

## Idiopathic Hypercalciuria in Iranian Children

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### Abstract

**Objective:** The aim of this study was to determine the prevalence of idiopathic hypercalciuria (IH) in school children in Ahvaz, a city with different ethnic groups located in the Southwest of Iran.

**Material & Methods:** In a descriptive cross sectional study from October to December 2006, we determined urinary calcium (UCa) and urinary creatinine (UCr) in the morning urine samples of 500 primary school children. The levels of 24-hour UCa and UCr were measured in these children. Level of 24-hour UCa exceeding 4 mg/kg/day was considered as hypercalciuria, and UCa/UCr ratio exceeding 0.21 (mg/kg) was considered abnormal. Children who had hypercalciuria with a normal concentration of serum Ca were categorized as idiopathic hypercalciuric.

**Findings:** Of 500 children aged 6-12 years, 231 were males and 269 females. In the first screening, 64 (12.8%) children (45 males, 19 females) had an abnormal UCa/UCr ratio. But in the end only 15 had the criteria of IH, i.e. the prevalence of IH was 3% (1.8-4.8%, confidence interval of 95%). The prevalence in females and males was 0.74% and 5.6%, respectively ( $P=0.003$ ). Of these children 10 had hematuria (including 2 cases of gross hematuria), 8 children gave a history of recurrent abdominal pain, 5 children suffered from dysuria and 3 persons had a history of personal or familial urolithiasis.

**Conclusion:** The study showed that 3% of primary school children in Ahvaz had IH predisposing to short-term and long-term complications of the disease. IH was significantly more common in boys than in girls.

**Key Words:** Renal stone; Hypercalciuria; Hematuria; Abdominal pain; Calcium

### Introduction

Calcium is the most important ion in the musculoskeletal system and kidney is the

major organ for calcium homeostasis<sup>[1]</sup>. Idiopathic hypercalciuria (IH) is a common metabolic abnormality in children of all ages. There is evidence of an association of IH with

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frequency-dysuria syndrome, enuresis, abdominal pain, hematuria, urolithiasis and osteoporosis<sup>[1,2]</sup>. Prior to development of kidney stones, hypercalciuria can present as frequency-dysuria syndrome, with or without microscopic or gross hematuria<sup>[3]</sup>.

Hypercalciuria, as currently defined, greater than 4 mg/kg/day or urinary calcium/creatinine (UCa/UCr) ratio greater than 0.21 is common, occurring in 2.9 to 3.8% of healthy children<sup>[4]</sup>. Idiopathic hypercalciuria has been identified in 20-30% of children with hematuria, dysuria, frequency-urgency syndrome, and voiding dysfunction<sup>[5-8]</sup>. It is postulated that the high concentration of calcium in the urine irritates the bladder, causing involuntary incontinence<sup>[3,9,10]</sup>.

The aim of this study was to determine the prevalence of IH in school children in Ahvaz, a city with different ethnic groups in Southwest of Iran.

## Material & Methods

In a descriptive cross-sectional study from October to December 2006, among 93703 primary school children from 432 schools in metropolitan Ahvaz, 500 children were randomly recruited. The children were examined and excluded from the study if they received chronic medications, had known kidney diseases, malnutrition and chronic illness. Randomly, non-fasting urine samples were obtained from each subject using cups. The urine was collected between 9-10 a.m. The collections were designed to resemble the common method of urine collection in ambulatory setting. Urine calcium concentration was measured by cresolphthalein complexone spectrophotometric method and was determined by kinetic Jaffe reaction<sup>[11]</sup>.

UCa/UCr (mg/mg) ratio was calculated for each subject. Ratio exceeding 0.21 was considered abnormal<sup>[4]</sup>. In children with abnormal UCa/UCr ratio, 24-hour urinary calcium and creatinine excretion (the latter as a control of urine collection) was also measured and rates of calcium exceeding 4

mg/kg were considered as hypercalciuria. All patients were clinically examined, urine samples for urinalysis and culture taken, and serum levels of calcium, phosphate, alkaline phosphatase, creatinine and BUN chemically determined. Children who had hypercalciuria with a normal concentration of serum Ca were considered as idiopathic calciuric. Informed consents were obtained from parents of children enrolled in the study. Statistical analysis of data was performed by using the SPSS (version 14) program. *P*-values <0.05 were considered significant.

## Findings

Random sample of 500 children aged 6 to 12 years were enrolled in the study. The sample consisted of 231 (46.2%) males and 269 (53.8%) females. The UCa/UCr ratio was abnormal (>0.21) in 64 (12.8%) children (45 males and 19 females). The amount of 24-hour urinary calcium excretion exceeded 4 mg/kg only in 15 (3%) children. Chi square test showed statistically a significant difference between the prevalence rate in males (5.6%) and females (0.74%) (*P*=0.003). All children presenting the criteria of IH had normal concentrations of serum calcium, creatinine and BUN. Ten (66.7%) children had hematuria (including 2 cases with gross hematuria), 8 (53.3%) had a history of recurrent abdominal pain, 5 (33.3%) suffered from dysuria and 3 (20%) had a personal or familial history of urolithiasis.

## Discussion

Although hypercalciuria may be caused by conditions resulting in hypercalcemia, such as hyperparathyroidism, vitamin D intoxication, corticotherapy, distal renal tubular acidosis, IH is the commonest type of hypercalciuria<sup>[3]</sup>. IH is also the most common cause of renal calculi<sup>[5]</sup>. Inherited forms have been well

described, may account for up to 40 to 60% of cases of IH, and appear to follow an autosomal dominant or codominant pattern, but the gene or genes responsible remain to be identified<sup>[12]</sup>. The cause of this abnormality is not clear. It has been attributed to either a defect in renal tubular reabsorption of calcium (renal hypercalciuria) or from enhanced absorption by gastrointestinal tract (absorptive hypercalciuria). In most cases absorptive type is responsible for IH<sup>[3,5]</sup>.

The diagnosis of hypercalciuria is confirmed by 24-hour urine calcium excretion exceeding 4 mg/kg, but in patients who can not collect a timed urine specimen, measuring the UCa/UCr ratio on random urine, is a practical use in screening for hypercalciuria.

In the present study, in 64 (12.8%) of 500 children the UCa/UCr ratio exceeded 0.21 which was more than the rate of IH in the study conducted by Moore in 6.22% of 273 school children<sup>[13]</sup>. It was less than the rate of the study conducted by Esfahani et al, reported in 25% of 778 school children<sup>[14]</sup>. In our study, based on a 24-hour urine calcium excretion, the prevalence of IH was 1.8-4.8% (with confidence interval 95%) which was less than the study of Tehran (3.5-5.3%)<sup>[14]</sup>, Ankara (4.7%)<sup>[15]</sup> and Milan (3.2%)<sup>[11]</sup>.

In this study there was a difference in the prevalence of IH between girls and boys (7.5 fold more common in males) which was significant. One possibility may be the pattern of inheritance in this region which remains to be identified in the future. Recent studies have showed that the UCa/UCr varies with age and geographic area. In Turkey a ratio greater than 0.24 was considered abnormal<sup>[15]</sup>. The most frequent findings in our series were hematuria (66.7%), recurrent abdominal pain (53.3%), dysuria-frequency (33.3%) and familial history of renal calculi (20%) which were similar to the results of study conducted by Escrbano with 46%, 37.5% and 27.6%, respectively<sup>[16]</sup>.

In the present study, the renal function tests of all these children were normal which were comparable with the results of Stephan on 5- to 16-year old children in Memphis<sup>[17]</sup>. Vachvanichsanong et al found that 23% of

children with IH had urinary incontinence (nocturnal 54%, diurenal 21%, nocturnal with diurenal 25%)<sup>[18]</sup>. Penido et al reported that there is an altered bone metabolism in IH with osteopenia already present at the diagnosis in 35-38% of the patients<sup>[19,20]</sup>. They suggested N telopeptide as the most useful marker of bone alterations in IH, especially at an early stage of the disease<sup>[19]</sup>. Polito et al found that the risk of stone formation in children with IH increases with age, and during follow-up more than half of them have microcalculi<sup>[21]</sup>.

However, these studies suggest that IH is not an uncommon disorder in children and its manifestations are relatively common. Moreover, an appropriate management including general regimen and thiazides are safe and effective for resolving hypercalciuria and hematuria and if initiated in childhood, may have significant long-term benefits<sup>[22]</sup>.

## Conclusion

This study showed that 3% of school children in Ahvaz had IH predisposing for short-term and long-term complications of the disease. IH was significantly more common in boys than in girls in the region. Therefore, it is recommended that not only the urine of children having hematuria, abdominal pain, recurrent UTI and siblings with urolithiasis, but also the urine of every child (particularly boys in the region) be routinely screened for hypercalciuria.

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