


Patient Perspective on Iron Chelation Therapy: Barriers and Facilitators of Medication Adherence

Journal of Patient Experience
Volume 8: 1-11
© The Author(s) 2021
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/2374373521996958
journals.sagepub.com/home/jpx


Chia Chee Chong, BPharm¹ , Adyani Md Redzuan, PhD¹,
Jameela Sathar, MD² , and Mohd Makmor-Bakry, PhD¹ 

Abstract

Nonadherence to iron chelation therapy (ICT) remains a long-standing and serious issue in thalassemia, especially in resource-constrained developing countries. Barriers and facilitators of adherence to ICT in transfusion-dependent thalassemia (TDT) adult patients in Malaysia are not completely understood. This qualitative study explored factors affecting adherence to ICT among TDT adult patients at a public tertiary hospital in Malaysia. Data were collected through 21 semistructured in-depth interviews conducted among purposively sampled patients using a pretested interview guide. All interviews were audio-recorded and transcribed verbatim. Data were analyzed manually using thematic analysis method and managed using Atlas.Ti software. The most frequently discussed subthemes of barriers to adherence included patient-related factors, medications-related factors, sociocultural-related factors, environmental context and resources, and patient–health care provider relationship factors. The facilitators to adherence included having insights of their illness, prevailing sources of motivation emphasizing on strong self-efficacy, low medication burden, and having enabling environment. This study has identified barriers and facilitators that are unique to Malaysian thalassemic adults related to medication adherence. Options for future multifaceted interventions are suggested.

Keywords

medication adherence, thalassemia, iron chelating agents, patient perspectives, qualitative methods, behavior, patient education, pharmacist intervention

Introduction

Thalassemia is the most common inherited monogenic hemoglobin disorder worldwide (1). An estimated 7% of the world population is a carrier for this disorder, and approximately 60 000 children are born with the severe type of thalassemia each year (2). The mainstay management for these patients includes regular blood transfusions and iron chelation therapy (ICT). Iron chelation therapy is used to prevent iron overload to numerous vital body organs (3). Currently, there are only 3 iron chelators licensed for clinical use, namely, deferoxamine, deferiprone, and deferasirox. Advancement in blood transfusions and ICT transforms this disease from fatal childhood disease to adult chronic disease (1). Numerous studies have reported that advancement in medical care and good adherence to ICT treatment are instrumental to increase patients' survival and quality of life (4–10).

Nonadherence to ICT remains a long-standing and serious issue in thalassemia (11). Worldwide, nonadherence rate

to iron chelators ranges from 30% to 80% (6). Issue of non-adherence to ICT is complex and multifactorial (9–13). It has been established that nonadherence to ICT increases mortality and morbidity, reduces quality of life, and incurs huge economic burden to the country (14–16). However, most of these studies were conducted in developed countries and among younger patients (17–19). In Malaysia, suboptimal ICT adherence among thalassemia patients remains a

¹ Faculty of Pharmacy, Centre of Quality Management of Medicines, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

² Hematology Department, Hospital Ampang, Pandan Mewah, Ampang, Selangor, Malaysia

Corresponding Author:

Mohd Makmor-Bakry, Faculty of Pharmacy, Centre of Quality Management of Medicines, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, 50300 UKM Kuala Lumpur, Malaysia.
Email: mohdclinpharm@ukm.edu.my



persistent problem, and limited studies have explored this issue (20). Thus, this study aimed to explore barriers and facilitators to treatment adherence among transfusion-dependent thalassemia (TDT) adult patients in Malaysian population.

Participants and Methods

Study Design

This study used qualitative methodology, adopting phenomenological approach, through semistructured, face-to-face in-depth interview with purposively selected participants. Qualitative methodology was deemed the most appropriate method to explore in-depth experience and perception of study participants (21,22).

The participants were enrolled from a transfusion day care and outpatient thalassemia clinic of a public tertiary hospital. It is the national hematology referral center, serving the largest number of adult TDT patients in Malaysia. This study was carried out according to the principles stated in the Helsinki Declaration and approved by the medical research and ethics committee of the Ministry of Health, Malaysia (NMRR-19-73-45840).

Participant Selection

A purposive sample of adult (aged ≥ 18 years) TDT patients and taking any types of ICT was included in this study. The following participants were excluded: persons with impaired cognitive abilities and persons who were unable to understand or speak either English, Malay (the national language), or Mandarin language. Participants were selected from both genders, diverse races, and religious and socioeconomic background for maximum variation. Participants who agreed to participate voluntarily and signed the written consent form were assured of their anonymity and confidentiality throughout the research. All research-related data were kept in a password-protected database, and result findings were solely presented in deidentified terms.

Development of Interview Guide

An interview guide containing a list of predetermined open-ended questions was developed, based on the objectives of the study. The interview guide was independently reviewed and validated by an expert in thalassemia and 2 experienced qualitative researchers to ensure the development of meaningful questions that will motivate relevant responses. A pilot study was conducted on 3 patients to improve consistency and to ensure the interview questions were clear and relevant.

Data Collection

The face-to-face semistructured interview was conducted in English, Bahasa Malaysia, or Mandarin languages, according

to the participant's preference by a researcher who is fluent in all 3 languages. Individual interviews with patients were conducted in a private room to ensure confidentiality. Ice-breaking was initiated to establish rapport. The average time for each interview session was 45 minutes. Probing questions were asked to reduce ambiguity and to further explore the participant's answers in depth. The researcher periodically summarized the information received and clarified with the participants to determine accuracy. A reflective journal was maintained after each interview. All interviews were audio-recorded and transcribed verbatim. Where necessary, a follow-up interview was conducted to reexamine certain issues in light of emerging ideas.

Through circular approach, a total of 21 participants were recruited, based on data saturation (23). Data were collected until no new themes were identified and no new information was forthcoming. Throughout the data collection process, ongoing data analysis occurred concurrently.

Data Analysis

Data were analyzed manually using thematic analysis method (24) and subsequently managed using both Atlas.Ti version 7.0 software. Transcripts were re-read multiple times, with notes taking at the margins. Memo-taking was done simultaneously to capture reflections and general idea about each interview transcript. Coding was performed line by line inductively (25). Each new code was entered into a codebook indiscriminately at first, and subsequently codes were then collapsed by removing overlapping codes. Codings from transcripts were compared to the list and finally categorized into similar, meaningful units called themes. These themes were then carefully listed, checked, compared constantly, and finalized. The main researcher conducted this coding and thematic analysis independently. To ensure consistency and reliability of the findings, 2 researchers reviewed and verified the codings and themes generated. During the event of discrepancy, the opinions of all research team members were sought and consensus obtained to finalize the themes and quotes representing the themes.

Rigor of Study

To ensure trustworthiness of data, peer debriefing and analytic triangulation were conducted throughout the research with skilled researchers. Upon study completion, findings were shared with a few participants to affirm the accuracy and completeness of the findings.

Results

The mean duration of the interview was 45 minutes (range from 27 to 73 minutes). Majority of them were females ($n = 13$), young adults (mean age = 31.8 years; range = 21-47 years old) and had received education above secondary school ($n = 16$). Patients were predominantly single and

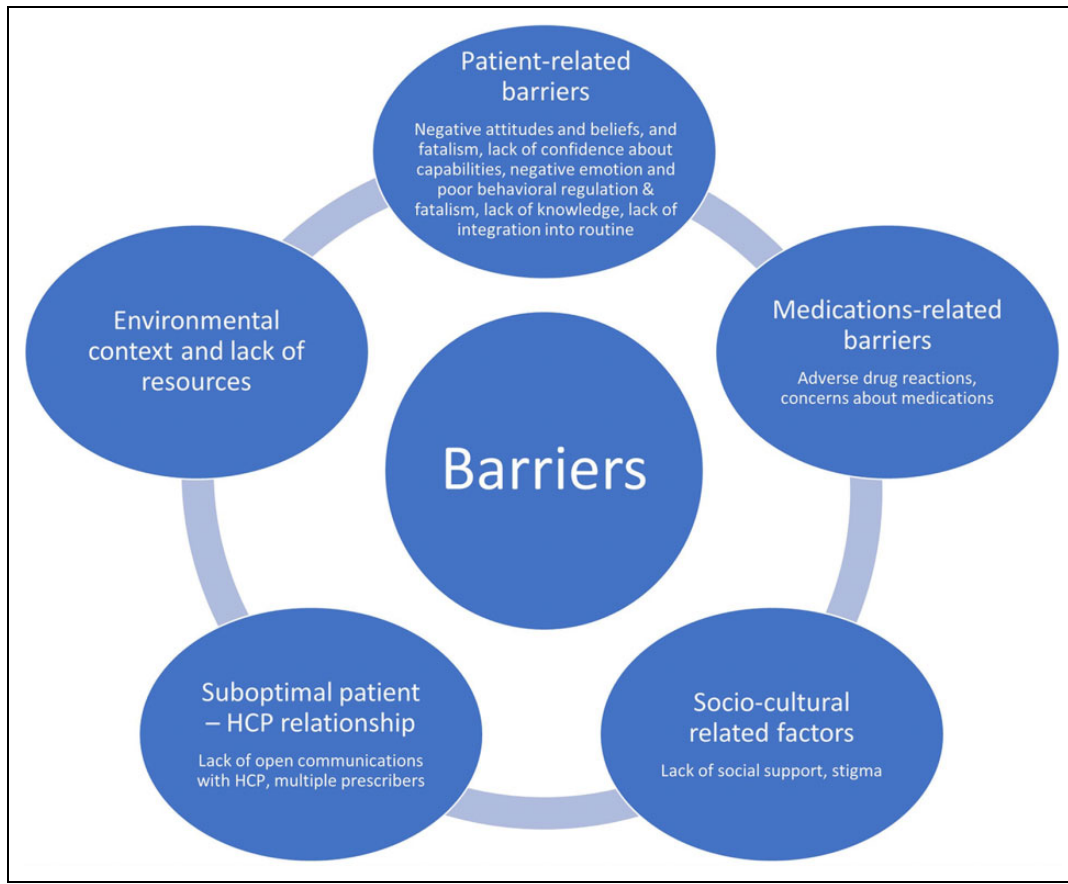


Figure 1. Diagram showing the themes and subthemes of the barriers to medication adherence.

staying with family. Most of them were from the lower middle-income bracket ($n = 16$). Two main categories emerged from the interview: barriers to adherence (Figure 1) and facilitators to adherence (Figure 2).

Barriers to Adherence

Five main subthemes of barriers to adherence (patient-related factors, medication-related factors, sociocultural-related factors, patient–provider relationship factors, environmental context and resources) emerged from the patients' interviews (Table 1).

Theme 1: Patient-related barriers. Five subthemes emerged in the patient-related barriers theme. Each of these subthemes is described in detail below without any specific hierarchy/order.

Negative attitude, beliefs, and fatalism. A few participants reported that they strongly dislike using the infusion pump as the injection caused damages to their skin and affected their sleep. Another participant narrated that he did not believe the ICT is effective due to unmatched outcome expectancy. A few participants also expressed fatalistic beliefs, particularly in areas of developing iron overload complications and mortality.

Lack of confidence about capabilities. A few of the young adult participants mentioned having no confidence to self-administer deferoxamine infusion. They felt this lack of confidence originated since their childhood, when they were being shielded from taking up responsibilities for their therapy by overprotective parents.

Negative emotion, poor behavioral regulation, and fatigue. A few participants described prevalent emotional distress and overt negativity that comes from having thalassemia, perpetuating their feeling of hopelessness. These participants claimed that negative emotions and fatigue during period of low hemoglobin further dampened their motivation to handle challenges. Therefore, they revealed adopting avoidance coping style to avoid dealing with the stressful situations in their lives. These underlying psychological constructs are important aspect of nonadherence to ICT.

Lack of knowledge. A few participants stated lack of understanding of the disease and drugs including the skills for correct medication administration and synergistic effect of different iron chelators.

Lack of integration into routine. A few participants discussed their struggles to integrate the time-consuming medication regimen into their daily routine due to their hectic life. This



Figure 2. Diagram showing the themes and subthemes of the facilitators to medication adherence.

was observed among participants who are working, having small children, or juggling heavy family commitments.

Theme 2: Medication-related factors. Medication-related factors were the most frequently mentioned barriers (85.7%) and consisted of 2 main subthemes, mainly adverse drug reactions and concerns about medications.

Adverse drug reactions. The majority of participants reported that they had experienced significant life-disturbing adverse drug reactions with ICT, causing them to withhold, alter, or skip the medications. A few participants experienced uncommon side effects, which include mood changes, impaired cognitive abilities, and unpleasant burning sensation.

Concerns about medications. Participants described perceived high burden to deferoxamine and oral ICT therapy as reason for medication nonadherence. Most participants consumed an average of 5 types of medications on top of iron chelators, further predisposing them to drugs-related problems. Many participants also expressed concern about their medications, including that oral ICT may cause kidney

damage, when taken for long term. Some believed that oral ICT has “heavy” effect on the body, thus should not be taken when feeling unwell.

Theme 3: Sociocultural-related factors. Lack of social support and stigma were constructs that emerged as sociocultural-related barriers to adherence.

Lack of social support. A few participants claimed lack of social support, particularly from influencing figures such as the parents, was found to discourage them from persisting with their medications.

Stigma. A few participants described their day-to-day interaction with others and revealed fear of stigma made them conceal their disease condition to others. Subsequently, participants intentionally refrained from taking medication in front of others, leading to missed doses.

Theme 4: Patient–provider relationship. There were 2 subthemes identified in this category: lack of open communications with health care providers and multiple prescribers.

Table 1. Themes, Subthemes, and Exemplar Quotations for Barriers to Iron Chelation Therapy Adherence Among Transfusion-Dependent Thalassemia Adult Patients.

Main theme	Subtheme	Exemplar quotations
1 Patient-related barriers	(1) Negative attitude, beliefs and fatalism	<p>"Because the effect of the iron overload is long term so I don't feel it immediately. That's why I lack the initiative to do it." (#9, male, Malay)</p> <p>"Before this, I don't take my medication because I am stubborn. I will still be sick even if I take it." (#18, female, Malay)</p> <p>"... The doctor said I am lying... I saw my iron level went up instead of coming down. I felt so disappointed and gave up hope. I had expected to see result once I started the treatment. After that, I don't take my medicine anymore." (#12, male, Malay)</p> <p>"Taking the iron chelator will cause my bone to decay... " (#12, male, Malay)</p> <p>"According to my belief, we can die anywhere. Even if we sit inside the vault, if God wants to take our lives, we will still die. To me, those who take their medications also will die, those who do not [take] also will die. It is the same. (laugh)" (#12, male, Malay)</p>
	(2) Lack of confidence about capabilities	<p>"I am scared that I will inject wrongly. I dare not poke myself." (#16, female, Chinese)</p> <p>"... Because my mum, she prepared it for me. Maybe if I personally get involved in it, I would be able to do it... Now, I am not confident to do it." (#9, male, Malay)</p>
	(3) Negative emotion, poor behavioral regulation, and fatigue	<p>"... I have encountered other thalassemia patients tried taking drug overdose hoping they can die faster." (#2, female, Malay)</p> <p>"My reason is... (hesitant)... because I am quite lazy to do it actually. Some doctors recommended to inject during the day, which is fine but I am not too comfortable to be walking around with the needle, the pump and the infuser. That's why I prefer to do it at night. But at night I prefer to sleep on my front... It is a very stupid reason but yeah..." (#9, male, Malay)</p> <p>"... I have not fully taken [iron chelation therapy] as part of my life. I turn to ignorance. Ignorance is bliss." (#9, male, Malay)</p> <p>"... When I experienced so much negative experience, even at home, I feel unbearable pressure. I thought before of not taking my treatment, including refusing blood transfusion. Maybe happier if I die." (#15, female, Malay)</p> <p>"... I don't talk about my illness to anyone because it makes me feel down. I feel tired you know, a lot of challenges... Always need to be poked..." (#18, female, Malay)</p> <p>"... I feel lazy... too many things... lazy even to think." (#12, male, Malay)</p> <p>"... When it comes to injecting desferal... Sometimes, I will feel like I simply do not want to inject, don't know why..." (#16, female, Chinese)</p> <p>"... You will feel very tired... Like you are working out in a gym. You are actually lying down, doing nothing, maybe play handphone, but you will feel very tired, the heart very tired, everything very tired." (#8, male, Chinese)</p> <p>"I am not very sure about my treatment... I don't know much... my mother used to handle all for me... She passed away 9 years ago. The hospital assumed I would know so they don't repeat to me." (#9, male, Malay)</p> <p>"I remember for my whole life, I eat vitamin C before injecting desferal... I have no idea I should take it an hour after the start of [desferal] infusion." (#9, male, Malay)</p> <p>"... I wondered before, why do I need to inject desferal when I am already taking the capsules... Now only I know due to different functions..." (#6, female, Malay)</p> <p>"Because of the busy schedule, I sometimes cannot take my medication... I don't have time to take the medicine because I need to prepare it. It takes time." (#7, male, Malay)</p> <p>"... Sometimes if I use it during daytime, it limits my movement. [Because] my kids, they want me to carry them. Whenever I think of taking care of the children and household chores, I feel stressed up. It affects [the iron chelation therapy]" (#1, female, Malay)</p> <p>"When I take the medicine, I will throw up... I will need to lie down. The whole day I can't do any work. I tried many times to take it but it happened each time. So I stop taking it." (#18, female, Malay)</p> <p>"The medicine made me feel nauseous and caused me to vomit. The effect is burning sensation on the skin. The drug made me feel very dizzy, unable to think properly... So I reduced the dose on my own." (#6, female, Malay, 32 years)</p> <p>"The previous brand had issues too but not as many as the current brand." (#2, female, Malay, 47 years)</p>
	(4) Lack of knowledge	
	(5) Lack of integration into routine	
2 Medications-related factors	(1) Adverse drug reactions	

(continued)

Table 1. (continued)

Main theme	Subtheme	Exemplar quotations
	(2) Concerns about medications	<p>"I feel burdened . . . the needles and all that. I feel scared and uncomfortable. Keep being poked . . ." (#18, female, Malay)</p> <p>" . . . I am the active type. When I am infusing the drug, I wouldn't move, I will just lie down. The doctors told me I can carry on normal activities while infusing but I am not keen. What if the needle gets dislodged? That will cause problems. Sometimes I will even skip meals while infusing the drug." (#15, female, Malay, 22 years)</p> <p>"The more I inject, the more I feel itchy . . . night time [when] I sleep, I can't sleep well." (#8, male, Chinese)</p> <p>"Sometimes when I feel unwell, I wouldn't take the medicine. The iron chelators have 'heaty' effect on the body, causing us to get fever more easily. I will make adjustments. If I feel unwell, I will stop my medication temporarily." (#11, female, Malay)</p> <p>" . . . We need to drink a lot of water if we take oral medication, otherwise it will spoil the kidney. I don't drink a lot of water every day, so I became scared to take the medicine." (#12, male, Malay)</p> <p>" . . . It tastes so bad. It is not like other medicine." (#15, female, Malay)</p> <p>"My mum passed away when I was 14 years old. Since then, I didn't have my own initiative to push myself to do it every night." (#9, male, Malay)</p> <p>" . . . My mother said it [infusing desferal] was a waste of time." (#12, male, Malay, 24Y)</p> <p>" . . . This is my own business . . . I can settle my own problems. The others will not know my situation, how the patient feels, what a patient needs to go through." (#15, female, Malay)</p> <p>"Recently, a local television drama portrayed wrong information about thalassemia. This perpetuated more misunderstanding about this illness. I feel upset." (#1, female, Malay)</p> <p>"The emotions caused me to skip my medicine. They [the peers] said thalassemia is like AIDS, it is dangerous and can be infected. The advertisement on the TV made them have that wrong knowledge." (#6, female, Malay)</p> <p>"The doctor talks with no facial expression. I feel lazy to see him. That's why I will not follow up every time . . ." (#8, male, Chinese)</p> <p>" . . . The doctor needs to build rapport with the patients. If patient's past record is not good, then they can ask why you can't take the medicine instead of scolding." (#18, female, Malay)</p> <p>"That doctor scolded me, ask me why I don't take the medication, I told him I did. He did not believe me. He thought I am lying . . . I stop taking my medicine after that . . ." (#12, male, Malay)</p> <p>"Every 3 months for my doctor's appointment, it is always different doctors telling me the same thing . . . If same doctor, maybe the doctor and patient can build some sort of relationship to see the progress and feels more personal . . ." (#9, male, Malay)</p> <p>"Those other doctors, the questions they ask . . . like I don't know what . . . repeat and repeat and repeat the same things . . ." (#8, male, Chinese)</p> <p>"When we [were] at the village, I [was] worried about the cleanliness. If we do it wrongly, or our hands are dirty, then it is easy to get infection. So, I don't use it." (#4, female, Malay)</p> <p>" . . . when I go back to hometown for the festive celebration, I will meet many relatives. I will take L1 at night only, not during daytime because it makes me sleepy. I am outside with relatives . . . Cannot be sleepy." (#2, female, Malay)</p> <p>" . . . I need to buy our own syringes. The syringes are not cheap. I need to find our own source to buy the syringes . . ." (#14, male, Chinese)</p> <p>"It is tough. I have young children, husband working, no one is around to help me . . . now my biological mother came back to stay with me . . . she does not understand my situation. It is very stressful . . . so I tend to miss my medications . . . you know . . . when life gets in the way . . ." (#1, female, Malay)</p>
3	Sociocultural-related factors	(1) Lack of social support
4	Patient-provider relationship	(1) Lack of open communications with health care providers
		(2) Stigma
5	Environmental context and resources	(2) Multiple prescribers

Abbreviation: AIDS, acquired immune deficiency syndrome.

Lack of open communications with health care providers. Participants highlighted that doctors with stoic facial expression who were paternalistic tend to discourage them from attending future clinics appointment. They developed mistrust when their doctors were reluctant to disclose the laboratory results or were not open in understanding reasons they cannot adhere fully to treatment.

Multiple prescribers. Participants reported that having multiple prescribers reduced rapport between patients and health care providers. Participants felt frustrated having to constantly repeat the same clinical history to different prescribers each time.

Theme 5: Environmental context and resources. Environmental context and resources refers to the circumstances of a person's situation or environment that influences the person's behavior. Almost 95% of participants claimed not taking ICT if they go overseas travelling, travel out of home during festive seasons, or attend social functions. Reasons given were obligation for socially desirable behavior during festival gatherings and concerns of environmental cleanliness for infusion. Some participants reported episodes of nonadherence during period of unfavorable life situations, such as during trauma or time of crisis. Majority of participants lamented the high cost of purchasing consumables (syringe, newer needles, alcohol swab) for deferoxamine infusion posed monetary burden to them. Consequently, participants will self-adjust their doses or administration frequency to reduce the cost.

Facilitators to Adherence

Four major categories were identified: having insights of the illness, prevailing sources of motivation, low perceived medication burden, and an enabling environment (Table 2).

Theme 1: Having insights. Participants who had insights of their illness knew the necessity of ICT, had good awareness of the complications of iron overload, perceived effectiveness of ICT either through outcome experienced by self or others, understood the synergistic effect of combination therapy, and appreciated the value of medicine.

Theme 2: Prevailing sources of motivation. Participants illustrated that they were motivated to persist with their treatment regimen through narratives of having strong self-efficacy, living for significant others, having positive reinforcement, having goals, having positive identity, and being optimistic.

Self-efficacy. Patients who possessed high self-efficacy were able to persevere with the treatment despite facing setbacks. Among the characteristics described were planning ahead, resilience, sense of capability, having positive emotion, high discipline, emotional management, fighting spirit, self-determination, problem-solving skills, making adjustments,

and taking initiatives. Even if they faced periodical lapses in adherence, such as having local injection site reactions or in times of personal crisis, they were able to quickly recover their sense of efficacy after these setbacks.

Living for significant others. A few participants reiterated that they drew strength from having the purpose to live for their significant others or for other purposeful endeavors including voluntary work. The hope of starting a family is a strong motivator for many female patients to be adherent to their treatment. Female participants were aware that therapeutic iron level might lead to better pregnancy outcome.

Positive reinforcement of minimal therapy when iron level is under control. Patients looked forward to needing only minimal therapy if they can get their serum ferritin level within the target range.

Having goals. Participants mentioned when they were able to set small goals for themselves and achieved it, that aided to their sense of accomplishment. Participants suggested incentives such as organizing a competition to reward patients who were able to lower their serum ferritin the most. Participants who have life goals, which include getting married, being successful in career, pursuing their hobbies, were more likely to persist with therapy.

Positive identity and optimism. Participants felt they are "normal," despite having thalassemia. They were motivated to keep their iron level under control to avoid changes in their outer appearance and skin bronzing, so they may also look "normal" to others. Participants also narrated being hopeful for better treatment in the future and staying optimistic.

Theme 3: Low medication burden. Most patients (66.7%) claimed that being compatible with the medications, having alternative infusion regimen, and having readily constituted deferoxamine or shorter infusion needle can lower the perceived burden from medication use.

Theme 4: Enabling environment

Social support and modeling. Majority of participants stated that good social support, particularly family support, is the pillar for good medication adherence. Quite notably, the construct of having a peer role model as facilitator highlighted the importance of support group and modeling. In addition, flexible working environment was also quoted as an enabling factor for better medication adherence.

Good patient–health care provider relationship. Participants reported that good rapport with health care providers, open communication between patient and health care providers, clear charting of treatment plan in health records, and honesty in broaching difficult topics helped patients feel involved in their health management.

Table 2. Themes, Subthemes, and Exemplar Quotations for Facilitators to Iron Chelation Therapy Adherence Among Transfusion-Dependent Thalassemia Adult Patients.

Main theme	Subtheme	Exemplar quotations
1	Having insights	<p>"Because I don't want to have additional complication." (#3, female, Chinese)</p> <p>"It helps in terms of my health. I feel stronger and more energetic. I can do what I like now." (#18, female, Malay)</p> <p>"Last time, desferal is extremely difficult to get. . . . It is very expensive. Once mixed, I don't want to waste. If don't want to do, means you are throwing the money down the drain." (#20, male, Chinese)</p> <p>"I need to plan ahead. . . . Daily, at night, I make sure I go back home before 12 so [that] I can take the treatment." (#7, male, Malay)</p> <p>"It all depends on ourselves. . . . We need to be disciplined in taking our medications." (#13, female, Malay)</p> <p>"I thought to myself, of course there will be problems in life but I must be strong to fight it." (#2, female, Malay)</p> <p>"When you self-inject, you don't feel so painful because you can adjust it." (#13, female, Malay)</p> <p>"I don't want my mother to be worried about me. I want her to see I can live like other normal person." (#19, female, Chinese)</p> <p>"I greet life with a smile amidst the humiliation that I felt from the people around me. Every day I wake up with the determination to be strong for my children." (#1, female, Malay)</p> <p>"I want a baby. My husband encouraged me to improve my health first so [that] we have higher chances of getting a baby." (#6, female, Malay)</p> <p>"(Thinking) My motivation is no need to use desferal, just use oral [iron chelator],[to-be] injection-free, just take oral [iron chelator] only." (#3, female, Chinese)</p> <p>"I want my ferritin [level] to continue be below 1000, that is why I continue taking my medication." (#3, female, Chinese)</p> <p>"My target is to lower down the readings. That's what motivates me to keep on complying to my medications." (#7, male, Malay)</p> <p>"All of my friends are very successful person in terms of their businesses and their lives. I want to be same (equally successful) like them." (#10, male, Chinese)</p> <p>"My hobby is travelling. I like to see the world. So that motivates me. . . ." (#7, male, Malay)</p> <p>"I want to stay alive because I want to go to Disneyland in the United States. . . ." (#17, female, Chinese)</p> <p>"I like them (others) to see me as a normal person. In fact, my colleagues do not know I have thalassemia. My skin is not dark." (#7, male, Malay)</p> <p>"Thalassemia is just like a car. . . . You need to fill up the petrol. When the petrol is full, then you are ready to go." (#8, male, Chinese)</p> <p>". . . . Nobody knows I am a thalassemic person, so they will treat me as a normal person." (#10, male, Chinese)</p> <p>"I just hope that one day there will be a cure for thalassemia." (#7, male, Malay)</p> <p>"I have no issues with my medications. So, I continue taking it. . . ." (#13, female, Malay)</p> <p>"For me, the new type of needle is easier to use and more comfortable. . . . better for me." (#18, female, Malay)</p>
2	Prevailing sources of motivation	<p>(1) Self-efficacy</p> <p>(2) Living for significant others</p> <p>(3) Positive reinforcement of minimal therapy when iron level is under control</p> <p>(4) Having goals</p>
3	Low medication burden	(5) Positive identity and optimism
4	Enabling environment	<p>(1) Social support and modeling</p> <p>(2) Good patient–health care provider relationship</p>

Abbreviation: ICT, iron chelation therapy.

Discussion

To the best of the researcher's knowledge, this is the first study conducted in Malaysia to explore both the barriers and facilitators to medication adherence among TDT adult patients using qualitative methodology. In line with Leventhal's Common-Sense Model (26), it is increasingly important to understand patient's perspectives of their illness condition that may influence their medication taking behavior, so health care policy makers can respond more appropriately.

Our study highlights that barriers and facilitators to ICT adherence are multidimensional. The elimination of certain barriers, specifically modifiable factors, can help patients to better adhere to ICT. Heightened understanding of facilitators, especially in self-efficacy and motivation, provides interesting options for future strategy. Most of these sub-themes can be further explored in future researches.

Patients-related barriers are the most reported barriers with strong emphasis at deficit of psychological capacity and motivation, particularly low perceived self-efficacy, to engage in medication adherence behaviors. This is reflected by participant's lack of confidence in their capabilities to self-administer complex regimen and to self-regulate complex emotions. Many studies supported that self-efficacy has mediating role in medication adherence, through development of multidimensional resilience, even among patients with psychological problems (27–29). It is one of the most important acquired skills for patient empowerment to self-manage the various facets of their complex illnesses (30). It is worrying that many young adult participants in this study have basic cognitive knowledge but have low perceived self-efficacy. The possible reason includes conventional thalassemia patient education is more cognizant based, mainly focusing on information giving and techniques teaching. This emphasizes the need to include pragmatic self-management interventions and programs as advocated by World Health Organization to empower persons with chronic illness to manage their health and health care (31).

High level of concerns about medication and suffering from adverse drug reactions emerged as the most compelling medication-related barriers to ICT adherence. Asian patients had higher levels of concern about chelation compared to white patients (13). According to Necessity-Concern Framework, unaddressed high concerns about medications predispose patients to problem of nonadherence (32). The occurrence of drugs-related problems, specifically adverse drug reactions, is disruptive to patients' quality of life and affects their adherence, evident from the many studies conducted among thalassemia patients (4,6–8). It is, therefore, important to address not only patients' knowledge but also their beliefs and concerns about medications, as emphasized by the UK National Institute for Health and Care Excellence (NICE) (33). Pharmacists play strategic role to recognize and to address these medications-related barriers commonly associated with iron chelators. Addressing these concerns

may require a more in-depth, nonconfrontational and collaborative approach, such as through motivational interviewing (34,35), while supporting efforts to enhance patient's perceived self-efficacy on symptoms management.

This study also highlighted the theme of enabling environment, particularly good patient–health care provider relationship and social support and modeling, in facilitating chelation adherence. According to COM-B framework, improved patient–health care provider relationship can provide the environmental and social influence that enhances opportunity for medication adherence (36). Patients are more likely to disclose to their physicians important information such as their concerns and self-adjustments made to their medications when positive therapeutic alliance is formed (37,38). This finding emphasized the need of concerted effort to strengthen patient–health care provider relationship and to align current practice with person-centered approach advocated by organizations such as NICE (39,40). Participants also highlighted the importance of role models and patient group. The establishment of a holistic specialized multidisciplinary adherence program, incorporating health-coaching initiatives, may be beneficial in this aspect.

There are some limitations to this study. Patients who refused to participate and those who could not speak English, Malay, or Mandarin language might have other important barriers or experiences that were not captured in this study. Being an interview-based research, social desirability and recall bias can undermine the quality of the data. However, this methodology is best to elucidate participant's perspectives and provide richer spectrum of barriers and facilitators encountered.

Conclusion

This study provides insights into various influencing factors of medication adherence for Malaysian TDT patients contextual to the local setting. Understanding of barriers and facilitators to ICT among these patients provides interesting options for future multifaceted interventions.

Authors' Note

This study was approved by the medical research and ethics committee of the Ministry of Health, Malaysia (NMRR-19-73-45840).

All procedures in this study were conducted in accordance with the medical research and ethics committee of the Ministry of Health, Malaysia, approved protocols.

Written informed consent was obtained from the participants for their anonymized information to be published in this article.

Acknowledgments

The authors thank Hospital Ampang for providing the facilities to conduct this project as well as hematology nurses at the specialist clinic and thalassemia daycare center for their help.

Declaration of Conflicting Interests


The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Chia Chee Chong, BPharm  <https://orcid.org/0000-0001-8003-9877>

Jameela Sathar, MD  <https://orcid.org/0000-0003-1943-0863>

Mohd Makmor-Bakry, PhD  <https://orcid.org/0000-0002-0592-0645>

References

1. Taher AT, Weatherall DJ, Cappellini MD. Thalassaemia. *Lancet*. 2018;391:155-67. doi:10.1016/S0140-6736(17)31822-6
2. Williams TN, Weatherall DJ. World distribution, population genetics, and health burden of the hemoglobinopathies. *Cold Spring Harb Perspect Med*. 2012;2:a011692. doi:10.1101/cshperspect.a011692
3. Cappellini MD, Cohen A, Porter J, Taher A, Viprakasit V. *Guidelines for the Management of Transfusion Dependent Thalassemia (TDT)*. 3rd ed. Thalassemia International Federation; 2014.
4. Sobota A, Yamashita R, Xu Y, Trachtenberg F, Kohlbray 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 US norms. *Am J Hematol*. 2011;86:92-5. doi:10.1002/ajh.21896
5. Ward A, Caro JJ, Green TC, Ward AHuybrechts K, Arana A, Wait S, et al. An international survey of patients with thalassemia major and their views about sustaining life-long desferrioxamine use. *BMC Clin Pharmacol*. 2002;2:3. doi:10.1186/1472-6904-2-3
6. Trachtenberg FL, Gerstenberger E, Xu Y, Mednick L, Sobota A, Ware H, et al. Relationship among chelator adherence, change in chelators, and quality of life in thalassemia. *Qual Life Res*. 2014;23:2277-88. doi:10.1007/s11136-014-0671-2
7. Bazi A, Sargazi-Aval O, Safa A, Miri-Moghaddam E. Health-related quality of life and associated factors among thalassemia major patients, Southeast of Iran. *J Pediatr Hematol Oncol*. 2017;39:513-7. doi:10.1097/MPH.0000000000000963
8. Trachtenberg F, Vichinsky E, Haines D, Pakbaz Z, Mednick L, Sobota A, et al. Iron chelation adherence to deferoxamine and deferasirox in thalassemia. *Am J Hematol*. 2011;86:433-6. doi:10.1002/ajh.21993
9. Porter JB, Evangeli M, El-Beshlawy A. The challenges of adherence and persistence with iron chelation therapy. *Int J Hematol*. 2011;94:453-60. doi:10.1007/s12185-011-0927-3
10. Evangeli M, Mughal K, Porter JB. Which psychosocial factors are related to chelation adherence in thalassemia? A systematic review. *Hemoglobin*. 2010;34:305-21. doi:10.3109/03630269.2010.485080
11. Emami Zeydi A, Karimi Moonaghi H, Heydari A. Exploring Iranian β -thalassemia major patients' perception of barriers and facilitators of adherence to treatment: a qualitative study. *Electr Phys*. 2017;9:6102-10. doi:10.19082/6102
12. Vosper J, Evangeli M, Porter JB, Shah F. Psychological factors associated with episodic chelation adherence in thalassemia. *Hemoglobin*. 2018;42:30-6. doi:10.1080/03630269.2018.1433686
13. Trachtenberg FL, Mednick L, Kwiatkowski JL, Neufeld EJ, Haines D, Pakbaz Z, et al. Beliefs about chelation among thalassemia patients. *Health Qual Life Outcomes*. 2012;10:148. doi:10.1186/1477-7525-10-148
14. Cutler RL, Fernandez-Llimos F, Frommer M, Benrimoj C, Garcia-Cardenas V. Economic impact of medication non-adherence by disease groups: a systematic review. *BMJ Open*. 2018;8:e016982. doi:10.1136/bmjopen-2017-016982
15. Delea TE, Edelsberg J, Sofrygin O, Thomas SK, Baladi JF, Phatak PD, et al. Consequences and costs of noncompliance with iron chelation therapy in patients with transfusion-dependent thalassemia: a literature review. *Transfusion*. 2007;47:1919-29. doi:10.1111/j.1537-2995.2007.01416.x
16. Vekeman F, Sasane M, Cheng WY, Ramanakumar AV, Fortier J, Qiu Y, et al. Adherence to iron chelation therapy and associated healthcare resource utilization and costs in Medicaid patients with sickle cell disease and thalassemia. *J Med Econ*. 2016;19(3):292-303. doi:10.3111/13696998.2015.1117979
17. Lee YL, Lin DT, Tsai SF. Disease knowledge and treatment adherence among patients with thalassemia major and their mothers in Taiwan. *J Clin Nurs*. 2009;18:529-38. doi:10.1111/j.1365-2702.2007.02150.x
18. Foe M, Treadwell MJ, Yamashita R, Lal A. Factors related to iron chelation therapy adherence in young adults with thalassemia: a framework from the patient perspective. *Blood*. 2017;130:2080. doi:10.1182/blood.V130.Suppl_1.2080.2080
19. Al-Kloub MI, A bed MA, Al Khawaldeh OA, Al Tawarah YM, Froelicher ES. Predictors of non-adherence to follow-up visits and deferasirox chelation therapy among Jordanian adolescents with thalassemia major. *Pediatr Hematol Oncol*. 2014;31:624-37. doi:10.3109/08880018.2014.939792
20. Lee WS, Toh TH, Chai PF, Soo TL. Self-reported level of and factors influencing the compliance to deferoxamine therapy in multitransfused thalassaemias. *J Paediatr Child Health*. 2011;47:535-40. doi:10.1111/j.1440-1754.2011.02017.x
21. Fontana A, Frey JH. The interview: from structured questions to negotiated text. In: *Handbook of Qualitative Research*. 2nd ed. SAGE; 2000.
22. Polit DF, Beck CT. Generalization in quantitative and qualitative research: myths and strategies. *Int J Nurs Stud*. 2010;47:1451-8. doi:10.1016/j.ijnurstu.2010.06.004
23. Creswell J. *Qualitative Inquiry and Research Design: Choosing Among Five Approaches*. 2nd ed. SAGE; 2007.
24. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol*. 2006;3:77-101. doi:10.1191/1478088706q.p063oa
25. Saldaña J. *The Coding Manual for Qualitative Researchers*. 2nd ed. SAGE; 2013.
26. Leventhal H, Brissette I, Leventhal EA. The common-sense model of self-regulation of health and illness. In: *The Self-*

- Regulation of Health and Illness Behaviour*. Routledge; 2003.
27. Náfrádi L, Nakamoto K, Schulz PJ. Is patient empowerment the key to promote adherence? A systematic review of the relationship between self-efficacy, health locus of control and medication adherence. *PLoS One*. 2017;12:e0186458. doi:10.1371/journal.pone.0186458
 28. Holmes EAF, Hughes DA, Morrison VL. Predicting adherence to medications using health psychology theories: a systematic review of 20 years of empirical research. *Value Heal*. 2014;17:863-76. doi:10.1016/j.jval.2014.08.2671
 29. Almahmoud SY, Coifman KG, Ross GS, Kleinert D, Giardina P. Evidence for multidimensional resilience in adult patients with transfusion-dependent thalassemias: is it more common than we think? *Transfus Med*. 2016;26:186-94. doi:10.1111/tme.12296
 30. Anderson RM, Funnell MM. Patient empowerment: myths and misconceptions. *Patient Educ Couns*. 2010;79:277-82. doi:10.1016/j.pec.2009.07.025
 31. Coulter A, Parsons S, Askham J, World Health Organization. *Policy Brief: Where Are the Patients in Decision-Making About Their Own Care?* World Health Organization Regional Office for Europe; 2008.
 32. West LM, Borg Theuma R, Cordina M. The 'necessity-concerns framework' as a means of understanding non-adherence by applying polynomial regression in three chronic conditions. *Chronic Illn*. 2020;16(4):253-65. Epub 2018;1742395318799847. doi:10.1177/1742395318799847
 33. National Institute for Health and Care Excellence (NICE). Medicines adherence: Involving patients in decisions about prescribed medicines and supporting adherence [internet]. NICE; 2009. [Accessed August 2, 2020; Updated 2019 Mac] <http://www.nice.org.uk/guidance/cg76>
 34. Salvo MC, Cannon-Breland ML. Motivational interviewing for medication adherence. *J Am Pharm Assoc*. 2015;55:e354-63. doi:10.1331/JAPhA.2015.15532
 35. Barnett NL, Flora K. Patient-centred consultations in a dispensary setting: a learning journey. *Eur J Hosp Pharm*. 2017;24:107-9. doi:10.1136/ejhpharm-2016-000929
 36. Jackson C, Eliasson L, Barber N, Weinman J. Applying COM-B to medication adherence: a suggested framework for research and interventions. *Eur Health Psychol*. 2014;16:7-17.
 37. Hadjidemetriou M. Thalassemia: yesterday, today, tomorrow. *Am J Hematol*. 2017;92:490-2. doi:10.1002/ajh.24744
 38. Ng YK, Shah NM, Loong LS, Pee LT, Hidzir SAM, Chong WW. Attitudes toward concordance and self-efficacy in decision making: a cross-sectional study on pharmacist-patient consultations. *Patient Prefer Adherence*. 2018;12:615-24. doi:10.2147/PPA.S159113
 39. Price AI, Djulbegovic B, Biswas R, Chatterjee P. Evidence-based medicine meets person-centred care: a collaborative perspective on the relationship. *J Eval Clin Pract*. 2015; 21:1047-51. doi:10.1111/jep.12434
 40. Person-Centred Care Toolkit. [internet] Royal College of General Practitioners; 2020 [updated February 11, 2021]. Retrieved August 2, 2020, from: <https://www.rcgp.org.uk/clinical-and-research/resources/toolkits/person-centred-care-toolkit.aspx>

Author Biographies

Chia Chee Chong is a postgraduate student and practicing pharmacist. She actively involved in medication management education for hematology patients.

Adyani Md Redzuan is a senior lecturer in clinical pharmacy. Her research interest covers medication adherence enhancement strategies and clinical pharmacy practice.

Jameela Sathar is a consultant hematologist at Ministry of Malaysia Hospital. Her research interest focuses on clinical hematology.

Mohd Makmor-Bakry is an associate professor in clinical pharmacy. His research interest focuses on medication adherence enhancement strategies and clinical pharmacy practice.