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Introduction:

Haemoglobin is an important component of blood that carries oxygen from lungs to the tissues. The ability to form haemoglobin is inherited from the parents (half each from the mother and the father). Some people are inherently deficient in making haemoglobin and this condition is called thalassaemia. Thalassaemia exists in two forms i.e. thalassaemia minor or trait and thalassaemia major. Thalassaemia minor is an asymptomatic disorder in which the abnormality is inherited from one of the parents. The abnormality of thalassaemia major is inherited from both of the parents and the affected child is completely unable to form haemoglobin. Such children require lifelong blood transfusions for sustenance of life.

Thalassaemia is the commonest inherited disorder in Pakistan. It is estimated that approximately 5% of the Pakistanis (~10 million) have thalassaemia minor (trait). It is also estimated that each year approximately 5000 new patients of thalassaemia major are born and at one time there may be 50,000-100,000 children with thalassaemia major who require regular blood transfusion each month for their survival.

Thalassaemia is a preventable disease. The objective of thalassaemia prevention is to avoid the births of children with thalassaemia major. In the Mediterranean populations, where thalassaemia is even commoner than Pakistan, effective programmes have brought the incidence of new births of thalassaemia major to almost zero. Thalassaemia prevention programme has the following components:

1. Awareness campaign
2. Carrier Screening and genetic counselling
3. Prenatal diagnosis (diagnosis in pregnancy and selective termination of pregnancy)

Awareness Campaign:

The affected families, health professionals and the general public should be made aware of thalassaemia and various options for its prevention.

Carrier Screening:

Since thalassaemia carriers do not have any symptoms there detection is always difficult. There are many approaches for screening of thalassaemia carriers.

Premarital screening of Thalassaemia (Mediterranean model):

This is a popular approach in the Mediterranean countries where thalassaemia carrier rate is 10-15%, the population is well educated and also understands the implications and consequences of being a carrier. The majority of the population has access to reliable lab facilities for testing of thalassaemia. In addition most of the population is covered by health insurance and very little financial burden rests on the individuals themselves.

Unfortunately none of these conditions apply to the Pakistani population. Thalassaemia is not as common a problem in Pakistan (~5%) as it is in the Mediterranean (10-15%), our people are least educated especially with reference to thalassaemia, and there are only a handful of labs, that too in the major cities and in the private sector only, who know how to test for thalassaemia. We are nowhere near to coverage by health insurance. The burden of testing rests mostly on the already poverty struck population.

A comparison of the economic and other conditions in Italy, Iran and Pakistan is presented in the following table. It needs no rocket science to understand why compulsory premarital screening for thalassaemia has been successful in Italy or Iran and why it is unlikely to succeed in Pakistan. *Enforcing compulsory premarital screening through law could prove counterproductive because (1) most people do not require it (as explained later in section on extended family screening) (2) there are very inadequate lab facilities where reliable testing is available and (3) vast majority of the people would find it as an additional financial burden.*

Parameters	Italy	Iran	Pakistan
Per Capita Income	$35,500	$11,500	$1250
Literacy	98%	80%	45%??
Health Spending	9% of GDP	4.2% of GDP	0.75% of GDP
Population	61 million	70 million	180 million
Thalassaemia	~12%	~4%	~5%

Thalassaemia Screening in Pregnancy (UK model):

Screening for thalassaemia in early pregnancy is a popular approach in the UK and other countries with a large number of ethnic minorities from Mediterranean and Asian countries having high prevalence of thalassaemia. When screening shows the woman to be a thalassaemia carrier then her husband is screened. If the husband is also found to have thalassaemia then the couple is offered prenatal diagnosis. This approach is not practical for a country like Pakistan with vast majority of the population living in rural areas having no access to qualified health care professionals. However, it may be applied to the major urban areas in Pakistan. This approach obviously needs no legislature for implementation.

Screening Extended Families of Thalassaemics (WHO proposed model):

WHO had suggested that carrier screening in the extended families of thalassaemic children could identify a large number of other family relatives with thalassaemia. In a country like Pakistan where consanguineous marriage (cousin marriage) is very common it is envisaged

that the genes for a recessive genetic disorder like thalassaemia get trapped in the family. This hypothesis was tested in a scientific study by carrying out screening of all available members of ten large Pakistani families with index cases of thalassaemia. The testing showed that on an average each family had ~30% carriers as against the ~5% in the general population of Pakistan. In a separate experiment the testing for thalassaemia in five large families with no apparent history of thalassaemia did not show a single carrier in the 400 people tested. This observation proved that, due to the longstanding tradition of cousin marriage, the genes, both normal and the abnormal, are trapped in the families.

Extrapolation of the above quoted research to the population of Pakistan means that genes for thalassaemia are not uniformly distributed. In a layman's language it means that the ~5% carrier rate of thalassaemia in the Pakistani population actually reflects that 5-10% of the families in Pakistan have thalassaemia and the rest over 90% of the families are free from this disorder. This finding has tremendous practical relevance in defining the approach for thalassaemia screening in Pakistan. For obvious reasons one should focus on the ~10% families that harbor the bulk of the carriers rather than involving the rest ~90% who probably do not need to be screened.

There are several advantages in carrying out screening in the index families:

- A large number of carriers and at risk couples can be identified with minimal effort.
- Families often already understand the condition because of the affected child present in the family.
- It avoids the problem of low level of literacy, because information and personal experiences are communicated directly among the affected families attending the centres.
- It avoids the problem of weak health care infrastructure because it can be run from the centres where thalassaemia is diagnosed and treated.

The Recommended Approach:

Out of the three approaches screening in the index families could be the most cost effective for Pakistan. The public sector hospitals in Pakistan are grossly deficient in facilities for diagnosis and management of thalassaemia. Most of the thalassaemics are diagnosed at private laboratories and are managed at centres run by large number of NGOs. At present these NGOs have over 20,000 registered patients of thalassaemia. A phenomenal progress can be made if the extended families of the 20,000 thalassaemics are targeted for screening. With very few exceptions the NGOs have not concentrated on establishing the screening facilities for thalassaemia. *In this regard it may be made compulsory through law that the NGOs dealing with thalassaemia should spend at least 20% of their budget on establishing facilities for thalassaemia screening.*

Prenatal Diagnosis:

It is possible to diagnose thalassaemia in early pregnancy (prenatal diagnosis). Prenatal diagnosis is offered to couples where both partners having thalassaemia trait. If the lab testing shows that fetus has thalassaemia major the couple has the choice either to accept a child with thalassaemia major or get the pregnancy terminated. Most religious scholars in Pakistan and abroad have consensus of opinion that Islam permits termination of pregnancy for a serious genetic abnormality in the fetus provided it is done before 120 days (17 weeks) of gestation.

Prenatal diagnosis of thalassaemia is available in Pakistan since 1994 and almost 10,000 couples have used this test. Over 90% of the couples who had affected fetuses opted to terminate the pregnancy.

References:

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