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**Pathology**

# A Rare Case of Haemoglobin J-Toronto in a Child

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**Abstract** **Case Report**

***Introduction:*** India is an ethnically diverse country with marked regional variation. This diversity is often reflected in the presence of different Hemoglobin variants. Hb variants arise due to mutations in the genes encoding for the α-chain and β-chain. Hb J is an infrequently found α-globin variant. It is a Fast moving hemoglobin. Haemoglobin J (Hb-J) was first described by Thorup et al. in an African-American patient (1956) and since then more than 50 variants of Hb-J are identified. Hb J-Toronto [alpha5(A3) Ala>Asp] is one of the rare variants identified. ***Case report*:** Blood sample of one year old child for high-performance liquid chromatography was received. The HPLC showed an abnormally high peak in P3 window on BIO RAD D10 machine. The high-performance liquid chromatography showed normal hemoglobin Hb F and Hb A2, but showed elevated levels of P3 (31.7%) which indicates presence of a Hb J variant. ***Conclusion*:** Hb J-Toronto is a rare variant of abnormal hemoglobin. It has little clinical significance in heterozygous state but when combined with other variants, they may give rise to severe disease.Prenatal analysis, especially by HPLC, is a key screening method to avoid hemoglobinopathies in off springs. One important clinical condition which may lead to a wrong diagnosis of FMH's is uncontrolled diabetes mellitus.

**Keywords:** Hemoglobin J- Toronto, HPLC, Parental screening, Fast moving haemoglobin (FMH's).



## INTRODUCTION

India is an ethnically diverse country with marked regional variation. This diversity is reflected in the presence of different Hemoglobin variants [1]. In recent times, abnormal haemoglobins (Hb) are generally discovered during a systematic study performed within programs for prevention of Hb disorders in off springs which are mostly picked up as abnormal peaks on high-performance liquid chromatography (HPLC) or electrophoresis [2]. Hb variants arise due to mutations in the genes encoding for the α-chain and β-chain that result in amino acid changes [3].

Fast moving hemoglobins (FMH's) are the rare hemoglobin variants. They are having tendency to migrate anodally to hemoglobin A on alkaline gel electrophoresis because of the mutation in the globin genes. The basic pathophysiology behind it is the substitution of a negatively charged aminoacid residue in either α, β or γ globin chains [4]. Hb J is an infrequently found α-globin variant.

Haemoglobin J (Hb-J) was first described by Thorup et al. in an African-American patient (1956)1 and since then more than 50 variants of Hb-J such as Hb-J Capetown [alpha92(FG4) Arg>Gln)], Hb J-Buda [alpha61(E10) Lys>Asn], Hb J-Chicago [beta76(E20) Ala>Asp], Hb JSardegna [alpha50(CE8) His>Asp), and Hb J-Toronto [alpha5(A3) Ala>Asp] are identified [5]. Due to these changes they move faster than haemoglobin "A" on cellulose acetate electrophorsis.

Some of Hb-J variants have abnormal properties and affect respective haematologic indices, while majority of them do not result in any abnormal clinical manifestation. For instance, Hb J-Cape Town, the most commonly seen Hb-J variant, in heterozygous case is associated with increased oxygen affinity and polycythemia.(5) Some variants like Hb J-Toronto and Hb J-Oxford will show a completely unremarkable clinical picture in the heterozygote patients. Hence, they are detected accidentally during family or antenatal screening by alkaline gel electrophoresis and/or HPLC. The Hb-J gene follows the pattern of autosomal codominant inheritance. The existence of Hb-J does not affect the longevity or survival of the foetus. (4) Prenatal as well as premarital screening and identification of the Hb variants are important due to the fact that certain

populations have a high prevalence of hemoglobinopathies.

## CASE REPORT

Blood sample of 1 year old child for abnormal haemoglobin studies by high-performance liquid chromatography was received. The HPLC showed an abnormally high peak in P3 window on BIO RAD D10 machine. On having suspicion of degenerated sample, the sample was recollected and rechecked. Persistence of high P3 peak was found.

The high-performance liquid chromatography also showed normal hemoglobin (Hb) F and Hb A2, but showed elevated levels of P3 (31.7%) which indicated the presence of a Hb J variant.

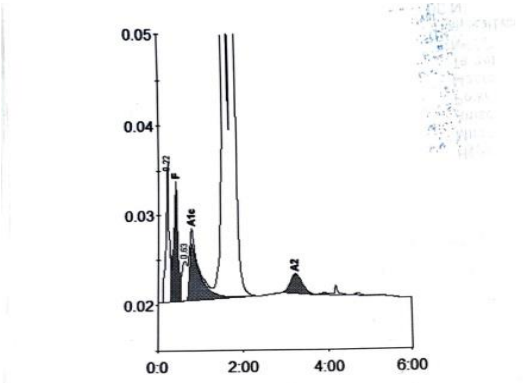
The patient was advised for Parental screening and DNA analysis for definitive diagnosis.

On testing mother's sample for abnormal haemoglobin, we found evidence for same P3 peak at same retention time on HPLC by D10 BIO RAD machine. While the father had no evidence of hemoglobinopathies.

A probable case of, haemoglobin J-Toronto [alpha 5 (A3) Ala > Asp] on globin gene, of a year old male patient who came to Desai Metropolis laboratory for investigation is described here. Haematological tests including haemoglobin, haematocrit, cell indices are as below (Table I).

**Table 1: Showing Hematological Parameters of Patient Investigation**

| | Result | Unit | Reference Range |
|---|---|---|---|
| Haemoglobin | 10.2 | g/dl | 11.5-14.5 |
| RBC | 4.90 | $10^{*6}$ /uL | 4.0-5.3 |
| Packed Cells Volume | 32.7 | % | 33-43 |
| Total Leucocyte Count | 12.4 | $10^{*3}$ /uL | 4000-12000 |
| MCV | 66.6 | fl | 76-90 |
| MCH | 20.9 | pg | 25-31 |
| MCHC | 31.4 | g/dl | 32-36 |
| Platelet | 357 | $10^{*3}$ /uL | 140-440 |
| RDW-CV | 18.1 | % | 11.5-15.0 |




Peak table - ID: 4019240005865

| Peak | R.time | Height | Area | Area % |
|---|---|---|---|---|
| A1a | 0.22 | 15484 | 82234 | 3.0 |
| F | 0.42 | 12509 | 76364 | 2.7 |
| LA1c/CHb-1 | 0.63 | 4380 | 37000 | 1.3 |
| A1c | 0.80 | 6300 | 106762 | 5.4 |
| P3 | 1.58 | 140375 | 881350 | 31.7 |
| A0 | 1.75 | 321428 | 1558347 | 56.0 |
| A2 | 3.24 | 2115 | 40829 | 1.7 |
| Total Area: | | 2782885 | | |

| Concentration: | % |
|---|---|
| F | 2.7 |
| A1c | 5.4 |
| A2 | 1.7 |

**Abnormal haemoglobin studies by high performance liquid chromatography, results were as Shown: P3 Peak – 31.7% at Retention time 1.58**

As shown above, P3 retention time is 1.58, which according to *BIO RAD's D-10 Hemoglobin testing system* [6] falls in Hb –J Toronto window.

| VARIANT NAME | RETENTION TIME As observed in the Library of Variants | ASSOCIATED MUTATION |
|---|---|---|
| Hb J-Mexico | 1.37 | α 54 (Gln→Glu) |
| Hb J-Meerut | 1.42 | α 120 (Ala→Glu) |
| Hb J-Oxford | 1.46 | α 15 (Gly→Asp) |
| Hb J Paris | 1.50 | α 12 (Ala→Asp) |
| Hb J Baltimore | 1.52 | β 16 (Gly→Asp) |
| Hb J-Bangkok | 1.56 | β 56 (Gly→Asp) |
| Hb J-Toronto | 1.58 | α 5 (Ala→Asp) |

One important clinical condition which may lead to a wrong diagnosis of FMH's is uncontrolled diabetes mellitus. Glycosylated hemoglobin (HbA1C), though not generally considered as true fast hemoglobin variants, should be kept in mind before giving impression of FMH's [4].

Proper identification of such variant Hb could avoid mismanagement of diabetic patients as it is earlier reported to show a falsely lower level of HbA1c than expected [2].

## CONCLUSION

Hemogram, HPLC and Parental screening are efficient tool to detect hemoglobinopathies. DNA analysis is gold standard tool for the diagnosis. Hb J-Toronto is a rare variant of abnormal hemoglobin. It has little clinical significance in heterozygous state but when combined with other variants, they may give rise to severe disease. Abnormal hemoglobins should be considered when a major discrepancy between the level of HBA1C and fasting plasma glucose is observed. Prenatal analysis, especially by HPLC, is a key screening method to avoid hemoglobinopathies in off springs. One important clinical condition which may lead to a wrong diagnosis of FMH's is uncontrolled diabetes mellitus.

**Declaration of interest**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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