

HEMOGLOBIN C**HEMOGLOBIN C_{HARLEM}****HEMOGLOBIN C**

Hemoglobin C is the second most common hemoglobin variant found in the United States next to sickle hemoglobin. Hemoglobin C is found primarily in African-Americans. Approximately 2-3% of African Americans are A/C heterozygotes.

The beta chain of hemoglobin C contains a lysine substituted for the glutamic acid A in the sixth position. (This is the same site as the amino acid substitution in hemoglobin S). This substitution gives hemoglobin C a relatively high positive charge and therefore slow mobility on electrophoresis. Hemoglobin C migrates with hemoglobin A₂ and hemoglobin E on cellulose acetate electrophoresis (pH 8.4). The mobility of these hemoglobins differs on agar gel electrophoresis (pH 6.2) and they can be distinguished by this method. Deoxyhemoglobin C forms intracellular crystals when the concentration is > 48%.

An individual with hemoglobin C as the principal hemoglobin but no hemoglobin A may have either homozygous hemoglobin C (C/C), or hemoglobin C/beta-thalassemia (C/β-thal). *Either diagnosis is associated with few clinical manifestations.* The best method to distinguish these is to test both parents.

Homozygous hemoglobin C: (C/C)

Patients who are homozygous for hemoglobin C are usually asymptomatic but may have a mild to moderate hemolytic anemia. Aplastic crises and cholelithiasis may occur. The following manifestations have been reported:

- enlarged spleen
- moderate reticulocytosis
- peripheral blood film showing target cells, microspherocytes and intracellular crystals
- packed cell volume ~25-30%

There is no significant fetal or maternal morbidity associated with pregnancy.

Hemoglobin C/ beta-thalassemia: (C/β-thal)

Patients who are heterozygous for hemoglobin C and beta-thalassemia are generally asymptomatic and have moderate hemolytic anemia. Those with hemoglobin C/beta⁺-thalassemia (some hemoglobin A present) tend to have mild anemia and the spleen is usually not palpable. In individuals with hemoglobin C/beta⁰-thalassemia (no hemoglobin A present), the anemia is more marked and the spleen is usually enlarged.

HEMOGLOBIN C_{Harlem}

Hemoglobin C_{Harlem} contains two amino acid substitutions in the β-polypeptide chain and migrates slightly anodal to HbC on cellulose electrophoresis pH 8.4. This hemoglobin has similar properties to sickle hemoglobin in that it gels on deoxygenation and in the deoxy form is relatively insoluble compared with hemoglobin A.

Patients who are homozygous hemoglobin C_{Harlem} or heterozygous for hemoglobin C_{Harlem} and beta-thalassemia may experience sickling and should be managed as sickle patients.

References:

1. Bunn and Forget: Hemoglobin: Molecular, Genetic and Clinical Aspects. Philadelphia, W.B.Saunders Company 1986
2. Weatherall and Clegg: The Thalassemia Syndromes. Oxford, Blackwell Scientific Publications 1981
3. Smith and Krevans: Clinical Manifestations of Hemoglobin C Disorders. Bulletin Johns Hopkins Hospital 104, 17-43. 1959
4. Bookchin R.M. et al, Biochem Biophys Res Commun 23:122, 1966