

## Nephropathic Cystinosis in Children: A Ten Year Experience from a Pediatric Nephrology Center in Mashhad, North East of Iran

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### Abstract

**Background:** Nephropathic cystinosis is a rare autosomal recessive lysosomal storage disease. Its clinical manifestations include: failure to thrive, fanconi syndrome, ocular findings, growth retardation and end stage renal disease.

**Methods:** This was a retrospective chart review of patients with a diagnosis of nephropathic cystinosis over a ten year period in Dr. Sheikh Children's Hospital in Mashhad, North East of Iran.

**Results:** 20 patients were included in the study. The most common symptoms leading to the diagnosis were failure to thrive, polyuria, and polydipsia. Kidney involvement was reported in 77% of patients. End stage renal disease was reported in 10% and 2 patients had died because of that. Extrarenal manifestations included: hypothyroidism (25%), anemia (55.5%) and hypophosphatemic rickets (80%).

**Conclusion:** The most important complication of nephropathic cystinosis is end stage kidney disease. Early diagnosis and timely treatment with cysteamine can prevent or delay the complications.

**Key Words:** Cystinosis, Cysteamine, ESRD, Nephropathy.

\* Please cite this article as: Moazzen N, Shahrahmani F, Azarfar A, Ravanshad Y, Atae Nakhai A, Khakshoor A, Bagheri S. Nephropathic Cystinosis in Children: A Ten Year Experience from a Pediatric Nephrology Center in Mashhad, North East of Iran. J Ped Perspect 2024; 12 (10):19098-19101. DOI: **10.22038/jpp.2024.84274.5510**

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Received date: Nov.25,2024; Accepted date:Dec.14,2024

## 1- INTRODUCTION

Cystinosis is a rare lysosomal storage disease caused by mutations in the CTNS gene on chromosome 17p13 and is inherited as an autosomal recessive pattern. More than 140 mutations of this gene have been described (1). It is characterized by the accumulation of amino acid cystine in different organs which leads to organ failure and dysfunction (2). Three categories of this condition are described: 1- the infantile or nephropathic form 2- late onset or juvenile 3- adult or benign form. The infantile form is the most prevalent and is estimated to be 1 in 100000-200000 children (2, 3). This form of cystinosis leads to end stage renal disease and many extra renal complications due to the deposition of cystine crystals in different organs from which cornea is the most prominent (4). Infants with this disorder are usually normal at birth but between 6 to 12 months of age they present with a generalized dysfunction of the proximal tubules called fanconi syndrome (5). Urinary waste of water, electrolytes, minerals, glucose, and amino acids leads to growth failure and other clinical symptoms like polyuria, polydipsia, vomiting, constipation, electrolyte imbalance, dehydration and hypophosphatemic rickets (6). Diagnosis of cystinosis can be confirmed by one of these 3 methods (7):

- a) Evaluation of cysteine content of fibroblasts or peripheral blood leukocytes.
- b) Examination of cornea by slit lamp and demonstration of cystine crystals.
- c) Genetic testing for pathogenic variants of the CTNS gene.

Treatment of cystinosis consists of symptomatic therapy for the amelioration of symptoms and administration of cysteamine which reduces the intracellular content of cysteine and delays the progression of disease (8). For those who have progressed to end stage kidney

disease, kidney transplantation is an option (9).

The frequency of nephropathic cystinosis in Iran is not studied.

This study represents the clinical course of infantile nephropathic cystinosis (INC) in North East of Iran.

## 2- MATERIALS AND METHODS

This was a retrospective chart review of all patients diagnosed with INC during a ten year period between 2013 and 2022 in Dr. Sheikh Children's Hospital. This hospital is affiliated with Mashhad University of medical Sciences and is a pediatric tertiary referral center in North East of Iran.

A checklist was used for gathering patient's information including demographic characteristics, clinical, laboratory and imaging findings and medications used by the patient.

The diagnosis of cystinosis was documented in all patients by demonstrating the cystine crystals in cornea using slit lamp examination.

The study was approved by the medical ethics committee of Mashhad University of medical sciences (MUMS) prior to performance.

### 2-1. Data Analysis

All statistical analyses were performed using the SPSS 16 statistical package. Mean and standard deviation was used for reporting the normally distributed data and categorical data were expressed as numbers and percentage.

## 3- RESULTS

A total of 20 patients were included in this study. 11(55%) of them were male and 9 (45%) were female. Mean age of the study population was 6.5 years old (range=2.5-14 years old). The median age at diagnosis was 28 months (range=5-108).

There was a history of parent's consanguinity in 60% of the study population.

The most frequent symptoms which led to the diagnosis were failure to thrive (90%), polyuria and polydipsia (80%). Poor feeding and vomiting, fever, muscular spasms, weakness, and skeletal deformities were among the other symptoms reported at the time of presentation. nephrocalcinosis and kidney involvement was reported in 77% of patients. 2 patients had died because of the complications of the disease. 2 patients were under hemodialysis due to end stage kidney disease (ESKD) and all other patients were receiving systemic cysteamine therapy.

Extrarenal manifestations in our study population included: hypothyroidism (25%), anemia (55.5%), and hypophosphatemic rickets (30%).

Hypokalemia (78%), hyponatremia(42%), metabolic acidosis(78%), hypocalcemia (38%), and hypophosphatemia (30%) were the most prevalent laboratory abnormalities in the study population.

#### 4- DISCUSSION

Nephropathic cystinosis is a severe chronic condition that has a great impact on patients' life. The first sign of this condition which is usually noticed by parents and physicians is failure to thrive (10) and this was the same in our study population. Mean age of our patients at the time of diagnosis was 28 months which is slightly higher than that reported in European countries (11, 12). This is due to the lack of diagnostic tests like cysteine content of the leukocytes and fibroblasts which is not available yet in our practice. The diagnosis of our patients was confirmed through eye examination and ophthalmologic manifestations which are usually not observed under the age of 12 months (13).

Three patients in our study population were diagnosed under the age of 10 months which was due to the presence of another affected child in the family.

This later diagnosis in our country may lead to a poorer prognosis as early diagnosis and timely management are important in the long term prognosis of this rare lysosomal disorder (14).

When the diagnosis of cystinosis is made, attention must be paid to the extrarenal manifestations of the disease and they should be screened and managed properly.

Impaired growth is an important issue in patients with nephropathic cystinosis and the patients must be also evaluated by a pediatric endocrinologist in order to manage their growth problems (15).

#### 5- CONCLUSION

Nephropathic cystinosis is a rare genetic disorder which is considered partially treatable. The main complication of the disease is its renal involvement that can lead to an end stage kidney disease. Most of the complications can be delayed or prevented with cysteamine therapy. Early diagnosis and management is mandatory.

#### 6- CONFLICT OF INTEREST

None.

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