

Short Communication

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Spectrum of clinical variability in the Indian HbS $\hat{\alpha}$ thalassemia patientsS.Pandey^{1*}, R.Saxena¹, R.M.Mishra², U.K.Chauhan³, M.Sharma⁴, S.W.Pandey³¹Dept of Hematology, All India Institute of Medical Sciences, Ansari Nagar, New Delhi-110029, (INDIA)²Dept of Environmental Biology, APS University, Rewa-486003, (INDIA)³Centre for Biotechnology Studies, APS University, Rewa -486003, (INDIA)⁴Dept of Hematology, Safdarjung Hospital, Ansari Nagar, New Delhi-110029, (INDIA)

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Received: 1st July, 2013 ; Accepted: 15th August, 2013**ABSTRACT**

Patients of sickle beta thalassemia show the clinical variability in mild to moderate manner. Co-inheritance of $\hat{\alpha}^+$ thalassemia and $\hat{\alpha}^0$ thalassemia showed great clinical variability. This phenotypic heterogeneity mainly depends on the $\hat{\alpha}$ thalassemia mutations. In our cases the hematological and clinical features were mild in HbS $\hat{\alpha}^+$ patients where the HbS $\hat{\alpha}^0$ patients showed the severe phenotype. Seven common thalassemia mutation present in the patients with variable frequency and mild to severe phenotypes of HbS $\hat{\alpha}^+$ as well as HbS $\hat{\alpha}^0$ thalassemia patients. Conclusion of the study was the HbS $\hat{\alpha}^+$ patient's clinical feature resulted as thalassemia intermedia while HbS $\hat{\alpha}^0$ -thalassemia patient's clinical feature closely related with sickle homozygous. © 2013 Trade Science Inc. - INDIA

KEYWORDS

HPLC;
Sickle cell;
Hemoglobinopathies.

INTRODUCTION

Sickle cell disease is quite variable in itself and few of the factors that contribute to this variability. Some are genetic, others likely involve environmental influences. One of the most important genetic factors is thalassemia. One form of thalassemia, called $\hat{\alpha}$ -thalassemia reduces the production of normal hemoglobin. Most clinical manifestation in the HbS syndrome are due to the $\hat{\alpha}$ s gene mutation and depend on amount of sickling^[1]. However when there is coinheritance of $\hat{\alpha}$ thal gene mutation, as in S $\hat{\alpha}$ thalassemia; the clinical picture may vary depending on the type of $\hat{\alpha}$ thal gene mutation present^[2,3]. Sickle cell $\hat{\alpha}$ -thalassemia also known micro drepanocytic disease. This disorder occurs when one beta gene carries HbS mutation and the other gene car-

ries beta thalassemia mutation (double heterozygous state). It is commonly observed in West Africa, the Mediterranean countries, and India. Clinical manifestations are decided by whether the beta thalassemia gene inherited is $\hat{\alpha}^0$ or $\hat{\alpha}^{+4}$. The severity of sickle $\hat{\alpha}$ -thalassemia varies. Some patients with sickle $\hat{\alpha}$ -thalassemia have a condition as severe as sickle cell disease itself. Others have few and relatively mild problems. It is well known that SS disease is more severe than $\hat{\alpha}$ -thalassemia patients^[5]. Our aim was to evaluate the clinical variability of Indian sickle cell beta thalassemia patients due to presence of various thalassemia mutations.

MATERIALS AND METHOD

Patient of sickle $\hat{\alpha}$ -thalassemia were recruited from

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Out patient department; All India Institute of Medical Sciences (AIIMS) New Delhi. Study was approved from institutional ethical committee. Five ml blood sample was collected from patients after taken signed consent. All investigations done in the department of hematology AIIMS. Diagnosis of sickle β -thalassemia patients and quantitative assessment of hemoglobin Hb F, Hb A, Hb A2 and Hb S done by high performance liquid chromatography (HPLC-Bio-Rad-Variant TMBio Rad, CA, USA). Complete blood count and red cell indices were measured by automated cell analyzer (SYSMEX K-4500, Kobe Japan).

Giemsa-stained peripheral blood smears were examined for red cell morphology. ARMS- PCR applied for the molecular study of beta mutations according to published literatures^[6]. Mean values, standard deviation & frequency distribution used to evaluate the hematological & clinical data.

RESULT AND DISCUSSION

Sixty five sickle β -thalassemia patients divided in two group; HbS β^+ and HbS β^0 according to the severity of disease. Nineteen patients were HbS β^+ with a mean age 10.7 \pm 6.2 (12 male and 7 female) while 46 patients were HbS β^0 with mean age 13.1 \pm 7.4 (27 male and 19 female). HbS β^- thalassemia patients red cells were microcytic hypochromic and sickle cell with few target cells. Peripheral blood smear shows feature of both sickle cell anemia and thalassemia. Red cell indices decreased. HbS 60-70%, HbA2 (4-10%) and HbF was 9-21%. HbA was almost nil in HbS β^0 -thalassemia (3.2 \pm 1.7) while 15.7 \pm 8.6 in HbS β^+ thalassemia patients. Molecular studies for thalassemia done by ARMS-PCR. IVS 1-5(G-C) mutation frequency was higher (26.08%) in HbS β^0 thalassemia while 619bp deletions was high (21.05%) in HbS β^+ thalassemia patients.

Hematological, clinical and thalassemia mutations details are given in TABLE 1, 2 and 3 respectively. Sub classification of Sickle cell β -thalassemia in to sickle β^0 thalassemia and sickle β^+ thalassemia on the basis of clinical features alone is difficult^[7]. The clinical features of HbS β^- thalassemia are extremely variable ranging from completely asymptomatic state to severe disease similar to homozygous sickle cell disease^[8]. The effect of β -thalassemia mutation on the clinical severity of β -thalassemia are well documented^[9]. The clinical severity largely

depend upon the nature or the β -thalassemia mutation i.e. β^0 or β^{+10} . In our cases the hemoglobin, reticulocytes and red cell indices were improved in comparison to HbS β^0 patients. Although 36.84% HbS β^+ patients were transfusion dependent but their clinical presentation was mild. Mild sickle cell β^+ thalassemia occurs predominantly in Africa and resembles sickle cell trait^[4].

TABLE 1 : Comparative hematological parameters of HbS β^0 -thalassemia patients and HbS β^+ -thalassemia

Hematological parameters	Mean \pm SD	
	HbS β^+ N=19	HbS β^0 N=46
HGB g/dl	8.3 \pm 1.6	7.2 \pm 1.4
RBCs millions/ μ l	3.7 \pm 1.9	3.2 \pm 1.4
HCT%	28.7 \pm 4.3	25.3 \pm 6.5
MCV fl	65.8 \pm 9.1	62.1 \pm 12.6
MCH pg	18.3.5 \pm 3.4	18.2 \pm 7.5
MCHC g/dl	24.8 \pm 4.1	23.7 \pm 3.2
S.iron μ g/dl	72.3 \pm 3	75.7 \pm 4

TABLE 2 : Comparative clinical parameters of HbS β^0 thalassemia and HbS β^+ thalassemia patients

Clinical features	Frequency %	
	HbS β^+ N=19	HbS β^0 N=46
Pallor	14 (73.68)	37(80.43)
DVT	Nil	2(4.34)
Splenomegaly	4(21.05)	15(32.60)
Painful crisis	12(63.15)	32(69.56)
AVN	Nil	2(4.34)
Weakness	8(42.1)	27(58.69)
jaundice	4(21.05)	9(19.56)
Hepatomegaly	5(26.31)	12(26.08)
Retinopathy	Nil	2(4.34)
Gall bladder stone	3(15.78)	14(30.43)
Septicemia	1(5.26)	3(6.52)
Hyper pigmentation	1(5.26)	4(8.69)
Blood transfusion	7(36.84)	38(82.60)

TABLE 3 : Beta thalassemia mutations in HbS β patients

Mutation	HbS β^+ N=19	HbS β^0 N=46
IVS 1-5(G-C)	3(15.78)	12(26.08)
IVS 1-1(G-T)	2(10.52)	9(19.56)
Cd8/9(+G)	2(10.52)	8(17.39)
Cd41/42(-CTTT)	3(15.78)	6(13.04)
619bp deL.	4(21.05)	4(8.69)
Cap site+1 (A-C)	3(15.78)	3(6.52)
-88 CT	2(10.52)	4(8.69)

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Patient with HbS β^+ thalassemia had mild to moderate presentation while those with HbS β^0 thalassemia showed more heterogeneity in clinical manifestation^[5,11-13]. The mild mutations of thalassemia in combination with other severe β^+ or β^0 mutations resulted in a very variable clinical presentation^[14]. In our cases the common thalassemia mutation present in the patients with variable frequency and mild to severe phenotypes of HbS β^+ as well as HbS β^0 thalassemia patients. The observation of the study concludes the hematological features of the HbS β^+ thalassemia patients similar to thalassemia intermedia with mild to moderate severity. While the HbS β^0 -thalassemia closely related with sickle cell anemia.

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