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RESEARCH ARTICLE

MANAGEMENT OF A PREGNANT PATIENT WITH PUNJAB HAEMOGLOBIN (HAEMOGLOBIN D TRAIT)

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ABSTRACT

Haemoglobin D trait (heterozygous form) is an abnormal haemoglobin variant which when present is clinically asymptomatic but its coinheritance with other haemoglobinopathies like haemoglobin S (Hb S) or thalassemia can cause sickle cell disease and chronic haemolytic anaemia of moderate severity. Also patients with haemoglobin D (Hb D) trait can pass the trait to their children. Hb D disease (homozygous form) is a rare disease and usually presents with mild haemolytic anaemia and mild to moderate splenomegaly. Case of a pregnant patient diagnosed incidentally with Hb D trait in her antenatal period posted for elective lower segment caesarean section has been reported.

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INTRODUCTION

A haemoglobin molecule is composed of four polypeptide globin chains. Each contains a haem moiety which has an organic part and a central iron ion in the ferrous state. HbD – Punjab is an abnormal haemoglobin variant which can occur in 4 forms: heterozygous Hb D trait, Hb D-thalassemia, Hb S-D disease and the rare homozygous Hb D disease. (Lukens, 1998; Ozsoylu, 1970) HbD trait is clinically asymptomatic but its homozygous form which is extremely rare, (Lukens, 1998; Ozsoylu, 1970; Firkin *et al*., 1996) is associated with mild haemolytic anaemia and mild-moderate splenomegaly. (Adekile and Muah-AlI, 2010; Taghavi Basmanj *et al*., 2011) Its coinheritance with thalassemia and HbS can cause moderate severity haemolytic anaemia and sickle cell disease. (Ahmed M, Stuhrmann *et al*., 2001) The trait can be passed to the off-springs. Hb D gene can be detected by DNA amplification and globin chain analysis. (Zeng *et al*., 1989; Lane *et al*., 1993) Prenatal diagnosis can also be used for the detection of Hb D in high risk couples. (Foder, 1999) An association between Hb D and haematological malignancies has also been reported. (Dash *et al*., 1988) There are less studies about this variant and therefore it is important that the variant be studied and cases be reported. (Jain, 1971) We report a case of a patient diagnosed incidentally in her antenatal period with HbD trait posted for elective lower segment caesarean section.

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Case report

26 year old female, primigravida with 38 weeks gestation, resident of Maharashtra, complained of generalised weakness for 20 days in the antenatal period for which she was evaluated. Blood samples were collected in a vacutainer containing EDTA as an anticoagulant. Complete blood count and red cell indices were measured. Iron studies were done. Blood smears were examined using the Leishman stain and Giemsa stain. Haemoglobin electrophoreses were obtained using cellulose acetate at pH 8.6 and citrate agar at pH 6.2 and HbA_2 and HbF levels were checked using variant Hb testing system which were in the normal range. The solubility test for the sickling was negative. The electrophoretic pattern on cellulose acetate at pH 8.9 showed bands at the positions of Hb A_2 and Hb S or D, the latter was confirmed to be Hb D on citrate agar electrophoresis at pH 6.2 with HbD concentration to be 33.6 % (heterozygous). She was diagnosed with Hb D trait (Punjab Hb) and iron deficiency anaemia. Following the patient's tests, her partner was investigated and had normal haemoglobin study, negative for sickling. Patient was started on ferrous sulphate and multivitamin tablets. She had no significant medical/ surgical history, no history of blood transfusion, no other drug history. Family history was not contributory. She was to be posted for elective lower segment caesarean section in view of breech. Prior to the procedure, her laboratory investigations- complete haemogram, coagulation profile, liver function tests and iron studies were normal. Cardiac, respiratory, abdominal and neurological systems

examination were normal. Airway examination revealed adequate mouth opening, neck extension and Mallampati class 2. Preoperative blood pressure and pulse rate were normal. Haematology reference was taken in view of HbD trait. Advice was to maintain Hb> 8 under PCV cover. Written, informed, valid consent taken after explaining the procedure and the risks involved. Nil per oral status confirmed. In the operating room, all routine monitors (five-lead ECG, non-invasive blood pressure monitor [NIBP], pulse oximeter) were attached. 20G intravenous cannula secured. Ringer's drip started. Pre-induction FHS heard. Patient was given spinal anaesthesia with 0.5% plain bupivacaine 2 ml (10mg). Following which supine position was given with monitoring of vitals. Level of anaesthesia was checked and the procedure was started. O_2 was given with Hudson's mask at 6L/min throughout the procedure. Temperature monitored along with urine output and blood loss monitoring. Our goal was to avoid hypoxia, hypotension, hypothermia, maintain adequate circulating blood volume, O_2 carrying capacity of blood and analgesia. Baby was delivered by breech extraction and baby cried immediately after birth. The procedure was uneventful.

Given below is table of the initial blood reports

COMPLETE HAEMOGRAM		
Hb	8.9 g/dl	↓
Hct	27.2%	↓
MCV	62.8 fl	↓
MCH	20.6 pg	↓
MCHC	32.7g/dl	
RDW	15.9%	
RBC	$4.33*10^6$mcL	Normal
WBC	$10.1*10^3$mcL	Normal
Differential count	Normal	
Platelets	$397*10^3$mcL	Normal
HAEMOGLOBIN ELECTROPHORESIS		
HbA2	2.6%	Normal
HbF	0.1%	Normal
Any other abnormal Hb	HbD- 33.6% HbD Punjab Heterozygous	
HbS and HbC	Not detected	
Blood group	B+	
IRON PROFILE		
Iron	22 mcg/dl	↓
TIBC	557mcg/dl	↑
% saturation	4%	↓
RBC MORPHOLOGY		
Anisocytosis	Nil	
Poikilocytosis	Nil	
Hypo/Poly – chromasia	Nil	
Macro/Micro-cytes	Nil	

DISCUSSION

Hb D-Punjab is a haemoglobin variant prevalent in Punjab region of India, Pakistan and Iran, with an estimated frequency of 2.0%, hence the name. (Firkin *et al*., 1996) There are several variants of HbD, amongst them Hb D-Punjab (also known as Hb D- Los Angeles) is by far the commonest. (Lukens, 1998; Foder and Eng, 1999) Initially, the geographic distribution of Hb D-Punjab suggests that this mutation originated in the central region of Asia, as it is prevalent in Punjab, a region of India, and North-western China. Then it spread to neighbouring countries by migration. (Husquinet *et al*., 2017; Yavarian *et al*., 2009) In western India, especially in Gujarat, the prevalence is low-1%. (Lukens, 1998) Hb D-Punjab is also common in countries such as Italy, (Fioretti *et al*., 1993) Belgium, (Husquinet *et al*., 2017) Austria, (Lischka *et al*., 1984) and Turkey. (Atalay *et al*., 2005) Hb D-Punjab is derived from a point mutation in beta-globin gene in the first base of the 121 codon with the substitution of glutamine for glutamic acid. (Baglioni, 1962) It was first described by Itano in 1951. (Itanot, 1951) The electrophoretic mobility of Hb D is similar to that of Hb S (slower than HbA) at alkaline pH- 8.6 in cellulose acetate, (Marengo-Rowe, 1965) while in acidic pH-6.2 in citrate agar, (Vella *et al*., 2017) it resembled Hb A. HbD can be distinguished from Hb S by normal solubility when in its reduced state. (Vella *et al*., 2017) Hb D in the form of heterozygote Hb D trait, Hb S-D disease and Hb D-thalassemia are commoner forms. By applying the Hardy-Weinberg formula, the expected frequencies of the homozygous Hb D disease can be estimated. (Serjeant, 1992) The expected incidence for the homozygous Hb D disease is 0.000025 %, or 1 case per 40000 births (considering the 1 % prevalence). When considering the almost negligible prevalence of Hb D in the Western Population, the number of cases of homozygous Hb D disease would at the most number a handful. Homozygous form is very rare, (Lukens, 1998; Ozsoylu, 1970; Firkin *et al*., 1996) and very few case reports have been reported. (Jain, 1971) Heterozygous state of Hb D does not produce any clinical or haematological symptoms, but its association with Hb S produces clinically significant, but less severe condition mimicking sickle cell anemia. (Lukens, 1998; Jain, 1971) Different Hb D variants appear to produce different severity of disease with Hb S. Hb D-Punjab produces clinically significant condition like sickle cell disease, whereas Hb D Iran and Hb D Ibadan are non-interacting and produce benign conditions like sickle cell trait. (Serjeant, 1992) Haemoglobin D trait is inherited from one's parents, like hair colour or eye colour. If one parent has haemoglobin D trait while the other parent has normal haemoglobin, there is a 50 percent chance with each pregnancy of having a child with haemoglobin D trait. Parents who have haemoglobin D trait can have a child with haemoglobin D disease, haemoglobin SD disease or haemoglobin D/beta thalassemia disease. Therefore, it is important to understand how it is passed on and its coinheritance with other haematological disorders. A report from Saudi Arabia has also emphasized the importance of careful analysis of the electrophoresis results and the usefulness of molecular studies in premarital screening and other haemoglobinopathy screening programs. (Owaidah *et al*., 2005) In today's ever changing population demographics with racial inter mixing, haemoglobin D disease should not be considered as an entity confined to the South Asian region. It is important to keep this important differential in mind when dealing with any suspected haemoglobinopathy. There are less studies about this variant therefore it is important that the variant be studied and cases be reported.

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