

# Case Report

# Transient hyperphosphatasemia in children

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# **ABSTRACT**

Transient Hyperphosphatasemia (TH) is a benign condition in which serum alkaline phosphatase (ALP) is transiently elevated in the absence of other systemic diseases. It mainly occurs in infants and children and very rarely seen in adults. The differential diagnosis may include liver, bone, kidney, intestinal, placental and blood diseases as well as other serious conditions as well as bone fracture due to accidental or non-accidental injuries. In this report, we present tow of our patients with TH and compare their clinical course with the natural history of TH described in literature. We also provide a focused review, in relevance to our presented cases, of this disease, which is rarely encountered in clinical practice.

#### **Key words:**

Alkaline phosphatase, Hyperphosphatasemia, hyperphosphatasia, Transient, Saudi Arabia

## INTRODUCTION

Transient Hyperphosphatasemia (TH) is a benign condition characterized by marked elevation of serum alkaline phosphatase (ALP) with absence of other associated disease such as in liver, bone or kidneys. In addition TH is also characterized by a return of ALP to normal levels within weeks or months of initial observation.

The exclusion of such causative illness before establishing a diagnosis of TH is of a paramount importance. As elsewhere, TH is generally rare to see in children managed in the inpatient and outpatient clinics at KKUH, Riyadh, Saudi Arabia. Yet the awareness of this condition, which is rarely encountered in practice, is important for both patients/parents and clinicians. This will encourage the avoidance of unnecessary concerns and investigations. We report on tow patients with TH to highlight the classic presentation as well as the natural history of the disease with a focused review of literature on the subject.

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#### How to cite this article:

Bassrawi R, Alsabie N, Alsorani D, Babiker A. Transient Hyperphosphatasemia in children. Sudan J Paediatr 2014;14(2):85 - 88.

### CASE REPORTS

#### Case 1

A 1-year- and 3- month -old girl was followed in clinic as a case of eczema and failure to gain weight. She was otherwise healthy with normal development. She fed on fortified milk formula, regular diet and she was on treatment for topical eczema. On examination, her weight was on 5-10 centile with unremarkable systemic exam suggesting organic disease or physical abuse. Her initial screening blood work at 1yr of

age was within normal including bone profile. At 1yr and 3 month of age accidentally found to have a serum alkaline phosphates (ALP) level of 3595U/L, which had further increased to 7273U/L after 2 weeks (normal lab value 175-476U/L). All her other investigation was normal (Table1). When followed in clinic, the ALP level started to drop dramatically from 7273U/L to 654,304,258U/L on monthly bases until normalized. It remained normal until her preschool vaccine visit when last reviewed (271U/L), and the patient appeared healthy.

Table 1 – Investigations of case 1 at presentation and during follow up

| Investigations                       | At presentation | After 1 month | After 2 months | After 3 months |
|--------------------------------------|-----------------|---------------|----------------|----------------|
| ALP<br>(N=175-476 u/l)               | 7273            | 654           | 304            | 258            |
| 25(OH) VIT D<br>(N=23-113 nmol/l)    | -               | 152           | -              | -              |
| PTH (N=1.65-6.9 pmol/l)              | 2.69            | -             | -              | -              |
| Corrected Ca<br>(N=2.25-2.75 mmol/l) | 2.5             | 2.5           | 2.48           | 2.4            |
| Phosphorus (N=1.45-2.16 nmol/l)      | 1.82            | 1.98          | 1.96           | 2              |
| ALT<br>(N=10-31 u/l)                 | 46              | -             | 25             | -              |
| Urea<br>(N=1.8-6.4 mmol/l)           | 3.3             | -             | 3.2            | -              |
| Serum creatinine (N=27-62 umol/l)    | 16              | -             | 33             | -              |
| Radiology:<br>Wrist X-ray            | -               | Normal        | -              | -              |

#### CASE 2

Was a 7-month-old healthy girl, on milk formula feeds, thriving well and developmentally normal with no social concerns. She presented to the children outpatient clinic at KKUH, SA with constipation and

overflow diarrhea for which she was investigated. Her physical examination was normal. Initial blood work was normal (table2), a part from a high ALP (3423U/L, N= 175-476U/L), which dropped spontaneously to 411U/L after 1 month.



Table 2 - Investigations of case 2 at presentation and during follow up

| Investigations                       | At presentation | After 1 month |
|--------------------------------------|-----------------|---------------|
| ALP<br>(N=175-476 u/l)               | 3423            | 411           |
| 25(OH) VIT D<br>(N=23-113 nmol/l)    | 130             | -             |
| Corrected Ca<br>(N=2.25-2.75 mmol/l) | 2.5             | 2.5           |
| Phosphorus<br>(N=1.45-2.16 nmol/l)   | 2.14            | 1.94          |
| ALT (N=10-31 u/l)                    | 39              | 37            |
| Urea<br>(N=1.8-6.4 mmol/l)           | 24              | -             |
| Serum creatinine (N=27-62 umol/l)    | 22              | -             |
| Radiology:<br>Wrist X-ray            | Normal          | -             |

### DISCUSSION

Transient Hyperphosphatasemia (TH) of infancy and early childhood is defined as a marked elevation of the serum Alkaline Phosphatase (ALP) activity in children younger than five year of age in the absence of clinical or laboratory findings of a systemic disease that may lead to similar biochemical picture [1]. ALP represents a group of isoenzymes originating mainly from kidney, bone, liver, placenta intestine and white blood cells [2]. The ALP level changes with age, it is generally higher in children than in adults, with a peak in the first six months of age and during pubertal growth spurt, because they have higher osteoblastic activity in this age [3,4]. In TH, as in our patients, the serum level of ALP is typically elevated four to five times above the upper limit of normal and gradually returns to normal within six months [5,6].

Although TH has been well known for decades its etiology and pathophysiology remain unclear. It is

considered as a benign condition in children and has also rarely been reported in adults [7]. The prevalence of TH is not known in Saudi Arabia or worldwide. In a series of 260 healthy infants, 1.5% (n=3) had unexplained and transient elevations in ALP, all of them had more than three times the upper limit of the normal range [8]. Most children with TH are healthy although TH can be incidentally identified in association with a variety of clinical conditions including gastroenteritis, respiratory infections, failure to thrive, chronic otitis media and asthma [9]. Case 1 in our report was assessed because of failure to thrive and case 2 presented with chronic constipation. This clearly highlights the difficulty in differentiating benign TH from an ongoing serious condition such as concomitant physical abuse and neglect and warrants a careful attention to family and social history. Follow up is required to document the return of serum ALP level to normal and it is critical for confirmation of the diagnosis. The sustained elevation of ALP beyond three to four month of initially being high should prompt reconsideration of other causes of Hyperphosphatsia [10]. However, children with TH should be spared from extensive investigations and unnecessary vitamin D treatment attempts. An initial thorough assessment including detailed social history, with infrequent biochemical follow up of ALP is the whole mark of diagnosing this condition and avoiding

missing other pathology.

## **CONCLUSION**

Though no accurate estimation of its prevalence worldwide, transient Hyperphosphatasemia (TH) seems to be rarely encountered in our community, as elsewhere in the world. Our tow reported cases demonstrated a classic natural history of the disease with regards to presentation and recovery.

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