Beta Thalassemia major: A Preventable disease, Where Do We Stand?

Globally, thalassemia is the most prevalent single gene disorder in human beings. Thalassemia is an autosomal recessive disorder which is characterized by reduced or absent synthesis of either alpha or beta globin chain, resulting of RBCs in reduced hemoglobin level in the Red Blood Cells, decreased production and rapid destruction of RBSs resulting in severe anemia. Depending upon the absence of chain, thalassemia is categorized into alpha or beta thalassemia. Thalassemia occurs with a high frequency in a broad belt extending from the Mediterranean basin through to the Middle East, Indian subcontinent, and Southeast Asia.[1] Worldwide 15 million patients have clinically apparent thalassemic disorder. Every year about 100,000 babies are born with severe form of thalassemia worlwide.[2] About 3% of the world population (200 million people) are carriers of the β-thalassemia gene.[3] The highest carrier frequency of Beta thalassemia is reported in Cyprus, Sardinia, and Southeast Asia.[4] The carrier frequency of Alpha thalassemia is highest in Southeast Asia (30-40%).

In Pakistan, the gene frequency of β-thalassemia is 5% - 8% and is present in all ethnic groups. It is estimated that there are approximately 9 million carriers of β-thalassemia, resulting in more than 5000 births of transfusion-dependent thalassemia (TDT) every year in Pakistan.[5,6] Presently there are estimated 100,000 cases of thalassemia in Pakistan, which makes up for almost 5% of world cases. Consanguinity is the main factor leading to high prevalence in Pakistan. There are 22,000 children registered with thalassemia federation of Pakistan however the actual figure is much higher as many patients are not registered with any thalassemia center. It is an alarming situation in our country because thalassemia may become a very serious threat in next fifty years due to lack of proper genetic counseling and proper screening.

The diagnosis of thalassemia is clinical along with laboratory help in the form of blood complete examination, Hb electrophoresis and confirmation by genetic analysis if required. The treatment strategy varies according to socioeconomic condition of parents and the country. The best treatment option is bone marrow transplant which is available in our country but the cost is a major hurdle resulting a very limited thalassemics to have this treatment option. The other treatment options are supportive in the form of repeated blood transfusion along with iron chelation therapy, splenectomy and Hb F augmentation. Over the past three decades, regular blood transfusions and iron chelation has dramatically improved the quality of life and transformed thalassemia from a rapidly fatal disease in early childhood to a chronic disease compatible with prolonged life.[6] Today life expectancy in certain centers of the world varies between 25-55 years with good compliance of medical treatment.[7]

In our country, repeated blood transfusion along with chelation therapy is the mainstay of treatment of thalassemic patients. This lifelong transfusion therapy along with iron chelation therapy puts an enormous financial burden on parents, society, blood banks and country. The limited facility of blood transfusion and chelation therapy leads to chronic anemia and iron overload resulting in various early complications of disease such as cardiac dysfunction, repeated infections and endocrine problems. These complications lead to compromised quality of life and poor survival with average life expectancy around 10 years in majority of centers. So, the only measure which will decrease the misery of parents regarding thalassemia is the prevention of birth of thalassemia major child.

As thalassemia is a preventable hereditary genetic disorder, chances of having thalassemia major fetus in each pregnancy is 25%, thalassemia minor 50% and normal 25%, if two thalassemia carriers get marriage. Worldwide, together with sickle cell anemia, 9 million carriers become pregnant annually and 1.33 million pregnancies are at risk for a thalassemia major. Most of these patients are born in developing and low-income countries where they create an enormous health burden.[8] According to World Health Organization, if for any disease, the birth rate of the affected infant exceeds 0.1/1000, an effective screening programme should be initiated.[9] So this should be for thalassemia, without preventive measures, the optimal treatment to thalassemics would not be complete.

Prevention is the most important advancement in the field of thalassemia. At present, several countries have set up comprehensive national prevention programs focusing on public awareness and education, carrier screening, effective counseling and prenatal diagnosis. This has been very successfully achieved in many countries i.e., Italy, Greece, Cyprus, Sardinia, UK, France, Iran, Thailand, Australia etc.In most programs, carrier screening and counseling are being performed on a voluntary basis. In Cyprus, however, the Orthodox Church requires a certificate of premarital screening for β-thalassemia but allows the final decision on marriage and reproduction option to be left to the couple. In a number of Muslim countries including Lebanon, Iran, Saudi Arabia, Tunisia, United Arab Emirates, Bahrain, Qatar, and Gaza Strip, the national premarital programs are mandatory and aimed at limiting carrier marriage.[8] In most of these countries, nowadays, interruption of the pregnancy is permitted for severe fetal disorders but only within the fourth month of gestation. By adopting these preventive strategies, birth of thalassemic major child has markedly decreased and ultimately disease burden of these countries has decreased.

Intensive education of health professionals, thalassemic patients & parents and general population regarding thalassemia disease and its prevention is the need of time worldwide and particularly in our country. There should be

regular meetings among pediatricians, obstetricians, family planning workers, nurses, and social workers, to discuss the clinical characteristics, the natural history, the principles of genetic counseling, and the methodologies for preventing the birth of affected child.

For the last few years (since 2009), Punjab thalassemia prevention program (PTPP) has been started in Punjab province regarding thalassemia awareness and its prevention. This program was initially started in limited cities but now it has been extended to many cities and providing thalassemic parents and general public its awareness and prevention. Carrier screening (Extended family screening and premarital screening) facilities are available in our country (Punjab) free of cost .The facility of genetic counseling is available in many centers of the country but prenatal diagnosis facility (chorionic villus sampling) is limited. Parents have to travel a long distance to avail this free facility by government. .

Though, thalassemia is a major public health problem but it is a preventable disease. Many of our neighbouring countries have successfully reduced the number of new cases by running an effective preventive program but we are far behind. In Province of Punjab, 18 districts have PTPP running efficiently but this need to be extended to whole of the Punjab as 50% of population of the country resides in Punjab. Moreover, there is a need to establish more centers for prenatal diagnosis. The condition is worse in rest of the provinces, where various Non-Government organizations and societies are working for this noble cause under the umbrella of Pakistan Thalassemia Federation but this is not sufficient. Khyber Pakhtunkhwa, Sindh and Punjab have passed laws on thalassemia prevention proposing compulsory screening of couples before marriage but Pakistan is still witnessing rise in thalassemic population due to lack of coordination and efforts to control and prevent the disease. This needs laws to be implemented with its full spirit with the involvement of religious and political leadership. Though a Fatwa, for termination of pregnancy within the first trimester is legal in Pakistan if the fetus is thalassemia major. With 5-6% prevalence, ante-natal diagnosis is required for 24,000 at risk pregnancies every year. Currently only small proportion of at risk pregnancies are being covered by ante-natal testing, so this has to increase many folds.

It is thus strongly recommended that in addition to provincial programs, an efficient and well-organized national preventive program in collaboration with Thalassemia Federation of Pakistan should be started addressing thalassemia as a national issue, with an emphasis on screening in schools, colleges /universities, premarital screening, prenatal diagnosis in known thalassemic couples and termination of pregnancy if having thalassemia major fetus. Above all there is a need to educate general public, medical professionals and paramedical staff to create awareness about the disease and its prevention in order to make thalassemia free Pakistan.

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