

A Clinical Pharmacist-Based Screening for Depression in Children with Transfusion-Dependent Thalassemia in Malaysia

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Abstract

An understanding of the psychosocial problems in pediatric patients with thalassemia is crucial, as depression has been shown to affect their adherence to long-term treatment including iron-chelating agents. This study was conducted to determine the prevalence of depression in children and adolescents with transfusion-dependent thalassemia through screening by a pharmacist in a tertiary care center. Of the 63 participants screened using the Children Depression Inventory (CDI), 19% (n = 12) were identified to have depression. The finding is consistent with those of the previous studies, suggesting that pharmacists could play a role in identifying the depressed patients by using a validated tool, refer them to physicians for clinical diagnosis, and make recommendations to change or modify the treatment if necessary.

Keywords: Adolescent, child, depression, pharmacists, thalassemia

INTRODUCTION

Regular blood transfusion and the use of iron-chelating agents have been the mainstay of supportive treatment in thalassemia.^[1] Nevertheless, the need for lifelong treatment was shown to potentially affect the psychological health and emotional functioning of patients with thalassemia. Over the past 10 years, research in psychosocial aspects of thalassemia has confirmed a considerably high prevalence of depression worldwide, ranging from 11 to 62%.^[2-8] However, only a few of them focused specifically on children and adolescents,^[3,4,7] whose psychosocial problems were commonly underestimated by their parents.^[1]

In Malaysia, most of the patients with thalassemia receive their treatment and long-term medical supervision in public hospitals, which are operated and fully subsidized by the Ministry of Health. Within this context, clinical pharmacists have expanded their role in the management of patients with thalassemia, mainly through ward-based clinical pharmacy services and the Medication Therapy Adherence Clinic. In view of the association between depression and nonadherence to thalassemia treatment,^[8] an understanding of the psychological health, particularly of non-adult patients, is crucial.

Aim of the study

The primary aim of this study was to determine the prevalence of depression in children and adolescents with transfusion-dependent thalassemia through screening by a

pharmacist in a tertiary care center. The investigators also sought to identify the factors contributing to depression, which could be used as guidance to develop appropriate pharmaceutical care plans for patients with thalassemia in the future.

Ethics approval

The study protocol was registered with the National Medical Research Register, Malaysia (NMRR-15-1772-28177) and was approved by the Medical Research Ethics Committee, Malaysia.

MATERIALS AND METHODS

This cross-sectional study was undertaken at a multidisciplinary, tertiary care center in Kedah State,

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Malaysia. The Pediatric Department is the referral center for all district hospitals and health centers in the state, catering to children and adolescents who seek general or specialized medical services.

Patients with transfusion-dependent thalassemia aged between 7 and 17 years, who were under the medical supervision of the Pediatric Department were included. Patients were excluded if they did not understand the Malay language or were diagnosed with depression or cognitive impairment. All patients receiving blood transfusion at the pediatric clinic during February and March 2016 were screened for eligibility. Potential participants and their parents were briefed on the study purposes while waiting for blood transfusion and were required to provide informed consent if they agreed to participate in the study.

Data collection was conducted by a clinical pharmacist stationed at the Pediatric Department. First, the parents were surveyed on the sociodemographics of the participants using a structured questionnaire. The clinical characteristics of the participants along with pertinent laboratory results were then obtained from the medical records and the electronic hospital information system. Subsequently, without assistance from

the parents, the participants were asked to complete the Children Depression Inventory (CDI), a 27-item scale, which was translated into the Malay language and validated for the use of children aged between 7 and 17 years (Cronbach's alpha value = 0.83). Each item was scored 2, 1, or 0 based on the severity of depressive symptoms in the past 2 weeks. A cutoff score of 18 was used to discriminate between the depressed and nondepressed patients (<18, nondepressed; ≥18, depressed).^[9]

Statistical analyses were performed using the Statistical Package for the Social Sciences version 20.0 software (IBM, New York, USA). Categorical variables were expressed as frequencies and percentages, whereas numerical variables were characterized using means and standard deviations (SDs) or medians and interquartile ranges, as appropriate. The associations between each variable and depression were determined by using simple logistic regression analyses, presented as odds ratios (ORs) and 95% confidence intervals (CIs). The backward stepwise multiple logistic regression analysis was then conducted, with all variables showing $P < 0.25$ in the univariable analyses included. The results of all statistical analyses were considered significant if $P < 0.05$.

Table 1: Participants' sociodemographics associated with depression (n = 63)

Variables	Depressed	Nondepressed	Crude OR (95% CI)	P
Age, years, mean (SD)	12.8 (3.4)	12.9 (3.1)	1 (0.8, 1.2)	0.98
Age group, n (%)				
12 or above (adolescent)	7 (17.9)	32 (82.1)	1	0.78
7–11 (children)	5 (20.8)	19 (79.2)	1.2 (0.3, 4.3)	
Gender, n (%)				
Female	3 (11.1)	24 (88.9)	1	0.18
Male	9 (25)	27 (75)	2.7 (0.6, 11)	
Ethnicity, n (%)				
Malay	9 (15.5)	49 (84.5)	1	0.03
Non-Malay	3 (60)	2 (40)	8.2 (1.2, 56)	
Weight, kg, mean (SD)	35.6 (8.2)	34.2 (10.3)	1 (0.9, 1.1)	0.65
Height, cm, mean (SD)	143.7 (11)	142.3 (15.3)	1 (0.9, 1.1)	0.77
Father's educational level, n (%) ^a				
Tertiary (college or university)	0 (0)	8 (100)	–	–
Nontertiary	12 (21.8)	43 (78.2)		
Mother's educational level, n (%)				
Tertiary (college or university)	2 (13.3)	13 (86.7)	1	0.52
Nontertiary	10 (20.8)	38 (79.2)	1.7 (0.3, 8.9)	
Family monthly income, n (%)				
MYR2000 or above	3 (16.7)	15 (83.3)	1	0.76
Below MYR2000	9 (20)	36 (80)	1.3 (0.3, 5.3)	
Number of siblings, mean (SD)	2.7 (1.6)	2.6 (1.5)	1 (0.7, 1.6)	0.87
Number of siblings with transfusion-dependent thalassemia, mean (SD)	0.3 (0.5)	0.7 (0.8)	0.5 (0.2, 1.4)	0.19
Absence from school in the past 6 months, day, median (IQR)	16 (13)	12 (4)	1 (0.9, 1.1)	0.28

CI = confidence interval, MYR = Malaysian Ringgit, OR = odds ratio, SD = standard deviation, IQR = interquartile range. ^aSimple logistic regression analysis was not performed due to the presence of "0" or "1" in one or more subcategories

RESULTS

Of the 66 eligible patients identified, 63 were enrolled in the study (response rate: 95.5%). Two patients, diagnosed with depression and autism, were excluded and one refused to participate in the study. The participants were predominantly Malay (92.1%), male (57.1%), and adolescents (aged 12 years or older; 61.9%). The majority of them had β -thalassemia (95.2%), and the most commonly used iron-chelating agent was deferasirox (87.3%). Twelve (19%) participants were confirmed to have depression, with a mean (SD) CDI score of 23.7 (4.7). The sociodemographics and clinical characteristics associated with depression were shown in Tables 1 and 2, respectively. Four variables showing $P < 0.25$ in the univariable analyses were included in the multiple logistic regression analysis; however, the only ethnicity remained significant, pointing to the higher risk for developing depression in non-

Malay patients (OR, 8.2; 95% CI, 1.2, 56).

DISCUSSION

Although a number of studies have observed the psychosocial aspects of thalassemia,^[2-8] this is the first study, to the investigators' knowledge, suggesting that a validated tool such as the CDI could assist pharmacists in screening for depression among the pediatric patients with thalassemia. Prior to this study, it was challenging for pharmacists to help in enhancing adherence to iron-chelating therapy when depression was an underlying issue.^[8] By effectively identifying the depressive symptoms, pharmacists will be able to quickly refer the patients to physicians and to make recommendations to change or modify the treatment if necessary.

Table 2: Participants' clinical characteristics associated with depression (n = 63)

Variables	Depressed	Nondepressed	Crude OR (95% CI)	P
Type of thalassemia, n (%) ^a				
β -Thalassemia	11 (18.3)	49 (81.7)	–	–
- β -Thalassemia	1 (33.3)	2 (66.7)		
Type of iron-chelating therapy, n (%) ^a				
Desferrioxamine	0 (0)	3 (100)	–	–
Deferiprone	0 (0)	4 (100)		
Deferasirox	11 (21.6)	40 (78.4)		
Desferrioxamine and deferasirox	1 (33.3)	2 (66.7)		
Deferiprone and deferasirox	0 (0)	1 (100)		
The use of parenteral iron-chelating agent (desferrioxamine), n (%) ^a				
Yes	1 (16.7)	5 (83.3)	–	–
No	11 (19.3)	46 (80.7)		
Pretransfusion ferritin level, mg/L, median (IQR)	3044.5 (2593)	3189 (3416)	1 (1, 1)	0.51
Pretransfusion hemoglobin level, g/dL, mean (SD)	9.5 (1)	9.5 (1.1)	1 (0.5, 1.8)	0.95
Age of onset of anemia, years, mean (SD)	2.6 (2.7)	2.1 (1.9)	1.1 (0.8, 1.5)	0.39
Age of starting blood transfusion, years, mean (SD)	3 (2.5)	3 (2.7)	1 (0.8, 1.3)	0.97
Age of starting iron-chelating therapy, years, mean (SD)	6 (2.9)	6.5 (3.6)	1 (0.8, 1.2)	0.63
History of hospitalization in the past 6 months, n (%)				
No	9 (16.4)	46 (83.6)	1	0.17
Yes	3 (37.5)	5 (62.5)	3.1 (0.6, 15.2)	
History of splenectomy, n (%)				
No	8 (16.3)	41 (83.7)	1	0.31
Yes	4 (28.6)	10 (71.4)	2.1 (0.5, 8.2)	
Short stature, n (%)				
No	6 (18.6)	27 (81.8)	1	0.85
Yes	6 (20)	24 (80)	1.1 (0.3, 4)	
Delayed puberty, n (%)				
No	7 (16.7)	35 (83.3)	1	0.5
Yes	5 (23.8)	16 (76.2)	1.6 (0.4, 5.7)	
Diagnosed with diabetes mellitus, n (%) ^a				
No	12 (19.7)	49 (80.3)	–	–
Yes	0 (0)	2 (100)		
Diagnosed with hypothyroidism, n (%) ^a				
No	12 (19.7)	49 (80.3)	–	–
Yes	0 (0)	2 (100)		

CI = confidence interval, Hb = hemoglobin, OR = odds ratio, SD = standard deviation, IQR = interquartile range. ^aSimple logistic regression analysis was not performed due to the presence of "0" or "1" in one or more subcategories.

This study found a 19% prevalence of depression, which is comparable to two previous studies that focused on pediatric patients with thalassemia.^[3,4] However, an Indian study reported a much higher prevalence (63%),^[7] likely attributable to the use of a different instrument. The relatively low prevalence in this study could also be due to the setting selected, which is a fully subsidized, tertiary care center. Specialized medical services along with blood transfusion and medications have been provided free of charge to patients. Therefore, it seems that the high cost of long-term thalassemia treatment did not profoundly affect their psychosocial development, even though the majority of them were from families with low socioeconomic status.

Furthermore, this study found an association between ethnicity and depression, which has not been reported in similar studies.^[3,4,7] Non-Malay patients were shown to have a higher tendency to develop depression compared to Malay patients. Nonetheless, it is noteworthy that the number of non-Malay patients recruited in this study was relatively small. Hence, a larger sample size of this particular subgroup is needed in future research to corroborate the finding.

The generalizability of the findings is primarily limited by the single-center design of this study. However, the data collection was conducted in a tertiary care center, which is a referral center for all the public health facilities in Kedah State, and efforts were made by the investigators to screen all patients with thalassemia presenting to the Pediatric Department for eligibility during the study period. Additionally, depression was assessed using the CDI, which is only a screening tool and may not be able to adequately distinguish between nondepressed and depressed children.^[10] Nevertheless, this instrument has been used in similar studies,^[3] and can still provide a means for pharmacists to reliably identify depressive symptoms in patients prior to clinical diagnosis by physicians.^[9]

CONCLUSION

By using a validated instrument, pharmacists could play a role in screening for underlying depression among children and adolescents with infusion-dependent thalassemia. This study confirms that approximately 20% of the patients presenting to a Malaysian tertiary care center have depression, underlining the importance for healthcare professionals to be aware of their psychosocial problems, which potentially affect their adherence to thalassemia treatment. Future research should evaluate not only the clinical outcomes following interventions made by pharmacists but also other psychosocial aspects of thalassemia, such as anxiety and quality of life, in Malaysia.

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Conflicts of interest

There are no conflicts of interest.

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