Comment on: oxidative stress and antioxidant status in beta-thalassemia heterozygotes

Hossain Uddin Shekhar
University of Dhaka, Bangladesh

The beta-thalassemias were among the first human diseases to be delineated at the molecular level. Heterozygous beta-thalassemia (synonyms: β-thalassemia minor - hereditary leptocytosis minor) is a rare blood disorder characterized by a moderately low level of hemoglobin in red blood cells (RBCs), that is, anemia. This disorder is inherited. People with thalassemia minor have one of a pair (heterozygous) of the thalassemia gene. If a person has two copies of the gene, they will have thalassemia major, which is a more serious disease. The beta-thalassemias (both homo- and heterozygotes) are a heterogeneous group with respect to molecular pathogenesis and populations and ethnic groups differ with respect to the predominating mutations. This variable spectrum of β-thalassemia mutations has resulted in extensive studies in each population and ethnic group to identify the major mutations.

Auto-oxidation of globin chains and iron overload are the suggested mechanisms for the increased oxidative stress in both major and minor β-thalassemia. It has been reported that thiobarbituric acid-reactive (TBARS) substances increase significantly in patients suffering from β-thalassemia major[1]. In another study it has been reported that the total serum antioxidant potential, measured as trolox equivalent antioxidant capacity appeared significantly lower (14%) compared to normal controls[2]. Similar results are expected with β-thalassemia minor but to a lesser extent.

More than 200 mutations in the β-thalassemia globin gene have been reported that result in β-thalassemia[3,4], together with a much smaller number of gene deletions ranging from 25 base pair (bp) to 67 kilobases (kb)[5]. However, genotypic variability at known loci is often insufficient to explain the disparate phenotypes of individual patients with the same genotype.

Studies have been carried out to find correlations between the hematological phenotype and the type of different β-thalassemia mutation[6]. It was found that a) heterozygotes for beta$^+$ IVS-I nt 6 and beta$^+$ -87 mutations produce larger and better hemoglobinized RBCs, and b) heterozygotes for beta$^+$ IVS-I nt 6 and beta$^+$ IVS-I nt 110 mutations have a less marked increase of hemoglobin (Hb) A2 levels compared to heterozygotes for the other mutations investigated.

Al-Mudalal et al.[7] studied super oxide dismutase (SOD) and catalase activity in RBCs in thalassemia major and minor. They observed that the SOD activity was increased in both thalassemia major and minor compared to healthy controls but thalassemia major patients have much higher SOD activity than in thalassemia minor. However this correlation was not found in the case of catalase activity. Increased red cell SOD values in thalassemic patients have previously been explained as a reaction to, or compensation for, the increased production of superoxide radicals, the amount of which is related to the excess globin chains[8,9]. A possible explanation for lower red cell catalase activity found in the more severe genotype of β-thalassemia is that the greater amount of hydrogen peroxide might cause direct toxic damage to catalase[10,11]. The concentration of this is considerably reduced in conditions of high oxidative stress[12]. In a three-month study period (April to June 2011) in Bangladesh, 600 individuals from peripheral rural areas suspected of suffering from anemia were referred to the city's hospitals[13]. Table 1 below represents the spectrum of hemoglobinopathies encountered during these three months. It is important to note that β-thalassemia minor is the most common form of hemoglobinopathy (21.3%). This study also reveals that all the hematological features of thalassemia minor have decreased to a lesser extent than in thalassemia major compared to normal healthy individuals.

However, to make a conclusive remark about the oxidative stress and antioxidant capacity in beta-thalassemia heterozygotes, the sample size should be big enough. And it is true that finding a particular incidence of a particular mutation type is really very difficult. So without making a cohort study over a long period of time, it is difficult to reach a conclusion about which type of mutation is more venerable to oxidative stress as well as the pattern of antioxidant status.

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Corresponding author:
Hossain Uddin Shekhar
Department of Biochemistry and Molecular Biology
Dhaka University
Dhaka -1000
Bangladesh
Phones : 88 02 9661900-70
hossainshekhar@yahoo.com

www.rbhh.org or www.scielo.br/rbhh

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Table 1 - Spectrum of hemoglobinopathies in Bangladesh

Type of hemoglobinopathy	Incidence					
	Male		Female		Total	
	n	%	n	%	n	%
Normal	166	48.8	87	33.5	253	42.2
β-Thalassemia minor	57	16.8	71	27.3	128	21.3
E-β-Thalassemia	48	14.1	33	12.7	81	13.5
Hemoglobin E disease	25	7.3	30	11.5	55	9.2
Hemoglobin E trait	38	11.2	35	13.4	73	12.1
δ- β-Thalassemia	1	0.3	2	0.8	3	0.5
β-Thalassemia major	2	0.6	1	0.4	3	0.5
Hemoglobin D/S trait	3	0.9	1	0.4	4	0.7
Total	340	100.0	260	100.0	600	100.0

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