The Change of Age at Diagnosis in Galactosemia Patients in Unscreening Population Over Time

Pelin Teke Kisa, Ayse Tuba Yurdusev, Semra Gursoy, Buse Soysal, Oguz Han Kalkanli, Senem Alkan Ozdemir, Filiz Hazan, Sebnem Calkavur, Tulin Gokmen Yildirim, Cigdem Omur Ecevit, Ozlem Bekem Soylu, Behzat Ozkan

Dr. Behçet Uz Child Disease Training and Research Hospital, Izmir, Turkey

Introduction

Galactosemia is an autosomal-recessive, inborn error of metabolism, caused by a disorder of the galactose metabolism. This pathway includes galactose mutarotase (GALM), galactokinase (GALK), galactose-1-phosphate uridylyltransferase (GALT) or uridine diphosphate galactose-4-epimerase (GALE). It is known that the diagnosis age was late in galactosemia patients in the unscreening population. In this study, we were investigated demographic, clinical and genetic findings of galactosemia patients from Turkey, where the diseaseis not yet included in the newborn screening programme. We also examined the age change at the time of diagnosis and the time to start lactose-free diet over the years.

Methods and Materials

The medical files of 25 patients (median age 47 [1-492] months, 10 female); demographic data, family history, presenting manifestations and time of presentation, physical examination and laboratory findings at presentation, time of diagnosis and GALT variants were retrospectively evaluated. Age at diagnosis was calculated for 7 (28%) patients diagnosed before 2015 (Group I), 10 (40%) patients diagnosed between 2016-2018 (Group II) and 8 (32%) patients diagnosed between 2019-2021. As it was determined that age at diagnosis and the groups were nonort mally distributed, they were compared using the Kruskal-Wallis test. Pairwise comparisons were performed using the Mann-Whitney U test.
The presenting complaints were neonatal jaundice in 18 patients (72%), poor feeding and vomiting in three patients (12%), respiratory distress and cyanosis in two patients (8%), cataract in two patients (8%). One patient was diagnosed via family screening. Parents of 16 (64%) were consanguinity. Patients’ median age at symptom onset was 11 [2-90] days, age at diagnosis was 51 [6-110] days. Age at diagnosis was the earliest in Group III (9 [1-37] days) (p=0.006). There was no difference between Group I (108 [60-492] days) and Group II (49 [38-58] days patients) in terms of age at diagnosis. Cataract was present in 6 (24%) of the patients and all of them had been operated. At presentation, median aspartate aminotransferase was 148 U/L [28-693], alanine aminotransferase was 94 U/L [11-556], total bilirubin was 7.2 mg/dL [1.1-24], direct bilirubin was 2.8 mg/dL [0.4-1.1]. All patients are on galactose-free diet therapy.

Table-1. The comparison of age at diagnosis patients with galactosemia in years

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<tr>
<td>Age (days)</td>
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<tr>
<td>Mean ±SD</td>
<td>158.7±152.5*</td>
<td>48.4±7.7*</td>
<td>15.1±13.3</td>
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<tr>
<td>Median(Min-Max)</td>
<td>108 [60-492]</td>
<td>49 [38-58]</td>
<td>9[1-37]</td>
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*Kruskal-Wallis (mann-Whitney u test), Difference from Group III p<0.05
Discussion

In our country, galactosemia is not yet included in the neonatal screening. It is thought that its addition to the national screening programme would provide early diagnosis in galactosemia patients. However, the efficacy of galactosemia in the neonatal screening program is controversial due to multiple reasons such as its effect on mortality and morbidity, high false positive rate, insufficient cost-benefit ratio. While studies conducted in our country showed that galactosemia patients used to be diagnosed months after the onset of clinical findings before, the present study revealed that the age at diagnosis declined over years. Evaluation of the age at diagnosis by year of diagnosis through a study that would include all galactosemia patients in our country may provide insight regarding the place of the galactosemia disease in the screening programme.