# PRIMARY HYPEROXALURIA TYPE I: RESULTS OF A TUNISIAN COHORT

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## Background

Primary hyperoxaluria type I (PH1) is an autosomal recessive inborn error of glyoxlate metabolism, characterized by the accumulation of renal oxalate and often resulting in end-stage renal disease (ESRD). Rare in Europe, It accounts for 13, 5% of cases of ESRD in children Tunisian.

## Objective

The aim of this study was to describe the clinical presentation, molecular analysis and evolution of HP1 in a Tunisian cohort.

## METHODS

The study includes a cohort of 133 patients (71 infantile form and 62 adult form) suspected suffering from PH 1, from 126 unrelated families. Ten of them were diagnosed after family screening.

- The genetic analysis was made by PCR/RFLP to detect mutations( I244T,33-34 insC, G170R, F152I, W108R,976delG and G190R) described as the most common.
- Clinical, biochemical, and radiological data were obtained by an information sheet review or provided by questionnaires sent to clinicians in charge of PHI patient.

## RESULTS

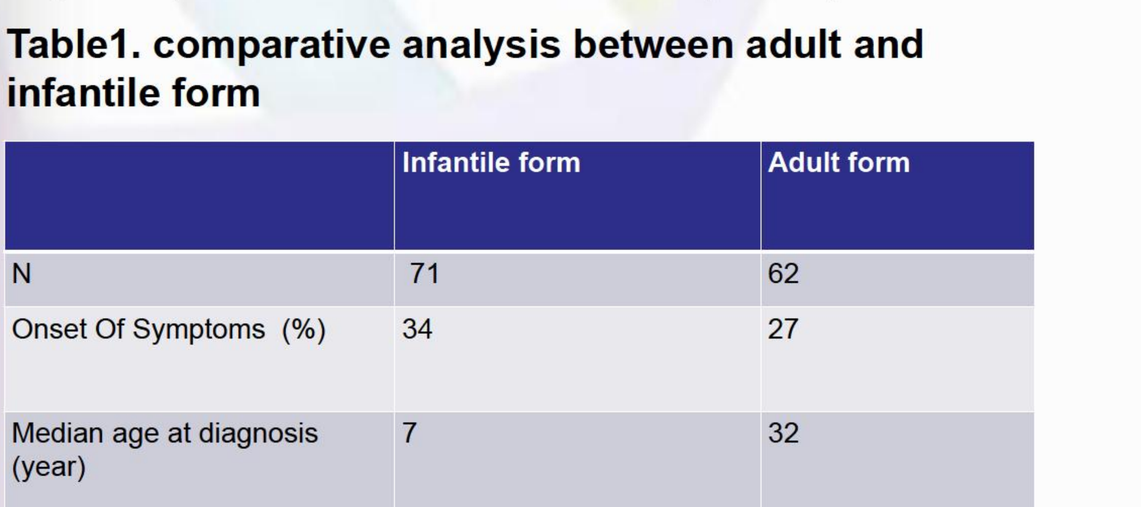
- Infantile onset (<1 years old) of symptoms occurred in 34%,whereas 27% of patients experienced the first manifestation of disease at an adult age (table1).
- Median age at diagnosis for infantile form was 7 years against 32 years for the adult form.
- ESRD was present at the time of diagnosis in 61 % of pediatric diagnoses patients versus 43 % of adult diagnosed patients.

**Table1. comparative analysis between adult and infantile form**

| | Infantile form | Adult form |
|---|---|---|
| N | 71 | 62 |
| Onset Of Symptoms (%) | 34 | 27 |
| Median age at diagnosis (year) | 7 | 32 |
| ESRD at the time of diagnosis (%) | 61 | 43 |

- The initial clinical presentation includes recurrent urolithiasis in 52% of cases, nephrocalcinosis in 38% and systemic oxalosis in 37% (figure1) .

**Figure1.systemic oxalosis: digestive, skin and in the venous**

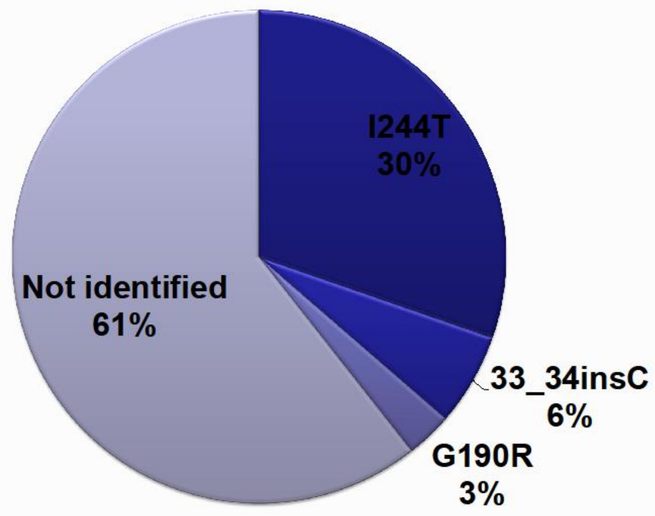


- The diagnosis was based on urinary oxalate level in 24 h (32%), stone analysis (28%), family history (27%), urinary oxalate-to-creatinine molar ratio (25%), renal biopsy (14%) and urine glycolate excretion (3%) (table2).

**Table2. Patient characteristics and clinical features**

| | |
|---|---|
| Total number of patients (N) | 133 |
| **Diagnosis** | |
| Mutation analysis (%) | 100 |
| Renal biopsy (%) | 14 |
| Stone analysis(%) | 28 |
| Urine analysis (%) | 32 |
| urine glycolate excretion(%) | 6 |
| **Symptoms at diagnosis** | |
| asymtomatic(%) | 9 |
| Urolithiasis (%) | 52 |
| Nephrocalcinosis (%) | 38 |
| Urolithiasis and nephrocalcinosis (%) | 13 |
| Other (urinary tract infection, failure to thrive...) (%) | 19 |
| **evolution** | |
| Death (%) | 9 |
| Oxalosis (%) | 37 |

**Figure2. results of molecular analysis**




- The most frequent mutation among Tunisian population is the I244T(figure2) , named the maghrebian, it results in a conformational unstable protein, prone to aggregation when is associated with the common polymorphism p.P11L.
- The 33_34insC is quite common PH1 patients, its high frequency can probably be attributed to multiple mutational events in the 8 cytosine residue repeat sequence in which it occurs (25). The 33dupC, which AGT is very low leads to a protein truncation and is the most common mutation found on the major allele .It is the second most common mutation in our cohort

## Conclusion

According to our study, our cohort is the highest cohort reported in Tunisia that systematically searched for PH1 patients in both pediatric and adult populations. Our results underscore the heterogeneity of the HP 1, delayed diagnosis and poor prognosis. The disease is probably underdiagnosed, particularly in the adult form. The molecular identification could provide an accurate tool for prenatal diagnosis, preserve kidney function and prevent diagnosis of adult diagnosed patients in ESRD.




DOI: 10.3252/pso.eu.51era.2014
Poster presented at: 51 ERA-EDTA CONGRESS AMSTERDAM 2014