleeding also affects their social life and ability to focus on daily tasks. Patients during diagnosis, who had skin manifestation (petechiae and ecchymosis) and epistaxis and wet purpura (mucous membrane bleeding) sign symptoms (P < 0.0001) were significantly associated with a higher impact of ITP on HRQoL. A study conducted in the United States of America confirmed that patients with ITP report feeling embarrassed in society because of the visible signs of the disease (bruising, ecchymosis, and petechiae) and that their participation in sports or other physical activities is limited [90]. Patients who develop corticosteroid side effects like iatrogenic Cushing's syndrome (p=0.02), physical appearance, emotional symptoms, and physical symptoms related (P=0.038) side effects were associated with a higher impact of ITP on HRQoL. In addition to that living far from the hematology clinic (outside Addis Ababa) (P=0.038) was also associated with a higher impact of ITP on their HRQoL. On the other hand, patients taking CPT (p<0.0001), PPI (P=0.007), and calcium with vitamin D3 supplementation (p= 0.034) were associated with a lower impact of ITP on their HRQoL; this could be due to the fact that these drugs taken as prophylaxis reduced the impact of corticosteroid side effects like infection secondary to immunosuppression, gastrointestinal ulcer and osteoporosis on their HRQoL.

Predictive factors for a higher impact of ITP on HRQoL included emotional-related corticosteroid side effects, fatigue during the assessment, not taking CPT, epistaxis and wet purpura (mucosal bleeding), place of residence, and skin symptoms (petechiae and ecchymosis). These were significantly correlated with a greater impact of ITP on HRQoL, with emotion-related corticosteroid side effects accounting for the highest value with 15.4% of the variance (adjusted R-squared=0.154, β= 0.392). When the number of patients experiencing emotional-related corticosteroid side effects increased by one, the impact of ITP on patients' HRQoL increased by 0.392 (β= 0.392, 95% CI: 5.160-9.961, P<0.001). This might be due to emotional side effects of steroids such as insomnia, depression, anxiety, restlessness, and anger which directly affect work capacity and concentration in daily activities and also reduce the energy capacity to perform a given activity greatly affecting

HRQoL. In addition, the number of patients with epistaxis and wet purpura (mucosal bleeding) during diagnosis increased by one, and the impact of ITP on patients' HRQoL increased by 0.191 (β= 0.191, 95% CI: 0.091-4.259, P=0.001) and the number of patients with clinical presentations of skin symptoms (petechiae and ecchymosis) of ITP patients increased by 0.041 (β= 0.041, 95% CI: 0.091-4.259 P=0.041) which is in line with other studies conducted in China and Serbia [58, 62].

A study conducted in the United States of America [91] and China [87] showed that fatigue was one of the most debilitating aspects of HRQoL of ITP. Moreover, in this study, the number of patients with fatigue during assessment also increased by one, and the impact of ITP on patients' HRQoL increased by 0.236 (β= 0.326, 95% CI: 4.394-9.475, P<0.001). The number of patients who did not take CPT increased by one, the impact of ITP on patients' HRQoL increased by 0.236 (β= 0.236, 95% CI: 2.236-6.570, P<0.001). This may be because immunosuppressive therapy, especially high-dose corticosteroids, predisposes patients to infections, which may also affect HRQoL in ITP patients. A study conducted in China found that infections are a common problem in patients with primary ITP, with an incidence of 24% in the first month of treatment, possibly due to immunosuppressive therapy. The number of patients living far from the clinic of hematology (out of Addis Ababa) increased by one, and the impact of ITP on patients' HRQoL increased by 0.166 (β= 0166, 95% CI: 1.107-5.114 P=0.003), which is in line with a study conducted in Serbia [58].

7. Limitations of the study

- ✓ The data were extracted retrospectively from the medical chart and cross-sectional directly from the patient and this study design limited the determination of causal relationships between the variables. It underlines the need for future research with repeated measures of treatment response and HRQoL.
- ✓ Due to the time concern, the data presented in this study were only quantitative; it needs qualitative or mixed descriptive data for more in-depth verification and comparison of qualitative data in the future study.
- ✓ The maximum time period (4 months) was used to recruit the study participants, but the event is rare; due to this the sample size was small and it is difficult to generalize the whole population.

8. Conclusion and Recommendation

8.11. Conclusion

The highest complete response rate was achieved at 12 months and the predictive factors for the partial response of ITP patients at 3 months were HRQoL, study site, heavy menstrual bleeding, and HBV-positive ITP patients were predictive factors for no response of ITP patients. ITP patients adhered well to their ITP medications, and more than half of the study participants had at least one side effect from corticosteroids throughout their treatment period. The impact of ITP on their energy levels and work life was high. The study on HRQoL domains and predictive factors for increasing impact of ITP on their HRQoL was the development of emotionally related corticosteroid side effects, presence of fatigue during the assessment, not taking CPT, living far from the hematology clinic (outside Addis Ababa), having epistaxis and wet purpura (mucosal bleeding), and skin symptoms (petechiae and ecchymosis) during diagnosis. The side effects of corticosteroids also affect the response to treatment and the quality of life of ITP patients. In general, concerted efforts must be made to reduce the impact of ITP on HRQoL and prevent/manage corticosteroid side effects.

8.12. Recommendation

Based on the findings of this study the following recommendations are forwarded:

- ✓ Therapeutic outcomes of ITP depend on multivariate factors, due to this, treatment should be tailored to the individual patient by considering factors such as age, lifestyle, comorbidities, compliance, patient preferences, the presence and severity of bleeding, and the potential side effects of treatment.
- ✓ The impact of ITP on HRQoL is greater, especially on physical functions such as the daily ability to work or study, fatigue, and daily energy levels; the clinicians should be concerned about the HRQoL of ITP patients in addition to treating low platelet counts and preventing life-threatening bleeding.
- ✓ The side effects of corticosteroids were high, to decrease the side effects the physician should optimize the treatment and the police makers/ institutions consider other medications like IVIg and TPO-RAs to incorporate into the guidelines.
- ✓ The response rate of ITP patients in SPHMMC was lower than ITP patients in TASH, due to this the SPHMMC should optimize the treatment strategies.
- ✓ The side effects of corticosteroid were a higher impact on the HRQoL of ITP patients, due to this further research need to check the causal association of corticosteroid side effect on HRQoL.

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Annex-I: Tool for ITP

The consent form and participant information sheet

Title of the study: Treatment outcomes, adherence, and health-related quality of life of patients with immune thrombocytopenia in two teaching hospitals (Tikur Anbessa Specialized Hospital and St Paulo's Hospital Millennium Medical College), Addis Ababa, Ethiopia.

Principal investigator: Dessale Abate (BPharm), Phone number: - 0921508009

Adviser: ***Eskindir Ayalew*** (BPharm, MSc, Assistant Professor of Clinical Pharmacy)

Co-adviser:

Amha Gebremedhin (MD, Associate professor in Medicine)

The objective of the study: To assess the treatment outcomes, adherence, and health-related quality of life in patients with immune thrombocytopenia at Tikur Anbessa Specialized Hospital and St. Paul's Hospital Millennium Medical College in Addis Ababa, Ethiopia.

Subject Participation and procedure: The method of the research is an institutional-based cross-sectional study. The expected duration of the participants' contact with the interviewer was not more than 20 minutes. Ask participants in this research because the trustful information provided an understanding of the purpose.

Confidentiality: To establish a secured safeguard of confidentiality of research data, the patient information was coded during the data collection period instead of using a name. The information is not disclosed in the way it identified your characteristics & privacy.

Benefit: The research does not have a short-term financial, health care, & capacity building benefit to the research participant as an individual or group but in the long run it will help the concerned organization & policy maker to have a policy consideration, direction, formation of strategy & design to improve the quality of life among ITP patient.

Incentive, & compensation: This study has no form of incentive or compensation for the respondent.

Risk and discomfort: The study has no health-related, psychological, economic, or social risks for the study participant.

Person to contact: The participant has the right to ask for information that is not clear about the context before and during the time of data collection; anyone can contact the principal investigator.

If you have/will have any questions or problems, you can contact the principal investigator by

Phone number: - 0921508009

Email: - dessale2010@gmail.com.

I voluntarily agree to participate in this research program. Yes ☐ No ☐

I understand that I will be given a copy of this signed Consent Form.

Name of Participant_____ Signature: _____ Date: _____

Person Obtaining Consent: _____Signature: _____Date: _____

Part One: Socio-demographic data of study participants.

1. Card/I-Care number_____
2. Sex A. Male B. Female
3. Age in year _____
4. Address (write the name of the town) _____
5. Marital status

   A. Married B. Unmarried
   C. Divorced D. Widowed

6. Occupation

A. Employed B. Housewife C. Retired

D. self-employed E. Student F. Unemployed

7. Educational level

A. unable to read and write	B. Only read and write	C. primary education (1-8)
D. Secondary education (9-12)	E. Diploma/certificate	F. Degree and above

8. How the medical services of the hospital were provided fees?

A. Free (government).	B. Out of pocket
C. Health insurance	D. Other company insurance

9. With whom do you live?

A. with family	B. Alone
C. with others (University dorm, Police, or other camps)	

Part-Two clinical characteristics of study participant

1. Date of diagnosis for ITP_____
2. Current/history of major comorbid diseases. A. Yes B. No
3. If your answer is yes for questions number **2**, please list them _____ _____
4. Current symptoms of ITP? (More than one answer is possible)

A. Fatigue	B. Bleeding
C. Depression	D. weight loss
E. Headache	F. Others_____

5. **Physical findings at presentations**

2.1. Signs of bleeding at presentations (more than one answer is possible)

A. wet purpura (mucous membrane bleeding)	B. Epistaxis
C. petechiae	D. if others

2.2. Signs of anemia (pallor) at presentations? A. Yes B. No

2.3. Neck stiffness (CNS bleeding) at presentations? A. Yes B. No

2.4. Splenomegaly or hepatomegaly at presentations? A. Yes B. No

6. Primary clinical/laboratory findings at presentations

Investigations	Value at presentation
WBC with differentials	
Hemoglobin (Hgb)	
Hematocrit (HCT)	
Platelet	

7. Secondary investigations at the presentation (during diagnosis)

Investigations		Result
Viral markers	HIV	
	HCV	
	Others (CMV, Epstein Barr virus)	
H. Pylori		
Bone marrow aspiration report (Megakaryocyte level)		
Drug-induced Immune Thrombocytopenia		

8. Platelet count during the treatment period

Platelet count										
Date	During DX									

9. Bleeding event

Bleeding									

events									
Date	During DX								

10. Treatment of ITP at presentation (first-line treatment).

A. Prednisolone	B. Dexamethasone
C. Methylprednisolone	D. platelet transfusion
E. Anti-D Ig	F. IVIg

11. Rescue treatment/second-line treatment of ITP

A. Rituximab	B. platelet transfusion
C. Splenectomy	D. IVIg
E. Azathioprine	F. others _____

12. Prophylaxis for Steroid SE

A. Cotrimoxazole	B. Omeprazole
C. Calcium with VtD3	D. Others____

Part Three: Immune thrombocytopenia treatment adherence by using the Morisky Green Levine scale (MGL)

	Morisky Green Levine scale (MGL)	Yes	No
1	Do you ever forget to take your ITP medications?		
2	Do you ever have problems remembering to take your ITP medication?		
3	When you feel better do you sometimes stop taking your ITP medications?		
4	Sometimes you felt worse when you take the ITP medications, do you stop taking them?		

Part Four: Steroid treatment side effects and complications in immune thrombocytopenia patients

1. The longest duration of prednisone or other steroids for ITP treatment _____
2. Which side effects of steroids do you experience?

2.1. Physical appearance-related side effects of steroid (≥ one answer is possible)

A. Moon face, bloating, swelling	B. Acne	C. Hair loss
D. Weight gain/increased appetite	E. Stretch marks	

2.2. Emotional symptoms (more than one answer is possible)

A. Insomnia, restlessness, and/or trouble sleeping	B. Anxiety and/or nervousness
C. Depression and/or stress	D. Anger and/or irritability

2.3. Physical symptoms (more than one answer is possible)

A. Generalized weakness, fatigue	B. Muscle weakness
C. Body pain (joint stiffness, muscle cramps)	D. Hot flushes and/or sweating
E. Visual problems (light sensitivity/decreased visual acuity)	F. Dizziness, headaches
G. Nausea, upset stomach, vomiting, diarrhea	

2.4. Other side-effects (more than one answer is possible)

A. Increased blood glucose (DM)	B. High blood pressure
C. Osteoporosis	D.

3. For each adverse event that you experienced, please indicate the severity by rating it on a scale from 1 to 5 using the following scale.

A. I did not experience these side-effects	B. These side effects did not bother me
C. These side effects bothered me a little	D. These side effects bothered me sometimes
E. These side effects bothered me a lot	

Part Five: Health-related quality of life in immune thrombocytopenia patients by using the ITP Life Quality Index (ILQI) tool

This questionnaire aims to measure how much your ITP has affected your **LIFE OVER THE PAST ONE MONTHS**. The aim is to standardize how; besides bleeding, your ITP affects your life.

1. How often has your ITP impacted your working life or studies?

A. Never	B. Some- times	C. More than half a time	D. All the time
E. I'm not currently working/studying due to ITP			
F. I'm not currently working/studying due to other reasons			

2. How often have you taken me off work or education because of your ITP?

A. Never	B. Some- times	C. More than half a time	D. All the time
E. I'm not currently working/studying due to ITP			
F. I'm not currently working/studying due to other reasons			

3. How often has your ITP impacted your ability to concentrate on everyday tasks?

A. Never	B. Some- times	C. More than half a time	D. All the time

4. How often has your ITP impacted your social life?

A. Never	B. Some- times	C. More than half a time	D. All the time

5. How often have your ITP impacted your sex life?

A. Never	B. Some- times	C. More than half a time	D. All the time
E. Not applicable/prefer not to say			

6. How often have your ITP impacted your energy levels?

A. Never	B. Some- times	C. More than half a time	D. All the time

7. How often has your ITP impacted your undertaking of daily tasks?

A. Never	B. Some- times	C. More than half a time	D. All the time

8. How often has your ITP impacted your ability to support people close to you?

A. Never	B. Some- times	C. More than half a time	D. All the time

9. How often has your ITP negatively impacted your hobbies?

A. Never	B. Some- times	C. More than half a time	D. All the time

10. How often has your ITP negatively impacted your normal capacity to exercise?

A. Never	B. Some- times	C. More than half a time	D. All the time

THANK YOU FOR YOUR COMPARATIVENESS' AND TIME!!!

Annex-II Amharic tool for ITP

የምርምር ወይም ጥናት ማብራሪያ እና የስምምነት መግለጫ ቅጽ

<u>የጥናቱ ርዕስ፡-</u> ከፕላትሌት ማነስ ጋር የተያያዘ መድማት (immune thrombocytopenia) ያለባቸው ታካሚዎች ላይ የህክምና ክትትል እና ውጤቶች፣ መድሃኒት በአግባቡ መወሰዳቸው እና ጤና ነክ የህይወት ጥራት/የኑሮ ሁኔታ እና ተዛማጅነት ጉዳዮች ላይ በጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል እና በቅዱስ ጳውሎስ ሚሊኒየም ሜድካል ኮልጅ ታካሚዎች ላይ የሚደረግ ጥናት።

<u>ዋና መርማሪ፡</u> ደሳለ አባተ (BPharm)፣ ስልክ ቁጥር፡- 0921508009

<u>ዋና አማካሪ፡</u> እስክንድር አያሌው (BPharm፣ MSc፣ የክሊኒካል ፋርማሲ ረዳት ፕሮፌሰር)

<u>ተባባሪ አማካሪ፡</u>

- ✓ አምሃ ንብረመድህን (MD, የሕክምና ተባባሪ ፕሮፌሰር)

<u>የጥናቱ ዓላማ፡</u> በአዲስ አበባ፣ ኢትዮጵያ በሚገኘው በጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል እና በቅዱስ ጳውሎስ ሆስፒታል ሚሊኒየም ሜዲካል ኮሌጅ ከፕላትሌት ማነስ ጋር የተያያዘ መድማት (immune thrombocytopenia) ያለባቸው ታካሚዎች ላይ የህክምና ክትትል እና ውጤቶች፣ መድሃኒት በአግባቡ መወሰዳቸው እና ጤና ነክ የህይወት ጥራት/የኑሮ ሁኔታ እና ተዛማጅነት ጉዳዮችን ለመገምገም።

<u>የርእሰ ጉዳይ ተሳትፎ እና አሰራር፡</u> የጥናቱ ዘዴ ተቋማዊ መሰረት ጥናት ነው። ተሳታፊዎች ከጠያቂው ጋር የሚገናኙበት የሚጠበቀው ጊዜ ከ20 ደቂቃ ያልበለጠ ይሆናል። ይህንን ጥናት ዓላማ የተፈለገው ግብ እንዲመታና በጥናቱ መሠረት የሚለዩ የተለያዩ ችግሮችን በመንግሥትና በሌሎች ድጋፍ ሰጪ ድርጅቶች አካላት ትብብር አማካኝነት በጥናቱ የተደረሰባቸውን ችግሮች ለመፍታት እርስዎ እንዲሳተፉ ተጋብዘዋል፡፡

በዚህ ጥናት ውስጥ ለመሳተፍ ከተስማሙ ስምምነቱን በደንብ መረዳትና እንዲሁም መፈረም ይገባዎታል፡፡ ከዚያ በመቀጠል በጥናቱ መረጃ ሰብሳቢዎች ለሚጠየቁት ጥያቄ እንዲመልሱ ፈቃደኝነትዎ ይጠየቃል፡፡ በዚህ ጥናት ሲሳተፉ የሚሠጡት መልስም ሆነ የሚገኘው ውጤት በምስጢር ይጠበቃል፡፡

<u>የጥናቱ ተሳታፊዎች መረጃ ሚስጥራዊነት፡-</u> ከዚህ ጥናት የሚገኝ መረጃ በሙሉ በምስጢራዊነት ይጠበቃል፡፡. ለዚህ ጥናት የሚሠበሰበው እርሰዎን የሚመለከት መረጃ በማህደር የሚቀመጥ ሲሆን ማህደሩም በስመዎ ሳይሆን በተለ የኮድ ሲቀመጥ ኮዱ ከዋናው ተመራማሪ ውጭ ለማንም አይገለጽም፡፡

የጥናቱ ተሳታፊዎች ጥቅማ ጥቅሞች፡- በዚህ ጥናት በመሳተፍዎ የተለየ ጥቅም አያገኙም፡፡ ነገርግን የርሰዎ በጥናቱ መሳተፍዎ ለጥናቱ መሳካት በጥናቱ በተለያዩ ችግሮች መፍትሄ ሲሰጥ እረስዎ እና ሌሎች ታማሚዎች ተጠቃሚ ይሆናሉ። ከዚህም ተጨማሪ የሚመለከተው ድርጅት እና ፖሊሲ አውጪ የፖሊሲ እይታ፣ አቅጣጫ እንዲይዝ ይረዳል።

ለጥናቱ ተሳታፊዎች ማበረታቻ እና ማካካሻ፡- ይህ ጥናት ለተሳታፊዎቹ ምንም አይነት ማበረታቻ ወይም ማካካሻ የለውም።

ለጥናቱ ተሳታፊዎች ስጋት/ጉዳት፡- ጥናቱ ምንም አይነት ከጤና ጋር የተገናኘ፣ ስነ-ልቦናዊ፣ ኢኮኖሚያዊ እና ማህበራዊ ስጋት/ጉዳት የለውም።

በጥናቱ ያለመሳተፍ ወይም ራስን የማግለል መብት፡ በጥናቱ ላለመሳተፍ ከፈለጉ በዚህ ጥናት ያለመሳተፍ ወይም ከአንድ በላይ ወይም ሁሉንም ጥያቄዎች አለመመለስ ይችላሉ፡፡ በዚህ ጥናት ባለመሳተፍዎ ወይም በከፊልም ሆነ በሙሉ ጥያቄዎችን ባለመመለስዎ ማንኛውንም አገልግሎት ከማግኘት አይከለከሉም፡፡

የመረጃ ሰብሳቢ፡- ተሳታፊው መረጃ ከሚሰበሰብበት ጊዜ በፊት እና በሚሰበሰብበት ወቅት ስለ አውድ ግልጽ ያልሆነ መረጃ የመጠየቅ መብት አለው። ማንኛውም ሰው ዋናውን መርማሪ ማነጋገር ይችላል።

ማንኛውም አይነት ጥያቄ ወይም ችግር ካለህ/የሚኖርህ ከሆነ ዋናውን መርማሪ በማግኘት ማነጋገር ትችላለህ

ስልክ ቁጥር፡- 0921508009 ኢ-ሜል፡- dessale2010@gmail.com.

በዚህ የምርምር ፕሮግራም ለመሳተፍ በፈቃዴ ተስማምቻለሁ ☐ አዎ ☐ አልተስማማሁም

የዚህ የተፈረመ የስምምነት ቅጽ ቅጂ እንደሚሰጠኝ ተረድቻለሁ።

የተሳታፊው ስም _____ ፊርማ: _____ ቀን: _____

ፈቃድ የሚያገኝ ሰው፡ _____ ፊርማ፡ _____ ቀን፡ _____

<u>ክፍል አንድ ፡- የጥናቱ ተሳታፊዎችን ማህበራዊመረጃ የሚመለከቱ ጥያቄዎች</u>

1.	ካርድ ቁጥር/ I-Care no_____				
2.	ፆታ	1. ወንድ	2. ሴት		
3.	ዕድሜ በዓመት ____				
4.	አድራሻ (የከተማውን ስም ይጻፉ) _____				
5.	የጋብቻ ሁኔታ	1. ያገባ/ች	2. ያላገባ	3. አግብቶ የፈታ	4. ባል/ሚስት የሞተበት
6.	ሐይማኖት	1.አርቶዶክስ ክርስቲያን	2. ሙስሊም	3. ፕሮቴስታንት	4. ሌላ ካለ ይግለጡ_____
7.	የስራ ሁኔታ	1.ተቀጣሪ	2. የቤት አመቤት	3. ጡረተኛ	
		4. የግለ ስራ	5. ተማሪ	6. ስራ የሌለዉ	
8.	የትምህርት ደረጃ	1.ማንበብና መጻፍ የማይችል	2.ማንበብና መጻፍ የሚችል	3.አንደኛ ደረጃ (1-8)	

		4.ሁለተኛ ደረጃ (9-12)	5.ቴክኒክና ሙያ/ዲፕሎማ	6. ድግሪ እና ከዚያ በላይ
9.	የህክምናውን አገልግሎት የሚያገኙበት መንገድ	1. በነጻ	2. በክፍያ	3. በጤና መድህን 4. ሌላ _____
10.	ከማን ጋር ነው የሚኖሩት?	1. ከቤተሰብ ጋር	2. ብቻዬን	3. ከሌላ ሰው ጋር (የዩንቨርስቲ ዶርም፣ ፖሊስ ካምፕ፣ ወዘተ)

ክፍል-ሁለት፡ የፕላትሌት ማነስ ጋር የተያያዘ መድማት (immune thrombocytopenia (ITP)) ሕክምና ውጤቶችን የሚመለከቱ መረጃዎች።

1. ከፕላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) የህክምና ምርመራ ካደረጉ ስንት ጊዜ ሆነዎት? _____
2. ከአሁን በፊት/አሁን ላይ ሌሎች ተጓዳኝ በሽታዎች አሉበዎት? 1. አዎ 2. የለብኝም
3. ለተራ ቁጥር 2 ጥያቄ መልስዎ አዎ ከሆነ እባክዎትን ሁሉንም ይዘርዝራቸዉ ___ _____ _____ _____ _____ _____ _____ _
4. በአሁኑ ሰዓት የሚሰማዎት/የሚታዩት የITP ምልክቶች የትኞቹ ናቸው (ከአንድ በላይ መልስ መስጠት ይቻላል)?

1. የድካም ስሜት	2. ደም መፍሰስ
3. የመንፈስ ጭንቀት/ድብርት ስሜት	4. ክብደት መቀነስ
5. የራስ ህመም	6. ሌሎች ካሉ ይዘርዝሩ_____

5. ለፕላትሌት ማነስ ጋር የተያያዘ መድማት ከነበረ ምርመራ በሚያደርጉበት ወቅት የነበሩዎት የመድማት ምልክቶች የትኞቹ ነበሩ (ከአንድ በላይ መልስ መስጠት ይቻላል)?

1. የቆዳ ላይ ምልክቶች ብቻ	2. በአፍ/በአፍንጫ መድማት
3. ለሕይወት አስጊ የሆነ የደም መፍሰስ (የጭንቅላት/የአንጅት ደም መፍሰስ)	
5. ሌላ ካለ ይጻፍት_____	

ክፍል-ሶስት፡ የሞሪስኪ ግሪን ሌቪን መስፈርት (Morisky Green Levine scale (MGL)) በመጠቀም ለፕላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) ሕክምና የሚታዘዙ መድሃኒቶችን በአግባቡ መወሰዱን ለማረጋግጥ የሚያገለግል መለኪያ/መስፈርት

	የሞሪስኪ ግሪን ሌቪን መስፈርት (Morisky Green Levine scale (MGL))	አዎ	በፍጹም
1	የእርስዎን ITP መድሃኒት ለመውሰድ ረስተው ያውቃሉ?		
2	የእርስዎን የITP መድሃኒት ለመውሰድ የማስታወስ ችግር አጋጥመውዎት ያውቃሉ?		
3	አንዳንድ ጊዜ ጥሩ ስሜት ሲሰማዎት (የተሻለዎት ሲመስለዎ) የITP መድሃኒትዎን መውሰድ አቁመው ያቃሉ?		
4	አንዳንድ ጊዜ የITP መድሃኒት ሲወስዱ የከፋ ስሜት ከተሰማዎት, መውሰድ አቁመው ያቃሉ?		

ክፍል-አራት: ለITP ሕመም የሚወሰዱ የስቴሮይድ መድሃኒቶች የሚያስከትሉትን የጎንዮሽ ጉዳቶች የሚገመግም ቅጽ .

1. ለITP ሕክምና የሚያገለግሉ የፕሬዴኒሶን(prednisolone) ወይም ሌላ ስቴሮይድ (**corticosteroids**) መድሃኒት ለምን ያክል ጊዜ ወስደዋል? _____ _____
2. **<u>ከሚከተሉት የስቴሮይድ መድሃኒት የጎንዮሽ ጉዳቶች ውስጥ የትኛዎቹ ኢጋጥመዎት ያውቃሉ?</u>**

   2.1. **ከስቴሮይድ መድሃኒት ጋር የተያያዙ የአካላዊ ገጽታ ጎንዮሽ ጉዳቶች (ከአንድ በላይ መልስ መስጠት ይቻላል)**

1. የፊት እብጠት	2. ብጉር
3. የፀጉር መርገፍ	4. ክብደት መጨመር / የምግብ ፍላጎት መጨመር
5. ቆዳ ላይ የመሰንጠቅ ምልክቶች (Stretch marks)	

2.2. ከስቴሮይድ መድሃኒት ጋር የተያያዙ ስሜታዊ ምልክቶች (ከአንድ በላይ መልስ መስጠት ይቻላል)

1.እንቅልፍ ማጣት፣ወይም የመተኛት ችግር	2. ጭንቀት
3. ድብርት ወይም ውጥረት	4. ቁጣ ወይም ብስጭት

2.3. ከስቴሮይድ መድሃኒት ጋር የተያያዙ የአካል ብቃት/የሰውነት ጥንካሬ ማነስ ምልክቶች (ከአንድ በላይ መልስ መስጠት ይቻላል)

1. አጠቃላይ የሰውነት ድካም ስሜት	2. የጡንቻ ድክመት/መዛል
3. የሰውነት ሕመም (የመገጣጠሚያዎች፣የጡንቻ መኮማተር)	4. የ ሰውነት ትኩሳት/ ላብ ላብ ማለት
5. የእይታ ችግሮች (የብርሃን ስሜታዊነት/ የእይታ መቀነስ)	6. ማዞር, ራስ ምታት
7. ማቅለሽለሽ፣ የሆድ ቁርጠት፣ ማስታወክ፣ ተቅማጥ	

2.4. ከስቴሮይድ መድሃኒት ጋር የተያያዙ ሌሎች የጎንዮሽ ጉዳቶች (ከአንድ በላይ መልስ መስጠት ይቻላል)

1. የደም ስካር መጠን መጨመር	2. የደም ግፊት መጨመር
3. የአጥንት መሳሳት	4. ሌላ_____

3. ላጋጠመዎት እያንዳንዱ ከስቴሮይድ መድሃኒት ጋር የተያያዙ የጎንዮሽ ጉዳቶች፣ እባክዎን የጎንዮሽ ጉዳቱ በህይወቶ ላይ ያሳደረውን ጉዳት/ ተፅዕኖ በሚከተለው መስፈርት መሰረት ከ1 እስከ 5 ደረጃ በመስጠት ያመልክቱ።

1. እነዚህ የጎንዮሽ ጉዳቶች አላጋጠመኝም	2. እነዚህ የጎንዮሽ ጉዳቶች አያስጨንቁኝም
3. እነዚህ የጎንዮሽ ጉዳቶች ትንሽ አስጨንቀውኝ ነበር	4. እነዚህ የጎንዮሽ ጉዳቶች አንዳንድ ጊዜ ይረብሹኝ ነበር.
5. እነዚህ የጎንዮሽ ጉዳቶች በጣም አስጨንቀውኛል/ይረብሹኛል	

ክፍል-አምስት፡- ከፐላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) ታካሚዎች ላይ የጤና ነክ ፣ የህይወት ጥራት/የኑሮ ሁኔታ እና ተዛማጅነት ጉዳዮች ላይ የሚያተኩር።

ይህ መጠይቅ ከፐላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) ህመም ባለፈው አንድ ወር ውስጥ በእርስዎ ህይወት ላይ ምን ያህል ጉዳት/ተፅዕኖ እንዳሳደረ ለመለካት ነው።

1. የእርስዎ ከፐላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) ህመም በስራ ህይወትዎ ወይም በጥናትዎ ላይ ምን ያህል ተፅዕኖ አሳድሯል?

1. በፍጹም	2. አንዳንድ ጊዜ	3. ከግማሽ ጊዜ በላይ	4. ሁል ጊዜ
5. በአሁኑ ጊዜ በ ከፐላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) ምክንያት እየሰራሁ/እያጠናሁ አይደለም			
6. አሁን በሌሎች ምክንያቶች የተነሳ እየሰራሁ/እያተጠናሁ አይደለም			

2. እርስዎ ከፐላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) ህመም ምክንያት ስንት ጊዜ ከሥራ ወይም ከትምህርት ተስተጓጉለው ያቃሉ?

1. በፍጹም	2. አንዳንድ ጊዜ	3. ከግማሽ ጊዜ በላይ	4. ሁል ጊዜ
5. በአሁኑ ጊዜ በፐላትሌት ማነስ ጋር የተያያዘ መድማት (ITP)ምክንያት እየሰራሁ/እያጠናሁ አይደለም			
6. አሁን በሌሎች ምክንያቶች የተነሳ እየሰራሁ/እያተጠናሁ አይደለም			

3. የእርስዎ በፐላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) ህመም በዕለት ተዕለት ተግባራት ላይ የማተኮር ችሎታዎን ምን ያህል ተጽእኖ አሳድሯል?

1. በፍጹም	2. አንዳንድ ጊዜ	3. ከግማሽ ጊዜ በላይ	4. ሁል ጊዜ

4. የእርስዎ በፐላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) ህመም በማህበራዊ ሕይወትዎ ላይ ምን ያህል ተጽዕኖ አሳድሯል?

1. በፍጹም	2. አንዳንድ ጊዜ	3. ከግማሽ ጊዜ በላይ	4. ሁል ጊዜ

5. የእርስዎ በፐላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) ህመም በወሲብ ህይወትዎ ላይ ምን ያህል ጊዜ ተጽዕኖ አሳድሯል?

1. በፍጹም	2. አንዳንድ ጊዜ	3. ከግማሽ ጊዜ በላይ	4. ሁል ጊዜ
5. ተፈፃሚነት የሌለው/ይሄ ጥያቄ እኔን አይመለከተኝም			

6. ከፐላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) ህመም በእርስዎ የሰውነት ጥንካሬ ላይ ምን ያህል ተጽዕኖ አሳድሯል?

1. በፍጹም	2. አንዳንድ ጊዜ	3. ከግማሽ ጊዜ በላይ	4. ሁል ጊዜ

7. ከፐላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) ህመም በዕለት ተዕለት ተግባሮችዎን በመከወን ላይ ምን ያህል ተጽዕኖ አሳድሯል?

1. በፍጹም	2. አንዳንድ ጊዜ	3. ከግማሽ ጊዜ በላይ	4. ሁል ጊዜ

8. ከፐላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) ህመም ለእርስዎ ቅርብ የሆኑ ሰዎችን የመደገፍ/የመርዳት አቅምዎ ላይ ምን ያህል ተጽዕኖ አሳድሯል?

1. በፍጹም	2. አንዳንድ ጊዜ	3. ከግማሽ ጊዜ በላይ	4. ሁል ጊዜ

9. የእርስዎ ከፐላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) ህመም የትርፍ ጊዜማ ሳለፈያዎችዎ (ለመደሰት፣ለመዝናናት የሚያሳልፉበት)ላይ አሉታዊ ተጽእኖው ምን ያህል ጊዜ ነው?

1. በፍጹም	2. አንዳንድ ጊዜ	3. ከግማሽ ጊዜ በላይ	4. ሁል ጊዜ

10. የእርስዎ ከፐላትሌት ማነስ ጋር የተያያዘ መድማት (ITP) በተለመደው የአካል ብቃት እንቅስቃሴ አቅምዎ ላይ ምን ያህል አሉታዊ ተጽዕኖ አሳድሯል?

1. በፍጹም	2. አንዳንድ ጊዜ	3. ከግማሽ ጊዜ በላይ	4. ሁል ጊዜ

ስለ ትብብርዎ እና ስለጊዜዎ ከልብ እናመሰግናለን !!!

በባለሙያ የሚሞላ/በመረጃ ሰብሳቢው የሚሞላ

Clinical characteristics of study participants assessed from medical chart

1. **Physical findings at presentations**

   1.1. Signs of bleeding at presentations (more than one answer is possible)

A. wet purpura (mucous membrane bleeding)	B. Epistaxis
C. petechiae	D. if others

1.2. Signs of anemia (pallor) at presentations? A. Yes B. No

1.3. Neck stiffness (CNS bleeding) at presentations? A. Yes B. No

1.4. Splenomegaly or hepatomegaly at presentations? A. Yes B. No

1.5. Others signs (more than one answer is possible)

A. Fatigue	B. Headache
C. Depression	D. weight loss
E. If others_____ _____	

2. Primary clinical/laboratory findings at presentations

Investigations	WBC with differentials	Platelet	Hemoglobin (Hgb)	Hematocrit (HCT)
Value at presentation				

3. Secondary investigations at presentation

Investigations	Result
Viral markers	
H. Pylori	
Bone marrow aspiration report (Megakaryocyte level)	
Drug-induced Immune Thrombocytopenia	

4. Platelet count during the treatment period

Platelet count													
Date	During DX												

5. Bleeding event

Bleeding events										
Date	During DX									

6. Treatment of ITP at presentation (first-line treatment).

A. Prednisolone	B. Dexamethasone
C. Methylprednisolone	D. platelet transfusion
E. anti-D Ig	F. IVIg, G. TAX

7. Rescue treatment/second-line treatment of ITP

A. Rituximab	B. platelet transfusion
C. Splenectomy	D. IVIg
E. Others _____	

8. Other medication used to comorbid/prophylaxis _____ _____ _____ _____

9. Platelet count if relapse/second-line treatment

Platelet count												
Date												

10. Prophylaxis for Steroid side effects.

A. Cotrimoxazole	B. Omeprazole
C. Calcium with VtD3	D. Others____