Transaminase Elevation in Nutritional Infantile Failure to Thrive

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ABSTRACT

Introduction: Laboratory investigations pursued for infants with failure to thrive (FTT) often show mild transaminase elevations, the incidence and significance of which are unknown.

Methods: This retrospective chart review included infants diagnosed with simple nutritional FTT at a single academic tertiary care system. Comparisons of diagnostic studies and outcomes between children with and without transaminase elevation were performed using chi-square and Wilcoxon rank sum tests.

Results: None of the infants with abnormal transaminases required additional follow-up or developed alternative diagnoses in the following year.

Discussion: Transaminase elevation may be common in infants with FTT and may not warrant further investigation if the history indicates an isolated etiology of insufficient nutrition.

BACKGROUND

Failure to thrive (FTT) is a common diagnosis made in otherwise healthy infants and can be a consequence of factors intrinsic to the infant and/or the environment.[1] Whether undernutrition is secondary to inadequate caloric intake, excessive caloric requirement, or malabsorption, the pathways lead to the same clinical phenomenon. Of infants diagnosed with FTT, 60% to 90% have laboratory or imaging studies performed in an attempt to delineate a possible etiology, including genetic, metabolic, and renal disease, among others.[2,3] FTT secondary to suboptimal caloric intake in otherwise healthy children accounts for the majority of infantile FTT cases, compared to a minority that are secondary to increased metabolic need or caloric losses.[4] In most infants with intrinsic causes of FTT, including genetic or metabolic conditions, the diagnosis is made with history or physical examination. Screening tests may provide reassurance but are unlikely to uncover an underlying disorder.[3-6] Some otherwise well infants diagnosed with FTT have mild transaminase elevations, which may compel clinicians to obtain further diagnostic testing. To date, no existing studies report the incidence of transaminase elevation in infants presenting with FTT, although the phenomenon has been well described in other populations experiencing starvation states.[7,8] It is also unknown how the finding of elevated transaminases may influence further diagnostic testing or predict diagnoses other than inadequate nutrition. The objective of this retrospective study was to determine the frequency and significance of transaminase elevation in infants diagnosed with FTT.

METHODS

Charts were identified for infants less than 1 year of age admitted to the hospitalist service or seen at the outpatient gastroenterology clinic at a single academic tertiary care system between July 1, 2012 and March 31, 2017 with FTT-associated International Classification of Diseases 9 and 10 diagnosis codes 783.41, 779.34, R62.51, and P96.2. Infants with Z scores for weight for age less than or equal to -1.64 were included in the study, consistent with a weight for age less than the 5th percentile.[4] Exclusion criteria included premature gestation less than 35 weeks; prior diagnosis of

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Table 1. Demographic Data for Infants Presenting to Pediatric Gastroenterology Clinic or for Admission to Hospital Medicine Service With Failure to Thrive Who Underwent Laboratory Studies

Patient Demographics	Elevated Transaminases (%) N=11	Normal Transaminases (%) N=28
Gender		
Male	4 (36)	14 (50)
Female	7 (64)	14 (50)
Race		
African American	0	2 (7)
White	9 (82)	17 (61)
Other	0	2 (7)
Unknown	2 (18)	7 (25)
Location		
Inpatient	6 (55)	21 (75)
Outpatient	5 (45)	7 (25)
Nutrition		
Breastfeeding	3 (27)	5 (18)
Formula	5 (45)	19 (68)
Both	3 (27)	4 (14)
Gestational age		
Term	11 (100)	23 (82)
Late preterm (35-36w7d)	0	5 (18)
Median age (months)	3 months (3 weeks-8 months)	4 months (3 weeks-10 months)

Abbreviations: w, weeks; d, days.

There were no statistically significant differences between the group who presented to the pediatric gastroenterology clinic or for admission to the hospital medicine service.

Table 2. Comparing Additional Studies Performed and Diagnostic Outcomes for Infants Presenting to Pediatric Gastroenterology Clinic or for Admission to Hospital Medicine Service With Failure to Thrive Based on Transaminase Status

Patient Evaluation	Abnormal Transaminases (%) N=11	Normal Transaminases (%) N=28	Odds Ratio (95% CI)
AST (mean, SD)[a]	70.2 +/- 15.5	39.8 +/- 12.4	NA
ALT (mean, SD)[a]	65.9 +/- 38.6	34.7 +/- 16.8	NA
Number of lab draws	2 +/- 1	1.5 +/- 1.8	1.17 (0.78-1.75)
Exclusive breastfeeding at discharge	4 (36)	3 (11)	4.76 (0.85-26.5)
Speech consult	6 (55)	11 (41)	1.75 (0.43-7.17)
Nutrition consult	10 (91)	27 (96)	0.37 (0.02-6.5)
Ultrasound (abdomen)	5 (45)	11 (39)	1.29 (0.32-5.27)
Upper GI study	5 (45)	13 (46)	0.96 (0.24-3.9)
Diagnosis leading to FTT	0 (0)	5 (18)	NA

Abbreviations: FTT, failture to thrive; AST, aspartate aminotransferase; ALT, alanine aminotransferase; upper GI study, water soluble oral contrast with a series of radiographs.

[a]Normal AST defined as 20-67 U/L and ALT 0-55 U/L..

genetic, cardiac, or metabolic diseases; and admission for illnesses other than FTT. Charts were abstracted for demographic data and diagnostic and therapeutic outcomes from the initial encounter through the subsequent year. Comparisons of diagnostic studies and outcomes between children with and without transaminase elevation were performed using chi-square and Wilcoxon rank sum tests. This study was considered exempt by the University of Wisconsin School of Medicine and Public Health's institutional review board.

RESULTS

A total of 670 patients were identified in the study period, with 95 meeting inclusion criteria. The majority were excluded due to age greater than 1 year, prematurity, or underlying illness contributing to FTT. The majority of patients were White, born at term, and formula fed at time of admission. There were no statistically significant differences between infants who did and did not undergo laboratory testing. Of the 39 (41%) infants undergoing laboratory testing, 11 (27%) had elevated alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) (ALT 23-138 U/L, AST 46-101 U/L). Infants with and without transaminase elevation did not have significant differences in demographic or presenting characteristics (Table 1). There was a trend toward additional investigations in infants with transaminase elevation, although this did not reach statistical significance (odds ratio [OR] 1.17; 95% CI, 0.78-1.75). None of the infants with abnormal transaminases required further clinic or hospital encounters for relapsing FTT or developed alternative diagnoses associated with FTT, and the transaminase elevation normalized within the following year (Table 2).

DISCUSSION

Approximately one quarter of infants with FTT who underwent laboratory testing were found to have elevated transaminases, and those patients were not found to have different exposures or outcomes compared to infants with normal transaminase levels. No infant with abnormal transaminases received a diagnosis explaining their FTT other than poor nutritional intake.

Transaminase elevation has been seen in other populations with suboptimal nutrition, with several proposed metabolic etiologies. In a study involving adolescents with anorexia nervosa, approximately one third of patients had transaminase elevation on admission, which resolved with refeeding and did not have long-term sequelae. Investigators have posited that this transaminase elevation was secondary to ischemic hepatitis from hepatic hypoperfusion, or to hepatic autophagy in the context of a catabolic starvation response.[7-10] Another proposed etiology for this phenomenon is that upregulation of transaminase production may occur in response to the increased need for uptake of amino acids to facilitate gluconeogenesis in the starvation state. Regardless of the etiology, patients in several studies show-

ing transaminase elevation during the starvation state showed laboratory normalization with nutrition and had no long-term sequelae.[7,8]

Over the last 40 years, evidence continues to show that laboratory and imaging studies are not necessary in the initial evaluation of FTT.[3-6] In several recent studies, only 1% to 3% of laboratory investigations revealed an underlying diagnosis, most of which were from genetic testing performed based on physical examination. Laboratory and imaging studies result in financial and emotional burden on families. A minority of infants may have an underlying medical diagnosis, but a focused history and physical exam with a period of observation prior to a more extensive evaluation is a reasonable first step.[2]

Our study is limited by its retrospective design, small sample size, single institution population, lack of ethnic diversity, and reliance on accurate coding of encounter diagnoses for chart identification. Additionally, the majority of patients were formula fed at the time of the study. Although patients were followed for 1 year, some may have received diagnoses outside of our system that were not imported to our electronic health record or could have received diagnoses after the follow-up period. Future work should verify our findings across multiple centers and in a larger and more diverse population.

Transaminase elevation associated with infantile FTT may be a common and insignificant finding that should not direct risk assessment or further diagnostic testing. Diagnosis and treatment of FTT should focus on optimization of nutrition rather than laboratory and imaging studies.

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