MOTHERS WITH MULTIPLE Β-THALASSEMIA MAJOR CHILDREN IN SABAH, MALAYSIA: A QUALITATIVE STUDY EXPLORING THE CONTRIBUTING FACTORS

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Abstract
Despite having the highest prevalence of thalassemia in Malaysia, studies exploring factors that contribute to high thalassemia births in Sabah is still lacking. This study aimed to explore the reasons that may contribute to mothers in Sabah having multiple children with β-thalassemia major (β-TM). In-depth, semi-structured interview was conducted on 18 mothers with more than one β-TM child in two thalassemia treatment centres in Sabah. Thematic analysis was performed by two researchers and comparison of codes and sub-themes were made to verify the themes emerged. The thematic analysis revealed five core themes for reasons of mothers having multiple children with β-TM: 1) intention to have more children and acceptance towards child's condition; 2) lack of understanding about thalassemia inheritance pattern; 3) barriers in prenatal screening; 4) barriers in abortion; and 5) ineffective family planning. Early identification of mothers with intention to have more children should be considered for active counselling. Providing continuous informational and financial support may increase uptake in prenatal screening, and involvement of local religious leaders to disseminate information regarding thalassemia prevention measures may improve effort to reduce thalassemia births in Sabah.

Keywords**:** Thalassemia Major, Qualitative studies, Mothers, Multiple children

Introduction

Thalassemia is an inherited disorder of red blood cells that is highly prevalent in the Middle East, Indian subcontinent, and Southeast Asia countries, including Malaysia (1). The current estimates of carrier rate for common thalassemia types in Malaysia is about 6.8% (2). Records from the 2018 Malaysian Thalassemia Registry showed a total of 7,984 registered thalassemia patients in Malaysia with highest cumulative prevalence in the state of Sabah (22.7%, 1,814 of 7,984). Almost half of the affected individuals in Sabah were from the indigenous ethnic group Kadazandusun (3). The population in Sabah is unique which made up of multi-ethnic indigenous and non-indigenous groups, with the largest ethnic group of Kadazandusun (25%), followed by Bajau (15%), Murut (3%) and other minority ethnics such as Rungus, Sungai, Lundayeh, Kedayan, Brunei, Suluk and others (4).

Despite having the highest thalassemia prevalence in Malaysia, studies exploring the factors that may contribute to this problem are still lacking in Sabah. One study suggested that marital consanguinity among the indigenous population in Sabah may have contributed to the high prevalence of β-thalassemia major (β-TM) in this population (5). However, recent findings showed that only 9.2% among thalassemia patients in Sabah had parents with marital consanguinity (6). Nonetheless, the low proportion of consanguinity reported in the study was likely to be underestimated as data was collected from two centres only (6).

To date, previous studies conducted in Sabah were mostly to characterize the molecular genetics of thalassemia (5, 7-10). Understanding the experiences on preventive measures and identifying the factors that contribute to having multiple thalassemia births in the

affected family is important, and this information will be useful for planning of effective preventive measures to reduce thalassemia births in Sabah. Hence, this study aimed to explore the factors that may contribute to mothers in Sabah having multiple children with β-TM.

Materials and Methods

Research design and sampling

A qualitative approach was adopted to identify the essence of mothers' experiences that may contribute to reasons for having multiple children with β-TM in the family. Purposive sampling was used for the selection of mothers with more than one β-TM child. The initial samples included in the study was 15 and subsequently added until data saturation reached.

Study participants and location

Mothers of β-TM patients attending thalassemia treatment clinic at two hospitals, namely Sabah Women and Children Hospital and Kota Belud Hospital in Sabah were identified from the records and invited to participate in the study. Initial contacts were made through phone calls and participants were provided with details of study purpose, length, time, and place of the interview if agree to participate in the study. The interview was conducted in a private space in the hospitals. On the interview day, written consent was obtained prior to the interview.

Data collection and analysis

In-depth, semi-structured interview lasting between 60 to 75 minutes were conducted with the mothers who agreed to be interview from July 2019 until January 2020. Two researchers conducted the face-to-face interview and referred to key questions to guide the interview progress. The lead researcher started the conversation with mothers by asking their demographic information and then referring to the key questions. To encourage mothers to talk more and explain the situation, further open-ended questions such as "Why?", "Explain more", "Tell more" were asked. The second researcher jot down relevant information for future reference.

The interview questions were adapted from a previous study which focused on parent's experiences and knowledge on preventive measures of thalassemia specifically prenatal screening and abortion (11). Additional key questions related to experiences when first affected child was diagnosed with thalassaemia, experiences when more than one child was diagnosed with thalassemia, knowledge on risk of thalassaemia occurrence, and practice of family planning were also included. The focus areas and key questions used to guide the interview are shown in Table 1.

Table 1: Focus areas and key questions to guide the interview

No.	Focus areas	Key questions
1.	Experiences when first child diagnosed with thalassemia	• How was your experience and feelings when told by the doctor that your child has thalassaemia major?
2.	Experiences when more than one child diagnosed with thalassemia	• How was your experience and feelings about having more than one child with thalassemia major?
3.	Knowledge about occurrence of thalassaemia	• What do you know about the risk of getting a child with thalassemia in your next pregnancy? • What do you understand about 25% risk of getting a child with thalassemia major in each pregnancy? • What do you know about the chance of getting a normal child in your next pregnancy?
4.	Knowledge and experiences about prenatal screening and abortion	• What do you know about prenatal screening? • Have you ever done prenatal screening? • What was your decision after learning the results of your prenatal screening? • Did you know about the option for abortion if thalassaemic foetus is confirmed after prenatal screening? • Have you ever been given option to do abortion? • If you made decision not to do abortion, what was the reason?
5.	Family planning practice	• Do you and your husband practice family planning now? • What contraceptive method do you use?

All interviews were conducted in Malay language and recorded digitally. Each recorded interview was then transcribed and re-read several times to gain a deeper insight into the subject matter. Line-by-line reading, and open coding was performed. Relevant statements related to reasons for having more than one thalassaemic children were extracted from each transcript and coded. Two researchers performed the thematic analysis and comparison of codes and sub-themes were made to validate the emerging themes.

The thematic coding analysis was performed in Malay language and later translated into English for academic purposes.

Results

A total of 24 mothers identified with more than one thalassemia child were invited to participate in the interview. However, only 18 mothers consented to participate in the one-to-one interview. Table 2 shows the characteristics of participants in this study.

Table 2: Participant characteristics

Participants	Age	No. of children	No. of thalassemia carrier children	No. of β-thalassemia major children	Has done BTL	Doing family planning (method used)
Participant 1	37	4	1	3	No	Yes (Injection)
Participant 2	53	3	1	2	Yes	NR
Participant 3	40	6	2	4	Yes	NR
Participant 4	55	5	1	3	No	Yes (IUD)
Participant 5	48	4	0	2	No	Yes (Pill)
Participant 6	34	2	0	2	No	Yes (Pill)
Participant 7	29	5	2	2	No	Yes (Injection)
Participant 8	36	2	0	2	No	Yes (Injection)
Participant 9	46	3	1	2	No	Yes (Natural)
Participant 10	50	6	3	3	Yes	NR
Participant 11	34	3	1	2	Yes	NR
Participant 12	42	6	2	3	No	Yes (Implant)
Participant 13	26	3	1	2	No	Yes (Pill)
Participant 14	39	4	0	3	No	Yes (Natural)
Participant 15	44	12	3	3	No	Yes (Injection)
Participant 16	39	6	1	3	Yes	NR
Participant 17	31	5	1	2	Yes	NR
Participant 18	41	4	2	2	No	Yes (Injection)

BTL – Bilateral tubal ligation; NR – Not relevant

The thematic analysis revealed five core themes for reasons of mothers having multiple children with β-TM; intention to have more children and acceptance towards child's condition, lack of understanding about thalassemia inheritance pattern, barriers in prenatal screening, barriers in abortion, and ineffective family planning.

Theme 1: Intention to have more children and acceptance towards child's condition

Majority mothers in this study expressed the intention to have more children regardless of their thalassemia status as they had already accepted the child's condition. This theme is divided into two sub-themes.

i. Intention to have more children

Several mothers knew their risk of having thalassemia baby in subsequent pregnancies, but intentionally become pregnant again to have more children as they desired to have a normal child or another gender whether a daughter or a son. Some were demanded by family members to have more children.

"After my third child diagnosed with thalassemia, I have intention to add another child because I want a normal child. After the birth of my fourth child, I did family planning for a while but pregnant again. All my children are boys, so I want to have a daughter" – Participant 10, 3 β-TM children.

"After my fourth child was born, I took injection for three years because I do not want another child, but my father-in-law insisted to have a grandson. We live in my in-law's house, so it was a pressure" – Participant 12, 3 β-TM children.

"I have many children because my husband wants many children" – Participant 15, 4 β-TM children.

"I want a healthy child, so I decided I wanted another child" – Participant 16, 3 β-TM children.

ii. Acceptance towards child's condition

Mothers with more than one thalassemia child tend to accept their children's condition and expressed it as the "will of God". They believed that child is a blessing from God and not an inconvenience. They also get used of the child's condition that required extra attention.

"I don't' think it's a burden. I just accept the situation" – Participant 4, 3 β-TM children.

"Child is a blessing. If God give a child with illness, how can we reject. We just accept, be patient" – Participant 6, 2 β-TM children.

"I am used to this situation" – Participant 18, 3 β-TM children.

Theme 2: Lack of understanding about thalassemia inheritance pattern

All mothers in this study did not know about their thalassemia carrier status prior to diagnosis of first affected child. However, after knowing their risk as carrier couples, most still lack the understanding of thalassemia inheritance pattern in each pregnancy and unable to tell the standard information provided to parents regarding risk of thalassemia (25% chance of unaffected baby, 25% chance of β-TM, and 50% chance of thalassemia carrier).

"Even if husband and wife are both carriers, sometimes can have a normal child. The first child can be normal. The second child, if not carrier, can have thalassemia major" – Participant 4, 3 β-TM children.

"It depends, some child can have thalassemia, some will not have" – Participant 5, 2 β-TM children.

Theme 3: Barriers in prenatal screening

This theme reflects the mothers' experiences that hindered them from doing prenatal screening. Although most mothers were aware about the opportunity to do prenatal screening, they described some barriers that hindered them to do prenatal screening at the time during their pregnancies due to cost issue, inaccessibility issue, or lack of information regarding prenatal screening.

i. Cost of prenatal screening

The expensive cost of prenatal screening influenced some mothers' decision to decline prenatal screening. Prior to 2013, prenatal screening facility was not available in Sabah and mothers are required to go Kuala Lumpur for prenatal screening which was perceived as inconvenient. Although prenatal screening was available in Sabah after 2013, some still could not afford the fees.

"I need to go to KL to do the screening. Doctor advised me to do the screening, and I need to be there for a long time. I'm working, I can't take off from work for a long time, so I decided not to go" – Participant 2, 2 β-TM children.

"I didn't do prenatal screening during my second pregnancy because it was not available in Sabah at that time" – Participant 8, 2 β-TM.

"I didn't do the screening because it was expensive" – Participant 3, 4 β-TM children.

"Prenatal screening was available at that time, but I did not have enough money" – Participant 10, 3 β-TM children.

ii. Late access to prenatal screening

Some mothers knew about prenatal screening during their pregnancies and requested the screening, but unable to proceed due to late gestation. One of the mothers stated that she was only able to attend the clinic in the fourth month of her pregnancy and was informed that she could not do prenatal screening due to late gestation. Another mother waited for a long time to get prenatal screening appointment and eventually not able to proceed with the screening due to late gestation.

"I was already four months pregnant, so the doctor said I cannot do the screening. We are no longer allowed to do the screening since my baby was already four months old" – Participant 18, 2 β-TM children.

"I waited for a long time but didn't get call to do the screening. After few months of waiting, I no longer can proceed with the screening because it was too late, so I didn't do the screening" – Participant 15, 4 β-TM children.

iii. Lack of information regarding prenatal screening

With regards to lack of information, some mothers did not know about prenatal screening during their pregnancies.

"I did not know about prenatal screening during my pregnancy" – Participant 11, 2 β-TM children.

"I know about prenatal screening during my last pregnancy, before that I never know" – Participant 15, 4 β-TM children.

Theme 4: Barriers in abortion

This theme revealed mothers' experiences and feelings in declining abortion for the confirmed thalassemia foetus following prenatal screening. Of the two mothers who undergone prenatal screening and found out about their thalassaemic foetus, one declined abortion due to religion prohibition and another declined as she was hoping the child can be cured with bone marrow transplant.

"I made a choice not to proceed with abortion because of religious restriction" – Participant 3, 4 β-TM children.

"I told my husband let's keep this baby, it's okay. I was hoping my fourth child can do successful bone marrow transplant just like my third child" – Participant 14, 3 β-TM children.

Theme 5: Ineffective family planning

i. Unsuitable type of contraceptive method

Issues regarding unsuitable type of contraceptives method were highlighted among mothers who did not wish to have another child after having one child diagnosed with thalassemia. Among the issues were inconsistent in taking oral contraceptive due to forgetfulness and unavailability of injection stock at the clinic which resulted in accidental pregnancies. Another issue was concern regarding the side effects of the oral contraceptive.

"After my second child was born, I took contraceptive pills but accidentally pregnant with my third child. I continue taking pills after my third child was born, but if the clinic run out of stocks, I need to wait for a while or need to buy from the pharmacy myself. I live far from the town, so this was inconvenient. I stop taking the pills and got pregnant with my fourth child. After my fourth child was born, I took depo injections at the clinic every month, but there was one time the clinic run out of stocks. I was given pills for one week…maybe I got accidentally pregnant with my fifth child during this time. I didn't know I was pregnant until five months. Now I continue taking injections at the clinic. If I forgot my appointment, the clinic staff will call me or they will come to my house" – Participant 7, 2 β-TM children.

"After my first child was diagnosed with thalassemia, I took contraceptive pills but did not take it according to the instructions. I was late to the clinic to get new stock when the pills run out, so I accidentally got pregnant" – Participant 8, 2 β-TM children.

"After my second child was born, I took contraceptive pills, but I accidentally got pregnant because I forgot to take the pills" – Participant 9, 2 β-TM children.

"I took contraceptive pill for five years until I gained weight" – Participant 3, 4 β-TM children.

ii. Non-compliance to family planning

Some mothers stated that it was their own choice to stop family planning and this was apparent among mothers that have intention to have more children.

"I did not do family planning after my first child was diagnosed with thalassemia. The clinic staff advised me to take but I choose not to take because I want to have another child" – Participant 11, 2 β-TM children.

"After my first child was diagnosed with thalassemia, I never do family planning until my last pregnancy because I want to be pregnant again, I want a normal daughter" – Participant 16, 3 β-TM children.

"I took contraceptive pills ever since my third child was diagnosed with thalassemia major. After 17 years, I stop taking the pills and pregnant again with my fourth child" – Participant 5, 2 β-TM children.

"After my fourth child was born, I took injections because I do not want another child. I stop the injection after three years because my father-in-law insisted to have a grandson" – Participant 12, 3 β-TM children.

iii. No family planning due to short pregnancy interval

Some mothers revealed they did not have any family planning until after the diagnosis of their first affected child. Six mothers stated that they were pregnant with another child when their first affected child was diagnosed with thalassemia. Hence, they were unable to plan for preventive measures due to short pregnancy interval between their first affected child and the subsequent pregnancy.

"My first child was eight months old when he was first admitted to the hospital and diagnosed with thalassemia. At that time, I was pregnant with my second child" – Participant 7, 2 β-TM children.

"When my first child was diagnosed with thalassemia, I was pregnant with my second child. Their age gap is very close" – Participant 13, 2 β-TM children.

Discussion

Despite the government's effort to reduce thalassemia prevalence in Malaysia, the prevention of thalassemia birth remains a challenge in Sabah seeing that new thalassemia births are still recorded and Sabah consistently reported the highest number of thalassemia births compared to other states (3). Health care workers constantly advised the affected families regarding prevention measures, but this often contradicts with the mothers' desire to have more children. This study identified several reasons that contribute to mothers in Sabah having multiple children with β-TM.

Intention to have more children and acceptance towards child's condition

The intention to have a normal or unaffected child revealed by mothers may have led to conscious decision to have more children despite knowing their risks. This was a unique theme found in Sabah population as no local studies have reported similar perspectives among mothers with thalassaemic children. Hence, when mothers expressed intention to have another child, health care workers should actively counsel mothers regarding reproductive options and undergoing prenatal diagnosis to find out thalassemia status of the foetus to ensure they received adequate information to make decision. Furthermore, a protocol of comprehensive follow up flowchart covering from the preconception, conception phase and to the postpartum phase of mothers with thalassaemic children should be established. This is to ensure standard treatment between all health care facilities given and well understood among the clinicians and others healthcare providers.

In line with previous studies, mothers with thalassaemic children shown acceptance towards their child's condition and believed the child's disease as a "will of God" (12-14). Moreover, with the advancement in iron

chelation therapy that enable thalassemia major patients to survive beyond childhood with good quality of life (15) and the possibility of curative treatment such as haematopoietic stem cell transplant (16), acceptance towards having a child with thalassemia might further increased among mothers.

Lack of understanding about thalassemia inheritance pattern

Lack of understanding about the risks of β-TM as a genetic disease was apparent among mothers in this study. When asked about the chance of getting thalassaemic baby, many could not explain the probability correctly. Other study reported similar findings in which lack of understanding about disease occurrence among mothers led to misinterpretation about thalassemia inheritance pattern, and consequently made decision to proceed with pregnancy despite knowing their risk (18). Inadequate knowledge about occurrence of thalassemia were commonly reported among mothers or parents of thalassaemic children (10, 17-19). Therefore, parental awareness and knowledge about the inheritance pattern is crucial for the prevention of thalassemia major in the family. Higher educational level among mothers has been shown to be correlated with lower number thalassaemic children in the family (25). Hence, continuous informational support should be given to mothers with low educational level to increase their knowledge and understanding about thalassemia risk and its prevention.

Barriers in prenatal screening

Several barriers to prenatal screening were encountered by mothers in this study such as unable to access prenatal screening due to high cost, late access to prenatal screening, and lack of information regarding prenatal screening. In countries such as Pakistan and India, high cost has been reported as one of the reasons for not doing prenatal diagnosis in subsequent pregnancies among mothers of thalassaemic children (21-23). Due to service unavailability in Sabah prior to 2013, the cost of travelling to Kuala Lumpur and its inconvenient was acknowledged as the reason for not doing prenatal screening. However, when the service become available, the affordability of prenatal screening remains a problem as majority mothers in this study belong to families with lower socioeconomic status (6). Fortunately, the local thalassemia society in Sabah has made effort in recent years to provide financial assistance for prenatal screening in hope to increase uptake of prenatal screening among the affected families in Sabah.

In a local study conducted in Johor, inadequate access to counselling and prenatal diagnostic services were identified as contributing factor for birth of thalassaemia major children (24). Previous studies have reported that knowledge regarding prenatal diagnosis among parents of thalassemia children are generally low especially among those with lower education level (25, 26). Therefore, effort should be intensified so that expecting mothers who already had one thalassemia child receive adequate information on methods of thalassemia preventions available, especially on prenatal screening and termination of pregnancy. However, given the limitation of health care providers are facing, giving an effective counselling is the art that is yet to be master by most clinicians.

Barriers in abortion

Religion prohibition and hope for a cure were reasons for declining abortion among mothers who had done prenatal screening in this study. In agreement with previous studies, religious belief was commonly cited reason for declining abortion of affected foetus (13, 27-30). In Malaysia, therapeutic termination of pregnancy is permissible within 120 days of conception. However, the termination criteria for thalassaemic foetus does not fully qualify the prerequisites of the Fatma committee in Malaysia which affected the acceptance of abortion among the local Muslim population. In contrast to other Islamic countries such as Pakistan and Saudi Arabia, termination is permissible for thalassaemic foetus (27).

In a study among thalassaemic parents in Iran, a small proportion of the respondents reported hope for future treatment as a reason for not terminating affected pregnancies (28). Hope for a cure also reported in qualitative studies of parents' experiences of having thalassaemic child (12, 31). Although curative treatment for thalassemia is possible with haematopoietic stem cell transplant, parents need to be made aware that the treatment is associated with complications and required matched donors (32).

Ineffective family planning

Unsuitable type of contraceptive method has led to unplanned pregnancies among several mothers in this study. The most common family planning method used in this study was tubal ligation and injection. Significant association between the type of family planning method used by parents and the number of affected children in the family has been reported in previous study (20). Hence, mothers of thalassaemic children should be regularly counsel at every given opportunity regarding suitable contraceptive method. For mothers with more than one affected child, tubal ligation method should be considered as the best family planning method rather than long term use of contraceptive pills to prevent thalassemia birth. However, in a situation in which tubal ligation is not best fit for the mother, factors such as distance from home to the nearest community health clinics, the availability of the contraceptive medications at the respective community health clinic, the sociodemographic condition, and the education level of the mother plays a major role in deciding which contraceptive methods to be given to ensure a good family planning is achieved.

Among mothers who stop family planning, this was due to their intention to have another child. A study in India

reported the most common reasons for not using contraceptive was intention to have another child (33). Therefore, mothers with intention to have another child should be identified early so they can be encouraged to undergo prenatal screening to prevent birth of thalassaemic child. In addition, mothers should be monitored for adherence to family planning method for successful prevention of thalassemia birth.

Several mothers in this study did not have any planning due to not knowing their risk of having thalassemia child prior to diagnosis of first affected child. After receiving the news about their carrier status, they could not do anything while being pregnant with another child. Similar experiences have been reported in other study where parents could not do anything about contraception as they did not know about their carrier status (34). This highlights the importance of premarital screening so that carriers have early awareness about their carrier status and make better decision when selecting future spouse.

Limitation

The emerged themes in this study were grounded in participants' perspectives, in which every factor developed in study represents the entire experiences, feelings, and intentions of participants based on their descriptions. It is acknowledged that evidence emerged from this study may present a unique experience in the state of Sabah, hence may lack the generalizability of the findings to mothers of thalassaemic children elsewhere. Interpretation bias was a possible limitation in this study. Two researchers independently analysed data for theme development to deal with bias. Codes were compared to prevent missing sub-themes and themes. Lastly, the themes developed was discussed among the researchers and interpretations of data were verified with a representative from the thalassemia community. Recall bias from mothers during the interviews may exist. However, researchers have no control over how each study participant answer the research questions.

Conclusion/Recommendation

In Sabah, where thalassemia is highly prevalent, prevention strategies tailored to the local population is required to reduce the number of thalassemia births. Early identification of mothers with intention to have more children to be considered so that active counselling without directive or coercion can be planned to enable informed decision regarding their reproductive options. Collaboration between health care providers and non-governmental organization to give mothers continuous support in terms of adequate family planning information and financial assistance will strengthen the effort to increase thalassemia knowledge among affected families and to increase uptake of prenatal screening. As religious belief plays important role in mother's decision related to termination of pregnancy, involvement of local religious leaders could aid in dissemination of information regarding thalassemia and its prevention to improve acceptance of abortion.

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Competing interests

The authors declare no competing interests in this study.

Ethical clearance

We obtained approval from the Human Research Ethics Committee of Universiti Sains Malaysia (USM/JEPeM/18010008) and the Medical Research and Ethics Committee Ministry of Health Malaysia (NMRR-18-218-39524).

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