

Increased knowledge of thalassemia promotes early carrier status examination among medical students

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ABSTRACT

BACKGROUND

Thalassemia is an autosomal recessive genetic disorder, in which the patient requires life-long blood transfusion. As Indonesia harbors 6 to 10% thalassemia carriers, thalassemia prevention measures such as early screening and education in the community are urgently needed. The aim of this study was to explore the knowledge, attitude and practice about thalassemia among young medical students.

METHODS

A cross-sectional analytic observational study was conducted on 179 subjects in 2015, using a questionnaire with items on knowledge, attitude and practice about thalassemia for data collection. After signing informed consent, the questionnaire was filled in by the students and a blood test was performed when the students agreed to be examined. Detection of probable thalassemia carrier status was done by determination of hemoglobin, mean corpuscular volume and mean corpuscular hemoglobin.

RESULTS

The knowledge about thalassemia of the first year medical students (n=179) was good (21.1%), moderate (70.9%) and poor (21.1%). Only 67 (38.3%) of the students agreed to a blood examination for determination of their carrier status after filling-in the questionnaire. The knowledge of thalassemia among first year medical students was statistically related to the timing when they would agree to have their thalassemia carrier status examined ($p=0.021$, one way ANOVA test).

CONCLUSION

A higher thalassemia knowledge score causes medical students to be willing to undergo thalassemia carrier status examination at an earlier point in timing. A well-organized educational program focusing on thalassemia and early screening in young adults may enhance the thalassemia prevention program.

Keywords: Early detection, knowledge, thalassemia, carrier status, medical students

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Pengetahuan thalassemia yang lebih baik berdampak pada pemeriksaan dini status karir thalassemia mahasiswa kedokteran

ABSTRAK

LATAR BELAKANG

Thalassemia merupakan kelainan autosomal resesif yang penderitanya membutuhkan transfusi darah sepanjang hidupnya. Di Indonesia terdapat 6 sampai 10% penduduk dengan karir thalassemia, sehingga tindakan pencegahan penyakit thalassemia seperti deteksi dini terhadap karir dan edukasi pada masyarakat mengenai beban penyakit thalassemia sangat diperlukan. Tujuan studi ini adalah untuk mendalami pengetahuan, sikap dan perilaku mengenai thalassemia pada mahasiswa kedokteran.

METODA

Penelitian potong lintang studi analitik observasional yang dilakukan pada 179 subjek pada tahun 2015. Kuesioner yang meliputi pertanyaan mengenai pengetahuan, sikap dan perilaku tentang thalassemia digunakan untuk pengumpulan data. Setelah mendatangi surat pernyataan persetujuan penelitian, mahasiswa mengisi kuesioner dan diperiksa darahnya bila berkenan. Deteksi untuk kemungkinan awal status karir thalassemia dilakukan dengan memeriksa nilai hemoglobin (Hb), mean corpuscular volume (MCV) dan mean corpuscular hemoglobin (MCH).

HASIL

Pengetahuan mahasiswa kedokteran tingkat pertama (n=179) mengenai thalassemia dapat dikategorikan baik (21,1%), sedang (70,9%) dan buruk (21,1%). Hanya 67 (38,3%) mahasiswa yang setuju untuk dilakukan pemeriksaan darah dalam menentukan status karir thalassemiannya setelah pengisian kuesioner. Pengetahuan thalassemia diantara mahasiswa fakultas kedokteran ini secara statistik berelasi dengan waktu mereka mau diperiksa status karir thalassemiannya ($p=0,021$, oneway ANOVA test).

KESIMPULAN

Nilai pengetahuan thalassemia yang lebih baik membuat mahasiswa kedokteran melakukan pemeriksaan status karir thalassemiannya lebih awal. Program edukasi yang organisasinya baik dan berfokus kepada thalassemia serta deteksi dini status karir thalassemia pada dewasa muda dapat meningkatkan program pencegahan penyakit thalassemia.

Kata kunci: *Deteksi dini, pengetahuan, status karir thalassemia, mahasiswa kedokteran*

INTRODUCTION

Thalassemia, an autosomal recessive genetic disorder involving hemoglobin (Hb) chain synthesis, is prevalent among populations in Mediterranean, Middle Eastern, South Asian and South East Asian countries.⁽¹⁻⁴⁾ The disease is not curable and the patients require life-long blood transfusion; however, new technologies offer the possibility for bone marrow transplantation.⁽⁵⁾ Due to life-long blood

transfusion, thalassemia patients may have complications of iron overload leading to abnormalities associated with iron deposition in tissues, ultimately resulting in death, thus necessitating iron chelation therapy.⁽⁶⁾ Infants with thalassemia major are born from parents who both harbor heterozygous mutations or are carriers, therefore their probability of having a child with thalassemia is one out of four pregnancies.

There are several tests in the laboratory to diagnose thalassemia carrier status. Early screening for possible thalassemia carrier status does not require special examinations, only routine blood examination for Hb, mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH).⁽⁷⁾ The heterozygous form of thalassemia carrier may manifest in healthy young adults as a low Hb. Since iron deficiency anemia due to dietary foods that are poor in iron accounts for approximately 75% of all anemia types in the developing countries,⁽⁸⁾ healthy young adults with low Hb need to be investigated accordingly. When apparently healthy young adults have low Hb, MCV and MCH, further examinations are necessary, including iron parameters to exclude iron deficiency, and Hb electrophoresis to measure the HbA2 level. A HbA2 value over 3.5% confirms β -thalassemia carrier status and a value less than 3.5% may indicate the presence of iron deficiency, α -thalassemia, or rare forms of β -thalassemia. However, the definitive diagnosis can only be determined following DNA analysis. A combination of Hb analysis and DNA testing seems to be the best way to confirm carrier status in a region with high frequency of thalassemia.⁽⁹⁾

The knowledge about thalassemia in some areas with high thalassemia carrier state varies. Unknown thalassemia carrier status may lead to high prevalence of thalassemia disease. Thalassemia can be prevented by premarital screening for early thalassemia carrier status or by prenatal diagnosis.⁽¹⁰⁾ A pregnancy with an affected fetus can be terminated after the carrier parents opt for the prenatal diagnosis; however, in some religions abortion of a fetus is definitely not an option.⁽¹¹⁾ Young adults from an area with high prevalence of thalassemia are prospective parents, and ideally they should be aware of their carrier status before pregnancy or even before marriage.⁽¹²⁾

Since Indonesia harbors 6 to 10% of thalassemia carriers, early screening and education of young adults and the community is

of interest.⁽¹³⁾ Therefore, early detection of thalassemia carriers in the general population, especially in school students and young adults is encouraged.⁽¹⁴⁾ The aim of the present study was to explore the knowledge and perception of thalassemia among first year medical students and their attitudes towards informed consent for thalassemia carrier testing. These students may be representative of young adults on their attitude towards managing their thalassemia carrier status.

METHODS

Study design

This study was of cross-sectional analytic observational design, and was conducted in March 2015 at the Faculty of Medicine, Universitas Padjadjaran, Bandung.

Research subjects

This was a study exploring the knowledge, attitude and practice of young adults using one questionnaire. Total sampling was used for sample size determination, therefore, all first year medical students were asked to participate. There were no exclusion criteria in this study.

Questionnaire about knowledge, attitude and practice of thalassemia

The questionnaire was comprised of 25 questions and divided into 3 parts. The first part was to explore the knowledge about thalassemia, consisting of 18 questions. In brief, participants were given closed questions with three answers of 'yes, no and don't know'. The answer was checked with the open questions to ensure that the questions were right- or wrong answered. For each question, the correct answer was given a score of one, and the incorrect or "don't know" answer was scored as zero, with a total possible score of 0 to 18. A score of 0-6 indicates poor knowledge, a score of 7-12 indicates moderate and a score of 13-18 good knowledge. Cronbach's alpha was used to assess the reliability of the knowledge scale, with values

of at least 0.7 indicating acceptability of the internal consistency.

The second part of the questionnaire was to assess the attitude toward thalassemia, and consisted of 5 questions. Participants were asked for their agreement on premarital screening, marriage between individuals who are both carriers, pregnancy of carrier couples, and termination of pregnancies with a fetus affected by thalassemia major. In the third part of the questionnaire with 2 questions, the practice or willingness to screen for possible thalassemia status were asked. The questionnaire was adapted and modified from a published article⁽¹¹⁾ and translated into Bahasa Indonesia.

Early screening for possible thalassemia carrier status

Students who had agreed to take part in the screening as stated in the third part of the questionnaire were invited to have their blood examined. Early screening for possible thalassemia carrier status was performed by routine blood examination, using as indicators low Hb or hypochromic anemia (mean corpuscular hemoglobin/MCH<27pg) and microcytic anemia (mean corpuscular MCV<80fl).⁽⁹⁾ The venous blood samples were collected in 3 ml EDTA vacuum tubes by well-trained laboratory technicians (Laboratorium Prodia, Bandung). Anemia was defined according to WHO criteria,⁽⁸⁾ corrected by gender, as a Hb concentration of <12g/dL and <13g/dL, for females and males, respectively. The severity of anemia was classified into three stages: mild (10-11g/dL), moderate (7-10/dL), or severe (Hb<7 g/dL). The laboratory results were distributed to the students in closed envelopes. Students who had probable thalassemia carrier status were counselled individually.

Statistical analyses

Responses to the questionnaire were expressed as percentages. Knowledge was scored and categorized as good, moderate, or poor; and

comparison between genders was analyzed using Pearson chi-square or ANOVA-test where needed. Hematological data were presented and analyzed for probable thalassemia carriers. The description and statistical analyses were conducted using SPSS 16.0 for Windows.

Ethical clearance

Information about the study had been given prior to the filling-in of the questionnaire, both verbally and written in the informed consent form that was signed, ensuring the confidentiality of the study results. The study protocol was approved by the Ethical Committee of the Medical Faculty, Universitas Padjadjaran, Bandung, Indonesia, under no. 715/UN6.C2.1.2/KEPK/PN/2014.

RESULTS

Questionnaires were distributed to 219 first-year medical students, but only 175 (70.9%) students responded and returned the questionnaire. These students consisted of 45 (25.7%) males and 130 (74.3%) females. The mean age of the students was 18.1 years (SD = 0.71), and the age range was from 16 to 21 years. The students identified themselves as Sundanese (n 55; 31.4%) or Javanese (n 47; 26.8%), the two dominant ethnicities on Java.

The reliability of the knowledge scale (Cronbach's alpha) for 18 questions was tested, resulting in high score of 0.86. Therefore, the questionnaire can be used to assess thalassemia knowledge. The data distribution of the knowledge scores among the students was not normal (Shapiro-Wilk score 0.012). The median knowledge score among the students was 9 and thus categorized as moderate knowledge. There was no difference between genders in knowledge about thalassemia (p=0.781, Pearson chi-square) as depicted in Table 1.

When exploring each item of the questionnaire, only 37.7% knew the definition of thalassemia as a disease with low numbers of red blood cells. This was in line with the low

Table 1. Knowledge among subjects about thalassemia and timing of thalassemia carrier status examination by gender

Variable	Gender		P
	Male (n,%)	Female (n,%)	
Knowledge criteria			
Good	3 (21.4)	11 (78.6)	0.871
Moderate	31 (25.0)	93 (75.0)	
Poor	11 (29.7)	26 (70.3)	
Timing of thalassemia status examination			
Directly after 1 month after interviews	18 (26.9)	49 (73.1)	0.582
Later before marriage	17 (24.6)	52 (75.4)	
Later but don't know when	6 (17.6)	28 (82.4)	

Note. Knowledge criteria: good (>12 good answers), moderate (7-12 good answers) and poor (<6 good answers) out of 18 questions. Statistical significance was set at $p < 0.05$ (Pearson chi-square)

number of students who successfully mentioned the types of thalassemia (30.9%) and thalassemia as an autosomal recessive inherited disease (57.1%). Despite their low percentage of general knowledge of thalassemia, most of the students knew that thalassemia was not infectious (93.1%) and required life-long blood transfusion (90.3%). They knew that thalassemia major is not curable (77.1%), but they did not know that iron chelators are needed for the iron overload (92.6%). The students knew that infants born as thalassemia carriers will remain carriers and do not develop into thalassemia major later in life (72.6%), but the majority of the students (81.1%) could not tell about the prevention of thalassemia carriers. Furthermore, they did not know the estimated prevalence rate of thalassemia in Indonesia (100%) and in West Java (97.1%). When stratified by gender, there was no statistically significant difference in all of these answers between female and male students (data not shown).

The majority of the students were of the opinion that premarital screening for thalassemia is necessary (99.4%). Should they know that their partner is also a carrier, they would agree not to marry their partner (77.1%), and that premarital counseling would therefore be necessary (98.9%). Termination of a pregnancy affected with thalassaemia major or abortion of the fetus was agreed to by 62.3%. Among Moslem students, 94 of 151 (62.2%) were for termination. We could not further compare the religious background for

the termination of an affected fetus as the percentage of non-Moslem students was low, with 13 of 17 Protestants and 1 of 5 Roman Catholics being for termination.

When the students were asked whether they would screen for thalassemia carrier status, 2 (1.6%) reported that they had indeed been screened for thalassaemia status, while 3 (1.7%) rejected screening and thought that it was not necessary as no one in the direct family line was affected. The majority of students ($n=170$; 95.6%), who had not been screened for thalassemia carrier status, indicated their willingness to undergo screening, but the timing of screening varied from soon after filling-in the questionnaire ($n=67$; 39.4%), some timing before getting married ($n=69$; 40.6%) to some timing in the future ($n=34$; 20.0%). When the willingness to undergo carrier status examination was compared between male and female students, no statistical difference was found between genders ($p=0.584$, Pearson Chi-square test, Table 1).

The results of further analyses of the knowledge and the timing of thalassemia carrier status examination indicated that the knowledge of these students had a statistically significant association with the timing of thalassemia status screening. Therefore, higher thalassemia knowledge scores signify earlier thalassemia status examination ($p=0.021$, one way ANOVA test) as depicted in Table 2. On post-hoc analysis, there was a significant difference between mean

Table 2. Relation between knowledge and timing of thalassemia carrier status examination among first year medical students in Bandung

Timing of thalassemia status examination	Knowledge score		P
	Mean	SD	
Directly 1 month after questionnaire	9.4	2.8	0.021
Later before marriage	8.5	2.6	
Later but don't know when	7.8	2.3	

Note: Statistical significance was set at $p < 0.05$ (one-way ANOVA)

knowledge scores of individuals who were willing to get their status examined directly after filling-in the questionnaire and mean knowledge scores of individuals who would postpone the examination until a later period in life (Bonferroni $p = 0.025$).

Students above 18 years old were considered to be young adults, but most students stated that they needed their parents' consent before undergoing definitive thalassemia screening (84.6%), and should they finally know that they were carriers, most of them (95.4%) would persuade their siblings and parents to check for their thalassemia status to prevent the disease and decrease the number of thalassemia cases.

One month after filling-in the questionnaire, the students were invited to have their blood examined for probable thalassemia carrier status. We expected that 67 students (Table 1) would come for direct blood examination as stated in the questionnaire. Surprisingly, the participation rate was higher, as there were 87 students who came up for the thalassemia carrier screening.

Laboratory hematology findings showed that 7 female students, corrected by gender according to WHO criteria, were identified as having mild anemia (Hb 10-11 g/dL). On the basis of Hb concentration only, the prevalence of anemia in these apparently healthy first year medical students in Bandung was 8% (7 out of 87 students). Interestingly, some of those who had normal Hb, had low MCV (< 80 fL) and MCH (< 27 pg) (Table 3), so that 24 of 87 students (27.5%) had probable thalassemia carrier status, and therefore needed further examination for determination of definitive thalassemia carrier status.

DISCUSSION

Thalassemia is prevalent in Indonesia,⁽¹³⁾ but studies on knowledge, attitude and practice related to thalassemia are relatively scarce. First year medical students in our medical faculty have lectures about 'Fundamentals of Basic Sciences' including the central dogma of DNA/RNA/

Table 3. Probable thalassemia carrier status among first year medical students in Bandung stratified by gender, according to triple parameters of Hb, MCV and MCH

	Male (n)	Female (n)	Total (n)
Low Hb:			7
Low Hb*only	-	1	1
Low Hb and MCH	-	2	2
Low Hb, MCV and MCH	-	4	4
Normal Hb:			
With low MCV and MCH	2	4	6
With low MCH	2	9	11
TOTAL	4	20	24

Note: * low Hb corrected by gender according to WHO⁽⁸⁾, low MCV < 80 fl, MCH < 27 pg; Hb - Hemoglobin; MCH - mean corpuscular hemoglobin; MCV - mean corpuscular volume. In total there were 24 out of 87 (27.5%) students with probable thalassemia carrier status

protein, and thalassemia is introduced as one of the cases in the problem-based learning program. It is shown that most of the first year medical students (70.9%) have a moderate knowledge about thalassemia after the lecture, but the knowledge of a substantial percentage still remains poor. Although the thalassemia knowledge level among the first year students is moderate, the median knowledge score of 9 out of 18 may reflect a general lack of knowledge among the students. The responses also indicated that specific knowledge on thalassemia was poor, with regard to the existence of different types of thalassemia, the genetic nature of the disease, and its pattern of inheritance. The limitation here is that the questions in the questionnaire may not be very understandable for first year students, therefore, the questionnaire may need further revision.

Owing to the genetic complexity of the disorder, it remains a challenge to educate the young adult. Regular educational efforts are needed to raise awareness of thalassemia in young adults at school and at the university.⁽¹⁴⁾ It is suggested to screen the Hb in young adults so they can become aware of their overall health condition, specifically with the extended MCV and MCH when Hb is low. Genetic counselling for thalassemia needs to be provided alongside with confirmation of the thalassemia carrier status, so the young adult carriers are reassured of their condition.

The awareness of carrier status in the Indonesian community has not yet been explored and this is reflected among the students as they do not know that the prevalence of the carrier status is quite high. In general, studies have shown that the awareness of thalassemia is higher in the higher educational and professional or managerial categories.⁽¹¹⁾ As for our students, this study confirmed that the knowledge is associated with the timing of examination for carrier status, thus, the better the thalassemia knowledge score, the sooner will they have their thalassemia status examined. In some countries, students and young adults have good responses for thalassemia screening.^(4,14) In our study, a very positive attitude

was expressed by the majority of the students toward screening for thalassemia, but what is of concern is that only one-third of the students would come for thalassemia status screening after the lecture, while two-thirds of the students would only want to be screened later in the future. Therefore, the thalassemia carrier screening program for young and unmarried women should be included in the national programs, and this may dramatically reduce the incidence of infants born with thalassemia major. For example, a screening program in Iran resulted in a 70% reduction in the annual birth rate of infants with thalassemia,⁽¹⁵⁾ and interestingly it has been reported from Italy that screening can reduce the number of births of affected infants in the Latium native population to zero.⁽¹⁴⁾ Identification of carriers is also offered early in pregnancy in most developed countries due to high migration rates of populations from high thalassemia prevalence areas to West European countries.⁽¹⁶⁾ Undoubtedly these studies have shown that thalassemia prevention programs including premarital and prenatal screening have been cost-effective in reducing the thalassemia prevalence.⁽¹⁷⁾

One should bear in mind that it is of utmost importance to dispel the misconception about thalassemia carriers, so that this genetic disorder is not stigmatized by society. The general public should be educated on the fairly high prevalence of thalassemia in Indonesia. Health care providers are encouraged to discuss thalassemia as a public health problem and therefore may enhance public awareness to prevent prejudice and discrimination against carriers. At the end of the study, a sharing experience about thalassemia and carriers was given by one of the researchers who is also a carrier. With her personal sharing, communication among the students was experienced as effective. The study by Wong (2011) showed that audio-visual aids and personal experience sharing have been suggested as an effective means for communication and education among young adults.⁽¹⁸⁾ Therefore, efforts to promote screening are of great interest to young adults.

Thalassemia can be prevented by prenatal diagnosis, but selective abortion is not widely accepted by the public. The majority of the first year students in our university were of the opinion that premarital screening for thalassaemia is necessary and when they know that their partner is also a carrier, then they agree not to marry their partner, so that premarital counseling is needed. These findings confirm those of studies that premarital screening is necessary as one of the early screening strategies or genetic counselling,⁽²⁾ and this can have an impact on families with thalassemia major. Early screening in the extended family is also very important, especially where resources and budgets for screening are limited.⁽¹⁹⁾ Undoubtedly public education in the community regarding thalassemia can impact on the prevalence of thalassemia and can direct the policy in the population.⁽¹⁴⁾

Religion has a significant impact on the decision for screening and may also be associated with refusal for prenatal diagnosis and termination of an affected fetus.⁽¹¹⁾ In Indonesian law, an abortion is only permitted if the pregnancy is likely to result in danger to the mother's physical and mental health.⁽²⁰⁾ We did not analyze this issue further since the religious issue is sensitive in the society. Given diversity in attitudes toward termination of a fetus in different religions, thalassemia prevention programs should consider the beliefs and preferences of individuals in the multiethnic society. When thalassemia prevention is offered to the population through carrier screening and premarital or prenatal diagnosis, then socio-economic, cultural and religious factors must be carefully taken into account.⁽¹¹⁾

This study has several limitations. This current study limits in-depth exploration of the reasons for delaying thalassemia carrier screening. Further investigations in future qualitative studies may be of great benefit to explore the reason for this delay. Although the questionnaire was adapted from a published article,⁽¹¹⁾ the translated questionnaire has not yet been validated. The small numbers of participants are not representative of first year medical students in Indonesia *per se*,

thus larger numbers from various regions in Indonesia are needed to represent the general thalassemia knowledge of young adults from differing ethnic groups and religions in Indonesia.

Despite the limitations of this study, there was a good response rate for the willingness to undergo laboratory screening. Our study has increased awareness of thalassemia among these young adults and their education needs to be enhanced. Carrier status screening at an early age in school and premarital screening programs aimed at identifying individuals before marriage has been proven to be effective and culturally acceptable when compared to prenatal diagnosis. The implication of this study is to increase the knowledge of young adults, especially first year medical students. It is therefore recommended that young first year medical students as future health care professionals need to have good knowledge for this disease, and in turn they can give better education in thalassemia prevention to the next generation.

CONCLUSIONS


This study has identified that thalassemia is not well known among our young adults. A higher thalassemia knowledge score causes medical students to be willing to undergo thalassemia carrier status examination at an earlier point in timing. The results of this study warrant further evidence-based surveys on a larger scale to validate these findings and to eventually set a well-organized educational program targeting young adult awareness of thalassemia and the complications of thalassemia therapy.

CONFLICT OF INTEREST

The authors had no conflict of interest to declare.

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