# EDITORIAL

## Thalassaemia in Pakistan

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Thalassaemia is the commonest single gene disorder of globin chain synthesis all over the world .[1,2] It is found as thalassaemia minor when the defect is inherited from one of the parents and as thalassaemia major when the defect is inherited from both of the parents. Studies of thalassaemia in Pakistan have shown that 5% of the population have thalassaemia minor.[3] Based on this figure it is estimated that each year in Pakistan approximately 5000 children with thalassaemia major are born and the total number of children with thalassaemia major may be over 50,000.[4]

Thalassaemia major is a serious disorder in which the affected child is unable to synthesize its own haemoglobin. The child remains well for the initial three to four months but after this the signs and symptoms of anaemia start appearing. The child looks pale, becomes irritable, and fails to thrive. Diarrhoea and frequent respiratory tract infections are other frequent symptoms. Examination may show hepato-splenomegaly. The lab investigations show moderate to marked hypochromic microcytic anaemia, numerous nucleated red cells and markedly raised Hb-F.[5] An early diagnosis and blood transfusions may halt further deterioration. The child has to be put on lifelong blood transfusions. As a result of regular blood transfusions a large amount of extra iron starts accumulation in the body. This iron can be very harmful for many important organs like heart and endocrine glands. The extra iron must be removed from the body by using iron chelating medicines. Stem cell transplantation is a curative treatment of thalassaemia major. When done early in life over 80% disease free survival can be achieved.[6] The facilities for stem cell transplant are available at several places in Pakistan but the procedure is expensive and due to the limited capacity it can be offered to only a small number of patients.[7]

There are more than 50,000 patients of thalassaemia major in Pakistan. Unfortunately the treatment facilities for such large number of patients are not adequate. Most of the patients are treated at the centres run by nongovernmental organizations (NGO) who have limited resources. Consequently the outcome is also not good. A report published in this issue of the Journal gives a detailed description of the outcome in a large number of patients at a local treatment centre.[8] Most of the children were chronically under-transfused and were also markedly iron overloaded. Majority had growth retardation below the fifth centile for the Pakistani population. The median age at death was just ten years. Although this is a single centre study but the situation at the other centres in Pakistan, with few exceptions, is not expected to be different.

Thalassaemia minor (carrier) is an asymptomatic disorder and most people do not even know about their abnormality. Most people with thalassaemia minor are detected during blood testing for some other reason or when they get married to another carrier and give birth to a child with thalassaemia major. Thalassaemia carriers usually have haemoglobin within the normal range, MCV < 75 fl and MCH < 25 pg. The diagnosis can be confirmed by haemoglobin electrophoresis that typically shows Hb-$A_2$ above 4.0%. A small number (<3%) thalassaemia carriers are silent i.e. their red cell indices and Hb-$A_2$ levels are within the normal range. Such carriers can be missed on routine screening methods and PCR is required to detect them.[5]

Thalassaemia is an autosomal recessive disorder. A child with thalassaemia major is born only when both of the parents have thalassaemia minor. In a carrier couple there is a 25% probability in each pregnancy that the child may inherit abnormality from both of the parents. Marriage of a carrier to a non-carrier will not result in thalassaemia major. The births of children with thalassaemia major can be avoided by premarital carrier screening and avoiding

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marriage between two carriers. The carrier couples who are already married can be offered prenatal diagnosis and selective termination of pregnancy if the fetus is found to be affected. Based on these two approaches excellent results have been achieved in many high risk populations in the Mediterranean countries and lately in Iran.[9] The birthrate of children with thalassaemia major in most of these countries has been brought down to almost zero. The success of thalassaemia prevention programs in the Mediterranean region and Iran has largely been attributed to a political will by the government, public awareness through mass communication media, allocation of funds, and the provision of quality diagnostic services.[9,10] Pakistan has one of the largest numbers of thalassaemia major children in the world and providing treatment facilities to these children is far beyond the available health resources.[2] The burden of disease is likely to increase with the passage of time if no measures are taken to implement a thalassaemia prevention program. The facilities for carrier screening of thalassaemia are available since early eighties. Prenatal diagnosis for thalassaemia is also available in Pakistan since 1994.[11] A study on the extended families of children with thalassaemia major in Pakistan has clearly shown it to be the most cost effective method for large scale application.[12] However, in spite of the two basic facilities for thalassaemia prevention there has not been any appreciable reduction in the birth incidence of thalassaemia major in Pakistan. There are several impediments, including the lack of awareness and the high cost, to the use of these measures in Pakistan.[13] The government of Punjab has initiated a thalassaemia prevention program (PTPP) that aims at providing free of cost carrier screening in the extended families of children with thalassaemia and the general public. PTPP also offers free of cost prenatal diagnosis (https://ptpp.punjab.gov.pk/). The program is in its early stages and it would take several years to see its long term benefits. There is need to initiate such programs in the other provinces of the country and to establish a central coordination cell in the federal ministry of health.[5,14]

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