Troia Med J 2025;6(3):97-99
DOI: 10.55665/troiamedj.1767889

CASE REPORT

High alkaline phosphatase level in a healthy child: A case of benign transient hyperphosphatasemia

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ABSTRACT
Benign transient hyperphosphatasemia (BTH) is a self-limited condition of early childhood, defined by a transient elevation of serum alkaline phosphatase (ALP) without evidence of underlying disease. This report emphasizes the importance of considering BTH in the differential diagnosis of elevated ALP and presents a case in light of the current literature. Recognition of BTH is crucial to prevent unnecessary investigations and referrals in pediatric practice.

Keywords: Benign transient hyperphosphatasemia, alkaline phosphatase, children

ÖZET

Yüksek alkalen fosfataz değeriyle başvuran sağlıklı bir çocuk: benign geçici hiperfosfatazemi olgusu

Benign geçici hiperfosfatazemi (BGH), erken çocukluk döneminde görülen, altta yatan herhangi bir hastalık bulgusu olmaksızın serum alkalen fosfataz (ALP) düzeylerinde geçici yükselme ile karakterize, kendini sınırlayan bir durumdur. Bu olgu sunumu, artmış ALP düzeylerinin ayırıcı tanısında BGH'nin göz önünde bulundurulmasının önemini vurgulamakta ve mevcut literatür ışığında bir olguyu sunmaktadır. BGH'nin tanınması, çocukluk çağında gereksiz tetkik ve yönlendirmelerin önlenmesi açısından büyük önem taşımaktadır.

Anahtar kelimeler: Benign geçici hiperfosfatazemi, alkalen fosfataz, çocuk

INTRODUCTION

Serum alkaline phosphatase (ALP) comprises of a group of isoenzymes primarily originating from bone, liver, intestines, kidneys, placenta, and white blood cells [1]. In healthy children, the bone and liver isoforms dominate, and levels vary with age. Notably, physiological increases in ALP are observed during infancy and adolescence due to rapid bone growth [2]. Six different ALP isoenzymes have been identified: high molecular weight ALP (ALP1), hepatic ALP (ALP2), bone ALP (ALP3), placental ALP (ALP4), intestinal ALP (ALP5), and IgG-bound ALP (ALP6) [3]. Elevated ALP levels beyond age-adjusted reference ranges warrant consideration of conditions such as rickets, fractures, hepatic disorders, renal tubulopathies, and medication effects. Since bone-derived ALP activity is physiologically higher in children than in adults, even values within the expected pediatric range may sometimes appear disproportionately elevated.
Benign transient hyperphosphatasemia (BTH) is characterized by a temporary elevation in alkaline phosphatase (ALP) levels without any underlying disease. It predominantly affects children under five years old and typically resolves spontaneously within four months. The diagnostic criteria, initially proposed by Kraut et al. and subsequently refined through further studies [4,5] (Table 1), help guide recognition of this condition. Being aware of BTH is important, as it can prevent unnecessary investigations and interventions while alleviating concern for both clinicians and parents; here, we report the case of a 14-month-old girl diagnosed incidentally during routine laboratory testing.

Cite as: Tekin SC, Kasap T. High alkaline phosphatase level in a healthy child: A case of benign transient hyperphosphatasemia.Troia Med J 2025;6(3):*97-99*.
DOI: 10.55665/troiamedj.1767889

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Date of arrival: 18.08.2025, *Date of acceptance*: 23.09.2025

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Kraut [7]	**Chu and Rothschild [8]**
Age <5 years	Age <5 years (median: 18 months)
No clinical or lab evidence of bone/liver disease	No history or physical findings suggestive of such diseases
Elevated bone and liver ALP isoenzymes	Normal liver tests (AST, ALT, bilirubin, GGT), electrolytes, calcium, BUN, and creatinine
Return to normal ALP levels within 4 months	Absolute increase in both bone and liver isoenzymes; predominance may vary
	Normal PTH and vitamin D levels
	Normalization of ALP within 3–4 months (median: 10 weeks)

Table 1. Diagnostic Criteria for Benign Transient Hyperphosphatasemia

CASE REPORT

A 14-month-old girl was referred to our clinic following the incidental identification of markedly elevated serum alkaline phosphatase (ALP) during routine laboratory evaluation at an external facility (ALP: 2750 U/L; reference range (N): 125–320 U/L). She exhibited no history of fever, night sweats, weight loss, or trauma, and her prenatal, perinatal, and postnatal courses were unremarkable. There was no consanguinity between the parents. There was no history of drug or toxin exposure. He was the first child in the family and had no siblings. Her immunization status was confirmed as up to date according to the national registry.

On physical examination, she appeared well, with stable vital signs. Anthropometric measurements included a weight of 9500 g (-0,12 SD), a height of 75 cm (-0,42 SD), and a head circumference of 47 cm (0,72 SD). A thorough systemic exam—including cardiovascular, respiratory, abdominal, musculoskeletal, and neurological systems—was normal. The anterior fontanelle was closed and her neurological development was appropriate for her age.

Laboratory investigations revealed an hemogram parameters and peripheral blood smear were normal, ALP 798 U/L (N: 125–320), serum calcium 9.5 mg/dl (N: 8,8-10,8), albumin 4.6 g/dl (N: 3,8-5,4), AST 37 U/L (N: 0-40), ALT 14 U/L (N: 0-41), GGT 9 U/L (N: 5-36), total bilirubin 0,4 mg/dl (N: 0-1,2), direct bilirubin 0,2 mg/dl (N: 0-0,3), normal renal function (urea and creatinine), INR 1,08 (N: 0,8-1,2), PT 12,6 sec (N: 10-13,8), aPTT 31 sec (N: 26,5-38,5), 25- hydroxy vitamin D 41 ng/ml (N:20-60), urine test was normal and parathyroid hormone of 25.7 pg/ml (N:0-40). Abdominal ultrasonography was unremarkable, and viral serologies (Hepatitis A-B-C, Toxoplasmosis, Cytomegalovirus, Epstein-Barr virus) were negative. Based on these findings, the patient was diagnosed with benign transient hyperphosphatasemia (BTH) and scheduled for follow-up. At one month, her ALP level had decreased to 213 U/L (Figure 1).

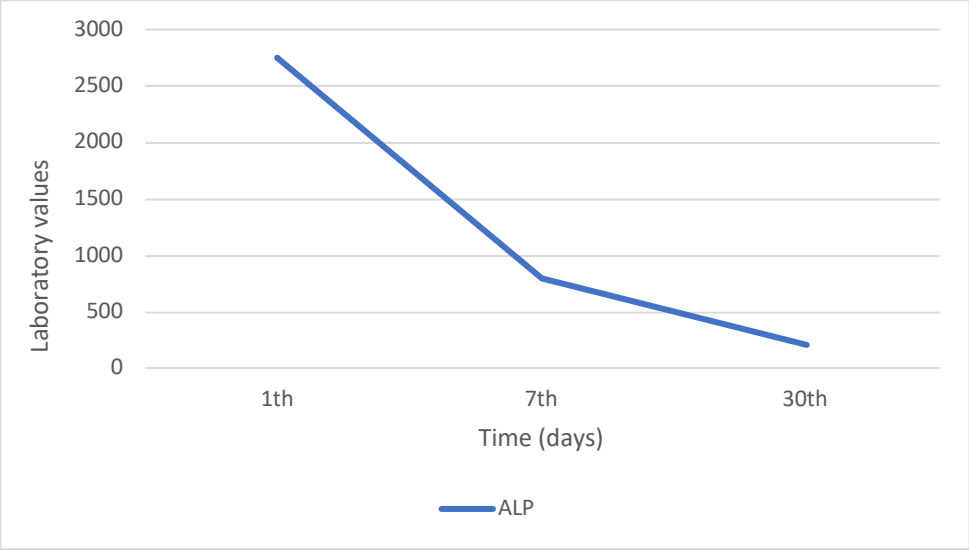

Figure 1. Laboratory changes protocols by day

DISCUSSION

The prevalence of BTH ranges from 2.5% to 5.1%, depending on the cutoff used [6]. Most cases occur in children under three years of age, with ALP levels ranging from 2- to 71-fold above the upper limit, and approximately 81% resolve within four months. Mean ALP elevation in children under two years has been reported as 7.4-fold, with no significant differences in normalization time between age groups [6,7]. Consistent with these findings, our patient was 14 months old and exhibited a 10-fold elevation in ALP, which normalized within six weeks. Most studies on the prevalence of BTH are retrospective and rely on incidental laboratory findings. The true prevalence remains difficult to determine, as routine blood tests are rarely performed in asymptomatic children under two years of age.

The etiology of BTH remains unclear. Several studies have suggested associations with viral infections, including respiratory syncytial virus (RSV), Epstein-Barr virus (EBV), human bocavirus, rotavirus, HIV, and SARS-CoV-2 [1,8–10]. Although our patient presented in October, a period associated with increased pediatric infections, she had no recent history of illness. Further research is warranted to elucidate potential etiologic factors.

ALP isoenzyme analysis can aid in differentiating elevations of bone and liver origin; however, in many centers where such testing is unavailable, as in our case, management relies on clinical monitoring. When hemogram, renal and liver function tests, thyroid function tests, parathyroid hormone, 25-hydroxy vitamin D, and abdominal ultrasonography are normal, the elevation is likely benign and physiological, and repeat measurement of ALP after one month may suffice, avoiding unnecessary investigations. Supporting this, a study of 62 pediatric patients with BTH and ALP levels above 1000 IU/L reported that 25% underwent unnecessary tests and 13% were inappropriately referred to tertiary centers [11]. Clinical monitoring in our patient demonstrated a progressive decline in ALP at follow-up, consistent with current recommendations for conservative management of asymptomatic children with transient ALP elevations.

BTH is a benign, self-limiting and transient condition most commonly identified incidentally during laboratory testing in otherwise healthy children under three years of age. It is characterized by marked elevations in serum alkaline phosphatase (ALP) despite normal findings on hemogram, liver and kidney function tests, thyroid function tests, parathyroid hormone, 25-hydroxy vitamin D, and abdominal ultrasonography, without evidence of underlying pathology. Although BTH is not associated with significant morbidity, such elevations may provoke concern among clinicians and caregivers. Recognition of these characteristic clinical and laboratory features is essential to ensure accurate diagnosis and to prevent unnecessary investigations and specialist referrals."

Conflict of interest: None
Funding: None

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