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Research Paper

Hb Q: An Uncommon Hemoglobin Variant, in a Native of West Bengal and Punjab – A Report of two Cases

Medical Science

KEYWORDS : Hemoglobinopathies, alpha chain variant, Hb Q India, HPLC

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ABSTRACT

Hb Q- India is a rare alpha chain variant and usually it presents in heterozygous form. It is caused by the mutation AAG - GAG (Aspartic acid – histidine) in the position of codon 64 of the alpha 1 gene. In High-performance liquid chromatography (HPLC), it is seen as an unknown peak in the retention time window of 4.77 minutes ± 0.02 minute. Most of the previous cases were reported in Sindhi family. Here we report two cases of HbQ India; one was 30 year old female native of West Bengal and another 22 year old female native of Punjab.

Introduction: Abnormality of hemoglobin synthesis are among the most common inherited disorders and can be quantitative (thalassemia syndrome) or qualitative (variants HbS or HbQ) [1]. Hemoglobin Q-India is a rare alpha-chain structural variant caused by the mutation AAG-GAG (aspartic acid-histidine) in the position of codon 64 of the alpha 1 gene [1]. This α chain variant does not cause hematological disorders because the residue involved is on the surface of the Hb tetramer and charge changes at these position does not affect the property of hemoglobin molecule. Hemoglobin Q India in heterozygous state with hemoglobin A does not show any abnormality. All the parameters of complete blood count remain within normal limit. In high performance liquid chromatography (HPLC), abnormal hemoglobin is seen as an unknown peak in the retention time window of 4.770.02 minutes. Hb Q levels in homozygous cases ranges from 32-35 %, while in Hb Q heterozygotes the level is 20 % [2].

Case report:

Case 1- A 30 year old women resident of West Bengal came for antenatal checkup in MGM's New Bombay Hospital,Vashi. Her hemoglobin was 11.8 gm/dL (normal 12 to 15 gm/dL), total leucocyte count 6600 / cu.mm (Normal 4000-11,000 / cu. mm) and platelets count was 1.85 lacs/cu mm (Normal 1.5 to 4.5 lacs/cu. mm). Erythrocytes were normocytic and normochromic. There was no reticulocytosis or anisopoikilocytosis. High performance liquid chromatography (HPLC) was done on Biorad Variant HPLC system. Result of HPLC are given in table 1-

Investigation	Observed value	Reference Interval
Hemoglobin A	80.9 %	94.3 -98.5 %
Hemoglobin A 2	1.3 %	1.5-3.7 %
Hemoglobin F	0.4%	0.0-2.0 %
Other	17.4 %	-

Table 1- Observed value of HPLC analysis

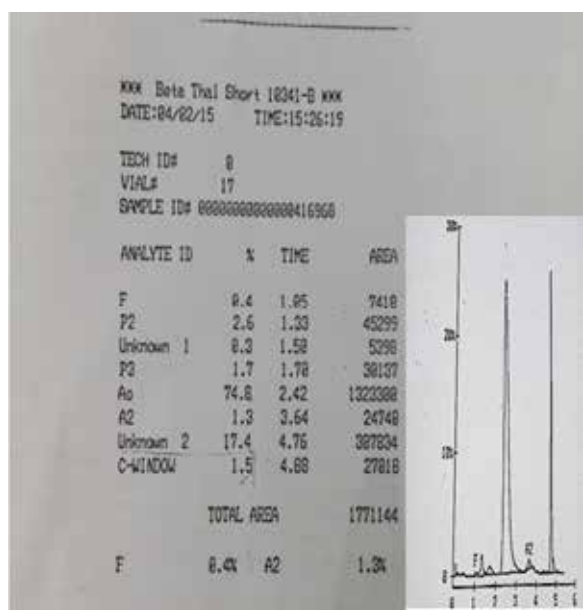

Image 1- Hemoglobin analysis by HPLC.Inset showing chromatogram (case 1)

On HPLC analysis an unknown peak (17.4%) noted at retention time of 4.76 minutes. This was suggestive of Hb Q-India. However, even after advice patient's DNA analysis could not be done.

Case 2- A 22 year old female resident of Punjab came for antenatal checkup and thalassemia screening. Her hemoglobin was 11.2 gm. /dl(normal 12 to 15 gm/dL), total leucocyte count 7700 / cu.mm (Normal 4000-11,000 / cu. mm) and platelets count was 2.02 lacs/cu mm (Normal 1.5 to 4.5 lacs/cu. mm). Erythrocytes were normocytic and normochromic. There was no reticulocytosis or anisopoikilocytosis. High performance liquid chromatography (HPLC) was done on BIORAD Variant HPLC system.Result of HPLC are given in table 2-

Investigation	Observed value	Reference Interval
Hemoglobin A	81.8 %	94.3 -98.5 %
Hemoglobin A 2	1.8 %	1.5-3.7 %
Hemoglobin F	0.5%	0.0-2.0 %
Other	15.7 %	-

Table 2- Observed value of HPLC analysis (case 2)

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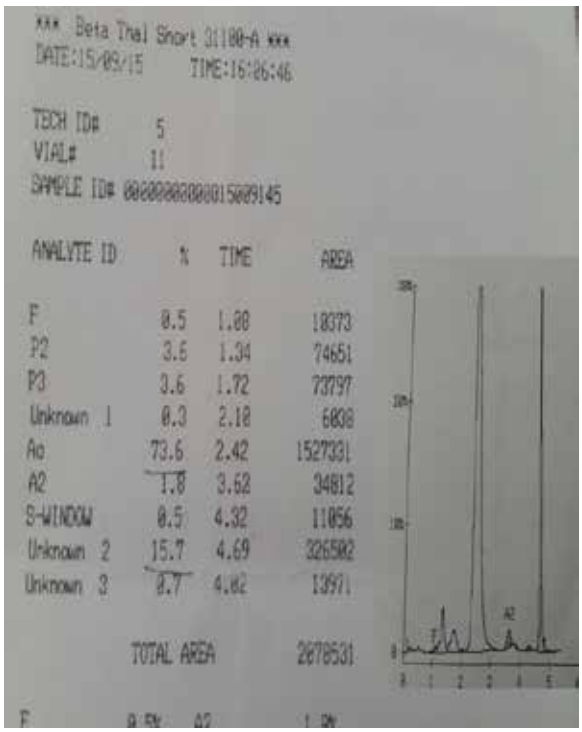

Image 2 - Hemoglobin analysis by HPLC, Inset showing chromatogram (case 2) On HPLC analysis an unknown peak (15.7%) identified at retention time of 4.69 minutes . This was suggestive of Hb Q India.

Discussion: The first case of Hb Q India was first reported by Sukumaran et.al in 1972 in a Sindhi family in association with beta thalassemia[3]. Hb Q India is a rare α chain structural variant caused by mutation in the position of codon 64 of α 1 gene with a replacement of aspartic acid with histidine. Three variants of Hb Q have been described. These include Hb Q- Thailand, Hb Q India and Hb Q-Iran. In Hb Q Thailand there is mutation in the position of codon 74 of α 1 gene with a replacement of aspartic acid with histidine and in Hb Q Iran mutation in the position of codon 75 with replacement of aspartic acid with histidine[4].The prevalence of Hb Q India in India is 0.4 %, found predominantly in Sindhi families. However our patients were natives of West Bengal and Punjab respectively.

Hb Q –India has a protein structure similar to the normal Hb molecule. In the heterozygous state, patients with Hb Q do not have the thalassemia phenotype or any other clinical manifestation. The replacement of aspartic acid with histidine is on the surface of the protein structure and does not affect the inner chain protein content and electrical charges of the molecule, and therefore does not cause any changes in the hematological parameters and indices.[5]

Hb Q levels in homozygous state are in the range of 32 to 35 % while in heterozygous state in less than 20 % [2]. In our patients Hb Q levels were 17.4 % and 15.7% respectively.

Hb Q may be associated with other abnormal hemoglobins. In one study interaction of Hb Q-India with Beta thalassemia have been reported in 64 cases[2]. Also the association of Hb Q with Hb S and Hb D also has been reported.[5]

HPLC provides reliable and reproducible data, enabling the retention time and position to be used to identify variants. However several variants are known to have identical retention times. Thus, the data are limited in suggesting a candidate variant when only one technique is used. One of the important methods for the detection of abnormal hemoglobin is ARMS-PCR. This is quite useful for the quick identification of α globin or α globin genes for which mutation is known. The definite method for the identification of Hb variants is DNA sequencing of α and α globin chain genes.[4]

Conclusion:Incidence of Hb Q in India is quite low may be because it is not diagnosed asit is not associated with clinical symptoms.Antenatal andPremarital screening tests by HPLC can detect or pickup such Hb variants hence such screening tests should beincluded in health checkups to prevent homozygosity of Hb Q and also other abnormal hemoglobin variants. HPLC forms a rapid, accurate and reproducible tool for early detection and management of hemoglobinopathies and itsvariants. However, for definitive diagnosis DNA sequencing and ARMS-PCR are required.

REFERENCE

1. Sachdev R, Dam AR, TyagiG.Detection of Hb Variants and hemoglobinopathies in Indian population using HPLC: report of 2600 cases. Indian Journal of Pathology and Microbiology 2010; 53(1):57-62. 2. Phanasgaonkar S, Colah R,Ghosh K, Mohanty D, Gupte S. Hb Q (India) and its interaction with beta-thalassemia: a study of 64 cases from India. Br J Biomed Sci.2007; 64(4): 160-3. 3. Sukumaran PK, Merchant SM, Dessaii MP. Hemoglobin Q India(alpha 64 (E13) aspartic acid to histidine) associated with beta-thalassemia observed in three Sindhi families. J Med Genet 1972; 9(4): 436-42. 4. RipalKumarBhimani, GunavatiB.Rathod, SachinAggarwal, Rushabh Patel, Rahul Goyal, N.K.Kuchhal. Hb Q –India: An Uncommon hemoglobin variant diagnosed in two patients- Case series. International Archeives of Integrated Medicine 2014; 1(4): 68-74. 5. Colaco S, Surve R, Sawant P, Nadkarni A, Ghosh K, Colah R. Hb D Punjab/ HbQ India Compound Heterozygosity: AN Unusual Association.Mediterr J Hematol Infect Dis 2014, 6(1): e2014072.