
Prevention of Thalassemia : Experiences from Samui Island

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Abstract

Thalassemia is one of the most important genetic disorders in Thailand. A model for prevention of thalassemia by combining 4 strategies including education, carrier screening, counseling and prenatal diagnosis was developed by a thalassemia task force. A thalassemia work group was formed in order to develop a mechanism to integrate the model for real use on Samui Island where thalassemia is common and a specific disease oriented program is required. 200 health professionals working on Samui Island participated in the thalassemia educational courses. The specific training courses were also provided for obstreticians, medical technologists and counselors. A team of well-trained health professionals was established to manage public education. Information booklets, posters, brochures and mass media including spot radio and newspapers were used as educational materials. For carrier screening, blood samples of pregnant women from all health care organizations on Samui Island were collected and screened for thalassemia carriers by using the osmotic fragility (OF) test/the dichlorophenol indophenol precipitation (DCIP) tests at Samui Hospital. Samples with positive results were sent to the Regional Medical Sciences Center in Surat Thani for thalassemia diagnosis. When a carrier was identified, her spouse was offered testing. For at-risk couples, details of the disorder were included in counseling to help them reach a decision that was right to them, in the context of their unique medical, moral and social situations. Amniotic fluid samples were collected for prenatal diagnosis. All patient information was registered by using computer software. After 1 year of integration by using facilities of the Ministry of Public Health service system, a wide range of problems were identified. They underlined the need for effective health service structure co-operation, adequate education of responsible health professionals, explicit policies and a clear line of responsibility at local, regional and national levels for service development and quality management. It is hoped that all information

conducted in the present study will be useful to health authorities to develop an explicit policy and promote the health service structure co-operation in the country that will finally lead to successfully reducing the frequency of severe thalassemia in the future.

Key word : Thalassemia, Prevention, Thailand

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Thalassemia is one of the most important genetic disorders characterized by defective synthesis of the hemoglobin molecule. In Thailand, α -thalassemia and β -thalassemia are prevalent⁽¹⁾. The frequencies of α -thalassemia have reached 20-30 per cent in Bangkok and Northern Thailand, those of β -thalassemia vary between 1-9 per cent, while hemoglobin E (Hb E) and hemoglobin Constant Spring (Hb CS) are the two most common hemoglobin variants found in Thailand⁽¹⁻⁵⁾. Estimation based on gene frequencies and number of babies born each year indicates that there will be approximately 1.2 per cent of newborns or 12,125 cases^(6,7) who have one of the common thalassemia diseases, i.e. homozygous β -thalassemia, β -thalassemia/HbE, Hb Bart's hydrops fetalis and HbH disease. If new births of severe thalassemia can not be prevented, patients will accumulate and thus will finally lead to health, social and economic problems in Thailand. Although the present management of thalassemic disease gives a probable life expectancy beyond the third or fourth decade, the quality of life of patients and their families and the burden that such treatment represents for public health services clearly underline the fundamental aspect of prevention rather than treatment.

Prevention of thalassemia by combining 4 strategies including education, carrier screening, counseling and prenatal diagnosis has proved to be effective, acceptable and highly cost-beneficial⁽⁸⁻¹³⁾. Deve-

lopment of a local strategy in each province is required according to local epidemiology, current service structure and available economic resources. However, it is difficult to develop a national program since it must be integrated into the general health system and a large element of professional and public education is needed. WHO monitoring shows that it is easiest to organize an effective program in a relatively small population where thalassemia is common and a specific disease-oriented program is required^(8,9,14,15).

Up to now, problems of thalassemia in Thailand have been recognized, technology concerning thalassemia diagnosis and treatment are available and the NGO, the Thalassemia Foundation of Thailand with more than 4,500 members is already organized in order to offer better care and successful prevention and control of thalassemia. Education, carrier screening, thalassemia diagnosis and counseling could be done in some regional hospitals but prenatal diagnosis could not, so patient management could be done but full prevention of thalassemia could not be achieved. Even though some prevention and control programs were reported in many parts of the country^(16,17), they were difficult to integrate for real use at the community level since many steps depend on the facilities of university hospitals. It is estimated that approximately 48,500 at-risk couples will require health services each year^(6,7), so university hospitals alone would not be enough to provide sufficient services.

In the present study a model for prevention of thalassemia in Thailand was developed by a task force and then integrated into the community on Samui Island by using the facilities of the Ministry of Public Health (MOPH) network. Experts from Prince of Songkhla University responsible for the south of Thailand were invited as consultants. Many aspects including studies of health service structure co-operation, establishment of a laboratory network and development of mechanisms to integrate the model for real use were studied. The model was evaluated and modified, to be utilized as a model for other communities throughout the country.

METHOD

Model development and integration

Creation of a thalassemia task force

A thalassemia task force comprising 25 thalassemia experts from various organizations such as university hospitals, the Thalassemia Foundation of Thailand and MOPH was formed to develop an appropriate model for prevention of thalassemia in Thailand based on four aspects including education, carrier screening, genetic counseling and prenatal diagnosis.

Integration of the model into a community

Study location

A feasibility study of the model was conducted on Samui Island where thalassemia is common and a specific disease oriented program is required. In addition, infrastructures and medical care services at Samui Hospital were available and considered strong enough to carry out the project.

Study population

The target population were mostly pregnant women and their spouses since new cases of thalassemia could be prevented in this population. Others were thalassemic patients and their family members.

Study period

October 2000-December 2001.

Creation of a thalassemia working group

A thalassemia working group comprising 23 health professionals from regional public health organizations was formed in order to develop a mechanism to integrate the model into the general health service system on Samui Island after October 2000.

Thalassemia registration

All patients and prenatal diagnosis information were registered by using the Thalassemia Prevention and Control System (TPCS) and the Thalassemia Registration System (TRS) computer software provided by Dr. Verapol Chandeying, Prince of Songkhla University.

Evaluation

The model was evaluated every 6 months by a team of evaluators from the Department of Medical Sciences. A random sample of 10 per cent of the records was reviewed. Reliability of laboratory diagnosis was monitored by reviewing the proficiency test results. All problems were discussed to achieve the effective network system that could be utilized as the model for other communities throughout the country.

RESULTS

Model development and integration

The model for prevention of thalassemia in Thailand was developed by a task force according to recommendations of WHO as follows:

Professional education and public education

200 health professionals including obstetricians, pediatricians, hematologists, nurses, medical scientists, medical technologists, laboratory assistants, counselors and health volunteers working on Samui Island were invited to participate in the thalassemia educational course. Thalassemia experts from Prince of Songkhla University and the National Institute of Health (NIH) were invited as lecturers. Information concerning the basis of thalassemia, genetic risk, screening protocol for thalassemia carriers, prevention and control of thalassemia were included in this course. In addition, the specific training courses were also provided for obstetricians, medical technologists and counselors. A team of well-trained health professionals was established to manage public education. Information booklets, posters, brochures and mass media including spot radio and newspapers were used as educational materials.

Creation of the laboratory network for thalassemia diagnosis

Appropriate laboratory tests of thalassemia diagnosis were set up at Samui Hospital and the Regional Medical Sciences Center (RMSC) in Surat

Thani province according to suggestions provided by a thalassemia task force.

Blood samples of pregnant women from all health care organizations on Samui Island were collected and screened for thalassemia by using the osmotic fragility test (OF) and the dichlorophenol indophenol precipitation test (DCIP) at Samui Hospital. Samples with positive results were sent to RMSC for thalassemia diagnosis. Laboratory results were sent back to Samui Hospital within 1 week after receiving blood samples. Elevation of Hb A₂ higher than 3.5 per cent was used in identifying β -thalassemia carriers. Thalassemic patients such as β -thalassemia homozygotes, β -thalassemia/Hb E, EA Bart's disease, EF Bart's disease and Hb H disease were identified by hemoglobin separation and quantitation results in combination with their clinical manifestation and other hematological analysis including complete blood count (CBC) and red cell morphology. Carriers for α -thalassemia 1 Southeast Asian (SEA)

type were identified by gap polymerase chain reaction (PCR). Common variant hemoglobins such as Hb E and Hb CS were identified by high performance liquid chromatography (HPLC), whereas rare abnormal hemoglobins were further identified by DNA sequencing technique. When a carrier was identified, her spouse was offered testing. In couples at risk of having a β -thalassemic child, types of β -thalassemia mutations were identified before fetal sampling by reverse dot blot analysis. Amniotic fluid samples were collected and subsequently sent to RMSC for DNA diagnosis by PCR. Maternal cell contamination in fetal samples was monitored by determination of the variable number of tandem repeats (VNTR) locus DIS80. Reliability of all laboratory diagnose was monitored by the proficiency test operated by NIH.

Genetic counseling

Counselors of Samui Hospital were trained by experts from Prince of Songkhla University. Genetic

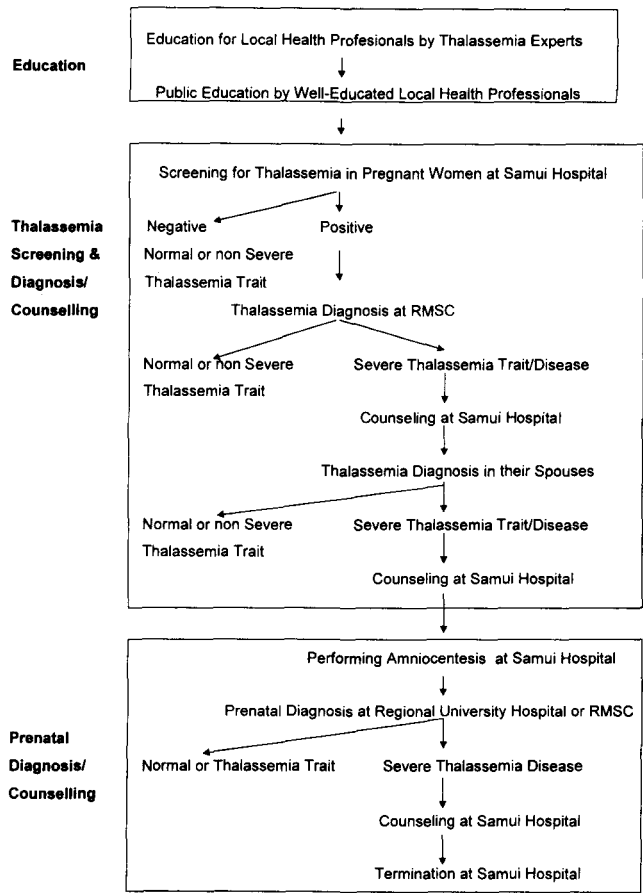


Fig. 1. The model for prevention of thalassemia on Samui Island.

counseling was done by well-trained counselors. Details of the disorder, the risk of obstetric procedure and the possibility of prenatal misdiagnosis were included in counseling to help at-risk couples to reach a decision that was right for them, in the context of their unique medical, moral and social situations.

Thalassemia registration

From October 2000 to September 2001, the number of pregnant women on Samui Island was 893 cases. 863 of them (96.6%) were willing to participate in the thalassemia prevention program. 392 of 863 (45.4%) had positive screening test(s). 21, 164, 23, 1, 3, 1, 1 and 1 pregnant women were identified as β -thalassemia carriers, Hb E carriers, homozygous Hb E, β -thalassemia/Hb E, homozygous β -thalassemia, Hb H disease, EA Bart's disease and Hb Malay carrier, respectively.

Among 392 pregnancies who had positive screening test(s), 310 (79%) spouses were willing to be investigated. 119 of 310 (38.4%) had positive screening test(s). 6, 59, 9, 1, 1 and 1 of the spouses were β -thalassemia carriers, Hb E carriers, homozygous Hb E, Hb H disease, Hb C carrier and Hb Malay carrier, respectively.

Risk was detected in 10 couples. Four of them were detected after 20 weeks' gestation and three of them moved to their hometowns. Overall, risk was recognized before 20 weeks' gestation in 3 pregnancies. Prenatal diagnosis was offered in these 3 pregnancies, they were found to be one Hb E carrier and two normal fetuses.

Evaluation

Almost all health professionals at Samui Hospital were willing to undertake this prevention program because of significant health benefits to their population. A random sample of 10 per cent of the records was reviewed by evaluators every 6 months. All information was completely recorded. Reliability of confirmatory test at RMSC in Surat Thani was excellent according to the national proficiency test result provided by NIH.

During one year of integration, many problems were observed. Their solutions were discussed and summarized as follows:

DISCUSSION

In the present study a model for prevention of thalassemia was established by a thalassemia task

force comprising experts from various organizations such as a university hospital, the Thalassemia Foundation of Thailand and MOPH. The model was integrated for real use into general health services by using facility of MOPH network system from October 2000 to December 2001. Samui Island was selected due to the availability of infrastructures and medical care services. In addition, the population on Samui Island (approximately 861,233) and number of pregnant women (approximately 800/year) was not too big to study. Thalassemia experts from Prince of Songkhla University were invited to be consultants for the study. The indicators of success could be evaluated by the increasing number of well-educated health professionals who participated in the educational course and the increasing number of pregnant women in the thalassemia registration. For health education, a total of 200 health workers including obstetricians, pediatricians, hematologists, nurses, medical scientists, medical technologists, laboratory assistants, counselors and health volunteers working on Samui Island participated in the thalassemia educational course. Obstetricians, counselors and laboratory persons also participated in their specific training course. Almost all of them were willing to integrate the prevention program model for real use into their community. They required appropriate tools such as information materials for carriers and at-risk couples. For the number of pregnant women in the thalassemia registration, almost all the pregnant women (863/893) were willing to participate in the prevention program in comparison with only 20 of 820 pregnant women who participated in the carrier screening protocol in 1999. However, the prevention model as currently practised identified the risk too late to provide satisfactory service to 4 of 10 at-risk couples. Therefore, it is necessary to establish policy promoting early in ANC visits in this community.

From this experience it was found that several factors might affect the integration of the model for real use as summarized as follows:

Health professionals' level of interest

Some health professionals did not want to integrate the model for real use, perhaps not all saw it as relevant. Others might have felt uncomfortable with a service that could lead to termination of a pregnancy. It is necessary to persuade them that the

Table 1. Problems and solutions for thalassemia prevention.

Category	Problems	Solutions
Health professionals	<ul style="list-style-type: none"> - Inadequate thalassemia information - Lack of awareness - Unclear responsibility - Difficulties in co-operation with other health service organizations - Not continuous in all activities 	<ul style="list-style-type: none"> - Provide adequate education - Establish a thalassemia support team - Establish the explicit policies that clarify roles and responsibility at local, regional and national levels - Develop a local thalassemia working group - Establish a time to time monitoring schedule by a team of auditors
Pregnant women and their spouses	<ul style="list-style-type: none"> - Late ANC visits - Unavailability of partner for blood testing - Inadequate information - Lack of awareness 	<ul style="list-style-type: none"> - Establish policy promoting early ANC visits - Provide adequate education and counseling materials
Laboratory	<ul style="list-style-type: none"> - Delay in DNA analysis - Overdiagnosis of β-thalassemia due to HPFH - Inappropriate laboratory tests 	<ul style="list-style-type: none"> - Establish an effective laboratory network to provide reliable and rapid diagnosis - Provide adequate education - Establish a thalassemia support team to assist laboratory staff - Establish national laboratory guidelines
Application of protocol	<ul style="list-style-type: none"> - Difficulties in identifying risk pregnancies - Impractical protocol for fetal sampling by cordocentesis 	<ul style="list-style-type: none"> - Provide adequate education - Revised protocol for fetal sampling by using amniocentesis
Data collection	<ul style="list-style-type: none"> - Too much information to collect 	<ul style="list-style-type: none"> - Provide software for thalassemia registration

prevention of thalassemia is practicable and benefits a large proportion of their patients.

Potential of laboratory diagnosis and effective network system

Prevention of thalassemia requires reliable and rapid diagnosis. National laboratory guidelines should be established and it is necessary to assist the regional health organizations to create an effective network system according to the guidelines. In the present study, OF and DCIP tests were used as screening tests. Samples with at least one positive screening test were confirmed by using HPLC for hemoglobin separation and determination. This confirmatory method is generally accepted by the hematological committees of WHO and of many countries^(9,18,19). The reliability of laboratory diagnosis was monitored by the proficiency test results.

Education for health professionals

Health professionals should periodically participate in educational courses. This is due to the fact that true success in informing the population and encouraging carrier screening requires educating health professionals that could offer information, screening and providing carriers with accurate information, so they become an information resource within the community. Production and dissemination of educational materials are also necessary. In addition, a team for thalassemia support should be established as consultants for health professionals.

Requirement of time to time monitoring and evaluation

It is necessary to monitor and evaluate health services from time to time, in order to stimulate all concerned professionals, locate problems and follow progress in all activities. Evaluation could be done most effectively through maintaining registers of patients and of prenatal diagnosis. All information conducted from evaluation should be subsequently proposed to health authorities to develop or modify

the policies in order to reach successful prevention and control of thalassemia.

Requirement of the explicit policies

It is generally accepted that the main cause of service failures is inadequate policy development (20-23). The national explicit policies should clarify roles and responsibility at local, regional and national levels for service development and quality management. However, it should be noted that health authorities in each community should also develop the local policies that solve local problems such as the policies promoting early ANC visits, early screening for carriers and immediate counseling for high risk couples.

One year after integration of the model into the community on Samui Island, improvements in quality of health care services have been brought about. Both health professionals and people in the community have adequate thalassemia information. Laboratory staff respond more precisely to the needs of obstetricians and counselors. Effective health structure co-operation has been created. Almost all pregnant women could be prevented from having children with severe thalassemia. It is hoped that all information conducted in the present study could be useful for health authorities to develop an explicit policy and promote health services co-operation in the country that will finally lead to successfully reducing the frequency of severe thalassemia in the future.

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การป้องกันโรคธาลัสซีเมีย : ประสบการณ์จากเกาะสมุย

สมชาย แสงกิจพร, พบ*, นฤมล จงกิตติวิทย์, วทบ**,
 เสริมศรี ปฐมพานิชรัตน์, พบ***, ลีริภากร แสงกิจพร, วทม*,
 บุญนิภา สงคราม, วทบ**, อุไร วัฒนโกคา, พยบ***, วันหนี่ เพชรทอง, วทบ***

ธาลัสซีเมียเป็นโรคทางพันธุกรรมที่มีความสำคัญมากที่สุดโรคหนึ่ง คณะผู้วิจัยได้พัฒนารูปแบบการป้องกันโรคนี้ ซึ่งประกอบด้วยกลยุทธ์ 4 ประการ ได้แก่ การให้ความรู้ การตรวจหาพาหะ การให้คำปรึกษาแนะนำทางพันธุกรรมและการตรวจวินิจฉัยก่อนคลอด จากนั้นจึงจัดตั้งคณะทำงานธาลัสซีเมียขึ้น เพื่อพัฒนากลไกการผสมผสานรูปแบบดังกล่าว สำหรับนำไปใช้จริงที่เกาะสมุย ซึ่งเป็นพื้นที่ที่มีปัญหาโรคนี้ โดยดำเนินการให้ความรู้แก่เจ้าหน้าที่ที่เกี่ยวข้องรวม 200 คน และอบรมหลักสูตรเฉพาะทางให้แก่ สูติแพทย์, พยาบาล และนักเทคนิคการแพทย์ ก่อนที่จะจัดตั้งคณะทำงานในการให้ความรู้แก่ประชาชน โดยใช้สื่อต่าง ๆ ได้แก่ หนังสือ, โปสเตอร์, แผ่นพับและการประชาสัมพันธ์ในรูปแบบต่าง ๆ รวมทั้งวิทยุและหนังสือพิมพ์ ห้างดังครุภัณฑ์มาฝากครุภัณฑ์ที่โรงพยาบาลเกาะสมุยจะได้รับการตรวจกรอง โดยวิธี OF/DCIP ตัวอย่างที่ผลการตรวจกรองเป็นบวกจะถูกส่งไปตรวจยืนยันที่ศูนย์วิทยาศาสตร์การแพทย์ สุราษฎร์ธานี หลังจากที่ได้รับผลจะตามสามของหญิงตั้งครรภ์ที่เป็นพาหะ เพื่อตรวจตามขั้นตอนดังกล่าวเช่นเดียวกับหญิงดังครุภัณฑ์ ในกรณีที่มีสาม-ภรรยาเป็นพาหะทั้งคู่จัดเป็นคู่เสี่ยงที่มีโอกาสให้กำเนิดบุตรเป็นโรคธาลัสซีเมียชนิดรุนแรง จะได้รับคำปรึกษาทางพันธุกรรม และมีสิทธิตัดสินใจในการวางแผนครอบครัวตามความเหมาะสมด้วยตนเอง การวินิจฉัยก่อนคลอดใช้วิธีเจาะเก็บน้ำคร่ำ เพื่อนำไปตรวจทางห้องปฏิบัติการ ข้อมูลทั้งหมดจะถูกบันทึกด้วยระบบคอมพิวเตอร์ หลังดำเนินการได้ 1 ปี พบปัญหาต่าง ๆ เช่น ความต้องการโครงสร้างสาธารณสุขที่มีความร่วมมือกันอย่างมีประสิทธิภาพ การให้ความรู้แก่บุคลากรที่เกี่ยวข้อง นโยบายที่ชัดเจน และการกำหนดความรับผิดชอบในระดับปฏิบัติการต่าง ๆ เช่น ระดับท้องถิ่น ระดับภูมิภาคและระดับชาติ ข้อมูลที่ได้จากการศึกษานับเป็นประโยชน์แก่ผู้บริหารในการตัดสินใจวางแผน แก้ไขปัญหาธาลัสซีเมีย เพื่อความสำเร็จในการลดจำนวนผู้ป่วยธาลัสซีเมียชนิดรุนแรงในอนาคตต่อไป

คำสำคัญ : ธาลัสซีเมีย, การป้องกัน, ประเทศไทย

สมชาย แสงกิจพร, นฤมล จงกิตติวิทย์, เสริมศรี ปฐมพานิชรัตน์, และคณะ
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