UNIVERSITI PUTRA MALAYSIA

HEALTH-RELATED QUALITY OF LIFE AND ASSOCIATED FACTORS AMONG PATIENTS WITH BETA THALASSEMIA ATTENDING THREE GOVERNMENT HOSPITALS IN SELANGOR, MALAYSIA

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BY

ASAUJI YUSNURYATI BINTI MD YUSOF

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfillment of the Requirements for the Degree of Master in Science

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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirement for the degree of Master in Science

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Chair: Sazlina Shariff Ghazali, MBBS, M. Med Fam. Med.

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Beta thalassemia is the most prevalent of all human genetic disease. In Malaysia, 600,000 carriers of beta thalassemia were reported. Each year, between 150 and 350 babies were born with beta thalassemia which mainly was Malay and Chinese. There were also about 5,600 blood transfusion dependent patients in Malaysia. The aim of the present study was to determine the health related quality of life among patients with beta thalassemia and its associated factors.

A cross-sectional study was conducted among patients with beta thalassemia who attended the Paediatric Clinics, Hospital Tengku Ampuan Rahimah, Hospital Serdang and Hospital Kajang in Selangor, Malaysia. Patients between

the age of eight and 18 years old were invited to participate in the study. Data was collected using a pretested structured questionnaire which included the socio-demographic profile of the participants, medical information and a validated Paediatric Quality of Life Inventory 4.0 (PedsQL version 4.0) which verbal and written consents were obtained from the patients and their parents. Data were analysed using Statistical Package Science System version 16.0 (SPSS version 16.0). A significant level was determined at p value less than 0.05.

The respondents were 70 beta thalassemia patients who fulfilled the inclusion criteria with a response rate of 97.2%. Majority 51 (72.9%) of the respondents were between eight to 12 years old, 52.9% were male and majority 87.1% were Malay. Most of the respondents had three or more siblings (65.7%) and did not have other siblings with beta thalassemia (65.7%). Mostly they were beta thalassemia major (58.6%) with less than 11 years duration of illness (58.6%) and received blood transfusion also desferrioxamine treatment (71.4%).

The lowest scores from all six domains of health related quality of life was school functioning (58.93 ± 17.93). This present study indicated that physical functioning was associated with types of beta thalassemia ($p = 0.005$), types of treatment ($p = 0.001$) and side effects of desferrioxamine treatment ($p = 0.001$). The emotional functioning of this study was significantly associated with age, education level and duration of illness with $p = 0.003$ respectively also the types

of treatment (p = 0.002). The social functioning significantly associated with age (p = 0.014), race (p = 0.011), especially Indian which compared with Malay the p = 0.004 and compared the Indian with Chinese the p = 0.024, other than that were education level (p = 0.014), types of beta thalassemia (p = 0.007), duration of illness (p = 0.001) and types of treatment (p = 0.017) but the school functioning was only significantly associated with frequency of blood transfusion (p = 0.039).

The psychosocial health summary score was associated with age and education level (p = 0.037), duration of illness (p = 0.003) and types of treatment (p = 0.005). Therefore, for the total scale score was significantly associated with age and education level which p value = 0.042 respectively, race (p = 0.030) which the Indian significantly difference with Malay (p = 0.009) and Chinese (p = 0.019), types of beta thalassemia (p = 0.011), duration of illness and side effects of desferrioxamine treatment with p = 0.006 respectively and also the types of treatment (p < 0.001).

Patients with not on any treatments will decrease of 16.47 units (p = 0.018), while those with no side effects of desferrioxamine treatment will increase of 14.60 units (p = 0.004) and every increases frequency of desferrioxamine treatment will increase of 2.30 units (p = 0.004), which were predicted physical functioning. The emotional functioning predictors were patients with not on

any treatments will decrease of 18.87 units ($p = 0.008$) and every increases duration of illness will increase of 1.56 units ($p = 0.009$). Social functioning was predict the increases of age with increase of 1.66 units ($p = 0.005$), patients who were non-Malay with decrease of 16.27 units (0.004) and non beta thalassaemia major with decrease of 9.65 units ($p = 0.014$). Only patients with no side effects of desferrioxamine treatment was predicted by increase of 11.28 units ($p = 0.047$) of school functioning scores. Thefore, the predictors for psychosocial health summary score and total scale score were patients with not on any treatment and increases frequency of blood transfusion with decrease of 29.87 units ($p < 0.001$) and decrease of 1.24 units ($p = 0.023$) of psychosocial health summary score also decrease of 21.16 units ($p < 0.001$) but every increases frequency of blood transfusion will increase of 8.99 units ($p = 0.018$) of total scale score of health related quality of life.

Abstrak Thesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

KESIHATAN BERKAITAN KUALITI KEHIDUPAN DAN FAKTOR - FAKTOR YANG BERKAITAN DENGANNYA DI KALANGAN PESAKIT MENGHIDAP THALASSEMIA BETA YANG HADIR KE TIGA BUAH HOSPITAL KERAJAAN DI NEGERI SELANGOR, MALAYSIA

Oleh

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Beta thalassemia ialah sangat lazim bagi semua penyakit genetik manusia. Di Malaysia, 600,000 pembawa thalassemia beta telah dilaporkan. Setiap tahun, di antara 150 dan 350 bayi yang dilahirkan dengan thalassemia beta iaitu umumnya kaum Melayu dan Cina. Lebih kurang juga seramai 5,600 pesakit yang bergantung kepada transfusi darah di Malaysia. Tujuan kajian ini adalah untuk menentukan kesihatan berkaitan kualiti kehidupan di kalangan pesakit menghidap thalassemia beta dan faktor – faktor yang berkaitan dengannya.

Satu kajian keratan-rentas sedang dijalankan di kalangan pesakit thalassemia beta bagi mereka yang hadir ke Klinik Pediatrik, Hospital Tengku Ampuan Rahimah, Hospital Serdang dan Hospital Kajang di Negeri Selangor, Malaysia.

Pesakit yang berumur di antara lapan hingga 18 tahun telah dijemput untuk menyertai kajian ini. Data telah dikumpul mengunakan soal – selidik bagi pra ujian iaitu termasuk sosio-demografi peserta, maklumat perubatan dan Inventori Kualiti Hidup Pediatrik versi 4.0 (PedsQL versi 4.0) iaitu persetujuan secara lisan dan bertulis diperolehi daripada pesakit dan ibubapa mereka. Data dianalisis mengunakan Pakej Statistik Sistem Sains versi 16.0 (SPSS versi 16.0). Peringkat signifikan telah ditentukan pada nilai p kurang daripada 0.05.

Responden adalah seramai 70 orang pesakit thalassemia beta telah tergolong dalam kriteria yang termasuk dalam kajian ini dengan kadar responden sebanyak 97.2%. Majoriti 51 (72.9%) orang responden telah berumur di antara lapan hingga 12 tahun, 52.9% adalah lelaki dan 87.1% adalah berbangsa Melayu. Kebanyakan responden menpunyai tiga atau lebih adik beradik (65.7%) dan tidak mempunyai adik beradik lain yang menghidap beta thalassemia (65.7%). Kebanyakan mereka adalah menghidapi thalassaemia beta major (58.6%) dengan mempunyai kurang daripada 11 tahun jangka masa penyakit (58.6%) dan menerima transfusi darah dan juga rawatan desferrioxamine (71.4%).

Skor terendah daripada kesemua enam domain kesihatan berkaitan kualiti kehidupan ialah kefungsian persekolahan (58.93 ± 17.93). Kajian ini menunjukkan bahawa kefungsian fizikal telah berhubung dengan jenis thalassemia beta ($p = 0.005$), jenis rawatan ($p = 0.001$) dan kesan sampingan bagi

rawatan desferrioxamine (p = 0.001).

Kefungsian emosi bagi kajian ini telah secara signifikannya berhubungkait dengan umur, peringkat pendidikan dan jangkamasa penyakit dengan p = 0.003 masing – masing, juga jenis rawatan (p = 0.002). Kefungsian social secara signifikannya berhubungkait dengan umur (p = 0.014), bangsa (p = 0.011), terutamanya kaum India, iaitu bila dibandingkan dengan kaum Melayu p = 0.004 dan dibandingkan dengan kaum Cina p = 0.024, selain dari itu, peringkat pendidikan (p = 0.014), jenis thalassemia beta (p = 0.007), jangkamasa penyakit (p = 0.001) dan jenis rawatan (p = 0.017), tetapi kefungsian persekolahan hanya berhubungkait dengan frekuensi transfusi darah (p = 0.039).

Ringkasan skor kesihatan psykososial telah berhubungkait dengan umur dan peringkat pendidikan (p = 0.037), jangkamasa penyakit (p = 0.003) and jenis rawatan (p = 0.005). Oleh itu, untuk jumlah skor skala telah secara signifikannya berhubungkait dengan umur dan peringkat pendidikan (p = 0.042), bangsa (p = 0.030), iaitu kaum Indian secara signifikannya berbeza dengan kaum Melayu (p = 0.009) dan kaum Cina (p = 0.019), jenis thalassemia beta (p = 0.011), jangkamasa penyakit dan kesan sampingan daripada rawatan desferrioxamine dengan p = 0.006 masing - masing dan juga jenis rawatan (p < 0.001).

Pesakit thalassemia beta yang tidak menerima sebarang rawatan akan menurun sebanyak 16.47 unit ($p = 0.018$), sedangkan mereka yang tiada kesan sampingan daripada rawatan desferrioxamine akan meningkat sebanyak 14.60 unit ($p = 0.004$) dan setiap penambahan frekuensi rawatan desferrioxamine akan meningkat sebanyak 2.30 unit ($p = 0.004$), iaitu telah mempredikkan kefungsian fizikal. Prediktor bagi kefungsian emosi adalah pesakit yang tidak menerima sebarang rawatan dengan menurun sebanyak 18.87 unit ($p = 0.008$) dan setiap kenaikan jangkamasa penyakit akan bertambah sebanyak 1.56 unit ($p = 0.009$). Kefungsian social telah mempredikkan umur iaitu dengan setiap penambahan umur akan meningkatkan sebanyak 1.66 unit ($p = 0.005$), manakala pesakit yang bukan berbangsa Melayu akan menurun sebanyak 16.27 unit ($p = 0.004$) dan mereka yang bukan thalassemia beta major akan menurun sebanyak 9.65 unit ($p = 0.014$). Hanya pesakit yang tiada kesan sampingan daripada rawatan desferrioxamine telah dipredikkan dengan kenaikan sebanyak 11.28 unit ($p = 0.047$) bagi skor kefungsian persekolahan. Oleh itu, prediktor untuk ringkasan skor kesihatan psykososial dan jumlah skor skala adalah pesakit yang tidak menerima sebarang rawatan dan kenaikan frekuensi transfusi darah dengan penurunan sebanyak 29.87 unit ($p < 0.001$) dan penurunan sebanyak 1.24 unit ($p = 0.023$), juga menurun sebanyak 21.16 unit ($p < 0.001$) tetapi setiap penambahan frekuensi transfusi darah akan meningkat sebanyak 8.99 unit ($p = 0.018$) untuk jumlah skor skala bagi kesihatan berkaitan kualiti hidup.

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of master. The members of the Supervisory Committee were as follows:

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DECLARATION

I declare that the thesis is my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or at any other institution.

ASAUJI YUSNURYATI BINTI MD. YUSOF

Date: 9 March 2011

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CHAPTER 1

INTRODUCTION

1.1 Background

Thalassemia is a genetic blood disorder which can be fatal if proper treatment is not given. It is characterized by partial or no production of alpha or beta globins chains, which form part of the structure of the haemoglobin in the red blood cells (Weatherall, 1999). Thalassemia is divided into two main groups, which is alpha thalassemia and beta thalassemia; depending whether the defect lies in the synthesis of alpha or beta globins chains, respectively (Weatherall and Clegg, 2001).

In alpha thalassemia syndrome, the defect is in either one, two, three or all four of the alpha globins genes (Higgs and Weatherall, 1993). Deletion of one or two alpha gene is not associated with anaemia, but the individual may have minor haematological changes and this is known as alpha thalassemia trait (Hoffbrand and Pettit, 1993). However, deletion of three and four genes causes HbH disease with enlargement of spleen, and Hb Bart's hydrop foetalis syndrome, which results in stillbirth. (Hoffbrand and Pettit, 1993; Higgs, 1993). The prevalence of alpha thalassaemias in Thailand, Malaysia, Indonesia and the West Africa was

between 20% and 30%, and they were also seen in southern Europe and the Middle East (Hughes-Jones and Wickramasinghe, 1996)

Beta thalassemia can be divided into three types, which are beta thalassemia minor, beta thalassemia intermedia and beta thalassemia major. Beta thalassemia minor is not life threatening on its own, but can affect one's quality of life. It causes mild to moderate anaemia and also often coexists with other diseases such as asthma and mood disorder (Palma-Carlos et al., 2005).

Beta thalassemia intermedia is in between beta thalassemia major and beta thalassemia minor. Affected individual often can lead a normal life, but may need occasional transfusions. This depends on the severity of their anaemia especially during an acute illness or during pregnancy (Maggio et al., 2002). The moderate anaemia will be present in individuals with beta thalassemia intermedia after the age of one or two years (Hughes-Jones and Wickramasinghe, 1996).

Beta thalassemia major is also known as Mediterranean or Cooley's anaemia, which occurs if both parents are carriers of beta thalassemia genes. Beta thalassemia major is usually due to inheritance of two

different mutations which each of its affecting beta globins synthesis (Hoffbrand and Pettit, 1993). Children with beta thalassemia major are characterized by severe anaemia, which usually developed between the second and twelfth months of life (Hughes-Jones and Wickramasinghe, 1996).

Beta thalassemia is a serious public health problem in the Mediterranean region, throughout the Middle East, the Indian subcontinent and South East Asia (Vullo et al., 1995). The thalassemia genes are widespread and it was considered the most prevalent of all human genetic diseases (Honig et al., 2000).

The carrier frequency of beta thalassemia in countries such as the Mediterranean and part of Africa, Middle East, the Indian sub-continent, South–East Asia, Melanesia and Pacific Islands, ranged from 1% to 20% (Weatherall and Clegg 2001). The prevalence of beta thalassemia trait in southern Europe was about 10 to 30%, South-East Asia 5% and Africa 1.5% and is was also frequently seen in the Pakistan and southern China (Hughes-Jones and Wickramasinghe, 1996).

In Malaysia, there are about 600,000 people who are carriers' beta thalassemia. Beta thalassemia occurs mainly in the Malay and Chinese Malaysians (Tam, 2005). The Ministry of Health of Malaysia estimated between 150 and 350 babies are born with thalassemia each year. In addition, there are about 5,600 patients who are blood transfusion dependent beta thalassemia in Malaysia (George et al., 2001).

Health related quality of life is a multidimensional concept that focuses on the impact of the disease and its treatment on the well being of an individual (Clarke et al., 2004). The measures of health related quality of life among beta thalassemia children enables to capture the patient's perspective of the disease and treatment. It also provides information on the patient's perceived need for healthcare and their preferences for treatment methods and disease outcomes (Bowling, 2003).

The measurement of quality of life also provides valuable information about the emotional and social impact of treatment on children especially in situations where there were no differences in the survival rates. The inclusion of quality of life measurement in paediatric research is becoming increasingly valued and mandatory (Abbott et al., 2003). However, reports on the use of health related quality of life measures in

paediatric clinical trials or clinical practice in particular on thalassaemia, are limited (Clarke et al., 2004).

The questions are increasingly raised about the quality of life of children with chronic diseases and efforts to measure a child's quality of life have proved complex but a number of generic and disease-specific measures have been reported (Eiser et al., 2001).

The objections to the inclusion of quality of life measures in trials involved the anticipated increased costs and the extra time needed to gain patient's and parent's consent (Bradlyn et al., 1995). There were some questions concerning the selection of quality of life measures and how best to report findings (Guyatt et al., 1991).

There were several types of measure in quality of life such as generic, disease specific, dimension specific and utility tools. Generic measures can be used across patient populations because it is broadly applicable. Disease specific measures focused on aspects of health that were selected to a specific health problem. Therefore, it has greater potential to be used for the necessary measurement criteria and for outcome measures in clinical research (Fitzpatrick et al., 1998).

Utility measures were used for making comparisons across treatments and health problems for the purposes of economic evaluation, which has preferences for the health status and produce a single index. (Ruta et al., 1999).

Generic measures were designed to provide valuable information for comparing outcomes between sick and healthy populations. It also assesses and compares health status of patients with different diseases. In addition, generic instruments were intended to be applicable to a wide range of health problems.

Generic instrument has been operationalized as a combination of psychological, social and physical measures or as a psychological concept. There are several generic instruments to measure health related quality of life in children such as the Child Behavioural Check List (CBCL), Paediatric Quality of Life Inventory (PedsQL 4.0), How Are You (HAY), Child Health Questionnaire (CHQ) and the TNO-AZL Children Quality of Life (TACQOL) (Breuning et al., 2004).

The other health status instrument measures the presence, absence, severity, frequency, and duration of specific symptoms, impairment, or

disabilities. Some examples were Child Health and Illness Profile (CHIP), Functional Status II (FS II) and Children's Health Sleep Questionnaire (CHSQ) (Riley et al., 2004).

In this present study the PedsQL version 4.0 was found to be most suitable to be used. PedsQL version 4.0 is validated and reliable instrument to be used in children and adolescent (Schwimmer et al., 2003). In addition, it also offers age-specific versions. The PedsQL 4.0 has instruments for ages 2 to 7, to 12, and 13 to 18 to measure the health related quality of life (Varni, 2009).

PedsQL integrated generic and disease specific modules into one measurement system and was described as a generic instrument (Varni et al., 1999). PedsQL 4.0 included further core dimensions such as physical, emotional and social functionings to match those described by World Health Organization (WHO). The success of PedsQL can be seen in its wide use in research and translation into many European and other international languages.

Chronic disease affects the quality of life of patients in their physical functioning, emotional functioning, social functioning and school

functioning (Atika et al., 2006; Shumaker et al., 1995). Patients with beta thalassemia sustain the disease for their whole life. Treatment such as blood transfusion and iron chelation therapy are extremely expensive and very costly. However, these treatments are very important for patients' survival (Weatherall and Clegg, 2001).

Patients receiving adequate transfusion and administration of the chelating agent may grow well and survive into adult life (Oliveri et a.l, 1994). Therefore, without these treatments, children do not live past their teens, and those who do not comply with these treatments may suffer and their quality of life will be affected.

Commonly, burden of illness in beta thalassemia major were related to its treatment; caused by iron-overload complications due to chronic blood transfusion. There were both direct and indirect costs which would affect the patient's physical and social well-being; that would influence their families too. There is a need to improve the management of thalassemia, as many patients with iron-overload complications also have both physical and social limitations and disability (Caro et al., 2002).

1.2 Problem statement

The chronic impact of the beta thalassemia, and high burden of the disease associated with regular treatment and complications due to treatment will increase burden to the patient and their family. Furthermore, burden of the treatment modalities have an impact on their parents,as well as the government, in providing the necessary support of the treatment to all patients, especially those blood transfusion dependent beta thalassemia in Malaysia.

It has been estimated that at least one in twenty Malaysians is a thalassemia carrier (Tam, 2005). The total number of thalassemia carriers was estimated approximately about 600,000 to 1 million people. The Malaysian National Thalassemia Registry reported only 3,650 patients were registered as of May 2008. Those who have not registered may be unaware of this disease. This could result in the increasing number of live birth with beta thalassemia in the future.

In Malaysia, there is limited information on the quality of life among patients with beta thalassemia. A case control study done in a paediatric hospital in Malaysia found the quality of life among children with beta

thalassemia were lower when compared to healthy controls of similar age (Ismail et al., 2006). There were studies that looked into factors influencing quality of life but were focussed on patients receiving desferrioxamine.

Hence, studies that looked into factors influencing quality of life in patients with beta thalassemia in general is not available in Malaysia. Therefore, this study aimed to investigate the health related quality of life of patients with beta thalassemia and its associated factors.

Research questions

1. What is the health related quality of life in beta thalassaemia patients, as measured by the Paediatric Quality of Life Inventory 4.0 (PedsQL version 4.0)?
2. What are the relationships between socio-demographic factors (age, sex, race, education level, number of siblings, number of siblings with beta thalassemia and marital consanguinity) and beta thalassemic patients' health related quality of life?
3. What are the relationships between medical information (type of beta thalassemia, duration of illness, type of treatment, frequency of blood

transfusion and desferrioxamine, compliance of desferrioxamine treatment, side effects of desferrioxamine treatment, complication related to thalassemia and other medical problem) and beta thalassemia patients' health related quality of life?

4. Are socio-demographic factors and medical information significant predictors of health related quality of life?

1.3 Objective

1.3.1 General objective

The aim of this study is to assess the health related quality of life (HRQoL) and its associated factors among patients with beta thalasaemia attending three government hospitals in Selangor 2008.

1.3.2 Specific objectives

1. To determine the health related quality of life of patients with beta thalassemia
2. To determine the socio-demographic characteristics (such as age, sex, race, religion, education level, family monthly income, number of

siblings, number of siblings with beta thalassemia and marital consanguinity).

3. To determine the medical information (such as type of beta thalassemia, duration of illness, type of treatment, frequency of blood transfusion and desferrioxamine, compliance of desferrioxamine treatment, side effects of desferrioxamine treatment, complication related to thalassemia and other medical problem).
4. To determine the association between HRQoL and socio-demographic characteristics.
5. To determine the association between HRQoL and its medical information
6. To determine the predictors of health related quality of life of patients with beta thalassemia

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