A Community-Based Thalassemia Prevention and Control Model in Northern Thailand

BOONCHIAN PANSATIANKUL, MD*,
SUPACHAI SAISORN, MD**

Abstract

Objective : To describe a community-based model for prevention and control of thalassemias and haemoglobinopathies in northern Thailand.

Design : Operational research composed of two components. First, a model to test whether thalassemic cases and carriers could be retrospectively detected from school children. Second, a model for prevention of prospective cases of thalassemic babies among pregnant women.

Setting : Phan District of Chiang Rai Province in northern Thailand.

Subjects : ***Component one*** **:** 5,617 preschool children and 21,123 school children were screened during May and July 1997. ***Component two*** **:** 256 pregnant women, 16 weeks or less gestation were screened during January and December 1997.

Material and Method : ***Component one*** **:** Sub-district public health officers and school teachers were trained to use pictures and simple clinical examination to detect suspected thalassemics among preschool and school children. Suspected cases were then referred for further clinical examination and blood testing. Blood smear examination was done at the Phan Community Hospital but Hb typing lusing on electrophoresis was done at the provincial hospital. The cellulose acetate was sent for re-reading at the Department of Medical Sciences. ***Component two*** **:** Osmotic fragility (OF) and dichlorophenol-indolephenol (DCIP) tests were abol in pregnant women ($\leq$ 16 weeks of gestation) in the Phan Community Hospital. If OF test was positive, Hb typing was done at a regional medical sciences center. Their spouses were also located and tested for Hb typing. Prenatal diagnosis was done and therapeutic abortion was. Offered, if indicated.

Main outcome measures : Cases, carriers, suspected cases, Hb typing, OF and DCIP tests.

Results : In ***Component one*** **:** 26,740 children were screened of whom 893 cases were suspected. Out of those suspected, 296 (33.2%) were normal, 140 (15.6%) were diseased, and 457 (51.2%) were carriers. 56 cases had major thalassemia diseases Their parents were counseled. Forty couples were determined to need some form of family planning and 39 (97.5%) accepted. In ***Component two*** **:** 256 pregnant women were screened and 56 were found to be carriers. Only 45 husbands could be located and Hb typed. Five couples were determined to require prenatal diagnosis (PND). One happened to undergo therapeutic abortion because of HIV infection in the mother without PND. Of the four who underwent PND, one was found to have a fetus with major thalassemia. However, this couple refused therapeutic abortion because of religious reasons.

Conclusion : This study combined both prospective and retrospective approaches and can be considered successful. However, as the only available option for pregnant women with affected fetuses is therapeutic abortion, this makes it difficult to expand the program because abortion may not be acceptable in certain communities. In addition, this model requires PND and other laboratory and clinical facilities as backups. Such backups may not be available in certain settings.

Key word : Prevention and Control, Community-Based Thalassemia

PANSATIANKUL B & SAISORN S
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* Department of Pediatrics, Queen Sirikit National Institute of Child Health, Bangkok 10400,
** Chiang Rai Provincial Health Office, Chiang Rai 57000, Thailand.

Thalassemias and hemoglobinopathies are the most common genetic hematologic disorders in Thailand. The prevalence rates of abnormal genes in Thailand are estimated as follows: 3.5-12 per cent for α-thalassemia-1, 16-19 per cent for α-thalassemia-2, 3-9 per cent for β-thalassemia, and 13-60 per cent for Hb E[1]. It is estimated that about 30-40 per cent of Thai people carry abnormal genes that can be transmitted to their offspring. The number of carriers is therefore, estimated to be around 18-24 million. About 5 per cent of all married couples are at risk of producing a homozygote for a major hemoglobinopathy (excluding the homozygous states for α^+-thalassemia, Hb Constant Spring, and Hb E)[2]. With approximately 0.9-1 million births per year, the number of at-risk pregnancies is 45,000-50,000 per year. One in four or approximately 12,500 babies born to these mothers will have a major hemoglobinopathy. Out of these babies, 625 would have homozygous β-thalassemia[3], 3,250 would have β-thal/Hb E[4], 1,250 would have Hb Bart's hydrops fetalis[5], and 7,000 would have Hb H disease[6]. Besides the Hb Bart's hydrops fetalis who usually die before birth, those with homozygous β-thalassemia and β-thal/Hb E require regular blood transfusion and those with Hb H disease are vulnerable to infections and may require blood transfusion as well. Despite the recent advances in gene therapy, thalassemias and hemoglobinopathies are still incurable. Bone marrow transplantation is done in only a few specialized medical centers in Thailand with a 20-30 per cent rejection rate. Those who survive the immediate rejection need life-long immunosuppressive drugs and are vulnerable to treatment failure due to resurgence of the disease. Thalassemias and hemoglobinopathies impose considerable economic and social burdens to Thailand[7]. In addition, affected individuals and families also suffer from psychological distress and social stigmatization. Intervention efforts for these disorders in Thailand have thus been towards prevention of new cases and carriers. The present paper describes a model for prevention of thalassemias and hemoglobinopathies in northern Thailand.

Setting

The study was conducted in Phan District of Chiang Rai Province. Chiang Rai is the northern most province that borders Myanmar on the west and the Lao People's Democratic Republic on the right. Its population in 1995 was 146,290. Phan is about 25 kms south the central district of Chiang Rai. with 107 schools in its community.

SUBJECTS AND METHOD

This model was composed of two main components. (Fig. 1) First, it was aimed to test a model of whether thalassemic cases and carriers could be retrospectively detected from preschool and school

children. Second, it tested a model for prevention of prospective cases of thalassemic babies among pregnant women.

Component one : Case and carrier detection from children

A group of 10 hemotologists and public health technical officers from the Queen Sirikit National Institute of Child Health and the Bureau of Medical Technical Development of the Department of Medical Services of the Ministry of Public Health were included in the working group of the project. The group developed a curriculum for doctors and nurses at provincial and community hospital levels (Curriculum A) and also a more simplified curriculum that could be used for subdistrict public health officers (SPHO) and school teachers (Curriculum B). The curricula contained the general situation, epidemiology, clinical and laboratory diagnosis, treatment, community screening, and counseling for thalassemias. Participants trained under Curriculum A were expected to train SPHO and school teachers using Curriculum B. Curriculum B was a simpler version of curriculum A but more emphasis was placed on the use of a newly-developed pictorial tool for screening. In addition, participants in Curriculum B were trained to have clinical skills in detecting anemia and jaundice. All participants were required to pass the course-end evaluation.

Another curriculum was prepared for laboratory scientists and technicians from the Chiang Rai Provincial Hospital and Phan District Hospital. The curriculum contained a brief introduction on the situation and epidemiology of thalassemias and hemoglobinopathies in Thailand, preparation and interpretation of blood smears the osmotic fragility (OF) test, dichlorophenol-indolephenol (DCIP) precipitation test, and Hb typing.

Preschool children (1-5 years) were then screened by SPHO. By using three key questions to ask the children's parents, pictorial tools and physical examination to detect anemia and icteric sclera to screen these children. The questions were history of sudden anemia after fever or an acute illness episode, history of chronic anemia in the family, and history of the anemic family members requiring blood transfusion. During the same period, the school teachers, screened school children in their classes by detecting anemia and icteric sclera. Suspected cases were referred to the Phan District Hospital where they were physically examined by doctors and also had blood tests. Complete blood count including blood smear morphologic examination was done at the Phan District Hospital. An aliquot of 2 ml of EDTA blood was sent to the Chiang Rai Provincial Hospital where a hemolysate was prepared and run electrophoretically on cellulose acetate (350 volts, 25 minutes). Based on patterns of bands, the results were classified as

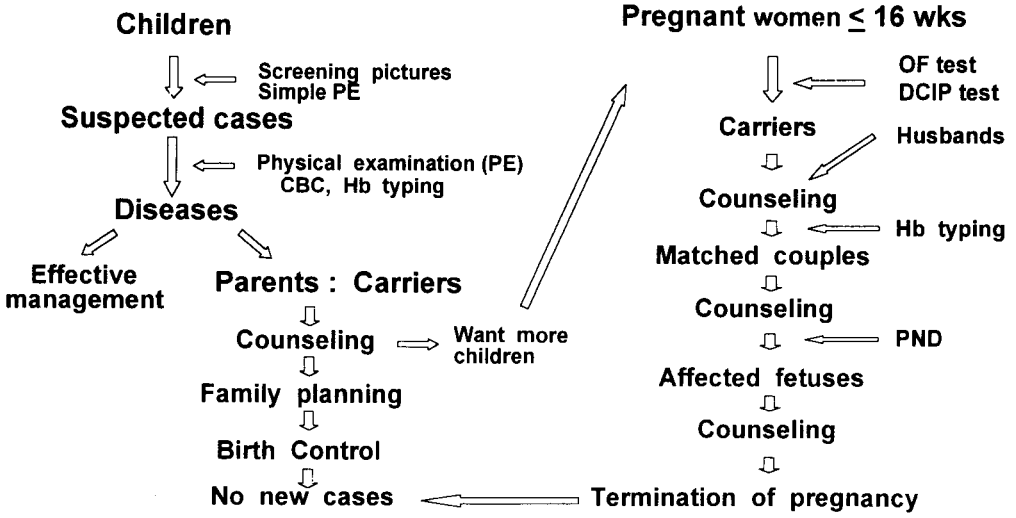

Fig. 1. Conceptual frame work of prevention and control of thalassemia in Thailand.

normal, β thalassemia trait, homozygous β^0 thalassemia, Hb H disease, Hb H-CS disease, and β^0 thal-Hb E disease, and homozygous -Hb E trait. The cellulose acetate specimen was then sent to the Haematology Laboratory Unit of the Department of Medical Sciences (DMSs) of the Ministry of Public Health for band re-reading. Performance of the Chiang Rai Provincial Hospital laboratory was checked against the results at the DMSs as quality control. Compared to the results from the DMSs laboratory, those from the Chiang Rai Provincial Hospital laboratory were 100 per cent consistent.

Peripheral blood smears from the Phan District Hospital laboratory were sent to the author for re-checking of red cell morphology (i.e. anisocytosis, poikilocytosis, presence of target cells, hypochromia, microcytosis, fragmented red cells, polychromasia, and presence of nucleated red cells). The author's readings served as the gold standard. Results from the Phan District Hospital were 92.8 per cent sensitive and 100 per cent specific when compared with the author's reading.

Component two : Prevention of new cases from pregnant women

Pregnant women, less than 16 weeks pregnant, who attended the antenatal clinic at the Phan Hospital were screened for clinical signs of anemia and tested for osmotic fragility of red cells for β-thalassemia trait identification and DCIP test for detection of Hb E, after pre-test genetic counseling. If OF or DCIP test was positive, blood was drawn and sent for Hb typing to the university medical center located in Chiang Mai province (located about 150 km from Chiang Rai) where a prenatal diagnosis facility was available. At the same time, husbands of these women were contacted and invited to join the study for Hb typing. Verbal informed consent was obtained. After consenting to participate, the couples were provided with individual and group counseling. Hb typing of the husbands was done at the same medical center as that for the women. Hb typing was done for detecting only β-thal and Hb E genes. If both were found to be matched carriers, putting their offspring at risk of β-thalassemia major and β-thal/Hb E, they were referred to the major medical center for prenatal diagnosis (PND) after post-test counseling. Those referred to Chiang Mai for PND were compensated for travel costs. If PND was positive, they were offered therapeutic abortion after counseling.

RESULTS

Case and carrier detection from children

There were 2 doctors, 1 nurse and 1 public health technical officer from the Chiang Rai Provincial Hospital, the Phan District Hospital, and the Chiang Rai Provincial Public Health Office who participated in training under Curriculum A. All successfully passed the course-end evaluation.

The participants from Curriculum A organized a training course using Curriculum B to train 90 subdistrict public health officers (SPHO) and 107 teachers from 107 schools in the Phan District.

During May and July 1997, the SPHO visited the Village Pre-School Children Centers where all pre-school children were registered. A total of 5,617 children were screened by the SPHO. During the same period, the school teachers screened 21,123 school children in their classes.

Out of the 26,740 (5,617 + 21,123) children screened, 893 were suspected. These cases were sent for physical, hematocrit and blood smear examination at the Phan District Hospital and blood specimens for Hb typing were sent to Chiang Rai Hospital laboratory. Two hundred and ninety-six (33.2%) were classified as normal, 140 (15.6%) as diseased, and 457 (51.2%) as carriers. Out of the 140 diseased cases, 8 cases (5.7%) had β-thalassemia major, 48 (34.3%) had β-thal/Hb E, and 84 (60.0%) had other minor types of thalassemic diseases (HbH, HbCS, HbH/HbCS) (Table 1)

The prevalence rates of thalassemia and hemoglobinopathies of preschool children, school children and total were 0.3 per cent, 0.6 per cent, and 0.524 per cent respectively. The prevalence rates of homozygous β-thalassemia, β-thalassemia/Hb E and other types of thalassemic diseases were 29.9, 179.5, and 314.1 per 100,000 population (Fig. 2).

Parents of the 48 cases of β-thalassemia/HbE and 8 cases of β-thalassemia major children were called for counseling and further investigation. Two affected children belonged to the same parents. Therefore, 55 couples were located and all agreed to participate. Of the 55 couples, 15 (27.3%) required no birth control because of separation, divorce or permanent sterilization. Of the remaining 40 requiring family planning, 39 accepted (21 using permanent methods and 18 temporary). Only one denied any form of family planning because of desire for more children. This couple was further counseled and provided with knowledge about PND and other therapeutic choices.

Table 1. Screening children by school teachers and subdistrict public health officers.

Screening Children	Hemoglobin typing						
	Normal	%	Traits	%	Disease	%	Prevalence* (%)
Preschool (5,617)	14	22.2	34	52.4	16	25.4	0.3
School (21,123)	282	34.0	423	51.0	124	15.0	0.6
Total (26,740)	296	33.1	457	51.2	140	15.7	0.524

* Based on the screened population of each age group.

1) Thalassemias and Hemoglobinopathies	
Preschool children	0.3%
School children	0.6%
Total	0.524%
2) Homozygous β-thalassemia	29.9/100,000 pop
3) β-thalassemia/Hb E	179.5/100,000 pop
4) Other diseases	314.1/100,000 pop

Fig. 2. Prevalence rate of thalassemia of children in Phan community, Chiang Rai province.

Prevention of new cases from pregnant women

During January and December 1997, 256 of 16-week-or-less pregnant women were screened by using CBC, OF, and DCIP tests and 56 were found to be carriers. Only 45 of their husbands (80.4%) could be located and Hb typed. Only 5 of the 45 couples met the criteria for prenatal diagnosis (PND). One couple was found to have one partner infected with human immunodeficiency virus (HIV) and the woman underwent therapeutic abortion because of reasons related to the HIV infection. No PND was done on the woman. Four other couples received PND and 3 were found to have normal fetuses and one had a thalassemic fetus (major thalassemia). The affected couple refused therapeutic abortion because of religious reasons.

DISCUSSION

Approaches to prevent new cases of major thalassemias and hemoglobinopathies can be either prospective and retrospective. The retrospective approach starts with identification and detection of diseased cases, either in communities or in hospitals, tracing their parents and other relatives to determine their disease or carrier status. After that, genetic counseling and family planning can be implemented. Such a population can also be located in the hospital, e.g. pregnant women attending ante-natal clinics. Again, genetic counseling and family planning will follow[8,9].

Both approaches have proved quite successful in this simplified model. Such success requires not only sophisticated laboratory and clinical backups but also strong networks of public health officers, teachers or grass-root workers who have access to community. These workers need specific training so that they are capable of carrying out the task. In addition, the laboratory work needs quality control.

The prevalence rates of major thalassemic diseases and hemoglobinopathies have shown to be quite high. This high rate of morbidity together with the high sensitivity of screening tools give a high yield of suspected cases. These cases are targets of further intensive but more definitive investigations. After such a definite diagnosis is made, therapeutic and

preventive approaches are put in place. This requires facilities such as prenatal diagnosis[8,9]. The only existing option for unborn but affected babies is therapeutic abortion. As seen in the present study, such an option may not be generally acceptable to affected couples, mostly due to religious reasons[10]. The unacceptability of such intervention in certain societies can be very serious and inhibits initiation of prevention programs like this right at the onset. Therefore, if preventive approaches based on abortion are to be used, it may be necessary to ascertain people's feelings toward abortion or other means of family planning before the start of the program.

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รูปแบบการป้องกันและควบคุมโรคธาลัสซีเมียในชุมชนในภาคเหนือของประเทศไทย

บุญเชียร ปานเสถียรกุล, พบ, ศุภชัย สายศร, พบ***

วัตถุประสงค์ : เพื่อบรรยายถึงรูปแบบของการป้องกันและควบคุมโรคธาลัสซีเมียและฮีโมโกลบินผิดปรกติในภาคเหนือของประเทศไทยที่อิงชุมชนเป็นฐาน

รูปแบบ : เป็นการวิจัยเชิงปฏิบัติการที่ประกอบด้วยสองส่วน ส่วนที่หนึ่งเป็นการทดสอบรูปแบบของการค้นหาผู้ป่วยและพาหะของโรคธาลัสซีเมียย้อนหลังจากกลุ่มของเด็กนักเรียน ส่วนที่สองเป็นการทดลองรูปแบบของการป้องกันทารกที่จะป่วยเป็นโรคธาลัสซีเมียรายใหม่ในหญิงตั้งครรภ์

พื้นที่ที่ทำการศึกษา : อำเภอพาน จังหวัดเชียงราย

ผู้ที่ถูกศึกษา : ***ส่วนที่หนึ่ง*** : เด็กวัยก่อนเรียนจำนวน 5,617 คน และเด็กวัยเรียนจำนวน 21,123 คนได้รับการคัดกรองในระหว่างเดือนพฤษภาคมและกรกฎาคม พ.ศ. 2540 ***ส่วนที่สอง*** : หญิงตั้งครรภ์ 16 สัปดาห์หรือต่ำกว่าจำนวน 256 คนได้รับการคัดกรองในระหว่างเดือนมกราคมและธันวาคม พ.ศ. 2540

วัตถุและวิธีการ : ***ส่วนที่หนึ่ง*** : เจ้าหน้าที่สาธารณสุขระดับตำบลและครูได้รับการฝึกให้สามารถใช้รูปภาพและการตรวจอย่างง่ายในการค้นหาเด็กวัยก่อนเรียนและเด็กวัยเรียนที่สงสัยว่าจะเป็นโรคธาลัสซีเมีย ผู้ที่สงสัยว่าจะเป็นโรคจะได้รับการส่งต่อเพื่อการตรวจร่างกายและการตรวจเลือด การตรวจเสมียร์เลือดทำที่โรงพยาบาลพาน ส่วนการตรวจ Hb typing โดยวิธี electrophoresis ทำที่โรงพยาบาลจังหวัด โดยส่ง cellulose acetate ไปอ่านยืนยันที่กรมวิทยาศาสตร์การแพทย์ ***ส่วนที่สอง*** : ตรวจหญิงตั้งครรภ์ 16 สัปดาห์หรือต่ำกว่าด้วยวิธี OF และ DCIP ที่โรงพยาบาลพาน ถ้าผล OF ให้ผลบวก จะได้รับการตรวจ Hb typing ที่ศูนย์วิทยาศาสตร์การแพทย์ และจะมีการติดตามสามีมารับการตรวจ Hb typing ด้วย และหากจำเป็นจะมีการตรวจ Prenatal diagnosis (PND) และมีการเสนอให้ทำแท้ง (therapeutic abortion)

ผลลัพธ์ที่สำคัญ : ผู้ป่วย, พาหะของโรค, ผู้ที่สงสัยว่าจะป่วย, ผลการตรวจชนิดฮีโมโกลบิน, ผลการตรวจ OF และ DCIP

ผลการศึกษา : ***ส่วนที่หนึ่ง*** : เด็กจำนวน 26,740 รายได้รับการตรวจคัดกรองและ 893 รายสงสัยว่าอาจจะเป็นโรค ในจำนวนผู้ที่สงสัยนั้น 296 ราย (ร้อยละ 33.2) ปรกติ, 140 ราย (ร้อยละ 15.6) เป็นโรค, และ 457 ราย (ร้อยละ 51.2) เป็นพาหะ ทั้งนี้มี 56 รายที่เป็นโรคธาลัสซีเมียชนิด major ซึ่งได้ติดตามพ่อแม่จำนวน 55 คู่มารับคำแนะนำ (มีเด็ก 2 รายที่เป็นพี่น้องกัน) พบว่าพ่อแม่จำนวน 40 คู่จำเป็นจะต้องได้รับการวางแผนครอบครัวชนิดใดชนิดหนึ่งและ 39 คู่ (ร้อยละ 97.5) ยอมรับการวางแผนครอบครัว ***ส่วนที่สอง*** : หญิงตั้งครรภ์จำนวน 256 รายได้รับการตรวจคัดกรองและพบว่า 56 รายเป็นพาหะ สามารถติดตามสามีมาตรวจ Hb typing ได้เพียง 45 ราย พบว่า 5 คู่ของสามีภรรยาจำเป็นต้องได้รับการตรวจ PND ปรากฏว่ามีหนึ่งรายได้รับการทำแท้งไปก่อนแล้วเพราะว่าติดเชื้อไวรัสเอดส์ ส่วนอีก 4 รายที่เหลือได้รับการตรวจ PND นั้นมี 1 รายที่พบว่าทารกป่วยเป็นโรคธาลัสซีเมียชนิด major แต่พ่อแม่ปฏิเสธการทำแท้งด้วยเหตุผลทางศาสนา

ข้อสรุป : การศึกษานี้ใช้ทั้งวิธีศึกษาไปข้างหน้าและย้อนหลังซึ่งพบว่าประสบผลสำเร็จเป็นอย่างดี แต่เนื่องจากทางเลือกสำหรับหญิงตั้งครรภ์นั้นจำเป็นต้องทำแท้งหากพบว่าทารกป่วยเป็นโรคที่ร้ายแรง ซึ่งทางเลือกนี้อาจจะไม่ได้รับการยอมรับมากนักในบางชุมชน นอกจากนั้น รูปแบบนี้จำเป็นจะต้องทำในหน่วยงานที่สามารถทำ PND และทำการตรวจทางห้องปฏิบัติการและทางคลินิกได้ดี ซึ่งอาจจะทำไม่ได้ในทุกที่

คำสำคัญ : โรคธาลัสซีเมียในชุมชน, รูปแบบการป้องกันและควบคุม

บุญเชียร ปานเสถียรกุล, ศุภชัย สายศร
จดหมายเหตุทางแพทย์ ฯ 2546; 86 (ฉบับพิเศษ 3): S576–S582

* กลุ่มงานกุมารเวชกรรม, สถาบันสุขภาพเด็กแห่งชาติมหาราชินี, กรุงเทพ ฯ 10400

** สำนักงานสาธารณสุขจังหวัดเชียงราย, เชียงราย 57000