INTRODUCTION

Beta-thalassaemia major is the commonest lethal single gene disorder in India with a prevalence of 1-17% among different population groups and a mean prevalence of 3.3% (1). This condition is characterized by ineffective erythropoiesis, bone-marrow expansion, and rapid destruction of erythrocytes. Beta-thalassaemia major is usually diagnosed by 4-6 months of age after which patients are put on regular blood transfusion followed by iron chelation therapy which is associated with serious complications. If not treated, children may die of heart failure in early childhood. The only curative treatment available for this disease is bone-marrow transplantation which is too expensive for a common Indian family.

The homozygous state of beta-thalassaemia is clinically severe. The disease is inherited as an autosomal recessive condition meaning that parents of affected children are symptomless carriers of the gene. The carrier couples have a 25% risk of having an affected child in each pregnancy. Since parents of affected children are carriers, their relatives (sibs of parents and consequently their children) may also be at a high risk of being carriers of thalassaemia gene (heterozygotes). If a carrier marries a carrier, there is a 25% chance of giving birth to an affected child. The carrier status of these relatives can be known by screening for thalassaemia. This concept is broadly known as extended family screening. Higher fertility has been observed among heterozygotes (carriers) of haemoglobinopathies than among homozygotes (2-4), which implies that
heterozygotes produce more children than normal or homozygotes of defective gene to compensate for loss due to elimination of homozygotes. This leads to a higher frequency of heterozygotes in population. Prevalence of consanguinity varies among Indian population groups. Consanguinity compounds the situation as it is an important issue in spreading the disease.

In India, over 25 million people are carriers of the disease, and approximately 8,000 thalassaemic babies are born every year. Thalassaemia is, thus, a major problem in India, and the only effective strategy to lower its incidence is to prevent conception of thalassaemic children, and for prevention, the key step is screening of carriers (5,6). Advances in biotechnology and molecular biology have made detection of carriers and prenatal diagnosis of beta-thalassaemia major possible. Effectiveness of these advances is visible by 10-20-fold reduction in thalassaemic children in Cyprus, Greece, Italy, Sardinia, and the UK (7).

Our experience shows that, despite repeated genetic counselling, relatives of thalassaemic children do not come forward for carrier detection test. Consequently, first-degree relatives (sibs) of parents of thalassaemic children continue to give birth to thalassaemic children. Screening of this high-risk group can possibly prevent birth of affected children, which is more cost-effective compared to screening of general population.

The present study was undertaken to explore the feasibility of extended family screening. The first objective was to evaluate willingness of parents to share information on their thalassaemic children with their relatives, and effectiveness of these parents in communicating the increased risk of having thalassaemic children to their relatives and, therefore, their cooperation and help in making extended family screening possible. The second objective was to evaluate attitudes of relatives and response toward extended family screening, and, if they did not allow extended family screening, then to assess what the barriers to its acceptance were.

MATERIALS AND METHODS

The study was conducted in the Department of Medical Genetics, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India, during 1998-1999. The Department registered 110 thalassaemic patients for a hypertransfusion programme. These patients visited the hospital every 3-4 weeks for blood transfusion. Parents of 100 thalassaemic patients were interviewed to evaluate how well they understood thalassaemia as a genetic disorder, and the risk of its recurrence among their relatives. Since most patients came from outside Lucknow, they were accompanied by both the parents. Relatives of parents did not accompany them to the hospital due to distance and financial reasons. Therefore, the relatives were not interviewed directly; instead, the parents were interviewed. The following selection criteria were used for including the parents in the study: (i) parents had sibs who desired more children and, therefore, were at a risk of giving birth to thalassaemic children, and (ii) sibs had children who were of marriageable age and were at risk of giving birth to thalassaemic children if they were carriers of thalassaemic gene.

The parents had been counselled repeatedly over the preceding few years on the increased risk of their relatives being carriers, and consequently, on the need for extended family screening. The parents were provided literature, written in local language, on thalassaemia for distribution among their relatives (sibs) to increase their awareness of the disease.

Prior to the interview, the parents were provided with a brochure. The brochure contained complete information on thalassaemia as a disease, its incidence in general population and high-risk groups, treatment, and prevention.

In the structured interview, the parents were asked: (i) if they had informed their families (sibs, first and second cousins), friends, and co-workers that they were carriers of thalassaemia gene and, therefore, had a thalassaemic child; (ii) if there was increased risk of their family members being carriers and of having a thalassaemic child; (iii) if they had informed their relatives about the availability of antenatal diagnosis for carrier couples; and (iv) if parents had any reservation in our approaching their relatives directly to counsel them on increased risk of their being thalassemia carriers and availability of carrier detection test.

To evaluate attitudes of relatives toward the above information, the parents were further asked: (i) if their relatives accepted the increased risk of being carriers and having a thalassaemic child; (ii) if their relatives accepted the risk of being carriers, whether they were willing to get screened or whether they had already got tested; and
(iii) if their response was negative, what the reasons of, or barriers to, getting their carrier status tested were.

RESULTS

Attitudes of parents

Of the 100 parents (couples), 96 had no reservations in sharing information on their thalassaemic children. Four percent, who were hesitant in sharing information on their thalassaemic children with others, gave the following reasons: (i) they considered thalassaemia as a social stigma which could affect their image in the society leading to social isolation and eventually affect future marital prospects of other normal/carrier unmarried children in the family; (ii) relatives were illiterate and from rural background and, therefore, would not be able to understand the seriousness of the disease; (iii) husband and parents-in-law blamed wife for causing the disease to her child. Of the 100 couples, only two had objections in our approaching their relatives directly for genetic counselling as they wanted to be highly secretive about their child’s disease.

Attitudes of relatives

Relatives of 62 (64.5%) of the 96 couples accepted the increased risk of being carriers, and the remaining did not accept that they could be carriers of the gene (Fig.). Of the 62 couples, sibs of 35 families (56.4%) were willing to get their carrier status tested, and 14 families (22.5%) had already got themselves tested. The latter families were educated and feared recurrence of the disease in the family. The parents mentioned the following reasons for not getting carrier status of their relatives tested: (i) relatives did not seriously take information on their increased risk of being carriers and having a thalassaemic child; (ii) relatives had desired no more children, and all of them had normal children; and (iii) there were no facilities for carrier detection in the towns where they were living or in the nearby towns.

DISCUSSION

Primary prevention, based on a combination of increased awareness of general population, screening of carriers, genetic counselling, and prenatal diagnosis, has led to almost total elimination of thalassaemic children in Cyprus and, to a considerable extent, in Greece, Italy, and Sardinia (8-10). The most important requirement for implementing awareness of, or control programmes for, any disease is to create awareness among the masses (i) about the disease, (ii) how it spreads, and (iii) how it can be controlled.

Birth of thalassaemic children in four different families of relatives (sibs) of parents with thalassaemic children prompted us to conduct the study. This happened despite our repeated counselling to the parents regarding the increased risk of their relatives of being carriers and consequently of giving birth to thalassaemic children. These parents were asked to get the carrier status of all their first-degree relatives tested. This study was designed to evaluate the feasibility of preventing or controlling birth of thalassaemic children in a high-risk population through extended family screening.

The results of our study showed that, although the majority of affected families had no reservations in sharing information on their thalassaemic children with their relatives and friends, there was a low acceptance (64%) by relatives of an increased risk of being carriers and having thalassaemic children. This low rate of acceptance and indifferent attitude toward detection of carrier status may be due to lack of first-hand experience of raising a thalassaemic child who is both a social and a financial burden on the family. To add to this, there was an element of fear of intrusion by unknown persons. Further, because a good number of relatives desired no more children, they were not able to comprehend the fact that the carriers are symptomless, and their children, if carriers, were at risk of having a thalassaemic child in future, and hence this indifferent attitude. However, in families where there has been an incidence of recurrence, there is good acceptance of secondary prevention.

Our results are supported by comparative studies on Indians and Cypriots. These studies have showed that there is an appreciable difference (in attitude) between Indians and Cypriots in acceptability of genetic counselling and antenatal diagnosis for thalassaemia.
Compared to Indians, there is an overwhelming demand for this service from the British Cypriot community and a resultant reduction in the number of normal pregnancies terminated. The difference in demand (visible in terms of rejection of information) for carrier detection and antenatal diagnosis for thalassaemia and sickle-cell anaemia is striking in case of Indians compared to other populations (11). Cypriots are distinguished from other groups studied by a high level of awareness of thalassaemia among health workers and the community. Historically, thalassaemia has been seen as a problem for Mediterranean population, and concerted awareness campaigns have greatly reduced its prevalence in the Mediterranean area (9). In Cyprus, there are now almost no new affected births (12). Usually, it is thought that migrated Indian families have a broader outlook but these studies have shown that Indian families living abroad have very strong cultural attitudes.

For a community with such an attitude (which could be cultural), the only alternative to prevent birth of thalassaemic children is to firmly press in thalassaemia control programmes. The main objective of such programmes should be to create awareness among masses through the community and health education to motivate high-risk groups for screening of carriers. Extended family screening should be the main focus of these programmes, since the first-degree relatives of a thalassaemic child have a 14% higher risk of having an affected child compared to general population. Family physicians and obstetricians can play an important role in motivating high-risk groups. Screening of pregnant women along with their spouses should be made compulsory and free of charge. Genetic disorders, especially thalassaemia, should become a part of school curriculum which will facilitate in erasing the image of this disease as a social stigma (as the public will be more adapted to hearing and knowing about the disease).

Emphasis should be laid on channels of communication of information, and to make information effective, it must be adequately supplemented with audiovisual coverage. Without personal experience, seriousness of the situation cannot be appreciated. Facilities for genetic counselling, detection of carriers, and antenatal diagnosis should be made readily available. This might require opening up of new centres all over the country. For this, financial support can be sought from major international agencies, with cooperation from the government and communities in countries where thalassaemia is emerging (12). Places and towns where carrier screening test is not available, provisions should be made for collection of blood samples and their transport to centres for carrier testing. Selective termination of affected foetuses should not be considered a taboo. Three main messages that need to be propagated are: (i) the carrier state has no disadvantage; (ii) the homozygous state is very severe and fatal; (iii) prenatal diagnosis is available and safe; and (iv) before planning family, the carrier boy/girl should get his/her spouse tested for carrier status and go for chorionic villous sampling during 10th–12th weeks of gestation (if both are tested to be carriers) (6).

More studies need to be carried out at different centres in India to know the reasons for not accepting extended family screening. At present, there are no studies on the feasibility of extended family screening for controlling thalassaemia in Indian context.

Diseases that are known to run in families and have a high-risk of recurrence become a social stigma when nothing or very little is known about them. Illiterate people are ignorant about medical, social and financial burden of the disease. This further compounds the problem. Primary prevention of thalassaemia is possible by detection of carriers and by antenatal diagnosis. In preventing this disease, attitude of population at large and that of families directly involved in care of affected children are of prime importance. Cyprus, Greece, Italy, and Sardinia are excellent examples of demonstrating the effectiveness of control programmes for prevention of birth of thalassaemic children. Prevention of thalassaemia in India is possible only by sensitizing the problem at the individual, social and state levels.

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