Annals of Pharmacy Practice and Pharmacotherapy
ISSN: 3062-4436
2024, Volume 4, Page No: 8-16

Available online at: www.galaxypub.co/page/journals

Galaxy Publication

Exploring Treatment Adherence and Quality of Life Among Patients with Transfusion-Dependent Thalassemia

Lee Wan Jin[1], Nurul Ain Mohd Tahir[1*], Farida Islahudin[1], Li Shu Chuen[2]

[1]Faculty of Pharmacy, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, 50300 Kuala Lumpur, Malaysia.
[2] School of Biomedical Sciences and Pharmacy, University of Newcastle, Callaghan, New South Wales, Australia.

***E-mail** ✉ nurulain1331@gmail.com
Received: 06 December 2023; **Revised:** 28 February 2024; **Accepted:** 06 March 2024

ABSTRACT

In patients with transfusion-dependent thalassemia (TDT), adherence to iron chelation therapy (ICT) is essential for avoiding iron excess consequences and preserving HRQoL. The present research sought to assess the relationship between adherence and HRQoL in TDT patients from Malaysia. A cross-sectional study was conducted among TDT patients aged 18 years and above at Hospital Ampang, Selangor. The adherence and the HRQoL (SF-36) were measured utilizing validated tools. Correlation analyses were performed to ascertain whether adherence to ICT and HRQoL was associated. 162 individuals were included in the trial, and 46.91% (n= 76) of the subjects reported being adherent. TDT patients had a mean SF-36 score of 74.58. The SF-36 questionnaire showed that adherent patients had significantly higher HRQoL (mean SF-36 score of 79.21) than non-adherent patients (mean SF-36 score of 69.47) (P= 0.00). In addition, the results showed that the patient's HRQoL was positively and significantly correlated with the following factors: age (P= 0.050), employment (P= 0.003), and being female (P= 0.032). Adult TDT patients have a subpar ICT adherence rate, and their HRQoL has been severely impacted by non-adherence. The TDT population may have improved HRQoL results if the rate of ICT adherence is increased by interventions such as patient counseling and support programs.

Keywords: Transfusion-dependent thalassemia (TDT), Iron chelation therapy (ICT), Health-related quality of life (HRQoL), Short form 36 (SF-36), Adherence

How to Cite This Article: Wan Jin L, Mohd Tahir NAM, Islahudin F, Shu Chuen L. Exploring Treatment Adherence and Quality of Life Among Patients with Transfusion-Dependent Thalassemia. Ann Pharm Pract Pharmacother. 2024;4:8-16. https://doi.org/10.51847/B8R85qakUv

Introduction

Iron chelation treatment (ICT) adherence is a critical predictor of efficient iron overload control for transfusion-dependent thalassemia (TDT) patients, and it requires much more clinical attention [1]. In clinical practice, medication adherence refers to the level of compliance with the healthcare provider's treatment suggestion involving frequency, dose, and schedule [2]. To help patients with their medication difficulties, healthcare practitioners should frequently evaluate their medication adherence. Nonadherence to medications can be caused by a variety of circumstances [3, 4]. By doing this, doctors won't underestimate the therapeutic effects and end up changing the treatment plan unnecessarily [5]. Furthermore, there are several health advantages linked to high ICT adherence in TDT patients, including decreased iron buildup and a decreased risk of iron overload consequences, including endocrinologic, hepatic, and cardiac morbidities [6–10].

Patients' lives are negatively impacted, and their health-related quality of life (HRQoL) is much lower as a result of the advancement of thalassemia illness, the danger of iron-related problems, frequent hospitalization, and the high expense of medical care. As a result, HRQoL should be regularly assessed as a crucial and supplementary measure of successful therapy for individuals with thalassemia. Based on the Centers for Disease Control and Prevention (CDC), the term "HRQoL" refers to a comprehensive assessment of how illness and therapy influence

a patient's impression of general performance and health. It has been noted that thalassemia patients suffer from psychological and social behavior issues, including low self-esteem, stress, depressive signs, anxiety, poor social skills, and low academic achievement [11]. A meta-analysis of 26 studies comprising up to 687 individuals worldwide further supported this, demonstrating that beta-thalassemia illness significantly reduced the patients' HRQoL, particularly in terms of social functioning and overall physical health [12]. The social, emotional, and physical states of nonadherent patients were negatively impacted by this drop in HRQoL [13].

Many studies have been carried out globally to evaluate HRQoL in beta-thalassemia patients using the SF-36, but not much is understood about the connection between HRQoL and chelation adherence [12]. Healthcare professionals would be able to optimize treatment and customize therapies to meet the requirements of thalassemia patients if more thorough research were done to better understand the impact of chelation adherence on patients' HRQoL. Therefore, this study's main goal was to assess HRQoL, ICT adherence, and their relationships with TDT patients in Malaysia. This study will offer clinical proof of the importance of adherence in thalassemia therapy by comparing HRQoL between adherent and nonadherent groups. Additionally, it would include suggestions for developing comprehensive plans for the highest caliber of patient care.

Materials and Methods

Study Design

This was a cross-sectional, questionnaire-based study performed at Hospital Ampang, Selangor, which serves as the main hematology center in Malaysia. Convenient sampling was used for data collection from 1st August 2021 to 30th December 2021, with informed consent obtained from all eligible individuals before engaging in any study-related activity. To reduce selection bias, the researchers were blinded to the patient's clinical features, such as type of ICT, serum ferritin level, and iron overload status, at the time of questionnaire administration.

Inclusion and Exclusion Criteria

Patients aged 18 years and older with a diagnosis of transfusion-dependent thalassemia (TDT), treated with at least one iron chelation therapy (ICT), and able to speak, read, and understand Malay and English were recruited for the study. Patients with comorbidities of sickle cell disease (SCD), myelodysplastic syndrome (MDS), and other hematologic diseases were excluded. Besides, the patient who had just begun their follow-up in Hospital Ampang or had incomplete clinical data during the study period was excluded.

Sample Size Estimation

The sample size in this study was calculated by using a single proportion formula through the Raosoft© calculator [14]. With an absolute precision set at 0.05, a confidence level of 95%, and a Malaysian TDT population of 4529. The proportion of nonadherence to iron chelation therapy of 0.086 was used based on the study by Lam *et al*. [15]. The calculated sample size was 118, and accounting for 10% of non-respondents, a minimal sample size of 135 was required.

Data Collection

Eligible TDT patients were approached and invited to participate in this study. A detailed explanation of the study's objectives and procedures was given to the patients, and written consent was obtained before the study. The questionnaires were available in English and Malay and consisted of three sections: Section 1 involved demographic information including race, gender, body weight, marital status, employment status, age of thalassemia diagnosis, and types of ICT. The researchers also collected the relevant clinical data of the baseline serum ferritin levels during the data collection period retrospectively using the electronic health informatics system (eHIS), the institution's electronic medical records.

Section 2 of the questionnaires involved measuring the adherence rate among the participants using the Malaysia Medication Adherence Assessment Tool (MyMAAT) [4]. It is made up of 21 questions under preliminary constructs of patients' attitudes towards taking medication, their perception of the medicine's utility in terms of benefits, cost, efficacy, barriers, severity, and susceptibility to disease, patients' sociocognitive theory, and others. Each question was scored from one to five. The patient's adherence status was then classified using the cut-off point of 54; for instance, scores 12-53 indicated non-adherence, while scores 54-60 indicated adherence. Meanwhile, section 3 included a questionnaire to measure patients' health-related quality of life (HRQoL) using

the SF 36 health survey tool [16, 17]. The tool evaluated the domains of physical function (PF), role limitations caused by physical unwellness (RP), role limitations due to emotional problems (RE), vitality (VT), mental health (MH), social function (SF), bodily pain (BP) and general health (GH). Each domain has a score between 0 and 100, with higher scores denoting better well-being and health.

Statistical Analysis

All data analyses were conducted using SPSS (Statistical Package for the Social Sciences) version 21.0. Descriptive statistics were applied to analyze patients' demographic data, clinical data, adherence, and mean SF-36 scores. Continuous data were presented in mean and standard deviation, while categorical data were presented in frequency and percentage. The Kolmogorov-Smirnov test was then performed to determine the normality of the data. The outcome variables were twofold: patient's adherence status (nominal variable) and mean SF-36 score, which served as a measure of the patient's health-related quality of life (HRQoL) (scale variable). As the data was found skewed, the correlation between patient adherence and serum ferritin levels was identified by using the Mann-Whitney test with a significance value of $P < 0.05$. The correlation of adherence and types of ICT, monotherapy, or combination of ICT was determined using a chi-square test. Only the potential factors with P-values < 0.05 were reported to have a significant association with patient adherence. Besides that, Mann-Whitney and Kruskal-Wallis tests are used to determine to association between patients' HRQoL and potential factors such as adherence, gender, ethnicity, marital status, working status, age, monotherapy, or combination of ICT, and injectable or non-injectable ICT using a significant P-value < 0.05. To further investigate the differences between age categories and HRQoL, a post hoc analysis of the Kruskal-Wallis test was performed to determine the pairwise comparisons

Results and Discussion

In all, 209 sets of surveys were sent out and filled out. Nevertheless, only 162 cases met the requirements; 31 patients were left out because their clinical information was insufficient, 10 patients were duplicated, 4 patients had non-transfusion dependent thalassemia, one patient did not follow up at the designated hospital, and one patient's data could not be located in eHIS.

Demographic and Clinical Characteristics

A summary of the recruited individuals' clinical and demographic characteristics was provided, along with a breakdown of their adherent and nonadherent group classifications. **Table 1**. Malay participants made up the majority (n = 115, 70.99%), followed by Chinese participants (n= 43, 26.54%). Women made up around two-thirds of the subjects (n = 107, 66.05%). The mean age of the study's participants was 32.88 years (SD = 10.45), with a range of 18 to 72 years. They were mostly employed (n= 112, 69.14%), and over half (n = 87, 53.7%) were unmarried. The blood ferritin levels of the adherent individuals were considerably lower ($U = 1774$, $P < 0.001$).

Table 1. The clinical and demographic characteristics of individuals with transfusion-dependent thalassemia based on their adherence status.

Demographic characteristics	**Total number of participants (n = 162), (n (%))**	**Adherent patients (n = 76) (n (%))**	**Non-adherent patients (n = 86) (n (%))**
Age (year), mean (SD)	32.88 (10.45)	35.12 (11.80)	30.91 (8.69)
Age category			
Young adult (18-25 years)	46 (28.40%)	18 (23.68%)	28 (32.56%)
Adult (26-44 years)	91 (56.17%)	41 (53.95%)	50 (58.14%)
Middle age (45-59 years)	22 (13.58%)	14 (18.42%)	8 (9.30%)
Old age (≥ 60 years)	3 (1.85%)	3 (3.95%)	-
Race			
Malay	115 (70.99%)	49 (64.47%)	66 (76.74%)
Chinese	43 (26.54%)	26 (34.21%)	17 (19.77%)
Indian	1 (0.62%)	0 (0%)	1 (1.16%)
Others	3 (1.85%)	1(1.32%)	2 (2.33%)
Gender			

Female	107 (66.05%)	50 (65.79%)	57 (66.28%)
Male	55 (33.95%)	26 (34.21%)	29 (33.72%)
Marital Status			
Married	73 (45.06%)	36 (47.37%)	37 (43.02%)
Single	87 (53.70%)	39 (51.32%)	48 (55.81%)
Divorced	2 (1.24%)	1 (1.31%)	1 (1.17%)
Employed	112 (69.14%)	57 (75%)	55 (63.95%)
Not employed	50 (30.86%)	19 (25%)	39 (45.35%)
Type of Thalassemia			
Beta-thalassemia major	57 (35.19%)	30 (39.47%)	27 (31.40%)
Haemoglobin E beta thalassemia	79 (48.77%)	31 (40.79%)	48 (55.81%)
Haemoglobin H disease	15 (9.25%)	10 (13.16%)	5 (5.81%)
Beta-thalassemia intermediate	10 (6.17%)	5 (6.58%)	5 (5.81%)
Others	1 (0.62%)	0 (0%)	1 (1.17%)
Mean Body weight (kg) (SD)	51.81 (7.59)	53.22 (7.63)	50.56 (7.38)
Average serum ferritin (ng/mL) (SD)	3111.22 (2857.53)	2103.15 (1973.63)	4002.07 (3212.15)

Adherence to Iron Chelation Therapy (ICT)

The overall iron chelation therapy (ICT) adherence rate was 46.91%. A significant correlation between ICT type and adherence was discovered by an independent chi-square test ($X2(4)=7.69$, $P=0.048$). Patients on combination therapy (n = 82) adhered at a rate of 41.67%, whereas patients on monotherapy (n= 78) adhered at a rate of 52.56% (**Table 2**). This difference was not statistically significant ($X2(1)=1.93$, $P=0.165$). With $X2(2)=3.59$, $P=0.166$, patients who were administered injectable ICT had lower adherence rates (36.36%) than those who received oral ICTs (55.22%) and injectable and oral ICT (41.67%).

Table 2. The number and proportion (%) of patients adherent to iron chelation therapy (ICT) by treatment type

ICT	Total participants (n)	Adherent Patients (n (%))	Nonadherent patients (n (%))
Total (N)	162	76 (46.91%)	86 (53.10%)
Monotherapy	78	41 (52.56%)	37 (47.44%)
DFO	11	4 (36.36%)	7 (63.64%)
DFP	62	32 (51.61%)	30 (48.39%)
DFX	5	5 (100%)	0
Combination	84	35 (41.67%)	49 (58.33%)
DFO & DFP	82	34 (41.46%)	48 (58.54%)
DFO & DFX	2	1 (50%)	1 (50%)
Injectable ICT	11	4 (36.36%)	7 (63.64%)
Combination of injectable and oral ICT	84	35 (41.67%)	49 (58.33%)
Non-injectable ICT	67	37 (55.22%)	30 (44.78%)

ICT: iron chelation therapy; DFO: desferrioxamine; DFP: deferiprone; DFX: deferasirox

Health-related Quality of Life (HRQoL)

Both the adherent and nonadherent groups' scores for the eight domains and the overall SF-36 score were computed and compared (**Figure 1**). Overall, TDT patients scored 74.58 on the SF-36 on average, with general health (GH) scoring 60.71 and physical functioning (PF) ranking 84.57. All indicators of HRQoL, except for bodily pain (BP) and social function (SF), were significantly greater for the adherent patient than for the nonadherent patient (**Figure 1**). The adherent group's average SF-36 score was 79.21, with dimensions that ranged from 66.47 for general health (GH) to 87.04 for physical functioning (PF). The nonadherent group's average score on the SF-36 was 69.47, with the role limitations due to physical health (RP) and physical functional (PF) categories scoring the lowest at 54.94 and the highest at 81.40, respectively.

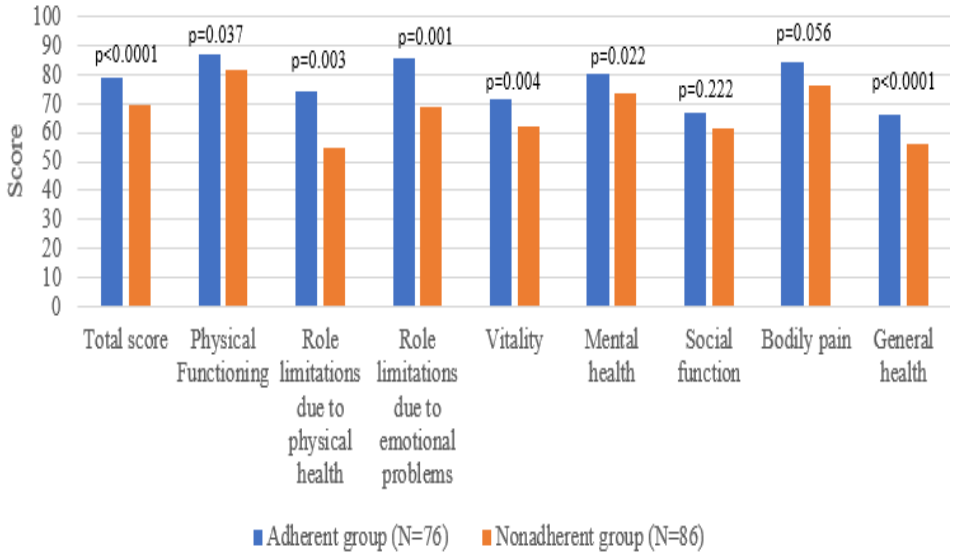

Figure 1. The 36-item short form survey results and their domains between transfusion-dependent thalassemia (TDT) patients' adherent and nonadherent groups, together with the P-value (Mann-Whitney U test)

When it came to HRQoL-related characteristics, the results showed that age, gender, working position, and patients' use of ICT were all significant determinants of HRQoL (P=0.032, P=0.003, and P=0.000, respectively). Patients with weaker ICT adherence, those without jobs, and women all showed much lower HRQoL. Young adults (aged 18–25 years) and adults (aged 26–44 years) showed notably higher HRQoL scores than those in the older age group (aged ≥ 60years) with P = 0.026 and P = 0.016, respectively, according to the post hoc analysis of the Kruskal-Wallis test evaluating the pairwise comparisons of age categories on HRQoL.

This study thoroughly investigated the relationship between ICT adherence and the HRQoL of individuals with transfusion-dependent thalassemia (TDT). To get an in-depth insight, two primary areas were examined in the present investigation: First, it assessed the ICT adherence rate among Malaysian adult TDT patients in particular. Second, it looked at how patients' HRQoL was affected by their ICT adherence. This methodology guaranteed a comprehensive analysis of how adherence affects TDT patients' health outcomes. The study found that adult TDT patients in Malaysia had a significant percentage of nonadherence to ICT of 53.09%, indicating a critical issue that needs particular attention.

The Short Form-36 Health Survey (SF-36) has been used in beta-thalassemia patients [12], which supports its applicability for assessing HRQoL in the TDT population and enables cross-national comparison. To the best of our knowledge, only a small number of studies have been conducted globally to evaluate the effect of adherence on TDT patients' HRQoL. This cross-sectional study's findings also demonstrated a connection between HRQoL and ICT adherence. Interestingly, patients with worse adherence reported worse HRQoL.

The current study's ICT adherence rate, as determined by MyMAAT, was in line with values reported globally, which varied from 20.93% to 75.3% [7, 8, 18, 19]. Significant variables contributing to the variation in reported adherence rates include the discussion and argument surrounding the definition of adherence and the best ways to measure it [20]. Numerous earlier studies have found that oral chelators, such as DFP and DFX, have a higher adherence rate than injectable DFO. With adherence rates ranging from 87.2 to 100%, the rates for oral chelators were higher [8, 21, 22]. The range of chelators compared to injectables was 48.84 to 85.1%. [10, 23–29]. This disparity in adherence indicates that the adherence rate is influenced by factors such as discomfort, annoyance, and adverse effects, particularly those related to parenteral administrations [30]. The findings of this study showed that patient adherence rates were statistically significantly impacted by the types of ICT. Interestingly, though, our study did not find that oral ICT was substantially better than injectable ICT or a combination of injectable and oral ICT in terms of adherence, even though oral ICT had a higher adherence rate.

The findings of the research demonstrated a strong favorable relationship between adherence and HRQoL, were consistent with a prior study conducted in Malaysia that found that TDT patients who were taking an optimal dosage of DFO (which indirectly indicated higher adherence) had better QoL scores than those who were taking a suboptimal dosage [31]. Moreover, the research by Haghpanah *et al.* [25] revealed that patients with ICT

adherence showed a markedly better HRQoL than those with inadequate ICT adherence. Interestingly, adherent patients had a far greater percentage than poor adherent individuals. It is clear from the similarities between these studies that ICT adherence is critical to improving TDT patients' HRQoL. Positive attitudes and perceptions of patients with better medication adherence may result in better management of disease-related problems [25], which may explain their higher HRQoL in the present investigation, particularly improved physical function, decreased role limitation because of physical function, raised vitality, and improved general health. Additionally, committed patients who receive better TDT management feel calmer and less nervous, which eventually improves their mental health and lessens the challenges that emotional discomfort causes them to face in their daily responsibilities. The social function of HRQoL and physical pain did not, however, change significantly between adherent and nonadherent individuals, according to our study. This outcome may be explained by the fact that thalassemia patients frequently endure persistent pain, weariness, and discomfort as a result of their underlying anemia and frequent blood transfusions. Some patients may develop asthenia and body weakness as a result of iron accumulation from repeated blood transfusions, often accompanied by joint and abdominal pain [32]. The physical discomfort and exhaustion they experience may deplete their energy and impair their social engagement. Our study also found substantial differences in HRQoL between age groups, even though age is frequently regarded as a key determinant of HRQoL [25, 33]. Adults and young adults often have better physical health and vigor than older persons. People are increasingly vulnerable to chronic illnesses and other health problems as they become older, which might have a detrimental impact on their HRQoL. A reduction in physical performance and HRQoL may also follow from the social isolation that older persons may face due to retirement, the loss of friends and family, and limited mobility [34]. These would explain the impact of nonadherence as well as the decreased HRQoL. It is widely acknowledged that poorer HRQoL ratings are influenced by female gender [33, 35]. In our study, TDT women had a considerably poorer HRQoL than males with TDT, encompassing characteristics of physical health, role constraints due to physical function, social activity, and bodily discomfort. Women may misrepresent their poor health condition in health self-reports, although studies have revealed that females suffer from psychiatric problems at a higher incidence than males in the population at large [36]. In addition, females are more prone to having low HRQoL due to their many duties, such as taking care of the home and children [37]. Additionally, the present investigation discovered that patients with thalassemia had significantly higher HRQoL. This conclusion is consistent with previous research demonstrating that occupational status had a favorable influence on HRQoL in individuals with diverse illnesses [38, 39]. Financial security can significantly reduce worry and tension associated with financial obligations, hence improving general well-being [40]. Overall, these three characteristics would have contributed to the influence of adherence to HRQoL in varying degrees.

The research's weaknesses have been noted. Initially, it was a single facility in Malaysia that carried out small-scale research. Generally speaking, single-center research lacks the external validity and scientific rigor required to justify broad practice changes. Nevertheless, this is somewhat mitigated by Ampang Hospital's standing as a significant hematology center in Malaysia, which allows it to specialize in TDT and access a sizable patient cohort. Second, patients' self-reporting was used to evaluate the HRQoL and adherence data. Inadequately, patients may overstate or underestimate the intensity of their signs. Additionally, during data collection, patients may suffer from recollection bias. Nevertheless, these are inherent issues that are hard to resolve in this kind of research. Due to expensive procedures, it was also challenging to get other clinical measures that might have been utilized to more accurately assess the severity of the iron overload, including the MRI T2* for the liver and heart. It was not feasible to compare the iron burden in the heart and liver throughout the data-collecting phase because not all patients had access to or multiple readings of MRI T2* for the heart and liver.

Several recommendations for enhancing adherence might be put into practice in the future, considering the low ICT adherence rate among TDT patients in Malaysia. Conventional thalassemia education concentrates on disseminating information about the condition, treatment, and DFO administration methods. Nevertheless, because of the medical, financial, and psychological strain, healthcare providers frequently overlook the mental and emotional well-being of TDT patients. The many numbers for blood transfusions, doctor follow-up, DFO administration, and oral iron chelators cause patients' opinions of adherence to change over time. This emphasizes how crucial it is to use practical self-management strategies, as suggested by the World Health Organization, to empower individuals with long-term conditions to take charge of their emotional and physical well-being [41]. Prior research [1] also demonstrated the importance of role models in patient groups. In this context, it might be beneficial to create a customized multidisciplinary adherence program that includes health coaching activities.

Additionally, establishing a positive rapport between a patient with thalassemia and a healthcare provider is essential to promoting the patient's use of ICT for the best possible therapy results [1, 42]. The connection between a patient and a healthcare provider is typically characterized as a fiduciary one, and a positive connection between a patient and a healthcare provider keeps patients motivated and helps them overcome the obstacles of ICT adherence and persistence, ultimately improving their well-being. Healthcare providers, including doctors, pharmacists, and nurses, should constantly assess their procedures to avoid patronizing behavior that would hinder rapport-building and incorporate deliberate efforts to strengthen their relationship.

Conclusion

In summary, our research showed that TDT patients in Malaysia had less than ideal ICT adherence. Additionally, it has been demonstrated that noncompliance with ICT dramatically lowers the entire HRQoL of TDT patients, except for social function and physical discomfort. Additionally, it was discovered that the patient's HRQoL was greatly impacted by variables including age, gender, and employment status. Consequently, it is essential to give ICT adherence top priority since it immediately enhances the health and quality of life of people with TDT. To increase adherence, healthcare providers should create individualized treatment plans that take into account each patient's particular needs and circumstances.

Acknowledgments: None

Conflict of Interest: None

Financial Support: The Fundamental Research Grants Scheme [FRGS/1/2020/SS02/UKM/02/5], which is sponsored by the Malaysian Ministry of Higher Education (MOHE), provides some of the money for this study, while the remainder is supplied by the University Kebangsaan Malaysia through the Geran Universiti Penyelidikan (GUP-2020-003).

Ethics Statement: Both the National University of Malaysia's Research Ethics Committee (UKM PPI/111/8/JEP-2022-231) and the Ministry of Health Malaysia's Medical Research Ethics Committee (NMRR-20-2814-57565) have approved the research.

References

1. Chong CC, Redzuan AM, Sathar J, Makmor-Bakry M. Patient Perspective on Iron Chelation Therapy: Barriers and Facilitators of Medication Adherence. J Patient Exp. 2021;8:2374373521996958.
2. Cramer JA, Roy A, Burrell A, Fairchild CJ, Fuldeore MJ, Ollendorf DA, et al. Medication compliance and persistence: terminology and definitions. Value Health. 2008;11(1):44-7.
3. Vrijens B, De Geest S, Hughes DA, Przemyslaw K, Demonceau J, Ruppar T, et al. A new taxonomy for describing and defining adherence to medications. Br J Clin Pharmacol. 2012;73(5):691-705.
4. Hatah E, Rahim N, Makmor-Bakry M, Mohamed Shah N, Ahmad M, Haron N, et al. Development and validation of Malaysia Medication Adherence Assessment Tool (MyMAAT) for diabetic patients. PLoS ONE. 2020;15(11):e0241909.
5. Nguyen TM, La Caze A, Cottrell N. What are validated self-report adherence scales really measuring? A systematic review. Br J Clin Pharmacol. 2014;77(3):427-45.
6. Mokhtar GM, Gadallah M, El Sherif NH, Ali HT. Morbidities and Mortality in Transfusion-Dependent Beta-Thalassemia Patients (Single-Center Experience). Pediatr Hematol Oncol. 2013;30(2):93-103.
7. Chai ASC, Draman N, Mohd Yusoff SS, Azman NF, Zulkifli MM, Yaacob NM, et al. Non-Compliance to Iron Chelation Therapy in Patients with Transfusion-Dependent Thalassaemia. Pediatr Hematol Oncol J. 2021;6(4):207-15.
8. Sukhmani S, Shruti K, Priyanka D, Namita B, Praveen S. Adherence to Iron Chelation Therapy and Its Determinants. Int J Hematol-Oncol Stem Cell Res. 2021;15(1):27.
9. Mahmoud RA, Khodeary A, Farhan MS. Detection of Endocrine Disorders in Young Children with Multi-Transfused Thalassemia Major. Ital J Pediatr. 2021;47(1):165.

10. Yassouf MY, Alquobaili F, Kabalan Y, Mukhalalaty Y. Compliance with Deferoxamine Therapy and Thyroid Dysfunction of Patients with beta-Thalassemia Major in Syria. Hemoglobin. 2019;43(3):218-21.
11. Pattanashetti M, Mugali J, Pattanashetty N, Patil S. A Study of Severity of Depression in Thalassemia Patients. Int J Indian Psychol. 2017;4(2):e05.
12. Arian M, Mirmohammadkhani M, Ghorbani R, Soleimani M. Health-Related Quality of Life (HRQoL) in Beta-Thalassemia Major (beta-TM) Patients assessed by 36-Item Short Form Health Survey (SF-36): a Meta-Analysis. Qual Life Res. 2019;28(2):321-34.
13. Martin LR, Williams SL, Haskard KB, DiMatteo MR. The Challenge of Patient Adherence. Ther Clin Risk Manag. 2005;1(3):189-99.
14. Raosoft. Sample Size Calculator. 2004. Available from: http://www.raosoft.com/samplesize.html.
15. Lam JCM, Lee SY, Koh PL, Fong SZ, Abdul-Kadir NI, Lim CY, et al. Clinical and Health-Related Quality of Life Outcomes of Transfusion-Dependent Thalassaemia Patients in Singapore. Blood Cells Mol Dis. 2021;88:102547.
16. RAND. Medical outcomes study: 36-item short form survey scoring instructions. 2009. Available from: http://www.rand.org/health/surveys_tools/mos/mos_core_36item_scoring.html.
17. Musa AF, Yasin MSM, Smith J, Yakub MA, Nordin RB. The Malay version of SF-36 health survey instrument: testing data quality, scaling assumptions, reliability and validity in post-coronary artery bypass grafting (CABG) surgery patients at the National Heart Institute (Institut Jantung Negara-IJN), Kuala Lumpur. Health Qual Life Outcomes. 2021;19(1):50.
18. Bazi A, Sargazi-Aval O, Safa A. Health-related Quality of Life and Associated Factors Among Thalassemia Major Patients, Southeast of Iran. J Pediatr Hematol/Oncol. 2017;39(7):513-7.
19. Theppornpitak K, Trakarnsanga B, Lauhasurayotin S, Poparn H, Chiengthong K, Sosothikul D, et al. A Study to Assess and Improve Adherence to Iron Chelation Therapy in Transfusion-Dependent Thalassemia Patients. Hemoglobin. 2021;45(3):171-4.
20. Reddy PS, Locke M, Badawy SM. A Systematic Review of Adherence to Iron Chelation Therapy among Children and Adolescents with Thalassemia. Ann Med. 2022;54(1):326-42.
21. Haghpanah S, Zarei T, Zahedi Z, Karimi M. Compliance and Satisfaction with Deferasirox (Exjade®) Compared with Deferoxamine in Patients with Transfusion-Dependent Beta-Thalassemia. Hematology. 2014;19(4):187-91.
22. Elalfy MS, Adly AM, Wali Y, Tony S, Samir A, Elhenawy YI. Efficacy and Safety of a Novel Combination of Two Oral Chelators Deferasirox/Deferiprone over Deferoxamine/Deferiprone in Severely Iron Overloaded Young Beta Thalassemia Major Patients. Eur J Haematol. 2015;95(5):411-20.
23. Al-Refaie FN, Wicken DG. Serum Non-transferrin-bound Iron in Beta-Thalassaemia Major Patients Treated with Desferrioxamine and L1. Br J Haematol. 1992(82):431-6.
24. Arboretti R, Tognoni G, Alberti D, Italian Colaborative Group on T. Pharmacosurveillance and Quality of Care of Thalassaemic Patients. Eur J Clin Pharmacol. 2001;56(12):915-22.
25. Haghpanah S, Nasirabadi S, Ghaffarpasand F, Karami R, Mahmoodi M, Parand S, et al. Quality of Life among Iranian Patients with Beta-Thalassemia Major Using the SF-36 Questionnaire. Sao Paulo Med J. 2013;131(3):166-72.
26. Kidson-Gerber GL, Francis S, Lindeman R. Management and Clinical Outcomes of Transfusion-Dependent Thalassaemia Major in an Australian Tertiary Referral Clinic. Med J Aust. 2008;188(2):72-5.
27. Lee WS, Toh TH, Chai P, Soo T. Self-Reported Level of and Factors Influencing The Compliance to Desferrioxamine Therapy in Multitransfused Thalassaemias. J Paediatr Child Health. 2011;47(8):535-40.
28. Richardson ME, Matthews RN, Alison JF, Menahem S, Mitvalsky J, Byrt E, et al. Prevention of Heart Disease by Subcutaneous Desferoxamine in Patients with Thalassaemia Major. Aust N Z J Med. 1993;23(6):656-61.
29. Wolfe L, Olivieri N, Sallan D, Colan S, Rose V, Propper R, et al. Prevention of Cardiac Disease by Subcutaneous Deferoxamine in Patients with Thalassemia Major. N Engl J Med. 1985;312(25):1600-3.
30. Hammond J, Thompson AA, Fogel MA, Hammond K, Kokroko J, Kwiatkowski JL. Combination Oral Chelation in Adult Patients with Transfusion-dependent Thalassemia and High Iron Burden. J Pediatr Hematol/Oncol. 2019;41(1):e47-50.
31. Dahlui M, Hishamshah MI, Rahman AJ, Aljunid SM. Quality of life in transfusion-dependent thalassaemia patients on desferrioxamine treatment. Singapore Med J. 2009;50(8):794.

32. Sandnes M, Ulvik RJ, Vorland M, Reikvam H. Hyperferritinemia- A Clinical Overview. J Clin Med. 2021;10(9):2008.
33. Sobota A, Yamashita R, Xu Y, Trachtenberg F, Kohlbry P, Kleinert DA, et al. Quality of Life in Thalassemia: A Comparison of SF-36 Results from the Thalassemia Longitudinal Cohort to Reported Literature and the U.S. Norms. Am J Hematol. 2011;86(1):92-5.
34. Philip KEJ, Polkey MI, Hopkinson NS, Steptoe A, Fancourt D. Social isolation, loneliness and physical performance in older-adults: fixed effects analyses of a cohort study. Sci Rep. 2020;10(1):13908.
35. Montazeri A, Goshtasebi A, Vahdaninia M. The Short Form Health Survey (SF-36): Translation and validation study of the Iranian version. Qual Life Res. 2005;14:875-82.
36. Hajian-Tilaki K, Heidari B, Hajian-Tilaki A. Are Gender Differences in Health-related Quality of Life Attributable to Sociodemographic Characteristics and Chronic Disease Conditions in Elderly People? Int J Prev Med. 2017;8:95.
37. Badr HE, Rao S, Manee F. Gender differences in quality of life, physical activity, and risk of hypertension among sedentary occupation workers. Qual Life Res. 2021;30(5):1365-77.
38. Lund RS, Karlsen TI, Hofso D, Fredheim JM, Roislien J, Sandbu R, et al. Employment is associated with the health-related quality of life of morbidly obese persons. Obes Surg. 2011;21(11):1704-9.
39. Rueda S, Raboud J, Mustard C, Bayoumi A, Lavis JN, Rourke SB. Employment status is associated with both physical and mental health quality of life in people living with HIV. AIDS Care. 2011;23(4):435-43.
40. Kakinuma Y. Financial literacy and quality of life: a moderated mediation approach of fintech adoption and leisure. Int J Soc Econ. 2022;49(12):1713-26.
41. Barnett NL, Flora K. Patient-centred consultations in a dispensary setting: a learning journey. Eur J Hosp Pharm. 2017;24(2):107-9.
42. Porter JB, Evangeli M, El-Beshlawy A. Challenges of adherence and persistence with iron chelation therapy. Int J Hematol. 2011;94(5):453-60.