First report on health-related quality of life among children with chronic immune thrombocytopenia in Vietnam

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ABSTRACT

Background: Immune thrombocytopenia (ITP) is a benign childhood disease. The aim of this study was to assess Health Related Quality of Life (HRQoL) among chronic ITP children in Vietnam.

Methods: A case - control study was conducted from January 2020 to April 2021. Case group consisted of 56 children with chronic ITP aged from 2 to 18 years and their parents selected in the Department of Nephrology-Hematology – Endocrinology, Haiphong Children's Hospital, Hai Phong city. Controls included 170 healthy children matched with the patients on sex, and age recruited from schools in the same city. The validated Vietnamese version of the Pediatric Quality of Life Inventory (PedsQL) 4.0 Generic Core Scale was used to assess QoL of the participants.

Results: The mean HRQoL physical, emotional, social, school functioning domains and total scores of the chronic ITP patients were significantly lower compared with that of the controls ($p < 0.001$ for all). Children in the age group 13–18 had the lowest overall HRQoL score compared other age groups (60.87 ± 7.66 , $p = 0.023$), especially in the emotional and social functioning domains (58.33 ± 6.83 ; 64.17 ± 11.58 , respectively) ($p < 0.001$). Chronic ITP patients with older age, longer treatment duration, and ongoing treatment status showed to be having lower HRQoL scores than the younger one, shorter treatment duration, and the stopped treatment group.

Conclusion: Chronic ITP has a negative impact on HRQoL in terms of physical functioning, emotional, social, school functioning, and overall scores when compared with the healthy sex, age-matched children.

1. Introduction

Immune thrombocytopenia (ITP) is a common bleeding disorder in blood and hematopoietic diseases. It is characterized by isolated thrombocytopenia (platelet count $<100 \times 10^9/l$) due to the unknown existence of autoantibodies in peripheral blood. These autoantibodies are directed against platelet membrane antigens.¹ Clinical features of ITP disease are emerged with some symptoms such as: spontaneous cutaneous bleeding (petechiae, purpura, or ecchymoses) or mucosal bleeding that involves to nasal passages, buccal, and gingival surfaces to intracranial hemorrhage.^{2–4} The estimated incidence of childhood ITP is about 4–5 per 100,000 person-years.⁵ Severe morbidity and mortality are rare and occur in approximately 0.1%–3% of patients.^{6,7} In more than 70% of cases, the disease resolves itself within six months, regardless of the treatment given.⁸ Although childhood ITP usually lasts

for a few weeks and months, it is estimated that 25–30% of children develop chronic situation in the world ($PLT < 100 \times 10^9/l$ and persisted for more than 12 months).^{9–11} One study conducted in Vietnam also found that the proportion of chronic ITP patients among the general ITP was 22.6%.¹²

ITP can cause fatigue, challenges with daily activities, reduced physical functioning, increased anxiety, and depression. In addition to certain risks of the problem such serious bleeding, patients experience both physical and emotional consequences living with their disease on a daily basis.¹³ Despite benign nature of chronic ITP, treatment and health services expenditures are a burden for families, especially for those with low income or no health insurance. For children, they have to undergo some restrictions in physical activities, disruption in education and social activities because of hospitalization and changes in emotion and psychology over the recurrences of illness.^{14–16}

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The World Health Organization defines that QoL as “an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns”.¹⁷ This is a wide concept and is influenced by many different factors such as economic status, accommodation, employment, affection, health,¹⁸ and the level of satisfaction in these areas that people consider the most important in life. When looking insights into the healthcare, people tend to consider the extent of the disease’s impact on patient’s satisfaction in areas of life and since then, scientists have isolated a ‘Health Related Quality of Life’ (HRQoL) concept. This is considered an important indicator of the effectiveness of disease treatment. Based on the definition about health of the World Health Organization, the being interested areas of HRQoL are: physical, mental, social and school functioning. The purpose of the assessment of HRQoL in a patient is to determine the extent of the impact of a disease on the life of patients, but not to evaluate the effectiveness or outcome of treatment.¹⁹

HRQoL is considered a measurement of the health state of an individual and is increasingly becoming an important evaluation tool to evaluate outcome of health improvement interventions and healthcare services.²⁰ In recent years, several researchers have concerned and supported HRQoL assessment for patients with chronic diseases.^{21,22} Regarding chronic ITP, although some studies were conducted to assess the HRQoL among the chronic ITP patients,^{23,24} knowledge on HRQoL among the group is still limited.²⁵ Literature showed that ITP have negative impact on HRQoL of children. The HRQoL of children with ITP and their parents were remarkably lower in comparison with the healthy children.^{26,27}

In Vietnam, research on HRQoL have been paid attention recently,^{28,29} however, HRQoL for chronic ITP patients is still lack of in the country. This study aims to evaluate the HRQoL among Vietnamese children with chronic ITP.

2. Methods

2.1. Patients

This case-control study was done at the Department of Nephrology – Hematology – Endocrinology, Hai Phong Children’s Hospital, Hai Phong city, Vietnam from January 2020 to April 2021. The enrolled patients were known recorded chronic ITP at the Department of Nephrology-Hematology – Endocrinology. The patients or their parents or legal guardians of the patients were interviewed in person by regular visits to pediatric hematology to collect data. Fifty-six patients aged 2–18 years with chronic ITP were selected into this study.

2.2. Inclusion criteria

Children aged from 2 to 18 years old diagnosed chronic ITP were selected into the study. Patients were diagnosed with chronic ITP if they had hemorrhagic symptoms such as spontaneous cutaneous or mucosal bleeding or to severe with internal bleeding and isolated thrombocytopenia (platelet count $<100 \times 10^9/l$ persisted for over 12 months) via complete blood count or peripheral blood smear.

2.3. Exclusion criteria

We excluded from the study: Patients with secondary ITP or symptoms of hepatomegaly, splenomegaly, swollen lymph nodes. Besides, those having disorders relating to physical function or congenital abnormalities (including both children and their parents) were excluded because of difficulties in answering accurately the questionnaire.

2.4. Control group

One hundred and seventy healthy age and sex matched students

selected during school days were invited to participate in this study as the controls. They were confirmed with no disease history including suffering from acute/chronic diseases or hospitalization in the past one month as well as no diagnosis with intellectual/psychological retardation by trained specialists. Schools were randomly selected based on the urban, rural criteria. In each area one pre-primary school, one primary school, one secondary school, and one high school were randomly chosen.

2.5. Data collection

General information of the participants, including age, sex, and residence were gathered. In addition, for the chronic ITP patients, information such as diagnosis age, treatment duration, treatment status and appearance characteristics were also obtained.

The PedsQL 4.0 Generic Core Scales³⁰ were utilized to assess the HRQoL of the study participants. The PedsQL 4.0 Generic Core Scales is a generic questionnaire that measures HRQL by a self-report and/or a parent-proxy report for patients aged from 2 to 18 years.³⁰ Parent proxy-reports and age-specific child self-reports were similar versions, with formulations appropriate to the understanding of the responder. We used the child version (self-report) for 8–12 years old, the teen version (self-report) for children aged 13–18 years. For young children who aged 2–7 years, we collected the parent’s answers since children cannot answer it by themselves.^{30,31}

This scale consists of 23 items, scored to assess the difficulty level of children about 4 essential domains: physical functioning (8 items), emotional (5 items), social (5 items) and school functioning (5 items) in the past one month. The difficulty levels are assessed 0–5 points with frequency of problem: never, rarely, sometimes, often, always, respectively. These raw scores are standardly transformed into scores on a scale from 0 to 100 and calculated following this formula: the mean score is represented by the sum of the items divided by the number of items.^{30,32}

This questionnaire was translated into Vietnamese and validated in the Vietnamese context. The validated questionnaire showed to be reliable and valid to assess HRQoL for children in Vietnam.³³

Researchers were trained carefully about the questionnaire and how to approach the study participants. Pilot data collection was done in both hospital and schools before the actual interviews were performed, making sure the researchers collected the data in the same manner in the two settings. The trained researchers based on the hospital and the schools on the day of interviewing. The participants were explained about the study. After getting the consent form signed, the parents or the patients/students were interviewed in a private room. They were allocated enough time to answer all of the question of the questionnaire.

2.6. Statistical analysis

Data were performed and analyzed by SPSS (Statistical Package for the Social Sciences) program version 26.0. Sociodemographic was presented in number, percentage, mean and standard deviation.

The HRQoL scores in each dimension and the total scores were presented with mean and standard deviation. Chi-square test was used to examine the equivalence between the case, and control group. In addition, One-way ANOVA and independent sample T test were used to compare the means between different groups, and the relationship between HRQoL and some characteristics among the patients. The level of significance for all statistical tests was set at $p < 0.05$.

2.6.1. Ethic

The research protocol was approved by the Institutional Review Board of Hai Phong University of Medicine and Pharmacy (264/QĐ-YDHP dated February 5th, 2021). The study was explained in detail to the participant children and their parents or legal guardians after assuring confidentiality of the data.

3. Results

Table 1 shows the socio-demographic details of study groups. No significant differences in age mean, age groups, gender and residence between the two groups ($p > 0.05$). More than 60% in both groups are male. Almost three quarters of participants in both groups reside in rural areas.

In terms of 56 chronic ITP patients, their diagnosis age was 4.37 ± 2.55 years. Most of them treated from 1 to 5 years (67.9%). There were 43 (76.8%) chronic ITP children were on treatment.

The mean scores of HRQoL were presented in Table 2. The HRQoL scores in five domains of the chronic ITP group were significant lower than that of the controls ($p < 0.001$). In general, the overall score of HRQoL among the patients and the controls were 68.10, and 91.12, respectively, $p < 0.001$. For all groups, school functioning was the domain with lowest scores while the emotional functioning showed to be the highest score of HRQoL.

The HRQoL in the chronic ITP and control groups classified by age groups, gender, and residence were reported in Table 3. For all sub-groups, higher score were found in the control group in comparison to the patient group ($p < 0.001$).

Table 4 illustrates the comparison of the HRQoL scores in all domains of the patient group based on some characteristics. There were significant differences in the scores based on age group, sex, treatment duration, and treatment status. For age groups, older group showed to be having lower overall score ($p = 0.010$). Males had higher scores than that of females in all domains. For the treatment duration, the longer treatment the lower HRQoL score reported ($p < 0.05$ except school functioning domain). Patients stopped treatment showed significant higher HRQoL scores in almost all domains than that of patients who were undergoing treatment.

4. Discussion

To the best of our knowledge, this is the first study that was conducted to measure the HRQoL among chronic ITP children in Vietnam after a comprehensive review. Our research encompasses 56 patients diagnosed with chronic ITP and 170 healthy children matched with age, gender. The study reported that chronic ITP patients had significant lower HRQoL scores compared with that of the healthy children ($p <$

Table 1
Characteristics of the chronic ITP group and control group.

Variables	Chronic ITP group n (%)	Control group n (%)	p
Age (Mean $\pm$ SD)	7.79 $\pm$ 3.63	8.41 $\pm$ 3.86	0.277
Age groups			0.994
2-7	28 (50.0%)	36 (49.9%)	
8-12	22 (39.3%)	67 (39.4%)	
13-18	6 (10.7%)	19 (11.2%)	
Gender			0.987
Males	34 (60.7%)	103 (60.6%)	
Females	22 (39.3%)	67 (39.4%)	
Residence			0.828
Urban	14 (25%)	45 (26.5%)	
Rural	42 (75%)	125 (73.5%)	
Diagnosis age (Mean $\pm$ SD)	4.37 $\pm$ 2.55		
Treatment duration			
<1 year	11 (19.6%)		
1-5 years	38 (67.9%)		
>5 years	7 (12.5%)		
Treatment status			
On treatment	43 (76.8%)		
Stopped	13 (23.2%)		
Appearance characteristics			
Cushing	30 (53.6%)		
Hirsutism	19 (33.9%)		
Acne	5 (8.9%)		

Table 2
The mean scores of health-related quality of life domains for chronic ITP patients and control group.

Variables	Children and adolescents 8-12 years (self-reported)			Children and adolescents 13-18 years (self-reported)			Total		
	Chronic ITP group (n = 22)	Control group (n = 67)	p*	Chronic ITP group (n = 6)	Control group (n = 19)	p*	Chronic ITP group (n = 56)	Control group (n = 170)	p*
	Mean $\pm$ SD	Mean $\pm$ SD		Mean $\pm$ SD	Mean $\pm$ SD		Mean $\pm$ SD	Mean $\pm$ SD	
Physical functioning	67.52 $\pm$ 7.86	92.63 $\pm$ 5.92	<0.001	72.42 $\pm$ 10.85	93.09 $\pm$ 5.76	<0.001	69.13 $\pm$ 10.18	90.55 $\pm$ 5.11	<0.001
Emotional functioning	79.29 $\pm$ 5.04	95.07 $\pm$ 4.80	<0.001	73.40 $\pm$ 8.50	86.31 $\pm$ 6.83	<0.001	74.73 $\pm$ 9.22	94.44 $\pm$ 5.64	<0.001
Social functioning	76.88 $\pm$ 9.69	92.38 $\pm$ 5.92	<0.001	67.27 $\pm$ 10.66	88.94 $\pm$ 5.15	<0.001	71.74 $\pm$ 11.37	92.21 $\pm$ 5.96	<0.001
School functioning	49.69 $\pm$ 8.85	89.47 $\pm$ 6.86	<0.001	56.81 $\pm$ 11.18	84.21 $\pm$ 7.50	<0.001	52.97 $\pm$ 10.14	86.93 $\pm$ 7.86	<0.001
Overall	69.64 $\pm$ 4.82	92.42 $\pm$ 2.68	<0.001	68.13 $\pm$ 7.18	88.78 $\pm$ 3.51	<0.001	68.10 $\pm$ 6.59	91.12 $\pm$ 3.21	<0.001

*: Independent sample T test.

Table 3

Comparison of the overall health-related quality of life score between the chronic ITP group and control groups based on some characteristics.

Parameters	Chronic ITP group Mean $\pm$ SD	Control group Mean $\pm$ SD	p*
Age groups			
2-7	69.64 $\pm$ 4.82	90.61 $\pm$ 3.12	<0.001
8-12	68.13 $\pm$ 7.18	92.42 $\pm$ 2.68	<0.001
13-18	60.86 $\pm$ 7.65	88.78 $\pm$ 3.51	<0.001
Gender			
Males	69.54 $\pm$ 6.01	90.78 $\pm$ 3.06	<0.001
Females	65.89 $\pm$ 6.95	91.65 $\pm$ 3.39	<0.001
Residence			
Urban	69.17 $\pm$ 7.03	91.31 $\pm$ 3.07	<0.001
Rural	67.75 $\pm$ 6.48	91.05 $\pm$ 3.28	<0.001

*: Independent sample T test or One-way ANOVA.

0.05). The research also found that chronic ITP patients having certain characteristics, including older age, longer duration of treatment, and undergoing treatment, had lower HRQoL scores than their counterparts.

In present study, the HRQoL of chronic ITP patients was significantly lower than that of healthy children for all domains, regardless of age, gender or residence characteristics. This result was in line with previous studies,^{27,34} but contrary with a study conducted in Dutch population which found no significant difference in HRQoL between newly diagnosed ITP patients and the reference group,¹⁶ both using the PedsQL questionnaires. The latter difference could be explained by the tools using to assess the HRQoL of that study and the current one.

Parental assessment may relate to the fear of bleeding and injury, as well as the uncertainty about their children's future. Meanwhile, for the patients who are teenagers and adolescents with a certain understanding of their conditions, their priorities might relate to the fear of interacting with people's surroundings, especially their peers. Study in China also showed that parents are much more concern with the disease than their children, resulting seriously influence their HRQoL.²⁷

Results from the current study also demonstrates significant differences between the HRQoL scores and some demographic and clinical characteristics. Children aged 13–18 years had lowest HRQoL overall and specifically in emotional and social functioning, while children in

the age group 2–7 years had impaired HRQoL in school functioning. As mentioned above, these findings could be interpreted by the different priorities related to the age group of children and parents. In terms of clinical characteristics, the patients being on treatment or having been treated for more than 5 years had lower HRQoL scores than those who stopped treatment or had treatment duration less than 5 years. This was predictable since previous studies revealed that children with persistent ITP had worse HRQoL.^{27,35} The reason for this could be attributed to the burden of prolonged treatment that the parents have to endure and leads to restriction of their child's daily activities, which might reduce the child's HRQoL. Besides, the long-term treatment with corticoids could also worsen HRQoL in children.³⁶ However, some studies found improvements in HRQoL of children with chronic ITP versus newly diagnosed patients, suggesting other possible aspects that could influence the HRQoL in addition to the time of treatment course. For the relationship between the HRQoL scores and gender, we found the worse overall HRQoL in females. Although HRQoL tends to decrease in females, the selection bias in assessing the HRQoL scores should also be taken into consideration. Parents' perception and/or the process of expressing emotions or socializing with their peers might be influenced by gender factor rather than the real ability of the children.

Given the negative impact of the problem on children, intervention program emphasizing spiritual growth, physical activity, and communications are necessary for children with chronic ITP. Additionally, different health issues such as pain, anxiety, fatigue have been reported by chronic ITP children.¹³ Those issues may have affect on quality of life among those patients. Future studies need to be conducted to measure the effect of those aspects on patients living with chronic ITP.

Some limitations of the current study need to be consideration. First, a relatively small sample size did not allow us to analyze clinically relevant subgroups such as acute ITP. In addition, the case of the present study was only selected in one hospital a city in the North of Vietnam. Second, although PedsQL 4.0 is an international tool to measure HRQL, it evaluates the HRQoL for children with general health, not particular ITP. Taking into account these limitations, it would be interesting to study the quality of life of the ITP patients with a larger cohort with different tools will be applied.

Table 4

Comparison between different health-related quality of life scores regarding demographic and clinical characteristics in the chronic ITP group.

Parameters	Physical functioning		Emotional functioning		Social functioning		School functioning		Overall	
	Mean $\pm$ SD	p*	Mean $\pm$ SD	p*	Mean $\pm$ SD	p*	Mean $\pm$ SD	p*	Mean $\pm$ SD	p*
Age groups										
2-7	67.52 $\pm$ 7.86	0.122	79.28 $\pm$ 5.03	<0.001	76.87 $\pm$ 9.68	0.002	49.68 $\pm$ 8.85	0.042	69.63 $\pm$ 4.82	0.010
8-12	72.42 $\pm$ 10.85		73.41 $\pm$ 8.51		67.27 $\pm$ 10.66		56.82 $\pm$ 11.19		68.13 $\pm$ 7.19	
13-18	64.58 $\pm$ 15		58.33 $\pm$ 6.83		64.17 $\pm$ 11.58		54.17 $\pm$ 7.36		60.87 $\pm$ 7.66	
Sex										
Males	70.79 $\pm$ 10.69	0.132	75.44 $\pm$ 8.91	0.479	73.46 $\pm$ 9.96	0.163	54.41 $\pm$ 10.03	0.188	69.54 $\pm$ 6.01	0.041
Females	66.58 $\pm$ 9.52		73.64 $\pm$ 9.78		69.09 $\pm$ 13.06		50.74 $\pm$ 10.12		65.89 $\pm$ 6.95	
Residence										
Urban	69.48 $\pm$ 10.83	0.883	73.57 $\pm$ 7.70	0.591	74.82 $\pm$ 10.58	0.245	56.43 $\pm$ 10.46	0.142	69.18 $\pm$ 7.03	0.487
Rural	69.01 $\pm$ 10.09		75.12 $\pm$ 9.72		70.71 $\pm$ 11.56		51.82 $\pm$ 9.88		67.75 $\pm$ 6.48	
Treatment duration										
<1 year	67.45 $\pm$ 8.19	0.047	79.09 $\pm$ 5.39	<0.001	81.36 $\pm$ 7.01	<0.001	50.27 $\pm$ 11.71	0.623	70.74 $\pm$ 4.94	<0.001
1–5 years	71.09 $\pm$ 9.56		76.05 $\pm$ 8.07		70.86 $\pm$ 10.30		53.64 $\pm$ 9.99		68.93 $\pm$ 5.51	
>5 years	61.16 $\pm$ 13.12		60.71 $\pm$ 7.32		61.43 $\pm$ 12.15		53.57 $\pm$ 9.0		59.47 $\pm$ 8.08	
Treatment status										
On treatment	67.71 $\pm$ 9.95	0.057	73.95 $\pm$ 9.17	0.254	70.29 $\pm$ 11.13	0.082	51.67 $\pm$ 10.82	0.021	66.84 $\pm$ 6.3	0.008
Stopped	73.83 $\pm$ 9.89		77.31 $\pm$ 9.27		76.54 $\pm$ 11.25		57.28 $\pm$ 5.92		72.29 $\pm$ 5.92	
Appearance characteristics										
Having Cushing	68.11 $\pm$ 10.49	0.425	74.50 $\pm$ 11.01	0.837	69.25 $\pm$ 12.13	0.078	52.26 $\pm$ 10.81	0.581	66.73 $\pm$ 7.6	0.094
No Cushing	70.31 $\pm$ 9.94		75 $\pm$ 6.78		74.62 $\pm$ 9.89		53.78 $\pm$ 9.45		69.69 $\pm$ 4.83	
Having Hirsutism	71.52 $\pm$ 11.21	0.212	71.84 $\pm$ 11.33	0.142	67.37 $\pm$ 11.59	0.038	53.51 $\pm$ 11.45	0.778	66.89 $\pm$ 8.36	0.325
No Hirsutism	67.91 $\pm$ 9.57		76.22 $\pm$ 7.67		73.99 $\pm$ 10.73		52.69 $\pm$ 9.55		68.73 $\pm$ 5.47	
Having Ance	70.0 $\pm$ 17.48	0.91	61.0 $\pm$ 6.52	<0.001	69.0 $\pm$ 6.52	0.577	57.0 $\pm$ 6.71	0.356	65.0 $\pm$ 6.85	0.272
No Acne	69.05 $\pm$ 9.48		76.08 $\pm$ 8.33		72.0 $\pm$ 11.75		52.57 $\pm$ 10.37		68.41 $\pm$ 6.54	

*: Independent sample T test or One-way ANOVA.

5. Conclusion

Chronic ITP has a negative impact on HRQoL in terms of physical functioning, emotional, social, school functioning, and overall scores when compared with the healthy sex, age-matched children. Patients with older age, longer treatment duration, and ongoing treatment status showed to be having lower HRQoL scores than the younger one, shorter treatment duration, and the stopped treatment group.

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Declaration of competing interest

No conflict of interest is declared.

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