SJIF Impact Factor: 6.711

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 9
Issue: 2
Page N. 63-68
Year: 2025

Original Article www.wjahr.com

OCULAR COMPLICATIONS IN CHILDREN WITH NEPHROTIC SYNDROM

[1*]Angam Tarek Hussein, [2]Baidaa Abdul Hussein Jasim, [3]Doaa Oday Hatem, [4]Taghreed Fadhil Mohammed and [5]Ameer A. Bananzada

[1,2]Babylon Health Directorate, Babylon. Iraq.
[3]Al Muthanna Health Directorate, Al Muthanna, Iraq.
[4]Baghdad Health Directorate - Al-Karkh, Baghdad, Iraq.
[5]Al-Rusafa Health Directorate, Baghdad, Iraq.

Article Received date: 04 December 2024 **Article Revised date:** 24 December 2024 **Article Accepted date:** 13 January 2025

***Corresponding Author: Angam Tarek Hussein**
Babylon Health Directorate, Babylon. Iraq.

ABSTRACT

Background: Nephrotic syndrome (NS) is a heterogeneous glomerular disorder commonly affecting children, characterized by proteinuria due to glomerular damage. Long-term corticosteroid therapy, a cornerstone of idiopathic NS treatment, is associated with ocular complications, including posterior subcapsular cataract, glaucoma, increased intraocular pressure (IOP), ptosis, mydriasis, eyelid atrophy, keratitis, corneal and scleral thinning, and recurrent hordeolum. Aim: To determine ocular complications in children with NS and their association with steroid dosing and duration. **Patients and Methods:** A cross-sectional observational study was conducted on 60 children with NS at the Department of Pediatric Nephrology, Central Child Teaching Hospital, from October 2019 to July 2020. Data on age, gender, disease duration, steroid treatment duration, type of NS, and prior ophthalmologic evaluations were collected. Comprehensive ophthalmic assessments were performed at a tertiary center. Histological diagnosis and treatment regimens were reviewed from patient records and caregiver interviews. **Results:** The study included 60 children aged 1–15 years (mean: 8.8 ± 3.5 years), with males comprising 58%. Most cases occurred before age five (mean: 5.23 ± 3.16 years). Half the patients had one or more ocular complications. Abnormal visual acuity was significantly associated with longer disease duration and treatment ($p = 0.024, 0.004, 0.043$). Cataract risk increased with prolonged steroid use and disease duration ($p = 0.036, 0.021$). Elevated IOP was linked to systemic hypertension ($p = 0.021$). **Conclusions:** Ocular involvement is common in children with NS. Longer steroid therapy increases cataract risk and decreases visual acuity, warranting regular ophthalmologic evaluation. Systemic hypertension elevates IOP risk, emphasizing blood pressure monitoring.

KEYWORDS: Ocular, Complications, Children, Nephrotic Syndrom.

INTRODUCTION

Nephrotic syndrome (NS) is a heterogeneous disease and one of the most common glomerular disorders among children. It is characterized by significant protein leakage from the blood into the urine due to glomerular damage. This condition is clinically defined by nephrotic-range proteinuria (≥40 mg/m²/hour, urine protein/creatinine ratio ≥200 mg/mmol, or ≥3+ protein on a urine dipstick), hypoalbuminemia (serum albumin concentration <30 g/L), and edema. Hyperlipidemia, though often present, is not universal.[1] NS primarily results from abnormalities in the glomerular filtration barrier, including changes in podocyte structure and function, leading to increased permeability to plasma proteins. Its pathophysiology involves both immune-mediated mechanisms and podocyte injury, with emerging evidence supporting the role of circulating permeability factors and podocyte dysfunction in disease onset and progression.[2-4] The clinical manifestations of NS vary, with edema being the hallmark feature. Edema typically starts in the periorbital region and progresses to generalized swelling (anasarca) with associated ascites, pleural effusion, and scrotal or labial edema. Other symptoms may include anorexia, malaise, abdominal pain, and fatigue. Hypertension, microhematuria, and infections are also observed in some patients. Notably, the clinical presentation of NS can vary based on its underlying cause, such as idiopathic, secondary, or congenital forms.[5,6] Idiopathic nephrotic syndrome (INS) is the most prevalent form in children, comprising approximately 90% of cases. The most common histologic subtype is minimal change nephrotic

syndrome (MCNS), accounting for about 85% of INS cases in children. MCNS is characterized by normal-appearing glomeruli under light microscopy, with effacement of podocyte foot processes observed under electron microscopy. It is associated with an excellent response to corticosteroid therapy, with over 95% of affected children achieving remission.[7] However, other histological subtypes, such as focal segmental glomerulosclerosis (FSGS) and membranoproliferative glomerulonephritis (MPGN), are more resistant to treatment and may carry a poorer prognosis.[8] Secondary NS occurs in association with systemic diseases, such as systemic lupus erythematosus, Henoch-Schönlein purpura, infections (e.g., hepatitis, HIV, malaria), or malignancies (e.g., lymphoma, leukemia). Congenital and infantile NS, presenting within the first year of life, often results from genetic mutations or secondary causes such as infections.[5] Epidemiologically, NS affects 2–7 children per 100,000 annually in the United States, with a cumulative prevalence of approximately 16 per 100,000. It predominantly affects boys under eight years, with a male-to-female ratio ranging from 2:1 to 3:2. Variations in racial and genetic predispositions have been documented, with higher incidence rates in South Asian and African American children, the latter showing a greater likelihood of progressing to end-stage renal disease (ESRD) due to higher rates of FSGS.[9,10] The prognosis of NS largely depends on the response to corticosteroid therapy. While most children with MCNS exhibit excellent outcomes, those with steroid-resistant nephrotic syndrome (SRNS) or secondary forms of NS are at higher risk for complications, including infections, thrombosis, acute kidney injury (AKI), and progression to chronic kidney disease (CKD).[8] Comprehensive management strategies, including dietary modifications, immunosuppressive therapy, and symptomatic treatments, are essential to optimize outcomes and reduce complications.[11-13] The aim of study is to determine ocular complications in children with NS and their association with steroid dosing and duration.

METHOD

This cross-sectional study included 60 patients diagnosed with nephrotic syndrome who attended the Pediatric Nephrology Department at the Central Child Teaching Hospital in Baghdad. The study was conducted from October 1, 2019, to July 31, 2020. Data collection involved a structured checklist capturing patient information, including age, gender, duration of disease, duration of steroid treatment, type of nephrotic syndrome, history of ophthalmologic evaluations (both steroid-dependent and independent), blood pressure measurements during sample collection, and prior ocular issues. Comprehensive ophthalmologic assessments were performed at the Medical City by an ophthalmologic consultant. These assessments included visual acuity testing using the Snellen chart, intraocular pressure (IOP) measurement with air-puff tonometry (Topcon Corporation, Japan), slit-lamp microscopy for anterior segment examination, fundus evaluation, optical coherence tomography (Topcon Corporation, Japan) for optic nerve analysis, and automated perimetry for visual field assessment (Humphrey, Australia). The IOP measurements followed pediatric age-specific norms: IOP: =0.71 x age (years) +10, up to age 10. Then, IOP tends to approach adult levels by 12 years of age[14] after which IOP approaches adult levels. Patient information, including histological diagnosis of nephrotic syndrome and treatment regimens, was obtained from hospital medical records, caregivers, and direct interviews with patients. While the initial sample size was larger, follow-up challenges and refusal to undergo ophthalmologic exams reduced the final sample size to 60. Inclusion Criteria: Patients aged 1–15 years with nephrotic syndrome characterized by proteinuria (>2 g/m²/day or 50 mg/kg/day), hypoalbuminemia (<2.5 g/dL), or hypercholesterolemia, and corticosteroid use for more than six months. Exclusion Criteria: Patients with syndromic forms of nephrotic syndrome (e.g., Pierson syndrome), systemic diseases other than NS, congenital nephrotic syndrome, prior ocular conditions, non-cooperation with ophthalmologic exams, or age <1 year were excluded. Statistical analyses were performed using SPSS (version 23.0). Continuous data were presented as mean ± standard deviation and analyzed using Student's t-test, while categorical data were compared using the chi-square test. Results were tabulated and visualized, with p-values <0.05 considered statistically significant.

RESULTS

Cross sectional study of 60 children already diagnosed with nephrotic syndrome were involved in this study. Their age was between 1-15 years with a mean of 8.8 (±3.5) years with male gender account about 58% of the sample. All are presented in figure 1.

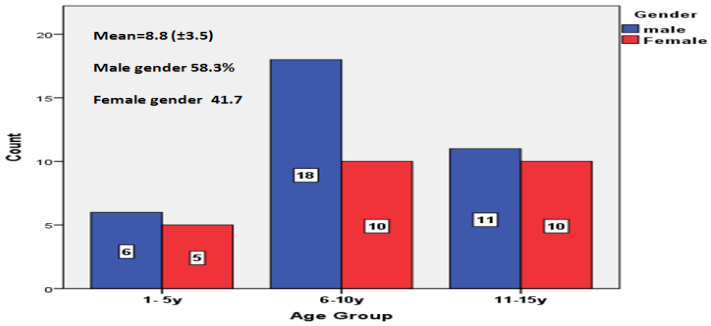

Figure (1) shows the distribution of the study sample according to age group and gender.

Most of cases of Nephrotic syndrome in the present sample tend to occur before the age of five years, with mean age of occurrence of 5.23 (±3.16) as in figure (2).

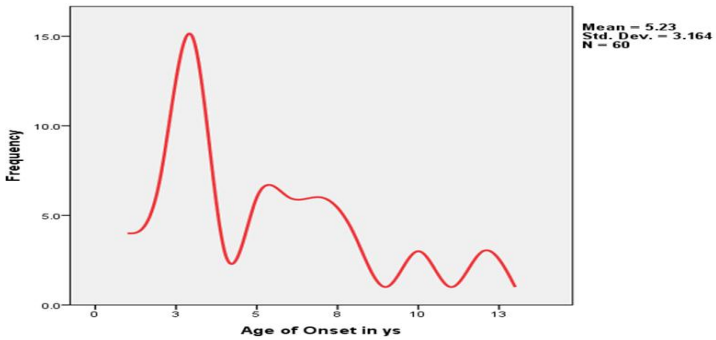

Figure (2): Distribution of the study patients according to age of onset of Nephrotic syndrome.

The majority of the study sample (More than 50%) are steroid sensitive and only 10% of them are resistant to steroid a condition may be obvious in figure (3)**.**

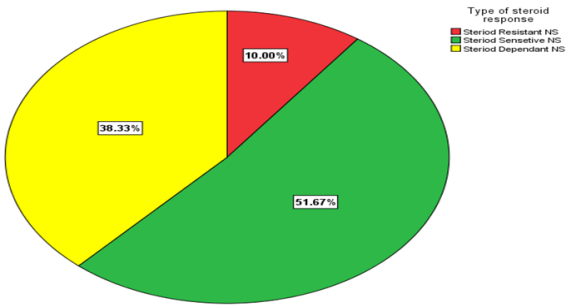

Figure (3): distribution of the study sample according to the type of steroid response.

Fifty percent of the sample had developed one or more ocular complications with abnormal visual acuity and high intraocular pressure been the most common complication as presented in table (1).

Table (1): Distribution of study sample according to presence and type of ocular complications.

Complications	Frequency	Percent
No ophthalmic complication	30	50.0
Only Cataract	3	5.0
Only abnormal visual acuity	7	11.7
Only High IOP	7	11.7
Two complications*	8	13.4
All three complications**	5	8.3
Total	60	100.0

*(Cataract& high IOP), (Cataract &Abnormal VA) or (High IOP & abnormal VA)
**(Cataract+ high IOP+ abnormal Visual acuity)

Chemotherapy used by the patients distributed among Cyclophosphamide, cyclosporine and calcept whether alone or in combinations as in table (2).

Table (2): The distribution of the nephrotic syndrome patients according to the type of chemotherapy used.

Type of chemotherapy	Frequency	Percentage (%)
Cyclophosphamide	10	55.56%
Cyclosporin	10	55.56%
Mycophenolate Mofetil	5	27.78%

Abnormal visual acuity was significantly associated with longer disease and hence longer treatment duration whether steroid treatment or even chemotherapy (0.024, 0.004 and 0.043 respectively) which also got a significant association with the development of abnormal visual acuity. Higher blood pressure also appeared as a

significant risk factor for such condition P value= (0.021) as in table (3).

Table (3): Shows the association between the development of abnormal visual acuity and different disease characteristics.

Disease Characteristic		Visual acuity		τ OR χ^2 value	P value
		Normal	abnormal		
Duration of the disease		3.14(±1.86)	4.76 (±3.56)	-2.31	0.024*
Duration of treatment (months)		14.34 (±8.1)	24.58 (±12.20)	-1.7	0.004*
Steroid Response	SSNS**	14 (60.9%)	9 (39.1%)	2.625	0.263
	SDNS***	25 (80.6%)	6 (19.4%)		
	SRNS****	4 (66.7%)	2 (33.3%)		
Bd pressure	Normal	40 (76.9%)	12 (23.1%)	5.307	0.021*
	raised	3 (37.5%)	5 (62.5%)		
use of chemotherapy	Not used	32 (80%)	8 (20%)	4.104	0.043*
	Used	**11 (55%)**	**9 (45%)**		

*significantly associated *** Steroid Dependent Nephrotic Syndrome
Steroid sensitive Nephrotic Syndrome ** Steroid Resistant Nephrotic Syndrome

As in visual acuity, both longer disease duration and treatment duration were significantly associated with ophthalmic Cataract (P value= 0.036 and 0.021 respectively). The type and steroid response (Steroid dependent and Steroid resistant) also play a role with P value = 0.019 as in table (4).

Table (4): Association between development of cataract and different disease characteristics.

Disease Characteristic		Cataract		τ OR χ^2 value	P value
		absent	present		
Duration of the disease		3.04 (±1.80)	5.27 (±3.61)	-2.28	0.036*
Duration of treatment (months)		15.26 (±9.6)	23.2 (11.01)	-2.49	0.021*
Steroid Response	SSNS**	26 (83.9%)	5 (16.1%)	7.49	0.019*
	SDNS***	13 (56.5%)	10 (43.5%)		
	SRNS****	6 (100%)	0 (0%)		
Bd pressure	Normal	41 (78.8%)	11 (21.2%)	3.070	0.079
	raised	4 (50%)	4 (50%)		
use of chemotherapy	Not used	34 (85%)	6 (15%)	6.40	0.024*
	Used	**11 (55%)**	**9 (45%)**		

*significantly associated *** Steroid Dependent Nephrotic Syndrome
Steroid sensitive Nephrotic Syndrome ** Steroid Resistant Nephrotic Syndrome

In contrast to the above two complications, only higher blood pressure seems significantly associated with higher intra-ocular pressure, but Neither chemotherapy treatment Nor steroid dependence appeared as significant risk factors for it, a condition presented in table (5).

Table (5): the association between development of high intraocular pressure and different disease characteristics.

Disease Characteristic		Intra-ocular Pressure		τ OR χ^2 value	P value
		Normal	High		
Duration of the disease		3.12 (±1.82)	4.82 (±3.59)	-1.867	0.077
Duration of treatment (months)		15.34 (±8.1)	22.06 (±22.06)	-1.857	0.078
Steroid Response	SSNS**	23 (74.2%)	8 (25.8%)	0.971	0.615
	SDNS***	15 (65.2)	8 (34.8%)		
	SRNS****	5 (83.3%)	1 (16.7%)		
Bd pressure	Normal	40 (76.9%)	12 (23.1%)	5.307	0.021*
	raised	3 (37.5%)	5 (62.5%)		
use of chemotherapy	Not used	30 (75%)	10 (25%)	0.675	0.418
	Used	**13 (65%)**	**7 (35%)**		

*significantly associated *** Steroid Dependent Nephrotic Syndrome
Steroid sensitive Nephrotic Syndrome ** Steroid Resistant Nephrotic Syndrome

DISCUSSION

In this cross-sectional study, 60 children diagnosed with nephrotic syndrome (NS) were evaluated for steroid-dependent and independent ophthalmologic complications. The age range was 2–15 years, with a mean age of 8.8 (±3.5) years. Males comprised 58% of the sample, and females accounted for 42%, aligning with findings from Alaleh Gheissari et al.[15] who reported a male-to-female ratio of 62% to 37%. The majority of NS cases in this study occurred before the age of five years, with a mean onset age of 5.23 (±3.16) years, similar to Vijay Agrawal et al.[16], who reported an onset age of 5 (±1.39) years. This is consistent with the well-documented observation that NS predominantly manifests in early childhood. More than 50% of the patients in this study were steroid-sensitive, 38% were steroid-dependent, and 10% were steroid-resistant. Regarding ocular complications, the observed issues were limited to cataracts, high intraocular pressure (IOP), and abnormal visual acuity. No cases of uveitis, ocular infections, astigmatism, or other steroid-related eye complications were recorded. These findings are consistent with those of Alaleh Gheissari et al.[15] but differ from Vijay Agrawal et al.[16], who reported myopic astigmatism as the second most common complication after posterior subcapsular cataract (PSC). Similarly, Jezeela K1 et al.[17] documented hordeolum internum and externum in 21.4% and blepharitis in 11.4% of 45 patients. Fifty percent of the patients in this study had one or more ocular complications, similar to the findings of Alaleh Gheissari et al.[15], who reported that 60% of patients had steroid-dependent or independent ophthalmologic symptoms. Among the therapeutic regimens used, cyclophosphamide was the most common, followed by cyclosporine and mycophenolate mofetil, either alone or in combination. Abnormal visual acuity was significantly associated with longer disease duration and treatment ($p < 0.05$), consistent with Jezeela K1 et al.[17] and Wenbo Zhang et al.[18] This association may be attributed to fluid accumulation in the retina and choroid caused by hypoalbuminemia. Additionally, the prolonged use of chemotherapy, particularly in steroid-resistant or steroid-dependent NS, was significantly related to visual problems, as noted by Wenbo Zhang et al.[18] and Jezeela K1 et al.[17] PSC was significantly associated with prolonged disease and treatment duration ($p = 0.036$ and 0.021, respectively). This is consistent with Jezeela K1 et al.[17] and Lee Ryan N et al.[19], who found a significant relationship between corticosteroid use and cataract formation ($p = 0.04$). Prolonged steroid use in SDNS, with or without chemotherapy, was a critical factor for developing PSC. Higher blood pressure was significantly associated with elevated IOP ($p = 0.021$), in line with findings by Marc Leeman[20], who identified hypertension as a significant risk factor for primary open-angle glaucoma ($p < 0.001$). However, steroid use and duration were not significantly linked to high IOP ($p = 0.078$), consistent with Jezeela K1 et al.[17] and J.S.K. et al.[21] The discrepancy with Alaleh Gheissari et al.[15], who found glaucoma to be the second most common complication, may be due to the smaller sample size in this study. These findings highlight the complex interplay of disease duration, treatment regimens, and systemic factors in ocular complications associated with NS.

CONCLUSION

Steroid eye involvement is common in N.S child. Pediatric patients with a longer duration of steroid therapy are at greater risk of cataract formation and decrease visual acuity Hence, pediatricians are advised to refer these patients to ophthalmologists for proper evaluation. Patient with high systemic blood pressure are risk factor to develop high intraocular pressure.

REFERENCES

1 Global Outcomes (KDIGO) Clinical Practice Guideline for Glomerulonephritis. Kidney Int., 2012; 2: 139–274.
2 Uwaezuoke SU. Pathogenesis of idiopathic nephrotic syndrome in children: molecular mechanisms and therapeutic implications. Integr Mol Med., 2015; 3(1): 484-487.
3 Bagga A, Mantan M. Nephrotic syndrome in children. Indian J Med Res., 2005; 122: 13-285.
4 Uwaezuoke SU. Pathogenesis of idiopathic nephrotic syndrome in children: molecular mechanisms and therapeutic implications. Integr Mol Med., 2015; 3(1): 484-487.
5 Kopac M. Nephrotic syndrome in children: present state and future perspective. J Nephrol Res., 2018; 4(1): 139-14.
6 Mahan JD, Patel HP. Nephrotic syndrome and proteinuria. In: Marcdante KJ, Kliegman RM. Nelson Essential of Pediatric. 7th edition. Elsevier Inc; 2015; 162: 557-8.
7 Pais P, Avner ED. Idiopathic Nephrotic Syndrome. In: Kliegman RM, Stanton BF, St Geme JW, eds. Nelson Textbook of Pediatric. 20th edition. Elsevier, 527: 3836-43.
8 Gbadegesin R, Smoyer WE. Nephrotic syndrome. In: Geary DF, Schaefer F. Comprehensive Pediatric Nephrology. 1st edition. Elsevier Inc; 2008; 12: 208-19.
9 Eddy AA, Symons JM. Nephrotic syndrome in childhood. Lancet, 2003 Aug 23; 362(9384): 629-39.
10 Warady BA, Chadha V. Chronic kidney disease in children: the global perspective. Pediatr Nephrol, 2007; 22: 1999– 2009.
11 Niaudet P, Boyer O. Idiopathic Nephrotic Syndrome in children In: Avner ED, Harman WE Niaudet, et al. Pediatric Nephrology. 7th edition. Springer, 2016; 28: 840-53.
12 Gipson DS, Massengill SF, Yao L, et al. Management of childhood onset nephrotic syndrome. Pediatrics, 2009; 124: 747–57.
13 Vaziri ND. Molecular mechanisms of lipid disorders in nephrotic syndrome. Kidney Int., 2003 May; 63(5): 1964–76.

14 BRESSON_DYMONT H.JFR ophtalmo, intraocular pressure measurement in children, Elsevier, 2009 mar, 32(3): 176-81.
15 Alaleh Gheissari, 1 Hossein Attarzadeh, 2 HodaSharif, et al. Steroid Dependent and Independent Ocular Findings in Iranian Children with Nephrotic Syndrome, 2011 Oct; 2(4): 264-8.
16 Vijay Agrawal, Kusum Devpura, 2 Laxmikant Mishra, 3 et al. Study on Steroid Induced Ocular Findings in Children with Nephrotic Syndrome, 2017 Mar; 11(3).
17 Jezeela K 1, Deleepkumar Kozhikkot Velayudhan 2, Rajini Chereyath 3, et al. 2018 March; 5 11: 1022-1026.
18 Wenbo Zhang 1, Yadi Zhang 1, Lei Kang 1et al. Retinal and choroidal thickness in paediatric patients with hypoalbuminaemia caused by nephrotic syndrome, 2019 Feb 6; 19(1): 44.
19 Lee Ryan N. Olonan, MD Catherine Anne G. Pangilinan, MD Mario M. Yatco, MD Department of Ophthalmology University of Santo Tomas Hospital Manila, Philippines JULY – DEC. 2009.
20 Marc Leeman, Philippe Kestelyn glaucoma and Hypertension Clinic, Erasme University Hospita, 2019 Mar; 73: 944–950.
21 J.S.K. Ng, William Wong, R.W.K. Law, et al, Ocular complications of paediatric patients with nephrotic syndrome, 2001 August Clinical and Experimental Ophthalmology, 29(4): 239-43.