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Etiological Profile of Nephrocalcinosis among Children a cross-sectional study

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Keywords:
Nephrocalcinosis, children, Hypercalciuria, RTA, distal RTA, Bartter syndrome, Dent disease.

Abstract
Introduction: Nephrocalcinosis is a condition that affects a small percentage of children but has the potential to result in chronic kidney disease. This study was designed as a cross-sectional investigation with the purpose of determining the etiological profile of nephrocalcinosis in children.
Methods: The research comprised a total of one hundred young people between the ages of one and eighteen who had previously been diagnosed with nephrocalcinosis. Investigations of the patient's clinical history, physical condition, and test findings were carried out. Imaging procedures such as renal ultrasonography and computed tomography were also conducted during this patient's examination.
Results: According to the findings, the most common cause of nephrocalcinosis in children was found to be hypercalciuria, which accounted for 54% of all cases. In addition to these important causes, RTA (16%), distal RTA (12%), and idiopathic reasons (10%) were also significant contributors. The research also found that 8% of instances were connected to inherited disorders such Bartter syndrome and Dent disease.
Conclusion: This study underscores the necessity for a complete examination and therapy of nephrocalcinosis in children, with a particular emphasis on the identification of underlying aetiologies to prevent the progression to chronic kidney disease.

1. Introduction

The buildup of calcium salts in the renal parenchyma characterises the uncommon but severe condition known as nephrocalcinosis in children [1]. Nephrocalcinosis is a significant source of morbidity and mortality in children and can result in chronic kidney disease. Nephrocalcinosis is a complex aetiology that can be affected by age, sex, and location [2].

The most frequent cause of paediatric nephrocalcinosis is hypercalciuria. It is a condition where the amount of calcium excreted in the urine is elevated. Numerous factors, including increased intestinal calcium absorption, decreased renal calcium reabsorption, or both, may contribute to hypercalciuria [3]. Another significant factor contributing to paediatric nephrocalcinosis is "*Renal Tubular Acidosis* (RTA)". A deficiency in renal acidification causes metabolic acidosis and acidic urine as a result of RTA. Nephrocalcinosis is more frequently linked to the distal RTA [4].

Hereditary conditions such Lowe syndrome, Bartter syndrome, and Dent disease are also uncommon causes of nephrocalcinosis in children [5, 6, 7]. A genetic condition known as Bartter syndrome causes hypokalemia, metabolic alkalosis, hyperreninemia, and hyperaldosteronism [8]. Low molecular weight proteinuria, hypercalciuria, and nephrocalcinosis are the hallmarks of the X-linked recessive illness known as Dent disease [9]. Oculocerebrorenal syndrome, hypotonia, and renal failure are the hallmarks of the uncommon X-linked condition known as Lowe syndrome [10].

Despite the fact that there are many potential causes of nephrocalcinosis, it is crucial to pinpoint the root of the problem in order to stop chronic kidney disease from developing. Renal failure and its associated problems can be avoided with early detection and effective care of nephrocalcinosis. The resolve of this research

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was to determine the etiological characteristics of paediatric nephrocalcinosis.

2. Materials and Methods

A cross-sectional clinical study was piloted in a tertiary care facility in India from January 2021- January 2022. The institutional ethics committee gave its approval to the study, and the parents or legal guardians of every kid who participated in it gave their informed consent. The study included 100 kids with a nephrocalcinosis diagnosis who were 1 to 18 years old. Kidney disease, chronic kidney disease, and other serious comorbidities in children were excluded from the study.

Each participant underwent a thorough clinical history, physical examination, and laboratory tests. Complete blood count, serum electrolytes, serum creatinine, serum calcium, and serum phosphorus were among the laboratory tests performed. Additionally, 24-hour urine collection and analysis for calcium and creatinine were done.

All of the children underwent imaging tests, such as renal ultrasonography and “computed tomography (CT)”, to confirm the diagnosis of nephrocalcinosis and determine the underlying cause.

The “Statistical Package for the Social Sciences (SPSS)” version 26.0 was used to analyse the data gathered. Calculated descriptive statistics included frequency distributions, percentages, means, and standard deviations. The underlying aetiology of nephrocalcinosis was identified, and the relationships between it and factors like age, sex, and clinical presentation were examined.

3. Results

54% of the 100 study participants were boys and 46% were girls. The participants' average age was 8.7 4.2 years. With 54% of cases, hypercalciuria was the most frequent cause of nephrocalcinosis. RTA (16%), distal RTA (12%), and idiopathic reasons (10%) were other important causes. 8% of cases were caused by hereditary illnesses, such as Bartter syndrome and Dent disease. **Table 1,2**

The underlying aetiologies of nephrocalcinosis had a highly variable age distribution. The most prevalent aetiology across all age categories was hypercalciuria, with children aged 5 to 10 having the highest prevalence (61%). Children over the age of 10 (29%) had a higher prevalence of RTA than younger children (7%). Boys (19%) had the distal RTA more frequently than girls (4%). **Table 3**

Nephrocalcinosis's clinical manifestations varied considerably according to its aetiology. Recurrent “urinary tract infections (UTIs)” were the most frequent presentation of hypercalciuria (52%). The most frequent RTA presentation was metabolic acidosis (64%), whereas the distal RTA was more frequently associated with nephrocalcinosis and rickets (60%). Proteinuria and hematuria were the primary symptoms of Dent disease, whereas polyuria, polydipsia, and hypokalemia were the primary symptoms of Bartter syndrome. **Table 4**

Table 1: Demographic Characteristics of Study Participants

Characteristic	**Value**
Number of Participants	100
Gender (Male/Female)	54/46
Age (years), Mean ± SD	8.7 ± 4.2

Table 2: Underlying Etiologies of Nephrocalcinosis in Study Participants

Etiology	**Number of Cases**	**Percentage**
Hypercalciuria	54	54%

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RTA	16	16%
Distal RTA	12	12%
Idiopathic	10	10%
Hereditary Diseases (Bartter Syndrome, Dent Disease)	8	8%

Table 3: Age Distribution of Underlying Etiologies of Nephrocalcinosis

Etiology	**Age Group (years)**	**Number of Cases**	**Percentage**
Hypercalciuria	<5	9	17%
	5-10	33	61%
	>10	12	22%
RTA	<5	1	6%
	5-10	3	19%
	>10	12	75%
Distal RTA	<5	1	8%
	5-10	7	58%
	>10	4	33%

Table 4: Clinical Presentations of Nephrocalcinosis

Etiology	**Clinical Presentation**	**Percentage**
Hypercalciuria	Recurrent UTIs	52%
RTA	Metabolic Acidosis	64%
Distal RTA	Nephrocalcinosis and Rickets	60%
Bartter Syndrome	Polyuria, Polydipsia, and Hypokalemia	100%
Dent Disease	Proteinuria and Hematuria	100%

4. Discussion

Children that have nephrocalcinosis, a rare but serious condition that can cause chronic renal damage. Nephrocalcinosis has a complex aetiology that differs by age, sex, and geographical location [2]. Current investigation showed that hypercalciuria is the most frequent aetiology of paediatric nephrocalcinosis. This result is in line with those of other research carried out in various parts of the globe [11,12].

Numerous factors, such as increased intestinal calcium absorption, decreased renal calcium

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reabsorption, or both, may contribute to hypercalciuria [3]. Recurrent UTIs were the most typical clinical manifestation of hypercalciuria in current investigation. This result is consistent with earlier research [13] that have found a link between hypercalciuria and UTIs. Uncertain pathophysiological mechanisms may underlie this association, but one possibility is that it results from the infection that can develop when calcium-containing crystals form in the urinary tract.

Another significant factor contributing to paediatric nephrocalcinosis is RTA. A deficiency in renal acidification causes metabolic acidosis and acidic urine as a result of RTA. The distal RTA was more frequent than the proximal RTA in current study. This result is in line with those of earlier research, which have indicated that children with nephrocalcinosis had a higher prevalence of distal RTA [14]. Metabolic acidosis, the most typical presentation of RTA, was the clinical manifestation in current study [15].

Current investigation also revealed Bartter syndrome and Dent disease as hereditary causes of nephrocalcinosis. A rare hereditary condition called Bartter syndrome is characterised by hypercalciuria, hypokalemia, metabolic alkalosis, and salt loss [16]. Low molecular weight proteinuria, hypercalciuria, and nephrocalcinosis are symptoms of Dent disease, an X-linked recessive illness that compromises proximal tubular function [17]. These illnesses' clinical manifestations in current investigation were consistent with previous reports of them.

Current research revealed that there were considerable differences in the age distribution of the underlying causes of nephrocalcinosis. In all age groups, hypercalciuria was the most prevalent aetiology, but children between the ages of 5 and 10 had the highest prevalence. This result is consistent with previous research [18] that indicated a higher frequency of hypercalciuria in younger kids. The distal RTA was more common in guys and in youngsters older than 10 years.

In current investigation, the gender distribution of the underlying nephrocalcinosis aetiologies differed. Boys tended to have more distal RTAs, but females tended to have more proximal RTAs. This result is in line with those of earlier research [19] which have demonstrated a higher prevalence of distal RTA in males.

Current research has some drawbacks. First off, it was a single-center study, which would limit how broadly current conclusions can be applied to other groups. Second, the sample size was relatively small, which might have reduced the analytical statistical power.

5. Conclusion

As a result, current study determined that hypercalciuria is the most frequent cause of nephrocalcinosis in children. RTA, distal RTA, and genetic factors were additional major reasons. The underlying aetiologies of nephrocalcinosis differed widely in terms of age and gender distribution. Depending on the underlying aetiology, nephrocalcinosis' clinical appearance changed as well. Current work emphasises the significance of a comprehensive analysis of the aetiology of paediatric nephrocalcinosis to direct proper management and avoid long-term consequences.

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