Original Article

Prevalence of Thalassemia Traits in People without Anemia or Microcytosis

Somchai Insiripong, Watcharin Yingsitsiri, Juree Boondumrongsagul and Jirawadee Noiwatanakul

Hematology Unit, Department of Medicine, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima 30000

Introduction: *The mean corpuscular volume (MCV) lower than 80 fL is always used as one clue for screening thalassemia/hemoglobinopathy.* ***Objective:*** *To survey the alpha-thalassemia-1, beta-thalassemia and hemoglobinopathy in the individuals who have normal hemoglobin (Hb) concentration and normal MCV.* ***Materials and Methods:*** *The participants with normal Hb level and normal MCV randomly selected from the physically normal people are investigated for Hb typing and PCR for alpha-thalassemia-1 genotyping.* ***Results:*** *From 152 participants, there are no alpha-thalassemia-1 trait (SEA and Thai types), 24 Hb E traits (15.8 %), 3 Hb Constant-Spring traits (2.0%) and 1 beta thalassemia trait (0.6%)* ***Conclusion:*** *The alpha-thalassemia-1 can be excluded in people with normal Hb concentration and normal MCV.*

Keywords : ● *Thalassemia traits* ● *Mean corpuscular volume* ● *Prevalence*

J Hematol Transfus Med 2014;24:25-9.

Introduction

Thalassemia is a group of genetic disorders resulting in the decreased production of globin chains, alpha or beta, leading to the decreased production of hemoglobin (Hb). For the heterozygous state, it can be recognized by the microcytosis of its red blood cell or the decreased mean corpuscular volume (MCV) of less than 80 fL. For alpha-thalassemia-1 or alpha(0)-thalassemia traits, they have slightly low or normal Hb level (Hb 10.3 ± 1.9 g/dL) with mild hypochromia (MCH 25.9 ± 2.1 pg) and microcytosis (MCV 69.2 ± 4.0 fL)[1,2] whereas in beta-thalassemia traits[3], only two of 450 beta-thalassemic patients have the MCV ≥78 fL. Therefore the MCV < 80 fL may be used as the cut point for screening alpha-thalassemia-1 and beta-thalassemia traits with the sensitivity, specificity, the positive predictive value (PPV) and the negative predictive values (NPV) of 92.9%, 83.9%, 37.9% and 99.1%, respectively[4].

When the MCV less than 78.1 fL is used to screen for alpha-thalassemia-1 and beta thalassemia, it cannot detect all cases because its sensitivity and specificity are demonstrated to be 93.0% and 93.4%, respectively[5]. In addition, the MCV of beta thalassemia traits is shown to range from 56.3 to 87.3 fL which overlaps that of the normal people[6]. Moreover, the MCH < 27 pg is demonstrated to have more sensitivity (98.5%) than the MCV < 80 fL (97.6%) for screening beta-thalassemia[7].

Because, the various thalassemias and hemoglobinopathies are strikingly prevalent in Thailand (the prevalence 61.1[8] - 62.2%[9]), just only few percentages of thalassemia or hemoglobonopathy which are possibly unrecognized by any screening method can become a serious problem, this paper

Received 4 December 2556 Accepted 15 February 2557

Requests for reprints should be addressed to Somchai Insiripong, Hematology Unit, Department of Medicine, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima 30000

e-mail: chaikorat@gmail.com

is aimed to find whether there is any thalassemia/hemoglobinopathy in the individuals who have normal Hb level and the MCV > 80 fL, the usual cut-point for generally screening thalassemia/hemoglobinopathy.

Materials and Methods

The participants were the healthy individuals who yearly came for check-up at the OPD of medicine, Maharat Nakhon Ratchasima Hospital. CBC was performed using Coulter® "LH-750" automate hematology analyzer, and other tests including creatinine, liver function test, FBS, lipid profile, chest film and urinalysis were performed and all results were within the normal limits.

The individuals who had the normal hemoglobin (Hb) concentration, ≥ 12 g/dL for females and ≥ 13 g/dL for males, and the normal MCV (> 80 fL), were randomly selected for further investigation: Hb typing using the high performance liquid chromatography method, VARIANT Hemoglobin Testing System II Bio-Rad®, for screening Hb E and beta thalassemia trait (if Hb A_2 > 4.0%) and the polymerase chain reaction (PCR) method for detecting the common alpha-thalassemia-1 genotypes among Thais, viz. Southeast Asian (SEA) and Thai deletion types, using the real time PCR-HRM protocol, DNA dye SYTO9 included in the reaction mixture. The assays were carried out on the Bio-Rad CFX96 Real Time System® platform using the precision melting software. The positive and negative controls would be included in each time of analysis.

The pregnant women and the participants who received blood transfusion within 4 months were excluded from the study. All participants were 20 years old or older.

The sample size could be calculated according to the formula: $N = Z^2.pq/d^2$, Z = 1.96, d = 0.05. The percentage of thalassemia/hemoglobinopathy who had normal Hb level and normal MCV = 10%[10], p = 0.1, q = 0.9, thus N = 138.2, approximate 150.

Results

There were 152 participants consisting of 74 males and 78 females. Their ages ranged from 20 to 83, mean 47.1 ± 11.5 years. The means ± SD of Hb concentration were 13.4 ± 1.1 g/dL for females and 14.0 ± 0.5 g/dL for males, the means ± SD of MCV were 86.7 ± 5.1 fL for females and 89.4 ± 7.5 fL for males. The means of MCH ± SD and of RDW ± SD of both sexes were 29.8 ± 2.6 pg and 15.3 ± 1.9%, respectively.

Of 152 participants, no one was found to be the alpha-thalassemia-1 trait but 28 of them carried some kinds of thalassemias and hemoglobinopathies (18.4%) that consisted of 24 Hb E traits (15.8%), 3 Hb Constant-Spring traits (2.0%) and 1 beta thalassemia trait (0.6%) whose Hb typing was found to be: Hb A_2A, Hb A_2 4.2%).

When the participants with thalassemia or hemoglobinopathies were classified according to genders, there were 16 females, consisting of 13 Hb E traits, 2 Hb CS traits and one beta-thalassemia trait, and 12 males, consisting of 11 Hb E traits, and 1 Hb CS trait.

Discussion

Among 152 participants with normal Hb level and normal MCV, there are 24 Hb E traits (15.8%), 3 Hb Constant-Spring traits (2.0%) and 1 beta thalassemia trait. The Hb E trait is very common in our study because of various factors, 1) the high prevalence of Hb E trait itself in Nakhon Ratchasima Province, ie., prevalence of Hb E trait, Hb E disease, alpha-thalassemia-1 trait and beta-thalassemia are 37.5%, 8.0%, 4.8% and 2.9%, respectively[11]. 2) The Hb concentration and the MCV of Hb E trait are 12.8 ± 1.5 g/dL and 84 ± 5 fL, respectively which mostly overlap the ranges of normal people[12]. And 3) around 9.4% of Thai people who have MCV of 80-90 fL are found to be Hb E trait[13].

Likewise Hb CS traits, its Hb concentration and the MCV are found to be 12.9 ± 1.4 g/dL and 88 ± 4 fL, respectively which also overlap the range of Hb concentration and MCV of normal people[14].

In addition, Liao et al demonstrate that 1.3% of beta thalassemia traits have MCV > 80 fL and all of them have the same abnormal beta globin genotype[15]. Moreover, Chan et al recommend that it is worth investigating the thalassemia and hemoglobinopathy in cases having the MCV of 80-85 fL especially if they are the spouse of thalassemia or hemoglobinopathy trait because they found 31 cases with deletion of one alpha globin genes, 1 Hb CS trait and 3 Hb E traits from 95 samples despite normal MCV[10]. Likewise, Insiripong et al also show that 10% of the patients with thalassemias / hemoglobinopathies can have the normal Hb level and normal MCV (> 80 fL), these consist of Hb E trait 88.5%, Hb CS trait 7.7%, beta-thalassemia/Hb E disease 1.9%, double heterozygote of Hb E and CS 0.9% and beta thalassemia trait 0.9%[16].

We do not find the alpha-thalassemia-1 heterozygosity despite the high prevalence of alpha-thalassemia in the whole country of Thailand, 2.7[17]-13.9%[18], and this conforms the study of Konblit, et al that none of 117 cases of alpha(0)-thalassemia traits has low MCV although there used to be the report of two Chinese people who carried alpha(0)-thalassemia (SEA type) heterozygosity in spite of having the normal RBC indices, MCV > 80 fL and MCH > 27 pg[19].

Conclusion

The alpha-thalassemia-1 heterozygosity can be excluded in the participants who have the normal Hb level and MCV > 80 fL.

References

1. *Schrier SL. Pathophysiology of alpha thalassemia. In: UpTo-Date, Basow DS(Ed), UpToDate, Waltham, MA, 2008.*
2. *Syed Riaz Mehdi, Badr Abdullah Al Dahmash. A comparative study of hematological parameters of α and β thalassemias in a high prevalence zone: Saudi Arabia. Indian J Hum Genet 2011;17:207–11.*
3. *Kornblit B, Hagve TA, Taaning P, Birgens H. Phenotypic presentation and underlying mutations in carriers of beta-thalassaemia and alpha-thalassaemia in the Danish immigrant population. Scand J Clin Lab Invest 2007;67:97-104.*
4. *Sirichotiyakul S, Maneerat J, Sanguansermsri T, Dhananjaya-nonda P, Tongsong T. Sensitivity and specificity of mean corpuscular volume testing for screening for alpha-thalassemia-1 and beta-thalassemia traits. J Obstet Gynaecol Res 2005;31:198-201.*
5. *Sirichotiyakul S, Wanapirak C, Srisupundit K, Luewan S, Tongsong T. A comparison of the accuracy of the corpuscular fragility and mean corpuscular volume tests for the alpha-thalassemia 1 and beta-thalassemia traits. Int J Gynaecol Obstet 2009;107:26-9.*
6. *Rund D, Filon D, Strauss N, Rachmilewitz EA, Oppenheim A. Mean corpuscular volume of heterozygotes for beta-thalassemia correlates with the severity of mutations. Blood 1992;79:238-43.*
7. *Karimi M, Rasekhi AR. Efficiency of premarital screening of beta-thalassemia trait using MCH rather than MCV in the population of Fars Province, Iran. Haematologia (Budap) 2002;32:129-33.*
8. *Panomai N, Sanchaisuriya K, Yamsri S, et al. Thalassemia and iron deficiency in a group of northeast Thai school children: relationship to the occurrence of anemia. Eur J Pediatr 2010; 169:1317-22.*
9. *Pansuwan A, Fucharoen G, Fucharoen S, Himakhun B, Dangwiboon S. Anemia, iron deficiency and thalassemia among adolescents in Northeast Thailand: results from two independent surveys. Acta Haematol 2011;125:186-92.*
10. *Insiripong S, Yingsitsiri W, Boondumrongsagoon J. Thalassemia and hemoglobinopathy despite normal level of hemoglobin concentration and normal mean corpuscular volume. Bull Department Med Service 2012;37;215-21.*
11. *Tienthavorn V, Pattanapongsthorn J, Charoensak S, Sae-Tung R, Charoenkwan P, Sanguansermsri T. Prevalence of thalassemia carriers in Thailand. Thai J Hematol Transf Med 2006;16:307-12.*
12. *Vichinsky E. Hemoglobin E syndromes. Hematology. Am Soc Hematol Educ 2007:79-83.*
13. *Pattoom P. The study of mean corpuscular volume for differentiation of hemoglobin E carrier from normal. J Med Tech Assoc Thailand 2012;40:1-8.*

14. *Fucharoen S, Thonglairuam V, Winichagoon P. Hematologic change in alpha-thalassemia. Am J Clin Pathol 1988;89:193-6.*
15. *Liao C, Xie XM, Zhong HZ, Zhou JY, Li DZ. Proposed screening criteria for beta-thalassemia trait during early pregnancy in southern China. Hemoglobin 2009;33:528-33.*
16. *Chan LC, Ma SK, Chan AYY, et al. Should we screen for globin gene mutations in blood samples with mean corpuscular volume (MCV) greater than 80 fL in areas with a high prevalence of thalassaemia? J Clin Pathol 2001;54:317-320*
17. *Nillakupt K, Nathalang O, Arnutti P, et al. Prevalence and hematological parameters of thalassemia in Tha Kradarn subdistrict Chachoengsao Province, Thailand. J Med Assoc Thai 2012;95(Suppl 5):S124-32.*
18. *Lemmens-Zygulska M, Eigel A, Helbig B, Sanguansermsri T, Horst J, Flatz G. Prevalence of α-thalassemias in northern Thailand. Hum Genet 1996;98:345-7.*
19. *Liao C, Li DZ. α^0-Thalassemia trait with normal red cell indices: a report of two cases. Hemoglobin 2012;36:589-91.*

ความชุกของธาลัสซีเมียแฝงในผู้ที่ไม่มีภาวะโลหิตจาง และขนาดเม็ดเลือดไม่เล็ก

สมชาย อินทรศิริพงษ์ วัชรินทร์ ยิ่งสิทธิ์สิริ จุรี บุญดำรงสกลุ และ จิราวดี น้อยวัฒนกุล

หน่วยโลหิตวิทยา กลุ่มงานอายุรกรรม โรงพยาบาลมหาราชนครราชสีมา นครราชสีมา 30000

บทนำ *ค่าขนาดเม็ดเลือดแดงเฉลี่ยที่น้อยกว่า 80 เฟมโตลิตร มักใช้เป็นค่าหนึ่งในการคัดกรองธาลัสซีเมีย / ฮีโมโกลบินผิดปกติ* ***วัตถุประสงค์*** *สำรวจหา แอลฟ่า-ธาลัสซีเมีย-1 เบต้า-ธาลัสซีเมีย และ ฮีโมโกลบินผิดปกติแฝง ในกลุ่มผู้ที่มีค่าความเข้มข้นเลือดปกติ และค่า MCV ก็ปกติ* ***วัสดุและวิธีการ*** *เป็นการศึกษาแบบตัดขวางด้วยวิธีตรวจปฏิกิริยาลูกโซ่โพลีเมอเรสสำหรับ แอลฟ่า-ธาลัสซีเมีย-1 แฝง และวิธีตรวจชนิดของฮีโมโกลบินเพื่อหา เบต้า-ธาลัสซีเมีย และ ฮีโมโกลบินผิดปกติแฝง ในผู้ที่มีความเข้มข้นเลือดปกติ ขนาดเม็ดเลือดเฉลี่ยปกติ โดยสุ่มจากคนปกติที่มาตรวจร่างกายประจำปี* ***ผลการศึกษา*** *จากตัวอย่าง 152 ราย ไม่พบว่ามี แอลฟ่า-ธาลัสซีเมีย-1 แฝงเลย มี ฮีโมโกลบินอีแฝง 24 ราย (ร้อยละ 15.8) ฮีโมโกลบินคอนสแตนต์สปริง 3 ราย (ร้อยละ 2) และ เบต้า-ธาลัสซีเมียแฝง 1 ราย (ร้อยละ 0.6)* ***สรุป*** *ไม่พบผู้ที่มี แอลฟ่า-ธาลัสซีเมีย-1 ในกลุ่มประชากรที่ความเข้มข้นเลือดปกติ และขนาดเม็ดเลือดแดงเฉลี่ยปกติ*

Keywords : ● *Thalassemia traits* ● *Mean corpuscular volume* ● *Prevalence*

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต 2557;24:25-9.