REVIEW OF CLINICAL AND RADIOLOGICAL STUDIES OF ORAL AND MAXILLO-FACIAL MANIFESTATION IN THALASSEMIA FROM PAKISTAN

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Abstract

Oral and maxillofacial manifestation in thalassemia has been discussed from Pakistan.

Introduction

Thalassemia is an inherited single gene recessive, autosomal, blood disease , where totally or partially hemoglobin is produced(Cooley & Lee 1925; Rund & Rachmilewitz, 2005; Verma *et al*., 2011). It is very common in Mediterranean region Flint *et al.* (1998). Hemoglobin is composed of four protein chains, two α-globin and two β- globin chains arranged into a hetro-tetramer Thein (2005). Patients suffering from thalassemia, defects occur in either the α or β- globin chain which produced abnormal red blood cells (Rund & Rachmilewitz , 2005)

Kinds of thallassemia

β –Thalassemia:-
In β-thalassemia mutations occur in the HB β gene at chromosome No.11, and severity of the disease depends on the nature of the mutation. According to severity it is classified in three subclasses. 1) Thalassemia major; 2) Thalassemia intermedia; 3) Thalassemia minor. Severity of disease depends upon the amount of α-globin, however in each sub class tetramer do not form and they bind to the red blood cell membranes, producing damage to membrane, further more at high concentrations they form toxic compounds. (Khan *et al*., 2000; Raihan, *et al.,* 2009; Galanello & Origa, 2010; Khan *et al*., 2012; Bejaoui & Guirat, 2013; Kang *et al*., 2013).

α- Thalassemia: In α-thalassemia two genes HB α1 and HB α 2 at chomosome16are involved and inherited in a recessive manner. The cause of. α - thalassemia is decreased in production of α- globin resulting excess of β chains in adults and excess **γ** chains in new born babies. The excess β- chains form unstable tetramers, which are characterized by abnormal oxygen dissociation curves. (Bridge, 1998; Rund & Rachmilewitz, 2005; Patil, 2006)

Delta (Δ) Thalassemia: Generally hemoglobin, is mainly composed of α and β –chains, however about 3% of adult hemoglobin is made of α and **Δ** chains. Mutations also effect the production of **Δ-** chains (Patil, 2006)

General Manifestation in Thalassemia: Patients suffering in thalassemia due to lack of total or partial production of α or β globins, causes serious effects on their bodies, details of effects has been fully discussed by many worker. (Van dis & Langlias, 1986; Rund & Rachmilewitz, 2005; Raihan *et al*., 2009; Galanello & Origa, 2010; Verma *et al*., 2011; Abdel-Malak *et al*., 2012)

β –thalassemia is also responsible of causing various manifestations and complications of various degrees on different organs of patients. Initially it start by anemia and for treatment of it, regular blood transfusion is necesssory, which not only causes iron overloading but infections are also transmitted which causes serious effects on different organs of patients. Thus a disease that starts just as hemolytic anemia change to a chronic disease with involving many system with various deformities. It effects on bones, liver, kidneys, eyes, spleen, bones of face, maxilla, mandible, pharynx and esophagus-aperture etc. (Cooley & Lee 1925; Chakraborty & Basu,1971, Logothetis *et al.,* 1971; Abu-Alhaija *et al.,* 2002; Seyyedi & Nabavizadeh, 2003; Cunningham *et al*., 2004; Hazza & Al-Jamal, 2006; Amini *et al.,* 2007; Mehdizadeh *et al.,* 2008; Hashemipour & Ebrahimi, 2008; Rashi *et al.,* 2010).

Oral and Maxillofacial Manifestation in Thalassemia: In β thalassemia, bones of face are also involved resulting in severe disfigurement face has been reported in several reports. (Poyton & Davey, 1968; Chakraborty & Basu, 1971; Logothetis *et al.,* 1971; Van dis & Langlias,1986; Well *et al.,*1987; Bassimiti *et al.,*1996; Abu Alhaija *et al.,* 2002; Baig *et al.,* 2006; Amini *et al.,* 2007; Hashemipour& Ebrahimi, 2008).

Changes occur are high and bulging cheek bones, retraction of the upper lip, protrusion of the anterior teeth, spacing of other teeth, over- bite or open-bite, and various degrees of malocclusion. The skeletal changes are due to proliferation of the bone marrow in the facial skeleton (Chakraborty &. Basu, 1971).This proliferated bone marrow is extensively used as an ancillary hematopoietic organ to compensate for the chronic hemolysis. Usually the mandible becomes less enlarged than the maxilla. The dense cortical plates of the mandible apparently prevent expansion and they may occur early in life and tend to persist, particularly in skull (Bassimiti *et al.*, 1996; Abu-Alhaji *et al.*, 2002; Amini *et al.*, 2007; Aminabadi *et al.*, 2006**).** In addition to, a tint of lemon color is also observed in oral mucosa due to existing bilirubin produced by the decomposition of red cells.

Radiological changes are also occur but not evident up to first year of age. These include large bone marrow spaces, one of the most important and diagnostic radiographic features of Thalassemia. This enlargement is due to the fact that, when ineffective erythropoiesis damages the membrane of RBC (red blood cells) causing severe anemia, and thus body responds by increasing the production of RBC, resulting expansion of the bone marrow up to 15-30 times the normal amount. Small maxillary sinuses are also due to bone marrow expansion, classical *"Chipmunk facies"* with depressed cranial vault, maxillary expansion, frontal bossing, retracted upper lip and saddle nose, yellowish tinge at the junction of hard and soft palate, yellow tinged finger nails and spaces with widened trabeculae (Hashemipour & Ebrahimi, 2008). In thalassemic patients, radiograph of The skull shows the increased diploid space and arrangement of trabeculae in the vertical rows, causing "hair on end" appearance.(Hazza & Jamal, 2006). In OPG images, thinning of cortical borders and short spiky roots causing hyperplasia of the alveolar processes of maxilla at the cost of the sinuses normal volume may be visible. Further more cortex, spiky shaped short root, faint lamina Dura and absence of inferior alveolar canals become evident. (Patil, 2006).

Thalassemia in Pakistan and Azad Kashmir: The Population of Pakistan was recorded 18.2490721 millions (Anonyms, 2012). Thalassemia is a major health concern in Pakistan and is the most prevalent genetically transmitted blood disorder with a carrier rate of 5-8 %.f this disease. 5000 children in Pakistan are diagnosed with thalassemia every year. (Anonym, 2012, 2013). The total number of thalassemic major children in Pakistan are 60000-100,000 (Anonym, 2013). It is prevalent in all provinces of Pakistan but total numbers of patient are more in Punjab since its population is 50% of all Pakistan. Further more South Punjab literacy rate is low (Baig, 2006).

The Pakistan Institute of Medical Sciences (PIMS) has diagnosed around 160 new cases of thalassemia major during the last four years (2008-2012). Furthermore 277 patients have been transfused for thalassemia by Pediatric department of the hospital during (2011-2012).

In Azad Kashmir the people suffering from thalassemia are 5% with only one blood bank in public sector which is insufficient for a large population, (Gilani *et al*., 2012).

Treatment: Prevention against thalassemia in developing countries is very challenging. (Mehrnoush, 2011). In big cities of Pakistan treatment facilities in public sector are available however they are insufficient. Some private sectors and ANGO'S are also working. For optimum treatment every thalassemic child needs frequent transfusion of screened packed red cells and regular iron chelation therapy. This cost more than Rs.15,000/ per month (Karnon *et al.*,1991, Anonyms, 2013). Thalassemia major patients required at least Rs, 12.0 billion each year, which is out of reach of health budget. Bone marrow transplantation is also a costly methods which cost 1-1.5 millions (Anonyms, 2013). This situation leaves only one alternative:- stop birth of thalassemic children. This is only possible by screening of thalassemia before marriages and stop consigenous marrariges. (Jaber *et al*., 1998; Hussain, 2000; Naidu *et al*., 2010). Literature survey revealed that work on oral and maxillofacial manifestation in thalassemia has been extensively carried out through out the world (Bassimiti *et al.*,1996; Abu-Alhaiji *et al.*,2002; Amini *et al.*, 2007; Aminabadi *et al.*, 2006;). In India this type of work has also been carried (Patil, 2006). In Pakistan no work of oral and-maxillo-facial manifestation in thalassemia is carried out, however work on other aspect of thalassemia were carried out in Pakistan (Baig, 2006; Jafry, 2007; Gilani *et al.*, 2012). Therefore it is necessary to do work on this aspect in Pakistan.

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