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Research Article

Factors Affecting Quality of Life in ITP patients: Case Control Study

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Abstract:

Background: Quality of life is usually a cornerstone in patients diagnosed with any chronic disease and its impairment may necessitate some modifications in the management plan. Immune thrombocytopenia (ITP) is a common blood disorder that in most adult cases becomes a chronic disorder. **The aim of the work:** to explore the effect of ITP on QOL of adult patients with emphasis on different factors that may affect QOL in ITP patients. **Methodology:** Two hundred subjects were involved in this study, including 100 adult ITP cases in comparison to 100 sex and age matched control. All of them were subjected to structured interview to take detailed data about the disease and treatment plan after that they fulfill the WHOQOL-BREF. Lastly a Blood sample was taken for laboratory investigation. **Results:** There is a highly significant difference in QOL of ITP patients in comparison to control (p=0.0001). The main impairment was found in chronic ITP patients when compared with acute or persistent patients. There is no difference between cases according to disease type. There is a positive correlation between QOL and platelet count and hemoglobin level while there is negative correlation with total leucocytic count, ITP bleeding score, number of treatment line used and splenoectomy. **Conclusion:** QOL in ITP patients is affected by several factors that all need to be addressed and modified in order to reach the main goal in ITP treatment to live a relatively normal life.

Keywords: Immune thrombocytopenia, Quality of Life, Platelet count, Total Leucocytic Count, splenectomy.

Introduction:

Immune thrombocytopenia (ITP) is one of the prevalent blood diseases with an incidence 2-4 / 100 000 [(1)]. It is manifested by thrombocytopenia (platelet count < 100 × 109/L). ITP may be a primary type which is characterized by isolated thrombocytopenia without the association of other causes or disorders. While secondary form is presented with thrombocytopenia in association with another disorder that is usually immune or infectious [(2)].

ITP can be classified according to onset of thrombocytopenia into; acute, persistent and chronic. Acute ITP refers to recently diagnosed ITP (not exceeding 3 months), while persistent type has a duration between 3-12 months. Finally chronic type defines an ITP of more than 12 months duration [(3)].

Clinical manifestations of ITP are highly variable. Cases with the same platelet count may experience different bleeding symptoms that range from no bleeding at all to severe bleeding symptoms. ITP bleeding usually manifests as spontaneous skin bruises, petechiae and purpura or mucous membrane bleeding (e.g orificial bleeding). Sometimes bleeding may be frank causing vaginal, gastrointestinal, or even intracranial hemorrhage [(4)].

Regarding treatment of ITP the American society of hematology (ASH, 2019) recommends several lines. In adults during acute phase, it recommends corticosteroids alone or intravenous immunoglobulin (IVIG) as a first line therapy. In ITP lasting ≥12 months that have no response to corticosteroids or corticosteroid-dependent it suggests either thrombopoietin receptor agonist (TPO-RAs) or rituximab or splenectomy which depends on the patient's overall condition and preferences [5].

The World Health Organization defines quality of life (QOL) as how individuals think of their place in life in relation to their aims, dreams, standards, and concerns as well as the society and system of values in which they live [6].

Patients who are diagnosed with a disease of chronic nature like ITP may experience depression, sleep disturbances, and fatigue concurrently, with the impact of their underlying disease [7]. Most ITP patients focus on the negative impacts of ITP on their lives, particularly on their psychological well-being, energy levels and ability to study or work. Despite many ITP patients describing their health as good, a large proportion reports that the condition significantly affects their energy, productivity, career progression, and emotional well-being [8,9].

Measuring QOL in ITP patients is important as one of target goals in ITP treatment is to help the patients to live a relatively normal life [10]. In addition, **Shimano et al.** [11] found that QOL may be used as an indicator for introducing second line therapy in children which both point the importance of giving special concern to measuring and improving QOL. The aim of our study is to explore the effect of ITP on QOL of adult patients in comparison to normal population with emphasis on different factors that may affect QOL in ITP patients as disease type (primary vs secondary), disease category (acute, persistent or chronic), lab investigations (PLT, HB, TLC), number of treatment lines.

Patients and Methods

Study design and participants

This is a cross-sectional case control study. One hundred Patients were recruited from both inpatient department and outpatient clinic of Internal Medicine Department/ Hematology Unit at Minia university Hospital from December 2023 to September 2024. Comparable number of sex and age matched healthy control were chosen from the apparent healthy relatives of the patients who were apparently free from any disorder.

The average number of adult ITP patients who visited Hematology unit in Minia University Hospital was nearly 300 patients in the last year. Sample size was calculated according to **Isaac and Michael** [12] formula (N= n×30/100) in which (N= sample size and n= total number of ITP patients who visited the hospital in the past year). Sample size = 300×30/100= 90. So, the research team includes 100 patients to confirm the validity of the sample size.

Inclusion criteria were; patients from both sex, aging from 18-65 years, diagnosed with isolated thrombocytopenia (platelets count less than 100.000/dl) either primary or secondary acquired immune thrombocytopenia. Give the informed consent to be involved in the study.

Exclusion criteria include; thrombocytopenia caused by other underlying medical diseases such as malignancy, Bone Marrow infiltration, megaloblastic anemia, aplastic anemia, liver disease, renal impairment, pregnancy, abnormalities in BM aspirate rather than typical Picture of immune thrombocytopenia (e.g. MDS), inherited thrombocytopenia with positive family history. In addition to exclusion of patients with history of psychiatric disorders prior to onset of ITP, and those with recent evidence of bacterial infection.

N.B. In the exclusion criteria, the authors referred to "malignancy" as solid tumors associated with bone metastases leading to thrombocytopenia, as well as chemotherapy-induced thrombocytopenia. In contrast, in the inclusion criteria, "malignancy" referred to lymphoproliferative malignancies associated with autoimmune thrombocytopenia, confirmed by bone marrow examination, which revealed peripheral destruction without bone marrow infiltration.

Tools of the study:

1. WHOQOL-BREF [13]:

The WHOQOL-BREF [13] has been developed to provide a short form quality of life assessment. It is an abbreviation of WHOQOL-100 which was developed by WHO in order to develop

a quality of life assessment tool that is applicable across different cultures.

The WHOQOL-BREF is an outcome instrument that is Patient reported to assess the global health status of patients irrespective of disease across 4 health domains (physical, psychological, social, environmental) with 24 different domain aspects. It is one of the best-known tools used for cross-cultural comparisons of quality of life and has been translated to more than 40 languages [14].

The internal consistency of WHOQOL-BREF is good with Cronbach's alpha coefficient equals 0.91 for the overall scale. It also has good convergent validity results [15].

2- Laboratory investigations:

Complete blood count was done under complete aseptic precautions; 5 ml of peripheral venous blood sample was withdrawn from each subject. This sample was collected on a tube containing ethylene-diamine-tetra acetic acid (EDTA). CBC was performed using automated hematology analyzer **(Celtac G 04635, NIHON KOHDEN CORPORATION, Japan).**

Data procedure:

A structured interview with the patients was performed to collect data about ITP (duration of illness, type of disease, treatment received, exclude other causes of ITP, record their last investigations, calculate bleeding severity according to ITP-bleeding score 2016 [16]. The second step was to answer the WHOQOL-BREF to assess their quality of life. Third step was to take a blood sample for CBC.

Statistical analysis:

SPSS version 21 was used for data entry and analysis. Quantitative data is showed as mean and SD while qualitative data is showed as frequency distribution. For comparison, independent sample t test, Man-whiteny test, kruskal Wallis test, and Chi square test were used. Spearman correlation test and Pearson correlation test were used for correlation while linear regression analysis was used for regression analysis. All studies used a p value <0.05 for significance.

Ethical consideration:

After delivering study approval from the research ethics committee of Faculty of Medicine, Minia University with an ethical approval No (753:5:2023) the research team started to interview different ITP patients fulfilling the inclusion criteria in order to explain the aim and methodology of the study in order to take informed consent from them to participate in the study. The collected data is preserved in a secure place where it could be only accessible by the research team in order to ensure privacy of the participants.

Results:

The studied sample composed of 100 cases of ITP patients with a corresponding control group composed of 100 participants also. Both groups are comparable regarding age and sex however, there is a statistically significant difference regarding HB, TLC, and PLT (P= 0.0001, 0.01, and 0.0001 respectively) (Table 1).

The studied cases (100 cases) are categorized into 22% in acute phase, 13% in persistent phase and the majority is in chronic phase (65%). Regarding disease type, 64% of cases are primary type of ITP while 36% are secondary. The number of treatment lines used is ranging from using one line in 21% to using 2 lines of treatment in 43% or using more than 2 lines in treatment in 36%. Only 5 cases undergo splenectomy while the majority doesn't (Table 2).

Comparison between ITP cases and control regarding QOL reveals the presence of statistically significant difference between them regarding total score in addition to all domains of QOL (physical, psychological, social and environmental) (p= 0.0001, 0.0001, 0.0001, 0.001, 0.0001 respectively). On deeper view of impact of disease stage on quality of life, acute and persistent cases show no statistically significant difference on comparison with control while there is a statistically significant difference regarding comparison between chronic patients and control. This difference is also significant on comparing QOL in chronic patients with acute or persistent cases (Table 3).

On the other hand, while comparing between primary and secondary ITP cases to control there is a statistically difference between them in all domains of QOL plus total score. However, this statistically significant difference disappears in

comparing primary ITP cases to secondary ITP cases (Table 4).

The correlation between QOL and PLT, HB, TLC in the studied sample reveals the presence of significant positive weak to fair correlation between QOL and both platelet count and hemoglobin level. On the other hand, there is negative non-significant correlation between QOL and TLC.

Regarding correlation between QOL and number of treatment lines, ITP bleeding score and Splenectomy**,** there is a negative significant correlation between QOL and both number of treatment lines and splenectomy (overall score and most of domains). Also, there is a negative correlation between ITP bleeding score and QOL which became significant regarding psychological and social domains only (Table 5,6).

The regression analysis of factors affecting QOL in ITP patients reveals that QOL is only significantly affected by disease stage (Table 7).

Table (1): Comparison between cases and controls regarding some demographic and laboratory data

Data	Cases No=100	Controls No=100	p
Age (years)			
Range	18-65	18-65	0.055
Mean±SD	31.6±11.3	35.02±12.8	
Sex (n,%)			
male	38(38%).	48(48%)	0.1
female	62(62%)	52(52%)	
HB (g/dL)			
Range	6-16	10-16	0.0001*
Mean±SD	11.5±2.03	12.9±1.3	
TLC (10^3/µL)			
Mean±SD	7.6±2.8	6.8±2.004	0.01*
PLT (10^3/µL)			
Range	2-91	150-420	0.0001*
Mean±SD	25.08±16.9	283.9±64.6	

-Independent sample t test to compare for quantitative data

*-Chi-square to compare for qualitative data***.**

Table (2): Clinical data of the studied cases (no=100)

Data	Frequency	Percent
Disease categorization		
Acute	22	22%
Persistent	13	13%
Chronic	65	65%
Disease type		
Primary	64	64%
Secondary	36	36%
Total line of medication		
Monotherapy	21	21%
Dual therapy	43	43%
Polytherapy	36	36%
Splenectomy		
Not done	95	95%
Done	5	5%

Table (3): Comparison between cases (acute, persistent, and chronic) and controls regarding QOL

Data		Acute No=22	Persistent No= 13	Chronic No= 65	Controls No=100	p
Overall QOL and general health	**Range** **Mean±SD**	25-100 74.2±17.8	37-87 69.8±15.7	12-100 52.8±21.9@#$	25-100 75±18.3	0.0001*
Physical Domain	**Range** **Mean±SD**	21-96 73.09±18.7	28-100 71.2±22.6	14-100 60.5±20.7@#$	32-100 77.4±16.8	0.0001*
Psychological Domain	**Range** **Mean±SD**	29-92 71.3±15.7	46-92 73.9±13.5	25-92 56.4±18.5@#$	25-96 71.6±16.5	0.0001*
Social Domain	**Range** **Mean±SD**	17-100 76.5±17.5	42-100 82.7±18.1	17-100 65.7±22.8@#$	25-100 79.4±16.3	0.001*
Environment Domain	**Range** **Mean±SD**	12-94 65.09±17.9	44-94 69.6±15.4	12-100 56.2±18.6@#$	25-97 73.07±17.7	0.0001*

- Independant sample t test used to compare numeric data between chronic and controls
-Mann–Whitney U tests were used to compare quantitative data between acute and control. Persistent and controls..
- Kruskal–Wallis test was used to compare quantitative data among the three groups.
** indicates a P value < 0.05 (two-tailed)*
@: Significant difference (p value ≤ 0.05) between chronic and control groups
#: Significant difference (p value ≤ 0.05) between the acute and chronic groups
$: Significant difference (p value ≤ 0.05) between the persistent and control groups

Table (4): Comparison between cases (primary, secondary) and controls regarding QOL assessment

Data		Primary No=64	Secondary No=36	Controls No=100	p
Over all QOL and general health	**Range** **Mean±SD**	12-100 58.1±22.3	12-100 62.6±22.4	25-100 75±18.3 @#	0.0001*
Physical Domain	**Range** **Mean±SD**	14-100 63.8±21.7	28-100 66.3±20.08	32-100 77.4±16.8@#	0.0001*
Psychological Domain	**Range** **Mean±SD**	25-92 60.8±16.8	25-92 64.06±22.2	25-96 71.6±16.5@#	0.001*
Social Domain	**Range** **Mean±SD**	17-100 70.9±21.2	17-100 69.2±23.6	25-100 79.4±16.3@#	0.004*
Environment Domain	**Range** **Mean±SD**	12-100 59.1±18.0	25-94 61.2±19.7	25-97 73.07±17.7@#	0.0001*

- Independant sample t test used to compare numeric data between primary and controls.
-Mann–Whitney U tests were used to compare quantitative data between secondary and controls.
- Kruskal–Wallis test was used to compare quantitative data among the three groups.
** indicates a P value < 0.05 (two-tailed).*
@: Significant difference (p value ≤ 0.05) between primary and control groups
#: Significant difference (p value ≤ 0.05) between secondary and control groups

Table (5): Correlation between PLT, HB, TLC and QOL (overall score and domains) in studied sample (n=200)

	PLT count	HB	TLC
Overall QOL score			
r	0.297	0.139	-0.019
P value	0.0001**	0.049*	0.791
Physical domain			
r	0.270	0.160	-0.020
P value	0.0001**	0.024*	0.781
Psychological Domain			
r	0.193	0.151	-0.033
P value	0.006**	0.033*	0.645
Social domain			
r	0.191	0.152	-0.065
P value	0.007**	0.031*	0.364
Environmental Domain			
r	0.309	0.159	-0.012
P value	0.0001**	0.025*	0.870

- *Hb:hemoglobin; Tlc: total leukocytic count; Plt: platelets count*
-The Pearson correlation test was used to correlate numerical data.
** indicates a P value < 0.05 (two-tailed).*
*** indicates a P value < 0.01 (two-tailed).*

Table (6): Correlation between number of Treatment lines, ITP bleeding score, Splenectomy and QOL in ITP patients (overall score and domains) (n=100)

	Number of treatment lines	ITP bleeding score	Splenectomy
Overall QOL score			
r	-0.252*	-0.142	-0.254*
p value	0.012	0.158	0.011
Physical domain			
r	-0.318**	-0.119	-0.263**
p value	0.001	0.239	0.008
Psychological Domain			
r	-0.310**	-0.283**	-0.212*
p value	0.002	0.004	0.034
Social domain			
r	-0.196	-0.210*	-0.192
p value	0.051	0.036	0.056
Environmental Domain			
r	-0.203*	-0.065	-0.205*
p value	0.043	0.523	0.040

- The Spearman correlation test was used to correlate nonparametric data.
** indicates a P value < 0.05 (two-tailed).*
*** indicates a P value < 0.01 (two-tailed).*

Table (7) Multivariate Regression analysis of factors affecting QOL and its domains among ITP patients

	Hb	PLT	TLC	Disease category	Disease type	Number of treatment lines	ITP bleeding score	Splenectomy
Overall QOL score Beta coefficient p value	-0.02408	-0.100.2	0.0030.9	-0.400.0001*	0.0120.9	-0.1470.17	-0.0550.59	-0.2180.02*
Physical domain Beta coefficient p value	0.0080.9	-0.170.06	-0.0030.9	-0.220.05	0.0190.8	-0.2760.01*	0.020.85	-0.2230.02*
Psychological Domain Beta coefficient p value	0.020.8	-0.080.34	-0.840.37	-0.330.003*	0.020.7	-0.1760.107	-0.1940.06	-0.1580.101
Social domain Beta coefficient p value	0.0540.6	-0.020.78	-0.080.4	-0.240.03*	-0.080.4	-0.0750.5	-0.1750.12	-0.1370.18
Environmental Domain Beta coefficient p value	-0.0140.8	-0.180.07	-0.060.5	-0.2690.02*	0.030.7	-0.1060.36	-0.0630.57	-0.1880.06

- *Hb:hemoglobin; Tlc: total leukocytic count; Plt: platelets count*
- *Linear Regression analysis was used * indicates a P value < 0.05 (two-tailed).*

Discussion:

As the majority of adults with ITP have the chronic form of disease so patients have to deal with their symptoms for a long period of time which impact their life. So it is necessary to explore the patients' QOL in order to help the patient to live a relatively normal life which is the main goal of management in ITP [10]. . The aim of this study is to assess quality of life in adult ITP patients with special emphasis on impact of disease type, category, laboratory investigations, and treatment lines on QOL.

This study reports a highly statistically significant difference between ITP cases and control group regarding QOL. This comes in agreement with **Tomasello et al.** [17] who conducted a multicenter study on 274 Norwegian patients and **Zhang et al.** [18] who include 175 Chinese patients. Which indicate that ITP patients suffer from poor QOL in comparison with control.

Cooper et al. [8] demonstrate that impact of ITP on patients' QOL was reported from both patients and their physicians. Patients report reduced energy levels, with increased fears about worsening of their condition also patients who were working experienced reduced productivity.

This impairment in quality of life may be explained by general factors contributed to nature of being diagnosed with a chronic illness that require lifelong follow up and medication in order to treat it and avoid possible complications. The physical limitations, social challenges, emotional burden, financial strain, and impairment in self-identity can all contribute to a reduced QOL [19].

In addition, QOL impairment in ITP patients affected by fear of bleeding at any time, fear of fatal complications that may occur, fear of side effects of the used medications as steroids and immunosuppressant, fear of splenectomy if needed and fear of disease stigma [20].

On comparing different ITP categories (acute, persistent and chronic) to control there is only a significant difference between QOL in chronic cases in comparison to control and also

this difference is significant on comparing chronic cases to acute or persistent cases. In addition, regression analysis of factors affecting QOL reveals the significant impact of disease category on QOL. So, chronicity of disease is related to more impairment in QOL.

These findings come in agreement with **Zhou & Yang** [20] who report that QOL may be affected by duration of illness as acute ITP patients have better QOL than chronic patients. While disagree with **Efficace et al.** [21] who reported that persistent ITP patients are the most impaired group in quality of life. This difference may be attributed to difference in used tool to measure QOL (HRQol), inclusion of primary ITP patients only but in our study both primary and secondary ITP patients were included.

The increase in impairment of QOL with increase of duration of disease may be attributed to feeling of despair to recover from illness, increase in lines of treatment needed, facing difficulties in accepting the chronic nature of the disease which incorporate difficulties in accepting possible complications and/or need to administer treatment for long duration or even for life.

On comparing primary to secondary acquired immune thrombocytopenia regarding QOL there isn't significant difference between them. Up to our knowledge there is no previous study that compare primary to secondary acquired immune thrombocytopenia ITP cases. However, this may be explained by exclusion of other types of secondary ITP which may suffer from more impairment due to the presence of underlying illness which may has its own effect on QOL. Sharing the same etiology of immune dysregulation in both primary and secondary ITP may explain the absence of difference in QOL.

In correlation between PLT count to QOL there is significant positive correlation which came in agreement with **Zhou & Yang** [20] and **Mathias et al.** [22] as they reported that The QOL is higher in patients with higher platelet counts.

The positive relation between HB and QOL was proved by several research who reported a direct relationship between hemoglobin increase and improvement in QOL in different diseases as different types of anemia either primary type or secondary [23,24].

ITP bleeding score has a negative correlation to QOL, but it isn't significant except regarding psychological and social domains only. This don't come in agreement with **Neunert et al.** [25] **or Zhou et al.** [26] who reported that the bleeding severity score did not correlate with the QOL. Our results can be explained by higher bleeding score is associated with more severe symptoms of bleeding companied with lower platelet count which was previously negatively correlated to QOL. However, this correlation isn't significant except in psychological and social domains which may reflect the presence of associated fears of developing bleeding in social situations which can threaten his life or embarrass him between his colleagues. Also, the subjective evaluation of the seriousness of his condition may contribute to worsening in psychological QOL.

There is a negative significant relation between QOL and number of treatment lines used and splenectomy especially in physical domain of QOL. **Tomasello et al.** [17] reported that ITP patients receiving treatment have worse QOL compared to those currently not on treatment but they don't mention number of treatment line used. According to ASH guidelines patients who are under treatment with more than one line of treatment usually suffer from active disease in persistent or chronic phase [27]. Worsening in QOL may be attributed to several factors including being in persistent or chronic stage with decrease in PLT count in addition to psychological factors and treatment side effects.

Regarding the effect of splenectomy on QOL we find a negative relation between it and QOL. This isn't in agreement with a previous study in children who reported improvement in QOL after splenectomy [28]. While another study in adults don't reveal significant difference in QOL after the operation [22]. The worsening in QOL after splenectomy in our study may be explained by long duration of suffering from ITP as splenectomy is done in chronic patients after 12 months of ongoing, active disease [27]. The chronicity of the disease may be the main cause of QOL worsening as mentioned before. Added to that some patients may be relapsed even after splenectomy.

The detection of QOL impairment in those patients is an important step during course of treatment as it may indicate some alternations in treatment plan. Interventions to improve QOL may

include some modifications in drug regimens to manage side effects or indicate treatment switch or even treatment discontinuation and consider watch-and-wait strategy [29].

So, it is important to measure QOL of ITP patients several times during their course in order to detect it early then trying to improve it according to which symptoms are present and what is the underlying cause [7]. The deterioration in QOL in ITP can be predicted by several laboratory investigations (PLT, HB, and TLC) which are regularly requested for those patients in addition to reviewing the treatment plan and patient's bleeding history. If patient suffers from high bleeding score associated with impairment in his lab investigation measuring QOL is advised in order to manage it even if the patient isn't complaining of it.

In conclusion QOL in adults with ITP is impaired in comparison with normal population. Chronic ITP patients suffer from more impairment than other categories. On the other hand QOL is not affected by disease type (primary or secondary acquired immune type). PLT count, HB level are positively correlated with QOL while TLC, ITP bleeding score, number of treatment lines and splenectomy are negatively correlated. Finally QOL is affected by several factors that need all to be addressed and modified in order to reach the main goal in ITP treatment to live a relatively normal life.

- **List of abbreviations**

ASH: American society of hematology

BM: Bone Marrow

CBC: Complete blood count

HB: hemoglobin level

HRQol: Health related quality of life

ITP: Immune thrombocytopenia

ITP-BAT: Immune thrombocytopenia -Bleeding Assessment Tool

IVIG: intravenous immunoglobulin

List of abbriviations:

MDS: Myelodysplastic syndrome

PLT: platelet count

TLC: total leucocytic count

TPO-RAs: thrombopoietin receptor agonist

WHO: World Health Organization

WHOQOL-BREF: world health organization quality of life brief version

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