INTRODUCTION

Thalassemia may have originated over 500, years ago, when **(Cooley & Lee, 1925)** described a form of sever anemia, splenomegaly and bone changes in Italian children. Because early cases were reported in children of Mediterranean origin, it called Mediterrancan anemia, until **(Whipple & Bradford, 1936)** attempted to convert various previous titles into one word Thalassemia from the Greek word for Sea ***(thala),*** blood ***(emia).*** According to this clinical syndromes and its severity the thalassemia are classified into four kinds:

1. Thalassemia major: severe anemia, red cells transfusion required to maintain life.
2. Thalassemia intermedia: moderate anemia, red cells transfusion occasionally required.
3. Thalassemia minor : slight if any anemia, microcytic red cells often with erythrocytosis.
4. Thalassemia minima: silent thalassemia, no clinical or hematologic abnormality demonstratable by family studies or gene analysis.

Thalassemia have in common deficient synthesis of one or more of the polypeptide chain of the normal human hemoglobin **(Bank, 1969)**. The primary feature is a quantitative one and contrasts with the qualitative change of hemoglobin structure that characterize the hemoglobinopathies **(Nienhuis, 1984)**.

Today the abilites of the cytogeneticist to look at the finer details of the chromosome have now converged with those the gene prober to produce a very complete picture of the globin therefore thalassemia result, from an imbalance in globin chain production that is almost always due to underproduction of one or two types of globin chains, rare examples in which overproduction of a globin chain causes the imbalance **(Thein *et al.*, 1984)**. Thus thalassemia are classified according to globin chain into five groups **α, β, δβ, δ** and **γ**. The two largest group are **α**- and **β**-thalassemia while **δ**- and **γ**- are much less common and of little clinical significance. Any imbalance in globin chain production involving reduction or absence of **β**-globin chains results in **β**-thalassemia. In contrast with **α**-thalassemia, the mutations resulting in **β**-thalassemia are almost exclusively point mutations **(Kazazian & Boehm, 1988)**.

These mutations diminishing production of mRNA and decreasing synthesis of structurally normal globin. Studies of globin chain synthesis in the homozygous reveals two major types of **β**-thalassemia, one with some residual **β**-chains (β^+-type) and another with no **β**-chains, (β^0-type). In individuals with β^+-thalassemia, the amount of **β**-globin mRNA in reticulocytes and bone marrow normoblasts is decreased three to ten folds **(Housman, 1973 ; Kacian, 1973 and Old, 1978)** whereas, in patients with homozygous **β**-thalassemia, **β**-globin synthesis is absent **(Godet, 1977; Bernards & Flavell, 1980 and Bunn & Forget, 1986)**. In general, in about half of patients, the **β**-globin mRNA in reticulocytes and red cell precursors is deficient or absent **(Kazazian, 1990)**.

In the last few years, the applications of DNA technology as research and diagnostic tools has permitted characterization of the molecular basis of deficient globin synthesis. The thalassemia were the interaction of a large number of different molecular defects. The β-thalassemia are known to result from mutations involving single nucleotide or small deletions characterized by mutation of genes necessitate examination of their expressions in tissue culture cells with the use of plasmid expression vectors **(Kazazian, 1985)**.

Using this technique, investigators have identified nearly 100 different mutations **(Kazazian, 1990)**. These mutations can be grouped into those that alter β-globin mRNA transcription (promoter region mutants and chain terminator mutants) and those that affect mRNA processing splice junction mutants, mutants producing consensus changes, mutants creating new splice signals, mutants enhancing cryptic splice sites, mutants causing defect cleavage as reported by **(Hasounah *et al.*, 1995)**.

Thalassemia is considered the most common genetic disorder worldwide, apporoximately 3% of the world's population (180 million individuals) carry β-thalassemia genes **(Lukens, 1999)**.

These genes are particularly prevalent in inhabitants of Italy and Greece and they extending from the Mediterranean basin throught the Africa, Middle East, Indian subcontinent, Burma and Southeast Asia including southern China, the Malay Peninsula, and Indonesia **(Kulozik *et al.*, 1988)**.