



## IMMUNOLOGICAL AND REGIONAL CHARACTERISTICS OF TUBULOPATHIES AND THEIR ASSOCIATION WITH INFECTIOUS DISEASE MORBIDITY

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### Abstract.

Tubulopathies are a common genetic disease in children, leading to impaired transportation of electrolytes and minerals in the body. These diseases are observed in children from an early age, leading to chronic renal failure (CRF). The high prevalence of these diseases in Uzbekistan is associated with environmental factors and genetic problems, as well as infectious diseases. Frequent infection with infectious diseases in patients affects the clinical course of tubulopathies. Therefore, the study of regional specifics of tubulopathies and infectious diseases and the improvement of immunotherapy are important goals of the study. Material and methods: 33 children with tubulopathies treated in the nephrology department of the Andijan Regional Children's Multidisciplinary Medical Center during 2023–2025 were studied; During the study, patients were divided into clinical types: Low syndrome (n=8), nephronophthisis-Fanconi (n=8), vitamin D-resistant rickets (n=13), tubular acidosis (n=2), de Toni-Debre-Fanconi (n=2). Control group - 25 healthy children. Results: In addition to the main disease, the following comorbidities were found to be significantly higher: urinary tract infections (81.8%), upper respiratory tract infections (57.5%), adenoiditis (48.7%), recurrent bronchitis (54.5%), chronic tonsillitis (45.4%), otitis media (36.4%), gastroduodenitis (24.2%) and pneumonia (24.2%). Patients with severe clinical signs of tubulopathies had higher levels of interleukin-2, maternal gestational age and TORCH infection, parental consanguineous marriage (57.6%), child gender (boy), place of residence (village), and frequent infections compared to patients without severe clinical signs. These factors were assessed as risk factors. When immunomodulators were added to traditional treatment, the incidence of infectious diseases decreased significantly ( $p < 0.01$ ). Conclusion: Regional factors, immune dysfunction, and perinatal risks in tubulopathies have a significant impact on the course of the disease. The developed “algorithm for regional assessment of tubulopathies and optimization of immunotherapy” allows preventing complications, reducing disability, and mortality.

**Key words:** tubulopathies, children, interleukin-2, TORCH, immunomodulator, regional characteristics.

### Introduction.

Tubulopathies are a group of diseases characterized by polyuria, polydipsia, bone deformities, and renal dysfunction, resulting from the dysfunction of the renal tubules due to various factors. These diseases can be caused by various mutations in genes, such as environmental factors, infectious diseases of the parents, and bad habits of the parents. In most cases, tubulopathies are diagnosed late or develop against the background of other diseases, leading to renal failure [1,2]. Methods for timely diagnosis and treatment of tubulopathies have not been sufficiently established. Delayed diagnosis and treatment, especially in children, are becoming a very important and urgent issue. [3]. Accurate clinical, laboratory, and genetic

analyses are required to diagnose tubulopathies. Genetic testing, biochemical analyses, and determination of the functional state of the kidneys are very important for these diseases. [4, 5]. In the diagnosis and treatment of tubulopathies, socio-ecological factors are important and the problems are complex, and new methods are required accordingly. Immunotherapy methods have been tested and shown to be effective in the treatment of tubulopathies [6, 7].

### Materials and methods

**Study Design and Setting.** This combined clinical and laboratory study was conducted between 2023 and 2025 at the Nephrology, Otorhinolaryngology, and Urology Departments of the Andijan Regional Multidisciplinary Children's Medical Center. **Study Population.** The main study group included 33 children aged 0 to 17 years who were diagnosed with tubulopathy based on clinical, biochemical, and instrumental criteria. The control group consisted of 25 age-matched healthy children from the same region with no history of renal, metabolic, or systemic diseases.

**Inclusion and Exclusion Criteria.** Inclusion criteria: confirmed diagnosis of tubulopathy, age 0–17 years, and written informed consent from parents or legal guardians. Exclusion criteria: acute infectious diseases, autoimmune disorders, acute glomerulonephritis, oncological diseases, and ongoing systemic corticosteroid therapy.

#### Laboratory Assessments.

All participants underwent standard laboratory evaluations including:

Serum biochemical tests: creatinine, urea, electrolytes, total protein, C-reactive protein, and other metabolic indicators.

Urinalysis: physical and chemical parameters, protein measurement, specific gravity, and urinary sediment microscopy.

#### Cytokine Profiling.

To assess immunological activity, serum levels of Interleukin-2 (IL-2) were measured using the enzyme-linked immunosorbent assay (ELISA) method. All analyses were performed in a certified laboratory following the manufacturer's protocols and standard operational procedures.

#### Instrumental Examinations.

Based on clinical indications, the following imaging studies were performed:

Renal ultrasonography: evaluation of renal parenchyma, echogenicity, pyelocaliceal system, and presence of nephrolithiasis.

Subclavian radiographic assessment: performed in standard projections to determine skeletal changes potentially associated with metabolic or renal disorders.

#### Statistical Analysis.

Data were recorded in MS Excel and analyzed using statistical software. Descriptive statistics included mean values, standard deviation, median, and interquartile ranges. Comparative analysis between groups was performed using the Student's t-test or chi-square ( $\chi^2$ ) test, depending on the data type. Statistical significance was set at  $p < 0.05$ . Confidence intervals (95% CI) were calculated where applicable.

### Results.

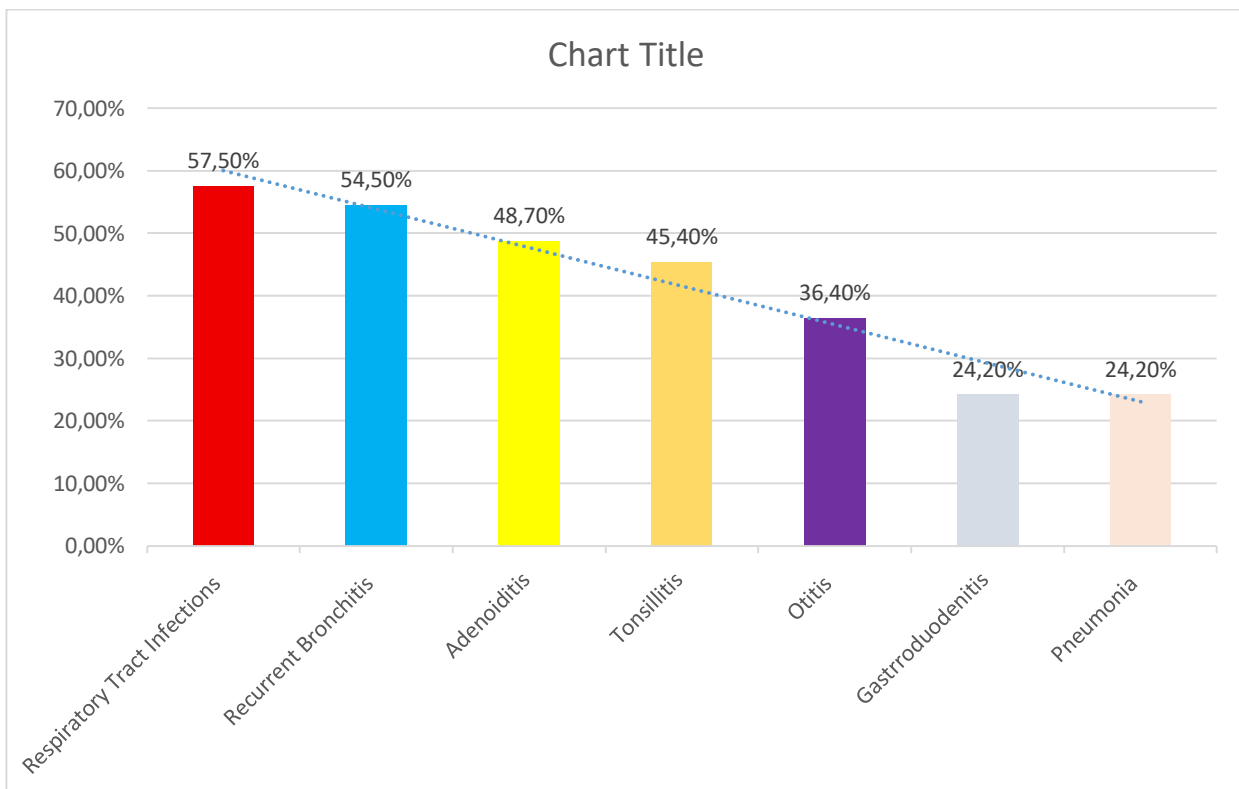
The regional and demographic characteristics of 33 different tubulopathies were studied. According to the results of the study, the number of tubulopathies increased from year to year, consanguineous marriages increased by 57.6%, 16%. Maternal age >30 years (71%) and <18

years (23%) - high risk. It was found that the frequency of occurrence in boys is higher than in girls. Table 1.

**Demographic and regional characteristics of 33 children with tubulopathies.**

Indicators	Values
Number of participants in the study	33 people
Consanguineous marriage	57.6%
Increase in consanguineous marriages	16%
Mother's age > 30 years	71%
Mother's age < 18 years	23%
Distribution by gender	
- Boys	high frequency
- Girls	lower frequency
The trend in the number of tubulopathies	It is increasing year by year

**The frequency of various infectious diseases in patients with tubulopathies along with the main disease was as follows (Figure 1).**



**Figure 1. Frequency of identified infectious diseases in patients with tubulopathies n=33**

The higher the incidence of infectious diseases, the more severe and severe the clinical signs of tubulopathy were.

Maternal health and perinatal risks

Passive smoking - 51%

Anemia, endocrine diseases, vegetative-vascular dystonia - high rates

Toxicosis, bleeding, placental abruption, labor discoordination, fetal hypoxia - significantly higher

Low birth weight - 58.3%



TORCH infections were associated with severe clinical conditions.

Immunological changes

In patients with high clinical activity, the IL-2 index was sharply increased, which confirms the susceptibility to infections and immune dysfunction.

The effect of immunomodulators

When immunomodulators were added to traditional therapy:

The frequency of infections decreased significantly ( $p < 0.01$ )

Clinical stability improved

The progression of metabolic disorders slowed down.

#### **Discussion.**

According to the results obtained, tubulopathies in Uzbekistan are multifactorial, due to genetic and perinatal causes. High incidence of infections aggravates the disease against the background of tubular dysfunction.

Elevated IL-2 indicates chronic activation of the immune system and allows for the justification of immunotherapy.

The developed algorithm is a multidisciplinary approach that combines regional risk factors, immune indicators and clinical data, and is of great importance in reducing the consequences of the disease.

#### **Conclusion.**

1. Tubulopathies in children often occur against the background of infectious comorbid conditions, which affect the progression of the disease.

2. The main risk factors are obstetric pathology in the mother, TORCH, passive smoking, consanguineous marriage, and male sex of the child.

3. Elevated IL-2 is important as a marker of immune dysfunction.

4. The use of immunomodulators reduces the frequency of infection and alleviates the course of the underlying disease.

5. The developed clinical diagnostic algorithm allows for early detection and prevention of complications of tubulopathy in children.

#### **Authors' contribution.**

Concept and idea: Nilufar Madjidova

Data preparation and collection: Nilufar Madjidova

Formal analysis: : Nilufar Madjidova

Study management: : Nilufar Madjidova

Methodology: : Nilufar Madjidova

Project supervision: : Nilufar Madjidova

Writing the first version of the text:

#### **Ethical committee approval.**

Ethical informed consent for the participation of children in the study was obtained from their parents in accordance with the requirements of the Geneva (Helsinki) Declaration. Ethical permission for this study was granted by the Ethics Committee of the Andijan State Medical Institute (Permit number: 2/60, date: 10.1.2023).

#### **Conflict of interest.**

The authors declare that there are no conflicts of interest in the preparation and publication of this article.

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