*The Journal of Microbiology and Molecular Genetics (JMMG)*
*Vol. 2, No. 2 (2021), pp. 1-8*

# A REVIEW ON RED BLOOD DISORDER: THALASSEMIA

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## Abstract

Thalassemia is classified as major (homozygous), minor (heterozygous) or intermedia (compound heterozygous). It's diagnosed is based on hematological findings whereas molecular genetic analysis has also been gradually developed. Due to untreatable nature of thalassemia, it is important to adopt preventive measures. In this regard, the community awareness, carrier testing and genetic counselling are important milestones. Region-wise division of thalassemia mutations is diverse in distinct provinces. HBB: c.92+5G > C represents raised incidence in Balochistan and Sindh. HBB: c.27_28insG is most common in KPK and Punjab. Similarly, NG_000007.3: g.71609_72227del619 has its roots previously in India subsequently in Gujratis along with Memon community populating Sindh. Widespread family testing can employ DNA-based genomic analysis in areas where consanguine marriages are usual. An assessed carrier ratio for HBV (3-5%) along with (4-5%) for hepatitis C virus being found in Pakistan due to asymptomatic distribution. Bone marrow transplantation is the only solution to get rid from thalassemia major complications and this facility is accessible ever since 1999 in Pakistan.

## I. Introduction

Thalassemia is a recessive single-gene red blood cell disorder characterized by microcytic anemia (Mahmoud *et al*., 2016). Thomas B. Cooley for the first time noticed splenomegaly in patients suffering from thalassemia hence named Cooley's anemia (Cooley and Lee, 1925). Whipple and Bradford in 1936 studied its pathogenesis and gave the name thalassemia (Ambroggio *et al*., 2016). Caminopetros and Angelini in 1936 and 1937 respectively recognized its recessive inheritance pattern (Zulkeflle *et al*., 2015).

## II. Types and Classification

Clinically it is classified as minor, major, and intermedia thalassemia. Thalassemia minor is asymptomatic and usually not required transfusions (Mahmoud *et al*., 2015). However, the major type requires frequent transfusions with severe clinical symptoms (Khan *et al*., 2015). It can be monogenic or form structural variants i.e., HbC, HbE, HbS which are clinically related to sickle cell anaemia (Galanello *et al*., 2012). Thalassemia intermedia are not transfusion dependent but are clinically more anemic than heterozygous carriers for alpha and beta-thalassemia (Tantiworawit *et al*., 2016). Genetically it is classified as alpha (*HBA1* and *HBA2* encode α-globin chains) and beta-thalassemia (*HBB* encodes β-globin) when there is no or reduced production of chains i.e., α- and β globin (Cebrian *et al*., 2016). Based on the molecular classification, thalassemia is classified as homozygous, heterozygous or compound heterozygous (Sripetchwandee *et al*., 2016).

## III. Molecular Pathology

Complications in thalassemia are mainly due to iron overload. The deadliest complication is heart failure which accounts for 71% of deaths in thalassemia (Higgs *et al*., 2013). Additionally, blood transfusions may also increase the risks of getting serological infections i.e., HCV, HBV, and HIV (Rahim *et al*., 2016).

## IV. Diagnosis and Management

Thalassemia can be diagnosed by hematological findings (complete blood count), qualitative and quantitative Hb analysis. With the advancement in techniques, molecular genetic analysis has progressively developed (Das *et al*., 2016). As thalassemia is not treated with ordinary treatments therefore its management is integral. It can be managed well using proper iron chelators, removing the spleen, and relatively expensive bone marrow transplantation (Kilshaw *et al*., 2015).

## V. Prevention of Thalassemia

Several countries have adopted successful prevention measurements against thalassemia (Ngim *et al*., 2015).

### *Community Training*

Immense understanding, as well as the awareness work, requires to be instigated together by the electronic media and print media. This may involve exclusive talk's placards, educational pamphlets at schools, colleges as well as university levels in addition to a broad setup to have room for every person. Furthermore, various communities' discussions, as well

as debates, can put out the word to the greatest number of individuals. In recent interest, the responsibility of community health employees cannot be forbidden (Williams and Weatherall, 2012, Cao and Kan, 2013).

### *Carrier Testing*

Extensive family testing believes to be the ameliorate method for examining the massive figure of thalassemia carriers (Das *et al*., 2016).

### *Genetic Guidance*

The primary objective in the wake of the genetic counseling is to offer the non-directive data regarding the nature of the illness, preventive measures, accurate diagnosis, risk towards children besides parents, therapy, plus very significantly moral assistance towards visiting couple aimed at deciding fair independent choice (Fucharoen and Weatherall, 2016).

### *Prenatal Diagnosis*

## Thalassemia Condition of Pakistan

Corresponding to the recurrent tribal relocations as well as attacks of Central Asia, the genetic pool stalks from South Asia. Nevertheless, local variants amongst Pakistan astonish the visitors from overseas. Amid an estimated populace of 182 million individuals, there are six main cultural groupings: Sindhi (14%), Balochi (3.5%), Punjabi (53.5%), Pashtun (Pathan) (15%), Muhajirs (7.5%), as well as other (6.5%) residing in Khyber Pakhtunkhwa (KPK) Punjab, Baluchistan along with Sindhi Muslim immigrants otherwise from pre-partition India besides minor cultural groupings correspondingly. The name of Punjab province is derived by the two words “Punj” implying five along with “aab” indicating waters. Punjab represents the land of five rivers. A massive system of canals combined with rivers makes up Punjab an agricultural land. Punjabi cultural grouping constitutes the leading group in Pakistan in conjunction with an estimated 80 million population (Joshi and Singh, 1976).

Khyber Pakhtuwan province is in the north of Pakistan. Its inhabitants are famous as Pathan having stunning fair skin color as well as features. They represent multi roots e.g., Arab, Persian, Jewish, Aiyan, and Greek (Bokhari, 1975). Having a populace of around 20 million are believed as the major ethnic group. Baluchistan is the largest province with minimum local population of Baluchi. Sindh population appears to be the multicultural kind which has its roots from Arabs, Aryans, Rajputs, Baluchis, Turks, Persians, as well as

Scythians (Khan, 1980). In Sindh province, the Mohajirs represent one more cultural grouping having a 15 million populace mass. Mohajirs come up with the background as of Bihar, Northern India, Gujrat along with primarily Urdu speaking people (Bokhari, 1975).

If we look at the Indian traditional caste system, the same system also flourishes in Pakistan having the slightest otherwise no community bias. The practice of the Baradari system is huge as compared to the kinship system. However, the members are interconnected either by far away otherwise close blood relationships or else matrimonies comprising a group of only some hundred to millions of individuals (Shah and Amjad, 2011, Thirumal, 2015).

Pakistan has been graded for the extraordinary proportions of consanguine marriages. 56% of marriages happened among. Ratio (54%) of blood cousin marriages is elevated in countryside areas as compared to (38%) urban areas (Agha, 2016). The probability associated with consanguineal marriages remains with an amplified probability for developing the recessively genetic condition in the family as well as if it is first cousin marriage then the probability gets two-fold (Kilshaw *et al*., 2015).

Various investigations have described distinct carrier frequency which is because of the variances in target population choice, lab practices are accessible as well as being employed but technological problems (Khattak, 1992). World Health Organization (1985) has described a 5% beta-thalassemia carrier ratio. In Pakistan, former investigations have described for more than 90% of entire genotypes of thalassemia (Moatter *et al*., 2012). The region-wise division of such mutations is likewise particularly diverse in distinct provinces. For instance, HBB: c.92+5G > C represents elevated incidence in Balochistan as well as Sindh province. HBB: c.27_28insG is most common in KPK as well as Punjab province. Correspondingly, NG_000007.3: g.71609_72227del619 has its roots earlier in India afterward in Gujratis plus Memon community inhabiting Sindh (Moatter *et al*., 2012, Thein, 2013).

In Pakistan the division of alpha thalassemia is non-evident. Not any otherwise extremely infrequent characteristic thalassemic patients have been detected in Pakistan. They are typically described as correlated to mutations of beta-thalassemia. An investigation by Khan *et al*. (2015) stated that the incidence of alpha allele (3.7) is 8.3% with it appearing in Sindhis, Balochis as well as Punjabis. Alpha (4.2) appears only in Sindhis. Delta beta-thalassemia is infrequently dispersed around Pakistan. Its identification over prenatal as well as the postnatal stage is available. Hematologic besides molecular classification exhibited 11.6g/dL hemoglobin, 70.9, 21.7 pg MCH, fL MCV, 14% HbF in addition 2.6% $HbA_2$ in

thalassemic individuals being heterozygous to delta beta-thalassemia whereas individuals homozygous to this mutation has 0% $HbA_2$, 10.6g/dL hemoglobin, 20.8pg MCH, 69.2 fL MCV as well as 100% HbF (Hanif *et al*., 2015). Extensive family testing can utilize DNA-based genomic examination in regions where consanguine marriages are usual (Finotti *et al*., 2015).

The unfortunate socioeconomic situation in Pakistan likewise reveals its consequences on the life quality of thalassemia. They are at present inadequately handled which results in the acute iron load with linked problems. Deferiprone is efficient as well as inexpensive iron chelator being utilized in Pakistan (Hejazi *et al*., 2016). An estimated carrier ratio for HBV (3-5%) along with (4-5%) for hepatitis C virus being detected in Pakistan owing to symptomless distribution. In Pakistan facility for bone marrow transplantation is accessible ever since 1999 (Shamsi *et al*., 2008). Elevated win ratios can be accomplished through cautious selection of patients along with early age transplantation (Wajid *et al*., 2016). Heterogeneity in haematologic, as well as medical factors in TM, demonstrates that monogenic ailments can appear through a wide-ranging scale in illness seriousness. Our findings detected unusual along with unique mutations which will be helpful for the avoidance of extremely widespread disorder of thalassemia all through Pakistan in the wake of countrywide awareness work.

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