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Evaluation of urine examination in Childhood Nephrotic Syndrome

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Abstract: Pediatric Nephrotic syndrome, which is a condition affecting the kidneys, is more prevalent in children than in adults.

Aims and Objectives: To investigate urine derangement in children aged 2-12 years with nephrotic syndrome.

Patients and methods: The current study was a prospective observational pilot study on children with NS from "The Nephrology Unit of Mansoura University Children's Hospital (MUCH)." over the years 2022 & 2023. The study included Nephrotic syndrome (NS) patients who suggested glucocorticosteroid conduct as a first-line therapy. Urine examination was measured, to understand the relation between uremia and comprised renal function and develop the life quality for children grappling with CKD.

Conclusions: Uremic toxins, including urea and creatinine, accumulate in the blood as kidney function declines. These toxins can have systemic effects and contribute to the progression of CKD

Keywords: Nephrotic syndrome, urine examination, Urinary protein, Urinary RBCs (/HPF), and Urinary WBCs (/HPF)

Introduction:

Nephrotic syndrome is a critical chronic disease in children, described by minimum change disease in the majority [1]. The following symptoms indicate the presence of excessive protein in the urine, which is known as proteinuria, low levels of a protein called hypoalbuminemia, swelling in specific parts of the body that is referred to as edema, and high levels of cholesterol and other lipids (fats) in the blood, also known as hyperlipidemia. The pathogenesis of idiopathic NS is believed to involve immune dysregulation, systemic circulating factors, or inherited structural abnormalities of the podocyte. Genetic risk is more common in children with steroid-resistant disease, although the cause remains unknown [2]. The nephrotic syndrome usually happens when the glomeruli are damaged, allowing too much protein to leak from the blood into the urine [3]. Edema in NS is affected by increased glomerular permeability to albumin and plasma proteins, increased liquid drainage, and increased risk of thrombosis in patients with prothrombotic genetic variations. The disease typically begins between ages 2 and 8, peaking at 3 to 5 years old [4]. The pathophysiological mechanisms of INS (idiopathic nephrotic syndrome) are not yet fully understood. However, it is believed that the disease is caused by an abnormal immune response which leads to an increase in the permeability of the glomerulus. This alteration in the capillary structure and integrity of the

glomerular membrane eventually results in INS [5].

NS needs chronic treatment with steroids or other immunosuppressants [6]. Long-term use of steroids or other medications that suppress the immune system is required for treatment. Biopsy is utilized to guide the course of treatment [7]. However, children with this condition have a positive prognosis in terms of maintaining normal kidney function, even if they experience regular relapses. Based on the response to steroids, SSNS is typically divided into broader categories, with 90% of children being diagnosed with steroid SSNS. About 25% of these children experience no additional relapses after the initial course of steroids and are effectively cured. The remaining 75% will continue to relapse, and their frequency of relapse will characterize them [8].

The present study aimed to study the derangement of urine examination in children 2 to 12 years old with nephrotic syndrome.

1.Patients and methods

The Nephrology Unit of Mansoura University Children's Hospital (MUCH) conducted a pilot study on children with NS from 2022 to 2023.

The study included Nephrotic syndrome (NS) patients who suggested glucocorticosteroid treatment as a first-line therapy. They are further given to subgroups upon their primary response to steroid treatment, according to the ISKDC definitions and guidelines: Steroid sensitive (SSNS): the response to steroid treatment can be categorized into steroid sensitivity and steroid dependence. Steroid sensitivity is indicated by complete remission within the initial four weeks of treatment without any relapses during this period, also known as primarily steroid sensitivity (PSS). The patient may suffer from steroid dependence (SDNS) if they experience two relapses while undergoing treatment or within two weeks of stopping steroid therapy. If a patient has two or more relapses in the first six months of treatment or four or more relapses in a year, they may be identified as frequently relapsing (FRNS). The term steroid resistance refers to the failure of a patient to achieve complete remission even after 8 weeks of corticosteroid therapy. To conduct the study, healthy children of similar age and sex will be selected from the General Outpatient Clinic of MUCH. Our study excluded individuals with Congenital Nephrotic Syndrome, Diabetes, Leukemia, and those who underwent transplantation. All patients in the current study underwent history-taking, including age, gender, and place of residence. The clinical presentation, date and age of onset of Nephrotic Syndrome, prior medical conditions, medications, family history of Nephrotic Syndrome, and response to treatment were recorded. Clinical information, particularly blood pressure, edema (location, severity, duration), as well as physical examination data such as weight, height, and BMI were collected. Renal Biopsy, Abdominal Ultrasound, or Renal Doppler Ultrasound, Magnetic Resonance Imaging (MRI), Computed Tomography were performed.

(CT) (Scan. Laboratory Information including Hemoglobin, Red blood cell count, White Blood Cell Count, Platelet Count, Serum Albumin, Creatinine, Albumin/creatinine ratio, Blood Urea Nitrogen, Total Cholesterol, Triglycerides, High-density Lipoprotein, Low-density Lipoprotein, Serum Calcium, Serum Phosphorus, Serum Potassium, Serum Sodium Urine analysis for (Protein- R.B. Cs-W.B. Cs).

2. Statistical Analysis:

The data collected underwent a process of revision, coding, and tabulation using the Statistical Package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). The normality of the data was evaluated using the Kolmogorov-Smirnov test. For numerical data, we used mean, standard deviation (± SD), standard error (± SE), median, and range.

Results

patients with NS. Their mean age was 9.2, ranging from 1.75 to 17.5 years. They were 56.7% males and 43.3% females. In addition to 43 healthy control subjects of matched age and gender. Out of the 60 patients, 3.3% had a nephrotic syndrome positive family history, while the majority (96.7%) had a negative family

history. Regarding consanguinity degree, 13.3% of patients had a positive consanguinity degree, while 86.7% had a negative consanguinity degree as shown in Table 1. The mean disease duration was 3.71 years with a standard deviation of 3.02 years. The median duration was 3.0 years, ranging from a minimum of 0.10 years to a maximum of 11.0 years. Puffy eye lids were observed in 1.7% of patients, while 6.7% had abdominal enlargement. Most patients experienced generalized edema (91.7%), ascites (5.0%), hypertension (5.0%), chronic renal failure (1.7%), and oliguria (26.7%) as shown in Table 2.

Table 1: Comparison between patients with nephrotic syndrome and control group regarding baseline parameters.

	NS patients (N = 60)	**Control (N = 34)**	P
Sex			
Male; № (%)	34 (56.7%)	23(67.6%)	0.295
Female; № (%)	26 (43.3%)	11(32.4%)	
Age (years)			
Mean ± SD.	9.20 ± 3.93	10.28 ± 3.30	0.135
Median	10.0	11.0	
Min. – Max.	1.75 – 17.50	3.0 – 15.0	
Residency			
Urban; № (%)	1(1.7%)	0(0%)	1.000
Rural; № (%)	59(98.3%)	34(100%)	
Disease duration (years)			
Mean ± SD.	3.71 ± 3.02		
Median (Min. – Max.)	3.0 (0.10 – 11.0)		

SD.: Standard deviation, Min.: Minimum, Max.: Maximum, U: Mann Whitney test, X2: Chi-Square, FE: Fisher Exact, p: Comparing NS and control group.

Table 2: Family history and consanguinity degree among patients with nephrotic syndrome.

Family history	**NS patients N = 60**	
	No.	**%**
Negative;	58	96.7
Positive;	2	3.3
Consanguinity degree		
Negative;	52	86.7
Positive;	8	13.3
Clinical manifestations		
Generalized edema;	55	91.7
Hypertension;	3	5
CRF;	1	1.7
Oliguria;	16	26.7

At sampling, 13.3% of nephrotic syndrome patients had hematuria, whereas only 11.7% were at the beginning of the disease. None of the control group had hematuria. The analysis between the NS and control groups showed a significant difference (p1=0.002, 0.001).

However, when comparing the presence of hematuria at the onset of the disease and at the time of sampling, there was no significant difference between the presence of hematuria at sampling and the onset of the disease (p3=0.541). Crystals and casts were significantly higher in NS at disease beginning and at the time of sampling when contrasted to a control group. Whereas no significant differences were found between the time of sampling and disease onset. The mean UPCR creatinine in urine ratio was 104.1 ± 162.8, with a median of 55.0 (range: 10.0 – 750.0). The UPCR protein in urine ratio had a mean of 870.0 ± 1092.3, and a median of 452.0 (range: 4.70 – 3700.0). These values indicate a wide variation in protein levels in the urine of patients with NS.

The mean UOP was 118.1 ± 314.0, with a median of 2.80 (range: 1.50 – 1000.0). The wide standard deviation and range indicate substantial variability in urine output among these patients. Urinary protein, Urinary RBCs and Urinary WBCs decreased significantly at sampling when compared to disease onset. Both times were

significantly higher than control group as shown in Table 3.

Table 3: Comparison between patients with NS and the control group regarding urine examination.

	NS patients (N = 60)		Control N = 34	p1	p2	p3
	At sampling	At the onset of the disease				
Hematuria; № (%)						
NIL	40(66.7%)	38(63.3%)	34(100%)	0.002*	0.001*	0.541
+	8(13.3%)	7(11.7%)	0(0%)			
++	4(6.7%)	7(11.7%)	0(0%)			
+++	8(13.3%)	8(13.3%)	0(0%)			
Crystals						
No	6(10%)	2(3.3%)	34(100%)	<0.001*	<0.001*	0.219
Yes	54(90%)	58(96.7%)	0(0%)			
Casts						
No	32(53.3%)	20(33.3%)	34(100%)	<0.001*	<0.001*	0.104
Yes	28(46.7%)	40(66.7%)	0(0%)			
Urinary protein	N = 58	N = 59				
Mean ± SD.	2.12 ± 1.14	2.78 ± 0.56	0.0 ± 0.0	<0.001*	<0.001*	<0.001*
Median (Min. – Max.)	3(0.0 – 3.0)	3(0.0 – 3.0)	0(0.0 – 0.0)			
Urinary RBCs (/HPF)						
Mean ± SD.	6.68 ± 13.79	9.22 ± 19.40	0.0 ± 0.0	<0.001*	<0.001*	0.043*
Median (Min. – Max.)	1(0.0 – 83.0)	3(0.0 – 100.0)	0(0.0 – 0.0)			
Urinary WBCs (/HPF)						
Mean ± SD.	6.44 ± 13.94	5.97 ± 5.22	0.0 ± 0.0	<0.001*	<0.001*	0.016*
Median (Min. – Max.)	3(0.0 – 100.0)	4(0.0 – 25.0)	0(0.0 – 0.0)			
UPCR creatinine in urine ratio						
Mean ± SD.	104.1 ± 162.8	-	-	-	-	-
Median (Min. – Max.)	55.0 (10.0 – 750.0)	-	-			
UPCR protein in urine ratio						
Mean ± SD.	870.0 ± 1092.3	-	-	-	-	-
Median (Min. – Max.)	452.0 (4.70 – 3700.0)	-	-			
UOP (ml/kg/hr)						
Mean ± SD.	118.1 ± 314.0	-	-	-	-	-
Median (Min. – Max.)	2.80 (1.50 – 1000.0)	-	-			

X2: Chi-Square, Mc: Monte Carlo, MH: Marginal Homogeneity, P1: Comparing NS and control group at sampling, P2: Comparing NS and control group at the onset of disease, P3: Comparing at sampling and at the onset of disease in NS group, *: Significant when p value <0.05.

No significant differences were found between SSNS, SDNS, and SRNS regarding sex, age, residence, FH, and consanguinity (p>0.05 for each). No significant differences were found between SSNS, SDNS, and SRNS regarding disease duration (p>0.05 for each).

SRNS was significantly associated with a higher incidence of oliguria (p=0.046). Otherwise, no significant differences were found between SSNS, SDNS, and SRNS regarding clinical data (p>0.05 for each) as shown in

Table 4 and Table 5

Table 4: Relation between treatment response and demographic data, family history, consanguinity, and clinical data among patients with NS.

		SSNS N = 7 № (%)	SDNS N = 16 № (%)	SRNS N = 37 № (%)	P
Sex	**Male; № (%)**	5(71.4%)	9(56.3%)	20(54.1%)	0.805
	Female; № (%)	2(28.6%)	7(43.8%)	17(45.9%)	
Age (years)	**Mean ± SD.**	7.46 ± 3.81	9.22 ± 2.94	9.52 ± 4.31	0.400
	Median (min-max)	8.5(1.75 – 12.50)	9.25(4.50 – 14.50)	10.5(2.00 – 17.50)	
Residency	**Urban; № (%)**	0(0%)	0(0%)	1(2.7%)	1.000
	Rural; № (%)	7(100%)	16(100%)	36(97.3%)	
Family history	**№ (%)**	0(0%)	0(0%)	2(5.4%)	1.000

SD.: Standard deviation, Min.: Minimum, Max.: Maximum, H: Kruskal Wallis test, X2: Chi–Square, MC: Monte Carlo, P: Comparing the different treatment responses.

Table 5: Relation between treatment response and demographic data, consanguinity, and clinical data among patients with NS.

		SSNS N = 7 № (%)	SDNS N = 16 № (%)	SRNS N = 37 № (%)	P
Consanguinity	**№ (%)**	0(0%)	1(6.3%)	7(18.9%)	0.383
Disease duration (years)	**Mean ± SD.**	2.10 ± 1.91	3.46 ± 2.51	4.14 ± 3.33	0.288
	Median	2.5(0.10 – 5.0)	2.75(0.40 – 8.0)	4(0.20 – 11.0)	
Puffy eye lids	**№ (%)**	0(0%)	0(0%)	1(2.7%)	1.000
Odema LL	**№ (%)**	0(0%)	0(0%)	0(0%)	–
Abdominal enlargement	**№ (%)**	1(14.3%)	0(0%)	3(8.1%)	0.297
Generalized edema	**№ (%)**	7(100%)	13(81.3%)	35(94.6%)	0.212
Ascites	**№ (%)**	0(0%)	0(0%)	3(8.1%)	0.686
Hypertension	**№ (%)**	1(14.3%)	2(12.5%)	0(0%)	0.076
CRF	**№ (%)**	0(0%)	0(0%)	1(2.7%)	1.000
Oliguria	**№ (%)**	0(0%)	2(12.5%)	14(37.8%)	0.046*

Urinary protein was significantly higher in SDNS and SRNS when compared to SSNS. Otherwise, no significant differences were found between outcome groups regarding urine examination at the time of sampling. At the onset of the disease, Urinary protein was significantly higher in SRNS compared to SSNS. Urinary RBCs were significantly higher in SRNS compared to SDNS. Urinary WBCs were significantly higher in SSNS, SRNS compared to SDNS. Otherwise, no significant differences were found between outcome groups regarding urine examination at disease onset as shown in **Table 6**

Table 7: Relation between treatment response and UPCR creatinine, protein in urine ratio among patients with NS.

	SDNS	SRNS	p
UPCR creatinine in urine ratio			
Mean ± SD	95.0 ± 106.1	105.0 ± 169.1	0.791
Median (Min. – Max.)	95(20.0 – 170.0)	55(10.0 – 750.0)	
UPCR protein in urine ratio			
Mean ± SD	42.0 ± 19.80	945.2 ± 1111.5	0.145
Median (Min. – Max.)	42(28.0 – 56.0)	563(4.70 – 3700.0)	

SD.: Standard deviation, Min.: Minimum, Max.: Maximum, U: Mann Whitney test, P: Comparing the different treatment responses.

Table 6: Relation between treatment response and urine analysis among patients with NS.

	SSNS	SDNS	SRNS	p
At sampling				
Hematuria				
NIL	7(100%)	12(75%)	21(56.8%)	0.400
+	0(0%)	3(18.8%)	5(13.5%)	
++	0(0%)	0(0%)	4(10.8%)	
+++	0(0%)	1(6.3%)	7(18.9%)	
Crystals				
No; № (%)	2(28.6%)	3(18.8%)	1(2.7%)	0.060
Yes; № (%)	5(71.4%)	13(81.3%)	36(97.3%)	
Casts				
No; № (%)	6(85.7%)	8(50%)	18(48.6%)	0.204
Yes; № (%)	1(14.3%)	8(50%)	19(51.4%)	
UOP (ml/kg/hr)				
Mean ± SD	334.7 ± 576.2	3.55 ± 1.34	88.09 ± 267.7	0.892
Median (Min. – Max.)	2(2.0 – 1000.0)	3.55(2.60 – 4.50)	2.9(1.50 – 1000.0)	
Urinary protein				
Mean ± SD	1.0 ± 1.0	2.19 ± 1.11	2.31 ± 1.08	P1=0.025*
Median (Min. – Max.)	1(0.0 – 3.0)	3(0.0 – 3.0)	3(0.0 – 3.0)	p2=0.028* p3=0.007* p4=0.679
Urinary RBCs (/HPF)				
Mean ± SD	3.43 ± 6.05	7.44 ± 20.28	6.97 ± 11.42	0.202
Median (Min. – Max.)	1(0.0 – 17.0)	1(0.0 – 83.0)	3(1.0 – 55.0)	
WBCs (/HPF)				
Mean ± SD	2.57 ± 1.62	3.06 ± 1.73	8.69 ± 17.51	0.057
Median (Min. – Max.)	3(0.0 – 5.0)	3(0.0 – 7.0)	3.5(0.0 – 100.0)	
At onset of disease				
Hematuria				
NIL	5(71.4%)	14(87.5%)	19(51.4%)	0.132
+	1(14.3%)	0(0%)	6(16.2%)	
++	0(0%)	2(12.5%)	5(13.5%)	
+++	1(14.3%)	0(0%)	7(18.9%)	
Crystals				
No; № (%)	0(0%)	1(6.3%)	1(2.7%)	0.625
Yes; № (%)	7(100%)	15(93.8%)	36(97.3%)	
Casts				
No; № (%)	4(57.1%)	5(31.3%)	11(29.7%)	0.407
Yes; № (%)	3(42.9%)	11(68.8%)	26(70.3%)	
Urinary protein				
Mean ± SD	2.29 ± 0.76	2.56 ± 0.81	2.97 ± 0.17	P1<0.001*
Median (Min. – Max.)	2(1.0 – 3.0)	3(0.0 – 3.0)	3(2.0 – 3.0)	p2=0.130 p3<0.001* p4=0.212
Urinary RBCs (/HPF)				
Mean ± SD	17.14 ± 36.66	2.56 ± 3.37	10.64 ± 18.80	P1=0.043*
Median (Min. – Max.)	3(0.0 – 100.0)	1(0.0 – 12.0)	5(0.0 – 100.0)	p2=0.217 p3=0.639 p4=0.012*
WBCs (/HPF)				
Mean ± SD	7.86 ± 7.90	2.81 ± 1.52	7.0 ± 5.20	P1=0.001*
Median (Min. – Max.)	5(3.0 – 25.0)	3(0.0 – 5.0)	5(1.0 – 23.0)	p2=0.024* p3=0.891 p4<0.001*

SD.: Standard deviation, Min.: Minimum, Max.: Maximum, H: Kruskal Wallis test, P1: Comparing the different treatment responses, P2: Comparing SSNS and SDNS, P3: Comparing SSNS and SRNS, P4: Comparing SDNS and SRNS, *: Significant when p value <0.05.

No significant differences were found between SDNS and SRNS regrading UPCR creatinine, protein in urine ratio (p>0.05 for each) as shown in **Table 7.**

Discussion

Nephrotic syndrome is a condition affecting the kidneys, which results in a significant loss of protein and fluid through urine due to irregularities in the glomerular capillary wall [9],[10]. The condition is characterized by symptoms such as hard proteinuria, which is the loss of more than 3.5 g/24 hr in adults or 40 mg/m2/hr in children, hypoalbuminemia, which is a low level of albumin in the blood (<2.5 g/dl), edema, and hyperlipidemia, which is an increased level of serum cholesterol (>200mg/dl) [8]. The present study showed that the mean age was 9.2 with male predominance in agreement with most earlier studies as in Egypt [11], Iran [12] , and New Zealand [13]. The childhood nephrotic syndrome has a male predominance [14, 15].

Family history and consanguinity grade between patients with nephrotic syndrome. In this study, out of the 60 patients, a small proportion of them (3.3%) had a positive family history of nephrotic syndrome. Most patients (96.7%) had no such history. It's noteworthy that the occurrence of positive family history was comparatively higher in this study than in other studies (such as the one conducted by Gulati et al, where it was 2%) [16]. Higher incidence was observed in Mattoo et al in a study done in Saudi Arabia, who reported a 6% positive family history [17]. This is probably due to the same cultural background in Saudi Arabia and Egypt. A previous study found consanguinity 23.3%. In Turkey, the consanguineous frequency marriage in patients with nephrotic syndrome was identified as 18.3% in the study conducted in Istanbul [18] and as 15.2% in a study carried out by [19], while the frequency was determined as 25.9% in the study by [20]. The mean disease duration was 3.71 years with a standard deviation of 3.02 years. The median duration was 3.0 years, ranging from a minimum of 0.10 years to a maximum of 11.0 years. Regarding clinical symptoms, Puffy eye lids were observed in 1.7% of patients, while 6.7% had abdominal enlargement. Most patients experienced generalized edema (91.7%), ascites (5.0%), hypertension (5.0%), chronic renal failure (1.7%), and oliguria (26.7%). This came in line with clinical finding among children with nephrotic syndrome as finding of Khanna [21]. Regarding urine analysis we observed that the mean UOP was 118.1 ± 314.0, with a median of 2.80. The wide standard deviation and range indicate substantial variability in urine output among these patients. Urinary protein, Urinary RBCs and Urinary WBCs decreased significantly at sampling when compared to disease onset. Both times were significantly higher than the control group. Crystals and casts were significantly higher in NS at disease onset and at the time of sampling when compared to the control group. At the same time, no significant differences were found between the time of sampling and disease onset. This came in line with previous findings about nephrotic syndrome which stated that urine analysis of children with nephrotic syndrome showed the presence of casts (hyaline, granular, fatty, waxy, or epithelial cells) [22, 23]. The present study showed that no significant differences were found between SSNS, SDNS, and SRNS regarding sex, age, residence, FH and consanguinity, disease duration, casts, crystals, clinical data, hematuria, creatinine, lipid profile at sampling, UPCR creatinine, protein in urine ratio, albumin, UOP, electrolytes at sampling nor the onset of disease. Moreover, SRNS showed significantly Urinary protein, Urinary RBCs were significantly higher in SRNS compared to SDNS. Urinary WBCs and WBCs count when compared to SDNS. Urinary protein was significantly higher in SDNS, SRNS when compared to SSNS. Also, previous studies observed that patients with SRNS have a circulating factor produced by lymphocytes that may induce proteinuria [24, 25]. Contrarily,

Kaddah et al, showed that female sex carried a significantly higher risk for the development of steroid resistance [26]. This was similar to the results of Kari and Halawani (2010), who found that 23 females and only 8 males were steroid resistant [27]. Difference between our study may be explained by small sample size.

Conclusion:

From our results we concluded that nephrotic syndrome had Uremic toxins, including urea and creatinine, accumulate in the blood as kidney function declines. occur mostly among cases with SRNS.

References

1. Bagga, A. and M.J.I.J.o.m.r. Mantan, (2005).Nephrotic syndrome in children. **122**(1): p. 13.
2. Noone, D.G., K. Iijima, and R.J.T.L. Parekh, (2018) Idiopathic nephrotic syndrome in children.. **392**(10141): p. 61-74.
3. Walz, G.J.D.I., (2003) Pathogenetic aspectics of nephrotic syndrome.. **44**(9): p. 1075-1082.
4. Gipson, D.S., et al., (2009).Management of childhood onset nephrotic syndrome. Pediatrics, **124**(2): p. 747-757.
5. Eddy, A.A. and J.M. Symons, (2003) Nephrotic syndrome in childhood. The lancet,. **362**(9384): p. 629-639.
6. Saleem, M. and A. Bierzynska, (2017) *R*ecent advances in understanding and treating nephrotic syndrome. F1000Research,. **6**: p. 1-7.
7. Noone, D.G., K. Iijima, and R. Parekh, (2018)Idiopathic nephrotic syndrome in children. The Lancet,. **392**(10141): p. 61-74.
8. Carter, S.A., et al., (2020). Prediction of short-and long-term outcomes in childhood nephrotic syndrome. Kidney international reports, **5**(4): p. 426-434.
9. Geary, D.F. and F. Schaefer, (2008) *Comprehensive* Pediatric Nephrology E-Book: Text with CD-ROM. : Elsevier Health Sciences.
10. Hampson, K.J., M.L. Gay, and M.E.J.N.i.C.P. Band, (2021).Pediatric nephrotic syndrome: pharmacologic and nutrition management. **36**(2): p. 331-343.
11. Kaddah, A., et al., (2012) Epidemiology of primary nephrotic syndrome in Egyptian children. *J Nephrol*,. **25**(05): p. 732-737.
12. Mortazavi, F. and Y.S. Khiavi, (2011) Steroid response pattern and outcome of pediatric idiopathic nephrotic syndrome: a single-center experience in northwest Iran. Therapeutics and clinical risk management,: p. 167-171.
13. Hacıhamdioğlu, D.Ö., S. Kalman, and F. Gök, (2015) Long-term results of children diagnosed with idiopathic nephrotic syndrome; single center experience. Turkish Archives of Pediatrics/Türk Pediatri Arşivi,. **50**(1): p. 37.
14. Özkaya, N., et al., (2004) Primary nephrotic syndrome during childhood in Turkey. Pediatrics international,. **46**(4): p. 436-438.
15. BİRCAN, Z., et al., (2002*)* Childhood idiopathic nephrotic syndrome in Turkey. Pediatrics international,. **44**(6): p. 608-611.
16. Soeiro, E.M.D., et al., (2004.) *I*nfluence of nephrotic state on the infectious profile in childhood idiopathic nephrotic syndrome. **59**: p. 273-278.
17. Mattoo, T.K., M.A. Mahmood, and M.S. Al-Harbi, (1990) *N*ephrotic syndrome in Saudi children clinicopathological study of 150 cases. Pediatric Nephrology, **4**: p. 517-519.
18. Hacıhamdioğlu, D.Ö., S. Kalman, and F. Gök, (2015) İdiyopatik nefrotik sendrom tanılı çocukların uzun dönem sonuçları; tek merkez deneyimi. Türk Pediatri Arşivi,. **50**(1): p. 37-44.
19. Van, A., et al.,(2001) Çocukluk çağı nefrotik sendromu: 230 olgunun değerlendirilmesi. *Journal of Experimental and Clinical Medicine*,. **18(2).**
20. Taner, S., et al., (2023) Evaluation of Children with Nephrotic Syndrome: A Single Center Experience..
21. Khanna, R., (2011). Clinical presentation & management of glomerular diseases:

hematuria, nephritic & nephrotic syndrome. Mo Med, **108** (1): p. 33-6.
22. Mejia, J.R., et al.,(2021) Diagnostic accuracy of urine dipstick testing for albumin-to-creatinine ratio and albuminuria: A systematic review and meta-analysis.. **7**(11).
23. Mohammed, E., et al., (2018) Clinical and laboratory findings of patients with diabetes undergoing kidney biopsy. **29**(6): p. 1290-1302.
24. Niaudet, P.J.P.n., (2004) Steroid-sensitive idiopathic nephrotic syndrome in children.. **5**: p. 543-556.
25. Suranyi, M.G., et al., (1993) Elevated levels of tumor necrosis factor-α in the nephrotic syndrome in humans.. **21**(3): p. 251-259.
26. Kaddah, A., et al., (2012) .Epidemiology of primary nephrotic syndrome in Egyptian children. **25**(5): p. 732-737.
27. Kari, J.A., M.J.S.j.o.k.D. Halawani, and Transplantation, (2010*)*Treatment of steroid resistant nephrotic syndrome in children.. **21**(3): p. 484-487.