Clinical profile of Hereditary Fructose Intolerance in children

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Hereditary fructose intolerance (HFI) is a potentially fatal inborn error of metabolism (IEM) unless detected in time and treated with dietary modification. HFI often has nonspecific symptoms and the literature on clinical features is scanty. We collated information of our patients diagnosed as HFI and analyzed their clinical and laboratory features.

9 cases of HFI were diagnosed during the period from Jan 2012 to Dec 2020. The age at diagnosis ranged from 10 months to 30 months, median 18 months. The presentation was vomiting in 7 (77%) (acute in 1, recurrent in 6), abdominal distension (hepatomegaly) in 4 (44%), recurrent diarrhea in 3 (33%) and Failure to thrive in 3 (33%). The child with acute presentation had severe metabolic acidosis and hypoglycemia. 2 (22%) children diagnosed before 12 months of age presented with hepatomegaly and sugar aversion in one each and had a previous sib affected leading to earlier diagnosis. Diet history showed strong aversion to sugar in 3 while definite dislike for sugar in 5. LFT was abnormal in 8 (88%) patients in the form of raised transaminases 3-10 times upper limit of normal. Ultrasound abdomen showed fatty liver in 5 (55%) patients. Seven children had a confirmed genetic mutation on *ALDOB* gene apart from suggestive laboratory abnormalities while the first two cases were diagnosed on the basis of oral fructose challenge test. The most common mutation noted was on exon 5, c.472 C > T (all homozygous) in 5 and on exon 3, c.178 C > T (both homozygous) in 2 children. One patient has succumbed to a vomiting and seizure at home possible due to hypoglycemia, the diagnosis was confirmed postmortem upon mutation report. Rests of the 8 children are doing fine on a fructose free diet.

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Prevalence of HFI has ranged from 1 in 20,000 to 1 in 60,000 (1). Severe forms generally present in the infancy when exposed to fructose containing diet either in the form of acute vomiting, hypoglycemia, acidosis (2) and in the chronic form as failure to thrive and hepatomegaly. If recognized and treated they have a normal life expectancy. Children develop an aversion for sweets and fruits which can lead to a suspicion of HFI.

On pubmed search on HFI clinical features, isolated case reports have variable presentation as acute liver failure in neonates (3), isolated hepatomegaly (4), Reye like syndrome (5), or refractory Celiac disease (6). Interestingly minor form of HFI learns to modify their diet and may remain undetected in childhood. Thus it is very important to take history of dislike to sweet or strong aversion to sugar which can be a strong clue towards the diagnosis (7). Unless this is suspected and treated, children tend to worsen as sugar (Sucrose) is present in all forms of medicine which comes in suspension form. Also sugar, honey, juices, fruits are very commonly used in children which can be harmful in HFI. Many ready to eat complementary food and some of the infant milk formulas also contains sucrose which needs to be carefully avoided in these children. The mutations noted in our patients were different from the one reported from another study from north India (8). The HFI is likely under diagnosed and should be considered in patients with above features as well as in individuals with significant aversion to sweets.

Further Reading:

1. Schrodi SJ, DeBarber A, He M, Ye Z, Peissig P, Van Wormer JJ, et.al. Prevalence estimation for monogenic autosomal recessive diseases using population-based genetic data. *Human genetics*. 2015 Jun 1;134(6):659-69.
2. Bouteldja N, Timson DJ. The biochemical basis of hereditary fructose intolerance. *Journal of inherited metabolic disease*. 2010 Apr;33(2):105-12.
3. Li H, Byers HM, Diaz-Kuan A, Vos MB, Hall PL, Tortorelli S, et.al. Acute liver failure in neonates with undiagnosed hereditary fructose intolerance due to exposure from widely available infant formulas. *Molecular genetics and metabolism*. 2018 Apr 1;123 (4):428-32.
4. Krawczyński M, Targońska B, Kostrzewa-Szymiec D, Walkowiak J, Cichy W. Congenital fructose intolerance diagnosed in a 13-year-old boy. *Wiadomosci Lekarskie* (Warsaw, Poland: 1960). 1994 Sep 1;47 (17-18):702-4.
5. Yang TY, Chen HL, Ni YH, Hwu WL, Chang MH. Hereditary fructose intolerance presenting as Reye's-like syndrome: report of one case. *Acta Paediatrica Taiwanica= Taiwan er ke yi xue hui za zhi*. 2000 Jul 1;41 (4):218-20.
6. Bharadia L, Shivpuri D. Non responsive celiac disease due to coexisting hereditary fructose intolerance. *Indian Journal of Gastroenterology*. 2012 Apr;31 (2):83-4.

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7. Newbrun E, Hoover C, Mettraux G, Graf H. Comparison of dietary habits and dental health of subjects with hereditary fructose intolerance and control subjects. *The Journal of the American Dental Association*. 1980 Oct 1;101 (4):619-26.
8. Bijarnia-Mahay S, Movva S, Gupta N, Sharma D, Puri RD, Kotecha U, et.al. Molecular diagnosis of hereditary fructose intolerance: founder mutation in a community from India. *InJIMD Reports*, Volume 19 2014 (pp. 85-93). Springer, Berlin, Heidelberg.