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Awareness and Screening of β-thalassemia trait in Sindhi community

KEYWORDS: β-thalassemia, Carrier status, Counseling, Screening.

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ABSTRACT *β-thalassemia is one of the most common single gene inherited conditions in the world characterized by reduced synthesis or absence of β-globin chain which causes anemia. Three classes of β-thalassemia have been recognized, beta thalassemia major, intermedia and minor. β-homozygous (major) state present with variable degree of anemia, intermediate condition which may have either heterozygous or homozygous pattern of inheritance has a milder anemia, β-heterozygous cases (minor) are almost asymptomatic with normal or slightly reduced level of hemoglobin. β-homozygous cases have to take the lifelong treatment; management includes regular blood transfusion, chelation therapy for iron overload. It was an utter amusement that even after careful blood administration practices; the patient experiences many complications both immediate and long-term including osteoporosis, cardiac dysfunction, endocrine problems, hepatitis B, hepatitis C, HIV infection etc. due to continuous blood transfusion and iron overload. Some bitter truths about management, although it increases the life span of patient, it prolongs the pain of both the patient and the family. The cost of treatment is very much expensive and stem cell curative therapy is out of reach for most of families. Screening for genetic diseases aims to reduce the burden on the society. Therefore the main objective of this study was population screening of Sindhi Community to identify asymptomatic carriers of recessive conditions, so that they are informed and understand their reproductive risks and options. Carrier status was found to be 8.58%,13.33%,16.60%,11.23%,13.79% and 9.09% for Akola, Murtijapur, Nandura, Akot, Khamgaon and Karanja respectively, which was followed by counseling of carriers .Thus it was concluded that public awareness and preventive measures such as premarital screening and prenatal testing should be done to eliminate this fatal disorder.*

Introduction:
β-Thalassemia is common autosomal disorder among the hereditary diseases worldwide. The β-Thalassemia refer to that group of inherited hemoglobin disorder which are characterized by reduced synthesis (β+ thalassemia) or absence (β° thalassemia) of β-globin chain production which causes anemia (Weatherall and Clegg, 2001). It is an important disorder that has attracted the attention of medical research towards the various paradigms of this multifaceted disease (Ataga, 2007, Barton,2007, Efremov, 2007, Ghosh,2007, Quek, 2007, Theodorsson, 2007) .

Hemoglobin (Hb) is responsible for oxygen delivery from the lungs to peripheral tissue (Bunn, 1984). It is a tetrameric iron containing protein, composed of two alpha-globin and two beta-globin chains join to form hemoglobin in developing erythrocytes and remain together for the life of the RBC's.

Reportedly, there are about 240 million carriers of β-thalassemia worldwide and in India alone the number is approximately 30 million with a mean prevalence of 3.3%. (Yashis, 2007, Verma, 1992, Yagnik, 1997).But among certain communities and religions like Punjabi's, Sindhi's, Bengali's, Jams and Muslim's the incidence of β-thalassemia trait ranges between 8-15 %. (Marwah and Lal, 1994)

In the event of altered beta-globin chain structure or function, in which one or both copies fails quantitatively or qualitatively to produce normal beta-globins, alpha-globin gene continues to produce quantitatively and qualitatively normal alpha-globin. This imbalance of the globin chains results in beta-thalassemia, with precipitation of excess alpha chains contributing to excessive destruction of RBC's, which begins with cascade that ends with significant morbidity and mortality.

Three classes of β-thalassemia have long been recognized clinically, β-thalassemia major, intermedia and minor. (Thein, 2004). β- Homozygous state presents with variable degree of anemia from early childhood and are generally transfusion dependent, a condition clinically known as thalassemia major. β-heterozygous cases (thalassemic minor) are almost asymptomatic with normal or slightly reduced levels of hemoglobin. However an intermediate condition which may have either heterozygous or homozygous pattern of inheritance, requires minimal or no blood transfusion and has milder clinical course than thalassemic major but is severe enough as compared to thalassemic minor. It manifests generally after two years of age and does not require regular transfusion therapy. (Rund, 1997, Tyagi, 2003))

Thalassemic major child is born if both parents carry a hemoglobinopathy trait, since there is a 25% chance with each pregnancy for an affected child. Genetic counseling and genetic testing is recommended for families that carry a thalassmia trait. (Talsania, 2011) Once a child is diagnosed to have thalassemia homozygous disorders, he/she has to take lifelong treatment. Management includes regular filtered packed red cell transfusion,chelation therapy for iron overload, management of complications of iron overload and transfusion, including osteoporosis, cardiac dysfunction, endocrine problem, hepatitis B and C, HIV infection etc. The cost of the treatment of an average weight 4-year old thalassemic child is around Rs.90, 000-100,000 annually in a private setup. Therefore not more than 5-10% of thalassemic children born in India receive optimal treatment. Stem cell transplantation as a curative treatment, which costs between 6 and 16 lac rupees is out of reach for majority of children. Besides bearing the cost of treatment the psychological stress to both the patients and the parents/family is phenomenal. (Mallik, 2010)

There is growing concern that thalassemia may become a very serious problem in the next 50 years, one that will burden the World's blood bank supplies and the health system in general. Therefore emphasis has shifted from treatment to prevention of birth of such children in future (Mallik, 2010). The most effective approach to reduce the burden on the society and to reduce the disease incidence is through implementation of a carrier screening programme, offering genetic

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counseling, prenatal diagnosis and selective termination of affected fetus.(Talsania, 2011). Need for prevention of thalassemia is obvious due to high frequency of the condition, the great expenses and difficulties in providing optimal treatment for patient. Prevention would not only be a good public health practice, but would be cost effective, as the ratio of treatment to prevention is 4:1 as shown in the study from Israel. (Ginsberg, 1998)

Thus the main objective of the proposed study was "Screening of β-thalassemia trait in Sindhi community especially in individuals having marriageable age, so that they should receive information about their personal health, future health and/or potential health of their offspring. **Materials and Methods:**

The study was conducted during the years 2011 and 2012 by organizing the camps at Akola, Murtijapur, Akot, Karanja, Nandura and Khamgaon of Maharashtra, in presence of Community authorized persons, Doctors and technicians, with two major objectives**:** To bring awareness about the disease in the community and to induce the individual to get their blood screened in order to find out its prevalence. For this,

- Every effort was made to involve the participation from individual. Medical persons from the community were involved as a link to induce the Boys and Girls having marriageable age, specially.
- Sindhi movie named "Masoom" was thrown on cable with a moral to make people understand the complication of β-thalassemia and get ready to participate in the camp.
- Booklets outlining the information of thalassemia were distributed in the community people.
- Before conducting the study informed consent was taken from the individuals participated in camp.
- 3 ml of blood was collected from each individual in EDTA bulbs. NESTROFT test was done for carrier detection of thalassemia as a preliminary screening test by using 0.36% buffered saline solution (Mehta, 1990, Manglani, 1997). Further confirmation was done by subjecting the samples for complete blood count on fully automatic analyzer Sysmex Kx-21.Samples with low Hb, MCV and MCH were run on Cation exchange HPLC system (Bio-Rad variant short programme) for quantification of Hb A_2 which was found to be most accurate method for β-thalassemia heterozygote detection (Ou,C.N,1983)

Result:
The study was carried out during the year 2011 and 2012 in various cities nearby and including Akola. Carrier status was found in general public belonging to age group 21-35 which is usually considered as marriage age in order to find out prevalence and to make people aware regarding seriousness of the disorder as well as future effect of disorder on their offspring. As shown in the graph, out of total 757 individual screened at Akola 65(8.58%) cases were found to be carrier of β-thalassemia, out of 210 individual screened from Murtijapur 28 (13.33%) cases were found to be β-thalassemic minor,44 individual(16.60%) out of 265 at Nandura were found to be β-thalassemia carrier, similarly 31 individual (11.23%) out of 276 ,16 individual (13.79%) out of116 and 24 individual (9.09%) out of 264 were found to be carrier of β-thalassemia from Akot, Khamgaon and Karanja respectively. We can also observed from the table no.1, that all the heterozygous or carrier of β-thalassemia showed the low Hb value with MCV of < 80 fl and MCH of < 27 pg, Hemoglobin A2 > 3.5% which was found to be hallmark of diagnosis for β-thalassemia. All the carriers of β-thalassemia trait were asked to meet the Counselors along with the family, friends and close relatives for detailed discussion. They all were cleared with the fact that they are asymptomatic and were emphasized not to marry with another carrier to avoid the chance of birth of β-thalassemic major child which is 25% with each pregnancy.

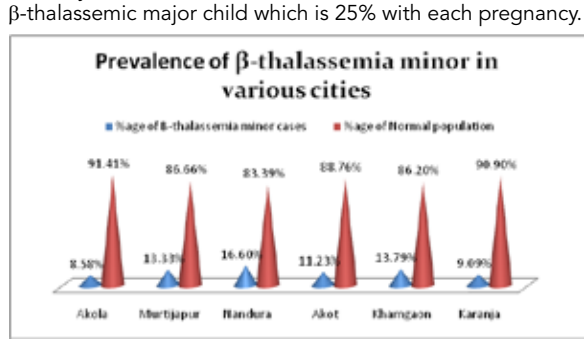

Fig. no. 1: Prevalence of β-thalassemia minor in various cities

Sr.no.	Area	Population	Hb (g/dl)	MCV (fl)	MCH (pg)	HbA_2 (%)	Hb F (%)
1	Akola	N-692	12.97±0.79	83.74±1.63	28.63±0.98	2.30±0.54	1.05±0.26
		C-65	11.02±0.52	72.77±2.96	22.95±2.42	4.74±0.33	1.05±0.25
2	Murtijapur	N-182	13.25±0.73	86.57±3.83	28.74±0.73	2.58±0.50	1.09±0.25
		C-28	10.58±1.10	73.01±2.15	22.62±2.34	4.78±0.77	1.23±0.26
3	Nandura	N-221	12.78±0.69	84.51±3.16	28.75±1.14	2.80±0.27	0.86±0.21
		C-44	10.19±1.28	72.01±4.34	21.92±2.31	4.84±0.48	0.99±0.26
4	Akot	N-245	12.71±0.74	86.21±4.08	28.72±1.01	2.85±0.35	1.01±0.30
		C-31	10.55±0.46	74.03±3.41	22.89±2.13	4.62±0.53	1.00±0.24
5	Khamgaon	N-100	12.35±0.48	84.44±3.83	28.60±0.89	2.83±0.31	0.97±0.30
		C-16	10.81±0.50	76.70±1.70	23.42±1.14	4.66±0.39	1.09±0.28
6	Karanja	N-240	12.71±0.74	85.27±3.98	28.68±1.06	2.91±0.33	1.04±0.30
		C-24	11.36±0.29	75.71±3.43	24.26±1.75	4.58±0.53	0.89±0.31

Note: (N=Normal population C=Carrier population)

Table no.1: Hematological data of Normal and heterozygous β-thalassemia individuals.

Discussion:
β-Thalassemia occurs Worldwide with a higher prevalence among Mediterranean population in the Middle East, in parts of India, Pakistan and South East Asia. Thalassemia major is an inherited blood disorder passed on from parents to their children, causing an inability to produce adequate amount of hemoglobin and leading to severe hemolytic anemia (Mallik, 2010).The management of β-thalassemia major in a developing country poses a major challenge to the health services. Lack of facilities and coordination to this multidisciplinary problem make the treatment difficult in a variety of ways. Availability of antenatal diagnosis is not readily available, bone marrow transplantation, is out of reach for most

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of parents because of financial constrains (Rahman, 2004, Zakerinia, 2005). The need for prevention of thalassemia is obvious due to high frequency of the condition, the great expenses and difficulties in providing optimal treatment for patients and the innumerable fatalities from untreated β-thalassemia. Prevention would not only be a good health practice but it would also be cost effective, as the ratio of treatment to prevention is 4:1,as shown in the study from Israel.(Ginsberg,1994).It would help tremendously in reducing the burden of the disease for patients, families and the health services. In the developed Countries much attention has been directed to the prevention of disease by detection of thalassemia carriers and marriage counseling. By using this prevention programme in Sardinia the incidence of thalassemia patients has decreased from 1:250 live births to 1:1000 live births. Similarly in Cyprus the incidence of thalassemia major cases dropped by 96%.(Buki,1998).The largest programme of screening for thalassemia in the population has been carried out in Gujarat by Indian Red Cross Society in Ahmadabad and other cities from 2004-2010. (IRCS,2010). Thus the objective of present study was also the same that is to reduce the burden of β–thalassemia in the most prevalent Sindhi Community and possibly eradication of fatal disorder β-thalassemia.

Conclusion:

Looking after a thalassemic patient according to standard management is tedious and very expensive with a life threatening complications. So all efforts should be concentrated on prevention of disease. It can be done by public awareness, population screening for carriers, genetic counseling and prenatal diagnosis. The programme of prevention through carrier screening and prenatal diagnosis should receive the highest priority in the future therefore it should be made mandatory by the Government for the all, in order to reduce drastically the birth of affected children.

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