



## FRUCTOSEMIA WITH AN EARLY ONSET AND ATYPICAL PRESENTATION– A CLINICAL CASE REPORT

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<p><b>Article Info</b></p> <p><i>Received 15/11/2014</i> <i>Revised 27/11/2014</i> <i>Accepted 12/12/2014</i></p> <p><b>Key words:</b> Hereditary fructose intolerance, Fructosemia, Aldolase B, Fructose.</p>	<p><b>ABSTRACT</b></p> <p>Fructosemia is an inborn error of fructose metabolism inherited as autosomal recessive disease due to absence of intestinal or liver enzyme aldolase B. The patients present with symptoms like hypoglycemia, failure to thrive, hemorrhage, jaundice, vomiting and seldom with liver and renal failure. Until date, very few such cases have been reported worldwide. We report a rare case of hereditary fructose intolerance born of non- consanguineous marriage diagnosed during laboratory investigation of an infant admitted with bleeding diathesis in a tertiary health care center of West Bengal.</p>
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### INTRODUCTION

Hereditary fructose intolerance is an autosomal recessive disorder resulting from deficiency of fructose 1-phosphate aldolase B (E.C.2.1.2.13) in liver, kidney and intestine. Aldolase B catalyses the lysis of F-1-P to glyceraldehyde and DHAP which are channelled as glycolytic intermediates. Deficiency of Aldolase B limits the patients' ability to handle fructose. This leads to accumulation of fructose-1-phosphate in the cytosol [1]. Hereditary fructose intolerance was first reported by Chamber & Pratt in a 24-year old woman having nausea, vomiting, abdominal cramps and transient loss of unconsciousness following ingestion of fructose [2]. They termed this as "idiosyncrasy to fructose" and suggested that some of the symptoms resulted from hypoglycemia. The population genetics revealed an incidence of about 1 in 20,000 births in Caucasian population [3]. Moreover, fructosemia presents a wide array of clinical features starting from nausea, vomiting, abdominal pain, jaundice,

hemorrhage, hypoglycemia, neurological features, acute liver failure and renal tubular acidosis [4]. In the present instance a case of fructosemia in a 9 month old infant presenting with itchy and hemorrhagic lesions, diagnosed as a case of Hereditary Fructose intolerance is reported [5-8].

### Case Presentation

A 9 month old infant was brought to pediatric department of a tertiary care institution with itchy lesions all over the body and history of development of multiple hematomas for last 3 months. On general examination, the weight of the infant was 6.5kg. The birth history of the child was uncomplicated and uneventful. The growth and development of this girl was otherwise normal. This child has received all the vaccines till date as per Immunization schedule. The girl was having moderate degree of icterus. There were several itchy nodular lesions on the left lumbar region. (Figure1).



On systemic examination, the liver was just palpable and the spleen was moderately enlarged. All other systems were within normal limit. There was no similar family history and sibling history.

Blood analyses showed an unconjugated hyperbilirubemia. The liver enzyme assays showed a transient increase of liver enzymes (ALT- 47IU/L and AST-78IU/L), a non-reactive and negative viral hepatitis screening. The coagulation profile showed prothombin time rose to 28 seconds against control of 11.6 seconds. The fasting plasma glucose concentration was reduced to 52mg/ dl. A normal hemoglobin concentration and hemoglobin electrophoresis excluded hemolytic anaemia. The urinalysis was positive for non-glucose reducing substance (Benedicts test but glucose oxidase negative) and ketose sugar. A normal ocular examination excluded galactose metabolism disorder. The serum urea and

creatinine were 41mg/dl and 0.9mg/dl respectively. The ultrasonography of the abdomen showed a mild hepatomegaly, contracted gallbladder and moderate splenomegaly. There was no ascites or bile duct or portal vein dilatation. A fructose tolerance test was avoided in apprehension of precipitating symptoms of acute hypoglycemia in the infant. The liver biopsy was undertaken following 2 units of FFP transfusion. The biopsy showed microvesicular steatosis with intralobular fibrosis. The hepatocyte lineage was negative for aldolase B. Due to financial constraints; the Genetic testing for the detection of aldolase B deficiency i.e mutations in the Aldolase B gene Chromosome 9p22 could not be done. The child was diagnosed as a case of hereditary fructose intolerance and discharged with a special advice on dietary restriction on fructose and sucrose.

**Fig 1. Showing nodular lesions**



There was a bruise on the right cheek of the patient (Figure2).

**Fig 2. Showing hematoma in cheek**



## DISCUSSION

The mode of onset of hypoglycemia is unique in Hereditary Fructose Intolerance as compared to other hepatic-hypoglycemic diseases. In these cases hypoglycemic attacks are precipitated by drinking sweetened liquids (containing fructose/sucrose) e.g. sugarcane juice. The fructose-1-Phosphate that accumulates in liver spares little phosphate for phosphorylating glucose to glucose-6-Phosphate. Consequently, the intracellular utilization of glucose is impaired. Moreover F-1-P inhibits the hepatic glycogen phosphorylase and so hepatic glycogenolysis is inhibited resulting in hypoglycemia despite the presence of high glycogen reserve. This specific clinical condition thus becomes apparent at the time of weaning when the child is introduced to artificial nutrients and fruit juices. Recurrent vomiting, abdominal pain and hypoglycemia are usual findings. However patient may present with jaundice, Haemorrhage, non-specific hepatic derangements and strained relationship with family members due to peculiar eating habits.

Sluggishness of liver function develops as a large proportion of phosphate available in the hepatocytes are trapped as F-1-P. So ATP production from ADP is hampered- this adversely affects energy requiring cellular functions e.g ATP dependent cation pump. Malfunctioning of these pumps fail to maintain normal ionic gradient across the cell membrane. Uncontrolled intracellular flow of ions and fluid cause swelling of hepatocytes and ultimate osmotic lysis. In this way functioning hepatocytes decrease in number. So liver failure is a consequence of long standing exposure and is the most probable cause of bleeding diathesis & jaundice in the present case.

Differential diagnosis from galactosemia and tyrosinemia is important as the histological features may resemble each other. A related enzyme deficiency is the fructose 1-6-diphosphate deficiency which has a different clinical presentation with lactic acidosis, somnolence, coma and hypoglycemia with ketosis. However hepatocyte lineage deficient of aldolase B clinches the diagnosis in this particular case.



The importance of study of laboratory parameters in suspected cases needs emphasis. Early diagnosis is crucial to prevent precipitation of fatal symptoms in the high risk neonatal period. In a certain percentage of cases diagnosis is not made upto adulthood as symptoms are misinterpreted as food allergy. Even in undiagnosed adult patients recurrent inadvertent fructose ingestion exposes them to the risk of hepatic failure. Many deaths have been documented in undiagnosed HFI individual challenged unknowingly. Fortunately most affected patients develop conditioned taste aversion that makes them avoid sweet tasting food. Dietary restriction of fructose, sucrose and sorbitol (<40 mg/kg/day) results in complete reversal of symptoms and a near normal healthy life span. This important ethical implication needs to be highlighted to

curb the increasingly widespread use of sugars as nutrients and sweeteners in ready to use foods.

### CONCLUSION

Thus in cases presenting with jaundice or bleeding diathesis, inborn error of metabolism needs to be ruled out. There after a laboratory work up is required to clinch the diagnosis.

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