Cystathionine Beta Synthase (*CBS*) Gene 844ins68 polymorphism in Sickle cell disease patients: Frequency of vaso-occlusive crisis.

1. EHA20(11-14 June; 2015) The 20th Congress of the European Hematology Association(Vienna)Abstract.

2.The Journal of The Egyptian Society of Hematology & Research. Vol: (13) No:(2) ;sept.2017.ISSN: 1687-6148.

Abstract:

Background: Sickle cell disease is (SCD) is a chronic hereditary hemolytic anemia characterized by a hyper-coagulable and inflammatory state which can lead to vaso-occlusive episodes. Increased serum homocysteine level is an independent risk factor for thrombo-embolism and cardiovascular disease and is therefore of interest in sickle cell disease. The 844ins68 mutation/polymorphism, occurring in the *cystathionine beta synthase (CBS)* gene which controls the CBS enzyme activity, is accompanied by hyper-homocysteinemia. This mutation, in homozygous or heterozygous state, lowers CBS enzyme activity and is thus considered an independent risk factor for artery occlusion. **Objectives:** To determine the frequency of the 844ins68 *CBS* gene mutation/polymorphism and its contribution to hyper-homocysteinemia and vaso-occlusive episodes in sickle cell disease and sickle/beta β thalassemia (Sβ-thalassemia) patients. **Patients and Methods:** Nineteen sickle cell disease, 32 Sβ-thalassemia and 2 sickle trait subjects together with 42 age and sex matched healthy controls (HCs) were included. Fasting serum homocysteine level was measured using immune-nephlometry. The *CBS* 844ins68 mutation/polymorphism was detected using conventional polymerase chain reaction (PCR). **Results:** The frequency of the CBS gene wild type was 78.8%, 73% and 81.3% in the HCs, SCD and Sβ-thalassemia groups respectively. The heterozygous variant was observed in 19%, 28.3% and15.6% respectively. The homozygous gene was detected only in the HCs and Sβ -thalassemia groups at a rate of 2% and 3.1% respectively. A significant increase in fasting serum homocysteine level was found in subjects with either homozygous or heterozygous variants compared to wild type subjects (p= <0.001). A significant increase in the frequency of vaso-occlusive crisis (VOC) was found in SCD patients exhibiting this variant (p = 0.05). Positive correlation was found between fasting serum homocysteine level and frequency of VOC (r = 0.30, p = 0.03). Positive correlation was also found between age and fasting homocysteine level (r = 0.36, p = 0.009).

Conclusion: The 844ins68 mutation/polymorphism of the *CBS* gene is a risk factor for VOC and hyper-homocysteinemia in sickle cell disease.

Key words: Sickle Cell Disease, Vaso-occlusive crisis, Cystathionine beta-synthase gene, Hyperhomocysteinemia.