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Hemoglobin Constant Spring is markedly high in women of an ethnic minority group in Vietnam: A community-based survey and hematologic features

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ABSTRACT

A community-based survey was conducted to determine the prevalence and gene frequency of Hemoglobin Constant Spring (Hb CS) and other forms of thalassemia among an ethnic minority in Vietnam. A total of 298 ethnic minority women, the Có-Tu, participated. Hematological parameters and hemoglobin profiles were analyzed using standard automated analyzers. Alpha- and beta-thalassemia mutations were identified using polymerase chain reaction (PCR) based technology. Of the 298 women, 141 (47.3%) carried thalassemia genes. Hemoglobin Constant Spring (Hb CS) is the most common with a markedly high frequency of 0.143 (overall prevalence = 26.2%). The heterozygous state of Hb CS was found in one-fifth (20.5%) of women participating. Seven women (2.4%) were Hb CS homozygote. The overall prevalence for Hb E was 13.8%, and 10.7% for α^{+}-thalassemia. Other forms of thalassemia included 0.67% β-thalassemia, and 0.34% Hb Paksé. None of the participants had the α^{0}-thalassemia gene. The study provides basic epidemiological information about Hb CS as well as other forms of thalassemia for a specific group of an ethnic minority in Vietnam. The data will be useful for further study on the distribution of thalassemia in Southeast Asia.

Introduction

Hemoglobin Constant Spring (Hb CS) is α-chain structural hemoglobin variant caused by a C–T substitution at the termination codon of the α_2-globin gene. As a consequence, an elongated and unstable α-globin chain is produced with a low rate. The Hb CS molecule in peripheral blood is also unstable and is presented at a very small amount, especially in the heterozygous state [1,2]. Although heterozygous Hb CS individuals usually have no clinical symptoms, interaction of Hb CS with α^{0}-thalassemia (α^{0}-thal) can cause Hb H disease with varying degrees of severity. The homozygous state of Hb CS may lead to mild to moderate hemolytic anemia [2]. Affected families require proper genetic counseling and care.

Hb CS can be found in many regions including the Middle East, the Mediterranean, Southeast Asia, and Southern China [2–4]. In Southeast Asia, it is particularly common in northeastern-Thai and Lao populations [5,6]. In northeast Thailand, a high frequency of Hb CS of 10% has been reported [7–9]. In Lao PDR, the prevalence of approximately 5–6% has been obtained from pregnant women living in the Vientiane capital city [9,10]. For other SEA countries including Vietnam, accurate data about the Hb CS frequency is limited.

In Vietnam, prevalence data on thalassemia and hemoglobinopathies from two community-based surveys have been reported, one from the southern part and the other one from the central region of the country. A study conducted in southern Vietnam showed a remarkable variation in the gene frequency of thalassemia and hemoglobinopathies among ethnic minorities [11]. A more recent study conducted in central Vietnam revealed an unexpectedly high proportion of Hb CS at 25% together with other forms of thalassemia and hemoglobinopathies when investigating a group of pregnant women derived from ethnic minorities [12].

To verify the findings mentioned above a further community-based survey for thalassemia and hemoglobinopathies among the Có-Tu minorities living in central Vietnam was undertaken and the results are reported here.

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Materials and methods

Population and samples

A community-based survey was conducted in the Nam Dong mountainous district, located 60 km westwards of the provincial capital of Hue city, Thua Thien Hue province in the North Central Coast region of Vietnam. Based on the World Malaria Report 2012, the distribution of confirmed malaria cases in this area ranged from 1.0 to 10.0 per 1000 population [13].

The total population of Nam Dong district is estimated to be 24,000 individuals. About 45% of the population belongs to an ethnic minority group, predominantly the Có-Tu ethnic minority. According to a report from the Department of Population and Family Planning, Thua Thien Hue Health Service (personal communication), the frequency of consanguineous marriages in 2012 was approximately 2.0%. The Có-Tu ethnic minority lives in five communes where the total population of Có-Tu reproductive age women is 2271. The sample size was calculated according to proportion estimation in the known population. The catchment areas and the number of subjects recruited from each commune are shown in Fig. 1.

A total of 298 unrelated Có-Tu ethnic women were randomly recruited. Demographic data including ethnicity and blood specimens were collected by local health staff. All women were healthy based on a physical examination and anthropometric measurement. All participants were informed about the objective of this project. Consent was received before data collection. After receiving consent, 3 ml of venous blood was drawn from each individual and stored at 2–8 °C before being transferred to the Hue Central Hospital where the measurement of red blood cell indices was done. A fraction of each blood sample was kept cold and transported to the Centre for Research and Development of Medical Diagnostic Laboratories (CMDL), Khon Kaen University, Thailand, where thalassemia and hemoglobinopathies were diagnosed.

The study protocol was approved by the Scientific Committee of Hue College of Medicine and Pharmacy, Vietnam and the Ethics Committee of Khon Kaen University, Thailand.

Laboratory methods

Red blood cell indices were measured by the KX-21 Sysmex automated blood cell counter (Sysmex Co., Kobe, Japan). Hb-type was initially identified by cellulose acetate electrophoresis (CAE) at alkaline pH (Helena Laboratories, Texas, USA.). Individuals with normal Hb-type with MCV < 80 fl and/or MCH < 27 pg as well as those suspected for Hb CS, i.e. the presence of the slow moving band on the CAE strip, were investigated further using an automated capillary zone electrophoresis (Sebia, Leisse, France). Beta-thalassemia was diagnosed in cases with Hb A_2 level greater 4% [14]. The accuracy and precision of all automated determinations were monitored using quality control products provided by the manufacturers.

DNA analysis for α-thal was carried out for all samples. The investigations included α^0-thal (SEA and THAI deletion), α^+-thal (3.7 and 4.2 kb deletions), α^{CS} and $\alpha^{Paksé}$. The PCR-based technology described previously was used for the DNA analysis [15–17].

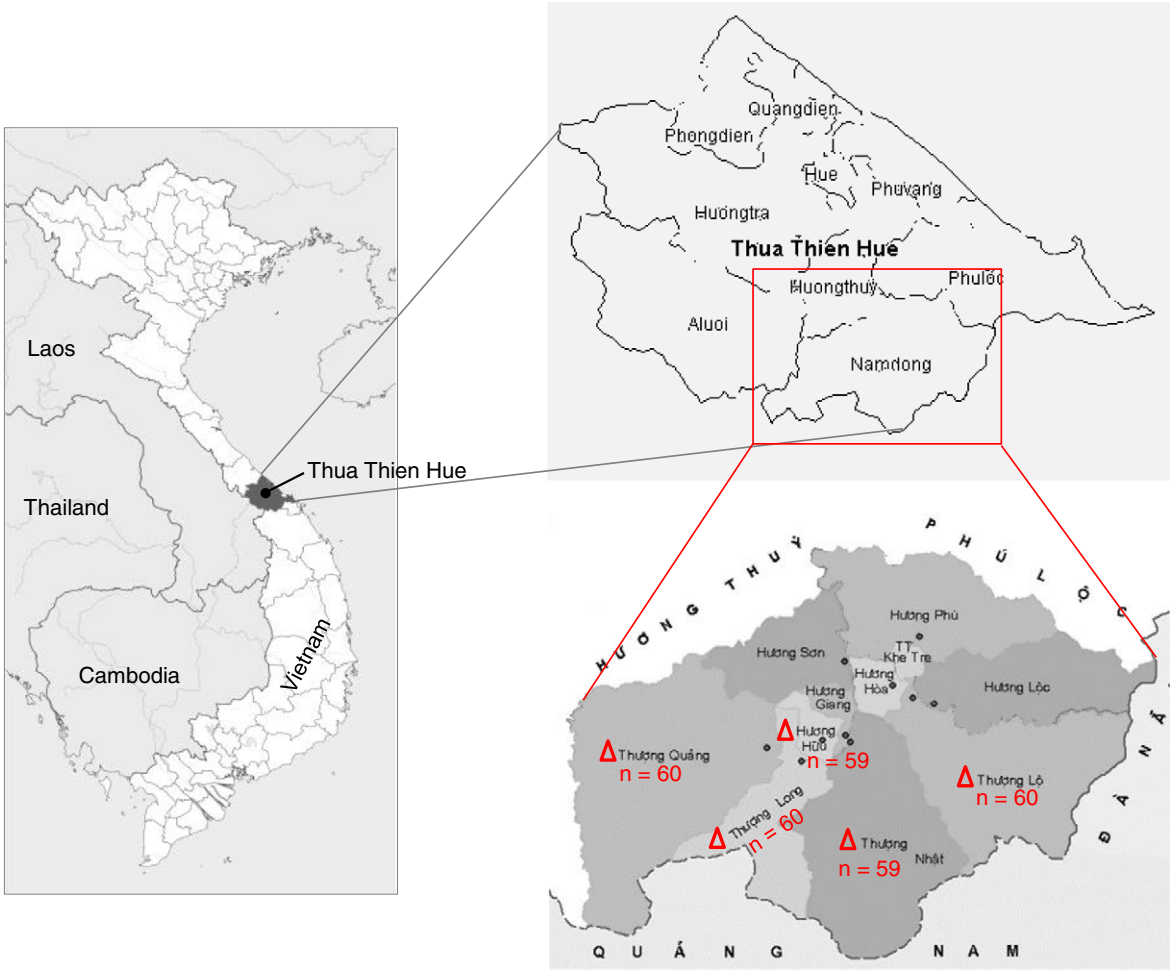

Fig. 1. Catchment areas in Nam Dong district, Thua Thien Hue, Vietnam. Open triangles represent 5 communes where the Có-Tu ethnic minority lives; "n" indicates the number of subjects recruited from each commune.