REVIEW ARTICLE

Prevention of Thalassaemia by Genetic Counseling

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ABSTRACT

Thalassaemia is the most common inherited disorder in the world with a wide geographical variation in incidence. According to World Health Organization (WHO) at last 30% of Bangladesh population are carrions of Beta thalassaemia and 4.0% are carriers of Hb-E in Bangladesh. It is presumed that approximately 6000 thalassaemic children are born each year in Bangladesh. A recent study showed that carrier state of Hb-E is 6.1% and as high as 40% in Tribal children in Bangladesh. Early genetic, diagnosis, proper counseling, Health Education Community based prevention are necessary for the improvement of this inherited disorder in Bangladesh.

Key Words: Thalassaemia, Bangladesh, Early Diagnosis, Counselings, Community Based Prevention, Health Education

Introduction

Thalassaemia and the haemoglobin disorder are the most common clinically serious single gene disorder in the world. About 60,000-70,000 children are born each year with severe form of thalassaemia. Majority are born in countries with limited resources where priority tends to be given to tackling high rates of infant and child mortality from infection diseases and malnutrition[1]. As a result, hereditary disorders receive little attention. Affected children of severe thalassaemia often do not receive adequate treatment and die during childhood.

The major reasons that justify developing a preventive programme for thalassaemia in Bangladesh include the high frequency of thalassaemia major and E-beta thalassaemia, the high incidence of fatalities from untreated patients, and the high expense (and difficulty) of providing adequate treatment which creates a burden on patients, families and national health services.

There is no definitive data regarding carriers existing in Bangladesh. A conservative WHO report has estimated 3% of population as carriers of β-thalassaemia and 4% of population as carriers of Hb-E in Bangladesh. More than two thousand thalassaemic children are born every year in Bangladesh[2]. A recent study showed that carrier status of Hb-E is 6.1% and as high as 40% in tribal children in Bangladesh[3].

The intuitive solution to such a problem is genetic counseling. Genetic counseling has been defined as the process "by which patients relatives at risk of a disorder that may be heredity are advised of the consequences of the disorder and the probability of developing and transmitting it and ways in which this may be prevented or ameliorated[4]."

Importance of Genetic Counselings

Genetic counseling in inseparable from genetic diagnosis, aiming to replace misunderstanding about causes with correct information and to increase peoples' control of their own and their family's health by informing them of the resources available for diagnosis, treatment and prevention.

For this, a correct diagnosis is necessary

- Explanation of the nature and prognosis of the disorder and treatment available and where to find it.
- Estimation of genetic risk for parents and family members.
- Communication of genetic risks and options for avoiding them including the chances of parents and other family members passing the disorder on to their children.

- The options for avoiding further affected children must also be addressed, including technique of prenatal diagnosis and associated problems.
- Supporting the individual or couple in making the decision that is right for them is also part of counseling.

Meeting the above needs requires specialist genetic knowledge, training in counseling skills, ability to communicate, and back-up from a trained genetic counselor.

Undergraduate medical training in Bangladesh rarely equips doctors to provide adequate genetic counseling and discuss complex issues with their patients and parents in order to help them reach their own decisions. Genetic diagnosis is often difficult in view of enormous diversity of conditions involved and misdiagnosis and misinformation can have disastrous consequences for individuals and their families.

A genetic counselor should be knowledgeable in molecular genetics of thalassaemia. For example, when both partners carry the thalassaemia mutation which results in mild clinical phenotype of mild E-beta thalassaemia, or mild thalassaemia intermedia poses an ethical dilemma far as termination of pregnancy is concerned. Phenotype modifying co-inheritance of alpha-thalassaemia is another factor. The counselor should have sufficient experience and expertise to communicate this information and likely outcome to patients. Indeed, prenatal diagnosis should not be considered in many such patients.

By contrast, counseling couples at risk for alpha-thalassaemia hydrop foetalis is more straightforward because of hopeless prognosis and prenatal diagnosis is always advisable. However, this condition is rare in Bangladesh.

Prenatal Diagnosis

In practice, people's options are influenced by the stage at which they learn of their risk and by whether prenatal diagnosis is available. If the risk is found before marriage, the options are to remain single, not to marry another carrier, or to marry irrespective of carrier status. If the risk is found after marriage, as it happens in most cases in Bangladesh because of absence of carrier-screening programme, the options are to separate and find a non-carrier partner which is not logical or practical, to have few or no children, to take a chance and have children as usual. The latter is the case in the majority of instances in Bangladesh, due to the nonavailability and lack of acceptability of prenatal diagnosis and selective termination of pregnancy.

It is difficult for people to deal with the idea of prenatal diagnosis unless they are already used to the concept of controlling their own reproduction. When genetic diagnosis became available in the 1950s, the options available to couples were to ignore the information and hope for the best, i.e. the very same choices now faced by couples in Bangladesh where prenatal diagnosis is unavailable.

Family planning was already becoming widely accepted in the west at that time and it became clear that when options were so limited, most people chose either to avoid or ignore information on risk or to limit the size of their family[5,6].

Through community based programmes for prevention of haemoglobin disorders in Europe now include the option of prenatal diagnosis and selective abortion, carrier screening and generic counseling were introduce in some countries either before prenatal diagnosis was possible[7,8,9] or before it was legal. This early experience produced useful information on acceptability of some alternative approaches in Europe and Cyprus.

It is often though that affected births can be prevented if at-risk couples are identified prior to marriage an assumption that they will then decide to separate and each find non-carrier partners. However, we understand too little about how most marriages come about to be able to make any valid assumptions about how choice of partner might be affected by genetic information. In many societies, marriage is a complex social phenomenon that involves many other family members besides the prospective couple, and marriage partners are usually selected either by strong personal preference, valid family reasons, or traditional reasons and/or a combination of the above. When a planned marriage is called off, it can cause social embarrassment/stigma to the individuals and their families.

Premarital Screening is feasible in Iran. For reasons of cost efficiency and to reduce the possible stigma for women, many centers test the man first, only testing the woman in the event of a positive result. Annual statistics on outcome returned are 2600 at risk couples identified, of which 50% proceeded with their marriage plans

whereas 37% separated. The remaining 13% were undecided regarding the issue. The majority found it unacceptable to select a partner on the basis of genetic screening information. Instead, there was high demand for prenatal diagnosis. (Prenatal diagnosis is now available in several less developed countries, some of which have also introduced carrier screening programmes[10].)

Thus, a fatwa was issued by religious leaders permitting first trimester abortion where a foetus is confirmed as having a serious disorder. A national network of DNA diagnostic laboratories is now being set up in order to make prenatal diagnosis available to all.

Most Muslims accept that life does not begin at conception, believing that human life requiring perfection commences some weeks after development of the primitive streak[11,12].

Two renowned religious scholars in Pakistan gave a clear verdict permitting the termination of pregnancy before 120 days where the foetus is confirmed as having a serious disorder.

Prenatal services aimed at the prevention of haemoglobin disorders are not yet comprehensive even in the most developed countries. The follow-up of children suffering from severe thalassaemia despite the existence of prenatal diagnosis indicates that most births are not due to rejection of prenatal diagnosis, but rather patients' and doctors' unawareness of risk and of services available. Poor service delivery is therefore a key ethical issue because it can deprive couples of the ability to make an informed choice.

The medical professions' responsibility starts from the time prenatal diagnosis becomes available and therefore a new social responsibility is generated in every subsequent birth. This responsibility can only be discharged by handing it on to the parent through adequate information and genetic counseling.

Conclusions

In Bangladesh prevention of thalassaemia can successfully be done by developing premarital screening through the primary health care system and mandatory blood test before marriage registration and counseling. At the same time, prenatal diagnosis should also be made available nationwide as it is done in Iran. Ethical issues governing the generic counseling need to be addressed and uniform policy should be made taking in account the local, social and religious structures.

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