

# Epidemiological Characteristics of Children with Nephrotic Syndrome Referred to Amir-Kabir Hospital in Arak, Iran: A Cross-Sectional Study

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**Introduction.** Nephrotic syndrome is one of the most common glomerular diseases in childhood and is associated with significant morbidity and healthcare burden. Understanding its epidemiological and clinical characteristics is essential for improving patient management and outcomes. To investigate the epidemiological, clinical, and laboratory characteristics of children diagnosed with nephrotic syndrome referred to Amir-Kabir Hospital, Arak, Iran.

**Methods.** This cross-sectional study was conducted on 100 children diagnosed with nephrotic syndrome. Participants were enrolled using a census sampling method. Demographic, socioeconomic, perinatal, clinical, and laboratory data were collected from medical records and structured interviews. Data were analyzed using SPSS version 21 and presented as mean  $\pm$  standard deviation, frequency, and percentage.

**Results.** Among the 100 patients, 51% were male and 49% were female. The mean age was  $7.87 \pm 3.12$  years. Preterm birth was reported in 53% of patients. Hypoalbuminemia ( $< 2.5$  g/dL) was observed in all patients, while hypercholesterolemia ( $> 350$  mg/dL) was present in 69%. Prerenal azotemia, microscopic hematuria, urinary tract infection, allergy, and hyponatremia were observed in 56, 54, 38, 42, and 55% of patients; respectively. Periorbital edema was the most common clinical presentation (43%). Maternal risk factors included preeclampsia (38%), diabetes (52%), and hypertension (45%).

**Conclusions.** Children with nephrotic syndrome demonstrated a high prevalence of metabolic abnormalities, edema, and maternal prenatal risk factors. Early recognition of these characteristics may improve disease management and prognosis.

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## INTRODUCTION

Nephrotic syndrome (NS) is one of the most common glomerular disorders in childhood and is characterized by massive proteinuria, hypoalbuminemia, edema, and hyperlipidemia. Despite advances in diagnosis and treatment, NS remains an important cause of morbidity in

children because of its relapsing course, risk of complications, and impact on quality of life.<sup>1</sup> The incidence of childhood nephrotic syndrome varies



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worldwide, with reported rates ranging from 2 to 7 cases per 100,000 children annually. Although most cases are classified as idiopathic nephrotic syndrome and respond well to corticosteroid therapy, many patients experience frequent relapses or develop treatment-related complications. In addition to renal manifestations, children with NS are at increased risk of infections, thromboembolic events, electrolyte disturbances, and acute kidney injury.<sup>2</sup>

Several demographics, environmental, and perinatal factors have been suggested to influence the occurrence and clinical presentation of nephrotic syndrome. Previous studies have reported associations between NS and factors such as sex, family history, consanguinity, preterm birth, maternal hypertension, diabetes, and other prenatal conditions.<sup>3</sup> However, the reported findings have varied across populations, indicating the importance of regional epidemiological investigations.<sup>4</sup>

In developing countries, comprehensive data regarding the epidemiological and clinical characteristics of childhood nephrotic syndrome remain limited. In Iran, most published studies have focused on treatment outcomes or pathological findings, while fewer studies have evaluated demographic, socioeconomic, maternal, clinical, and laboratory characteristics simultaneously.<sup>5</sup>

A better understanding of the epidemiological profile of children with nephrotic syndrome may facilitate early diagnosis, improve patient management, and identify potential risk factors associated with disease development and progression. Therefore, the present study aimed to investigate the demographic, perinatal, clinical, and laboratory characteristics of children diagnosed with nephrotic syndrome who were referred to Amir-Kabir Hospital in Arak, Iran.

## MATERIALS AND METHODS

### Study Design and Setting

This cross-sectional study was conducted at Amir-Kabir Hospital, a tertiary pediatric referral center in Arak, Iran.

### Participants

The study population consisted of all children diagnosed with nephrotic syndrome who attended

the pediatric nephrology clinic during the study period. A total of 100 patients were included using a census sampling method.

### Inclusion Criteria

- Confirmed diagnosis of nephrotic syndrome.
- Age < 18 years.

### Exclusion Criteria

- Presence of chronic hematological disorders.
- Presence of other chronic systemic diseases.
- Use of medications or supplements for unrelated chronic illnesses.
- Incomplete clinical records.

### Data Collection

Data were obtained from medical records and face-to-face interviews with parents or guardians using a structured questionnaire.

Collected variables included:

- Demographic characteristics
- Socioeconomic status
- Parental educational level
- Birth history
- Maternal medical conditions
- Family history
- Clinical manifestations
- Laboratory findings
- Treatment-related variables

### Statistical Analysis

Data were analyzed using SPSS software version 21. Quantitative variables were presented as mean  $\pm$  SD, while categorical variables were expressed as frequencies and percentages.

### Ethical Considerations

The study was approved by the Ethics Committee of Arak University of Medical Sciences (IR.ARAKMU.REC.1395.277). Written informed consent was obtained from parents or legal guardians before participation.

## RESULTS

### Baseline Characteristics of Study Population

A total of patients with nephrotic syndrome were categorized into four clinical response groups: steroid-responsive (SR), steroid-dependent (SD),

steroid-resistant (SRNS), and frequently relapsing nephrotic syndrome (FRNS). Baseline demographic and clinical characteristics were compared among the four groups.

### Sex Distribution Among Nephrotic Syndrome Subgroups

A significant difference was observed in sex distribution among the studied groups ( $P = .004$ ). Female patients represented the majority of the steroid-responsive group (76%), whereas male predominance was observed in steroid-dependent (76%), steroid-resistant (52%), and frequently relapsing groups (52%) (Table 1).

### Clinical Manifestations at Diagnosis

**Urinary Tract Infection and Microscopic Hematuria.** The prevalence of urinary tract infection did not significantly differ among the four groups ( $P = .133$ ). However, microscopic hematuria showed a significant association with clinical subgroup ( $P = .001$ ). The frequency of microscopic hematuria was markedly higher among steroid-resistant (76%), steroid-dependent (68%), and frequently relapsing patients (64%) compared with steroid-responsive patients (8%) (Table 2).

**Inflammatory Marker and Electrolyte Abnormalities.** Positive CRP levels were significantly more frequent in patients with steroid-dependent, steroid-resistant, and frequently relapsing disease compared with steroid-responsive patients (60, 56, and 64% vs. 16%; respectively,  $P = .001$ ). Serum sodium abnormalities also differed significantly among groups ( $P = .001$ ). Hyponatremia was more prevalent in steroid-resistant (80%) and frequently relapsing patients (64%), whereas normal sodium levels were predominant in steroid-responsive patients (84%) (Table 2).

**Edema Characteristics at Initial Presentation.** The distribution of edema location at diagnosis significantly differed among clinical groups ( $P = .001$ ). Periorbital/facial edema was the most common presentation in steroid-responsive patients (64%). In contrast, anasarca was predominantly observed among steroid-resistant patients (60%), while ascites was more frequent in steroid-dependent patients (44%) (Table 3).

### Perinatal and Maternal Factors Associated with Disease Subgroups

**Mode of Delivery.** A significant association was observed between mode of delivery and

**Table 1.** Demographic and Baseline Characteristics of Children with Nephrotic Syndrome According to Clinical Subgroup

| Variable         | Category    | Steroid-responsive<br>(n = 25) | Steroid-dependent<br>(n = 25) | Steroid-resistant<br>(n = 25) | Frequently<br>relapsing (n = 25) | P    |
|------------------|-------------|--------------------------------|-------------------------------|-------------------------------|----------------------------------|------|
| Sex              | Male        | 6 (24%)                        | 19 (76%)                      | 13 (52%)                      | 13 (52%)                         | .004 |
|                  | Female      | 19 (76%)                       | 6 (24%)                       | 12 (48%)                      | 12 (48%)                         |      |
| BMI at diagnosis | Obesity     | 1 (4%)                         | 5 (20%)                       | 13 (52%)                      | 4 (20%)                          | .001 |
|                  | Overweight  | 5 (20%)                        | 7 (28%)                       | 5 (20%)                       | 11 (44%)                         |      |
|                  | Normal      | 14 (56%)                       | 10 (40%)                      | 6 (24%)                       | 2 (8%)                           |      |
|                  | Underweight | 5 (20%)                        | 3 (12%)                       | 1 (4%)                        | 8 (32%)                          |      |
| Delivery mode    | Vaginal     | 16 (64%)                       | 19 (76%)                      | 13 (52%)                      | 18 (72%)                         | .001 |
|                  | Cesarean    | 9 (36%)                        | 6 (24%)                       | 12 (48%)                      | 7 (28%)                          |      |

**Table 2.** Clinical and Laboratory Characteristics at Diagnosis According to Nephrotic Syndrome subgroup

| Variable              | Category | Steroid-responsive | Steroid-dependent | Steroid-resistant | Frequently<br>relapsing | P    |
|-----------------------|----------|--------------------|-------------------|-------------------|-------------------------|------|
| UTI                   | Present  | 6 (24%)            | 9 (36%)           | 9 (36%)           | 14 (56%)                | .133 |
|                       | Absent   | 19 (76%)           | 16 (64%)          | 16 (64%)          | 11 (44%)                |      |
| Microscopic hematuria | Present  | 2 (8%)             | 17 (68%)          | 19 (76%)          | 16 (64%)                | .001 |
|                       | Absent   | 23 (92%)           | 8 (32%)           | 6 (24%)           | 9 (36%)                 |      |
| CRP                   | Positive | 4 (16%)            | 15 (60%)          | 14 (56%)          | 16 (64%)                | .001 |
|                       | Negative | 21 (84%)           | 9 (36%)           | 11 (44%)          | 9 (36%)                 |      |
| Serum Na              | Normal   | 21 (84%)           | 9 (36%)           | 5 (20%)           | 9 (36%)                 | .001 |
|                       | High     | 0                  | 1 (4%)            | 0                 | 0                       |      |
|                       | Low      | 4 (16%)            | 15 (60%)          | 20 (80%)          | 16 (64%)                |      |

**Table 3.** Clinical Presentation and Maternal Factors Associated with Nephrotic Syndrome Phenotype

| Variable                    | Category              | Steroid-responsive | Steroid-dependent | Steroid-resistant | Frequently relapsing | P    |
|-----------------------------|-----------------------|--------------------|-------------------|-------------------|----------------------|------|
| Edema location at diagnosis | Face / eyes           | 16 (64%)           | 11 (44%)          | 9 (36%)           | 7 (28%)              | .001 |
|                             | Ascites               | 0                  | 11 (44%)          | 0                 | 1 (4%)               |      |
|                             | Hands / feet          | 0                  | 2 (8%)            | 0                 | 2 (8%)               |      |
|                             | Anasarca              | 2 (8%)             | 0                 | 15 (60%)          | 5 (20%)              |      |
|                             | Face / eyes + ascites | 6 (24%)            | 1 (4%)            | 1 (4%)            | 7 (28%)              |      |
| Maternal preeclampsia       | Present               | 1 (4%)             | 11 (44%)          | 13 (52%)          | 13 (52%)             | .004 |
|                             | Absent                | 24 (96%)           | 14 (56%)          | 12 (48%)          | 12 (48%)             |      |
| Maternal eclampsia          | Present               | 3 (12%)            | 0                 | 1 (4%)            | 1 (4%)               | .432 |
|                             | Absent                | 22 (88%)           | 25 (100%)         | 24 (96%)          | 24 (96%)             |      |
| Maternal diabetes           | Pregestational DM     | 2 (8%)             | 6 (24%)           | 10 (40%)          | 5 (20%)              | .118 |
|                             | Gestational DM        | 6 (24%)            | 6 (24%)           | 9 (36%)           | 8 (32%)              |      |
|                             | No DM                 | 17 (68%)           | 13 (52%)          | 6 (24%)           | 12 (48%)             |      |

nephrotic syndrome subgroup ( $P = .001$ ). Vaginal delivery was the predominant mode in all groups; however, cesarean delivery was relatively more frequent among steroid-resistant patients (48%) compared with other groups (Table 1).

**Maternal Pregnancy Complications.** A history of maternal preeclampsia was significantly associated with nephrotic syndrome phenotype ( $P = .004$ ). The frequency of preeclampsia increased from 4% in steroid-responsive patients to 44%, 52%, and 52% in steroid-dependent, steroid-resistant, and frequently relapsing groups, respectively.

No significant difference was observed regarding maternal eclampsia history among the groups ( $P = .432$ ) (Table 3).

**Anthropometric Characteristics at Diagnosis.** BMI classification differed significantly among the studied groups ( $P = .001$ ). Obesity was most prevalent among steroid-resistant patients (52%), whereas normal BMI was more common in steroid-responsive patients (56%). The frequently relapsing group showed a higher proportion of overweight (44%) and underweight (32%) patients compared with other groups (Table 1).

### Corticosteroid Initiation Timing and Disease Phenotype

The interval between edema onset and

corticosteroid initiation was significantly associated with clinical phenotype ( $P = 0.001$ ). Early initiation of corticosteroid therapy within one week was most common among steroid-responsive patients (76%). Conversely, delayed initiation was observed more frequently among steroid-resistant patients (68% after two weeks) and frequently relapsing patients (64% after three weeks) (Table 4).

**Maternal Diabetes Status.** Maternal diabetes status was not significantly associated with nephrotic syndrome subgroup classification ( $P = .118$ ). However, pregestational diabetes was more frequent among steroid-resistant patients (40%), while absence of maternal diabetes was more common among steroid-responsive patients (68%) (Table 3).

### DISCUSSION

Childhood nephrotic syndrome is a heterogeneous glomerular disorder characterized by significant proteinuria, hypoalbuminemia, and edema, with a highly variable response to corticosteroid therapy. Although the majority of children achieve remission with glucocorticoids, a considerable proportion experience steroid dependency, frequent relapses, or steroid resistance, which are associated with prolonged immunosuppressive treatment and increased risk of chronic kidney

**Table 4.** Relationship Between Corticosteroid Initiation Timing and Nephrotic Syndrome Subgroup

| Time from edema onset to corticosteroid initiation | Steroid-responsive | Steroid-dependent | Steroid-resistant | Frequently relapsing | P    |
|----------------------------------------------------|--------------------|-------------------|-------------------|----------------------|------|
| ≤ 1 week                                           | 19 (76%)           | 13 (52%)          | 3 (12%)           | 2 (8%)               | .001 |
| 2 weeks                                            | 4 (16%)            | 6 (24%)           | 17 (68%)          | 7 (28%)              |      |
| 3 weeks                                            | 2 (8%)             | 6 (24%)           | 5 (20%)           | 16 (64%)             |      |

disease. Identification of clinical and laboratory factors associated with unfavorable phenotypes may improve early risk stratification and allow more individualized therapeutic approaches.<sup>2,6</sup>

In the present study, several demographic, clinical, laboratory, and maternal factors were associated with different clinical phenotypes of nephrotic syndrome. Sex distribution differed significantly among the groups, with a higher proportion of females in the steroid-responsive group and a predominance of males among steroid-dependent, steroid-resistant, and frequently relapsing patients. Childhood nephrotic syndrome has consistently been reported to have a male predominance, particularly in younger children; however, the association between sex and steroid response remains inconsistent across studies. Previous investigations suggest that sex alone is unlikely to determine treatment response, and differences may instead reflect variations in genetic susceptibility, immune regulation, or underlying histopathological patterns.<sup>7</sup>

Microscopic hematuria was significantly more frequent among steroid-dependent, steroid-resistant, and frequently relapsing patients compared with steroid-responsive patients in our cohort. Hematuria is considered an atypical finding in classic minimal change disease, which accounts for the majority of steroid-sensitive nephrotic syndrome cases. In contrast, persistent hematuria may suggest more extensive glomerular injury and has been associated with pathological lesions such as focal segmental glomerulosclerosis (FSGS), which is more commonly associated with steroid resistance and poorer renal outcomes.<sup>5,8</sup> Therefore, the presence of microscopic hematuria at presentation may serve as a useful clinical marker for identifying patients who require closer monitoring and further evaluation.

We also observed a significant association between inflammatory status and nephrotic syndrome phenotype. Elevated CRP levels were considerably more common among steroid-dependent, steroid-resistant, and frequently relapsing groups compared with steroid-responsive patients. Although nephrotic syndrome is primarily driven by immune dysregulation and podocyte injury rather than systemic inflammation,

increasing evidence indicates that inflammatory pathways, cytokine abnormalities, and immune cell activation contribute to alterations in glomerular permeability and disease progression.<sup>9</sup> The higher frequency of CRP positivity among patients with unfavorable responses may therefore reflect greater inflammatory activity or more severe disease expression.

Serum sodium abnormalities, particularly hyponatremia, were significantly associated with disease subgroup in our study. Hyponatremia was more prevalent among steroid-resistant and frequently relapsing patients, whereas normal sodium levels were more common among steroid-responsive children. Electrolyte disturbances in nephrotic syndrome may occur as a consequence of severe proteinuria, reduced effective circulating volume, activation of neurohormonal pathways, and increased secretion of antidiuretic hormone despite total body fluid excess.<sup>10</sup> The association between hyponatremia and unfavorable disease characteristics may indicate a greater degree of physiological disturbance at disease onset.

The pattern of edema at diagnosis showed significant differences among clinical groups. Periorbital edema was the most common initial manifestation in steroid-responsive patients, whereas generalized edema (anasarca) was more frequent among steroid-resistant children. The severity of edema reflects the extent of urinary protein loss, hypoalbuminemia, and disturbances in fluid distribution. Although edema pattern is not currently included among formal predictors of steroid response, extensive edema at presentation may represent a marker of higher disease burden and more severe clinical presentation.<sup>2</sup>

An important finding of the present study was the association between BMI category and nephrotic syndrome phenotype. Obesity was markedly more frequent among steroid-resistant patients, whereas normal BMI was more common among steroid-responsive children. Obesity has emerged as an important modifier of kidney disease through mechanisms involving chronic inflammation, oxidative stress, insulin resistance, altered adipokine production, and podocyte injury. Previous studies have demonstrated that increased body weight may be associated with increased proteinuria and

accelerated progression of renal disease; however, whether obesity directly contributes to steroid resistance or reflects underlying disease severity remains uncertain.<sup>11,12</sup>

Maternal preeclampsia was significantly associated with unfavorable nephrotic syndrome phenotypes in our study. Children born to mothers with a history of preeclampsia showed higher frequencies of steroid dependency, steroid resistance, and frequent relapse compared with steroid-responsive patients. Preeclampsia is characterized by placental dysfunction, endothelial injury, and impaired fetal development, and accumulating evidence suggests that adverse intrauterine environments may influence lifelong renal susceptibility through altered nephron development and renal programming.<sup>13</sup> Although this association is biologically plausible, further prospective studies are required to confirm whether maternal vascular disorders contribute directly to childhood glomerular disease susceptibility.

In contrast, maternal eclampsia and diabetes status were not significantly associated with nephrotic syndrome phenotype. The absence of significant associations may be related to the relatively small number of affected mothers, limiting statistical power. Additionally, the relationship between maternal metabolic disorders and childhood kidney disease is complex and may involve multiple genetic, environmental, and developmental factors.

The timing of corticosteroid initiation was strongly associated with clinical phenotype. Steroid-responsive patients were more likely to receive corticosteroid therapy within one week of edema onset, whereas delayed initiation was more common among steroid-resistant and frequently relapsing patients. Early diagnosis and prompt initiation of standard corticosteroid therapy remain central components of childhood nephrotic syndrome management.<sup>2</sup> However, delayed treatment may represent a consequence of more severe or atypical disease rather than an independent cause of poor response. Therefore, this finding should be interpreted cautiously and requires confirmation in prospective studies.

Taken together, our findings indicate that childhood nephrotic syndrome phenotypes are

associated with a combination of clinical, laboratory, anthropometric, and maternal characteristics. The presence of microscopic hematuria, elevated CRP, hyponatremia, severe edema, obesity, maternal preeclampsia history, and delayed corticosteroid initiation may help identify patients at increased risk of steroid resistance or frequent relapse. Incorporating these factors into early clinical assessment may improve prediction of treatment response and support individualized management strategies.

The present study has several limitations. The observational design limits the ability to establish causal relationships between associated factors and disease outcomes. In addition, kidney biopsy findings, genetic testing, and long-term renal outcomes were not available for all patients, which may have provided further insight into mechanisms underlying steroid resistance. Future multicenter prospective studies integrating clinical, pathological, and molecular data are warranted.

## CONCLUSIONS

The present study identifies several factors associated with unfavorable nephrotic syndrome phenotypes, including microscopic hematuria, elevated CRP, hyponatremia, severe edema, obesity, maternal preeclampsia, and delayed corticosteroid initiation. Recognition of these characteristics may improve early risk stratification and facilitate personalized management of children with nephrotic syndrome.

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