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Socio-Demographic Factors of Children with Nephrotic Syndrome and Their Clinical Correlation

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Abstract **Original Research Article**

Background: Nephrotic syndrome (NS) is a chronic kidney disease in children marked by variability in treatment response, potentially influenced by socio-demographic and clinical factors. In resource-limited settings such as Bangladesh, understanding these potential influences is crucial for tailored healthcare strategies. This study investigates the socio-demographic profile of children with nephrotic syndrome and its clinical correlation to treatment outcomes. ***Methods:*** This cross-sectional study was conducted at Dhaka Shishu (Children) Hospital over six months, involving 168 children with nephrotic syndrome selected through convenient purposive sampling. Data were collected via structured interviews, focusing on socio-demographic factors and clinical outcomes. Statistical analysis was conducted using SPSS, with chi-square tests used to examine associations between socio-demographic factors and treatment response. A p-value <0.05 was considered significant. ***Results:*** Of the 168 participants, 61.31% were male, and half were aged 4 to 7 years. Most participants (70.24%) resided in rural areas, with 64.88% belonging to the lower socio-economic class. In terms of treatment response, 48.81% achieved remission, 38.10% experienced a relapse, and 13.10% were resistant to treatment. Although trends were observed, such as higher relapse rates among male children and resistance in females, no statistically significant associations were found between socio-demographic factors and treatment outcomes. ***Conclusion:*** The study highlights observed trends in socio-demographic characteristics and treatment outcomes in children with nephrotic syndrome in Bangladesh; however, no significant associations were identified. These findings underscore the importance of larger, more comprehensive studies to further investigate these variables and support the development of tailored management approaches in resource-limited settings.

Keywords: Nephrotic Syndrome, Pediatric Nephrology, Socio-Demographic Factors, Treatment Response, Steroid Resistance, Bangladesh, Healthcare Disparities.

INTRODUCTION

Nephrotic syndrome (NS) is one of the most common kidney diseases in children, characterized by significant proteinuria, hypoalbuminemia, edema, and hyperlipidemia. Globally, nephrotic syndrome in children presents in two primary categories: steroid-sensitive nephrotic syndrome (SSNS), which generally responds well to corticosteroids, and steroid-resistant nephrotic syndrome (SRNS), which is more challenging to treat and often progresses to end-stage renal disease (ESRD) if not adequately managed. The overall incidence of pediatric nephrotic syndrome ranges from 2 to 16.9 per 100,000 children, with regional variations based on genetics and environmental exposures [1]. This disease is not only a leading cause of morbidity in children but also a significant risk factor for chronic kidney disease (CKD) and ESRD, particularly in children with SRNS or those presenting with histological findings such as focal segmental glomerulosclerosis (FSGS) [2]. The clinical presentation of NS includes hallmark symptoms such as generalized edema, caused by hypoalbuminemia, as well as proteinuria, often exceeding 3.5 grams per day, and hyperlipidemia, characterized by elevated cholesterol and triglyceride levels. These symptoms result from disruptions in the glomerular filtration barrier, which includes podocytes, endothelial cells, and the glomerular basement

membrane. In children, the disruption of this filtration system, due to either genetic mutations or environmental factors, is often severe and can lead to significant complications such as infections, thrombosis, and progressive kidney dysfunction [3]. Children who do not respond to steroid treatment are particularly vulnerable, as steroid-resistant cases are frequently associated with genetic mutations affecting podocyte structure and function, and such cases often exhibit early-onset SRNS with rapid progression to ESRD [4]. The clinical outcomes of nephrotic syndrome, particularly SRNS, are heavily influenced by both socio-demographic and clinical factors. Socio-demographic variables such as ethnicity, socioeconomic status, access to healthcare, and parental education have been shown to significantly impact disease progression and treatment responsiveness. Ethnic differences in the incidence and outcomes of NS have been reported, with higher incidences in South Asian children and differences in relapse rates and steroid responsiveness compared to European or African children [5]. In countries like Bangladesh, where the healthcare infrastructure is limited, children from lower socioeconomic backgrounds may experience delayed diagnosis and limited access to appropriate treatment, exacerbating disease progression and increasing the risk of relapse and poor outcomes [6]. Poverty, rural residence, and overcrowded living conditions are associated with more frequent relapses, as children in these settings may have limited access to corticosteroids and follow-up care [7]. Furthermore, clinical predictors such as steroid responsiveness, hypertension, hematuria, and histological findings like FSGS are key factors in determining the progression of NS to CKD or ESRD. Children with steroid resistance are at greater risk of poor outcomes, with those showing histological evidence of FSGS or minimal change disease (MCD) being particularly vulnerable to progressive renal dysfunction [8]. Hypertension, commonly observed in SRNS, further exacerbates the risk of CKD, as it accelerates renal damage over time [9]. Additionally, the presence of hematuria and recurrent infections, especially in low-income regions like Bangladesh, are strong indicators of disease severity and are associated with worse clinical outcomes in nephrotic children [10]. Genetic factors also play a pivotal role in the disease's etiology and progression, particularly in SRNS. Mutations in genes encoding podocyte-related proteins such as NPHS1, NPHS2, and ACTN4 are frequently associated with SRNS, leading to early-onset disease and rapid progression to ESRD [11]. In Bangladeshi children, the NPHS2 R229Q polymorphism has been identified as a significant genetic risk factor for SRNS, with children carrying this mutation being at nearly three times the risk of progressing to ESRD compared to their counterparts with steroid-sensitive disease [12]. Additionally, studies have shown that compound heterozygosity in genes like NPHS2 can further increase the risk of SRNS and poor renal outcomes [13]. Infections and environmental exposures, particularly in low-income regions, also contribute significantly to the clinical course of NS. In Bangladesh and other developing countries, infections are a major concern, as children with NS are more susceptible to bacterial infections due to urinary protein loss and weakened immunity [14]. These infections, combined with poor access to healthcare and inadequate treatment options, further complicate disease management and lead to worse outcomes in children from impoverished regions [15]. The higher burden of infectious diseases in rural Bangladesh, coupled with socio-economic barriers, makes it imperative to address both clinical and socio-demographic factors when managing pediatric nephrotic syndrome. In conclusion, pediatric nephrotic syndrome, particularly in regions like Bangladesh, is a multifactorial disease with outcomes influenced by both clinical and socio-demographic variables. Genetic predispositions, environmental exposures, and access to healthcare play crucial roles in the progression and management of the disease. Understanding the interplay between these factors is essential for improving outcomes in children with NS, particularly those with SRNS who are at the highest risk of progressing to ESRD.

METHODS

This study employed a cross-sectional design and was conducted at Dhaka Shishu (Children) Hospital, Shere-e-Bangla Nagar, Dhaka, during a six-month period. The study population included all nephrotic syndrome (NS) patients admitted to the hospital during this period, with a total sample size of 168 participants. The sampling method used was convenient purposive sampling. Inclusion criteria consisted of both new and relapse cases of NS, while the exclusion criteria involved any guardians who refused to participate in the study. Informed written consent was obtained from the guardians of all patients before their inclusion in the study. Data collection was performed through face-to-face interviews using a semi-structured questionnaire, which captured socio-demographic data and relevant clinical information about the child suffering from NS. The researcher conducted all interviews, ensuring adherence to proper ethical standards. Following data collection, the information was coded and entered into SPSS version 16 for statistical analysis. Ethical approval for the study was obtained from the ethical review committee of Dhaka Shishu (Children) Hospital. Confidentiality of participants and their data was strictly maintained, and no unauthorized person had access to the data. Participants were informed about the purpose and procedures of the study, their right to refuse participation, and the fact that no financial benefit would be provided. Data were analyzed using SPSS version 17 for Windows. Continuous variables were expressed as mean ± standard deviation (SD). Chi-square tests were

conducted to assess relationships between treatment responses and variables such as gender, age distribution, and socio-economic status in children with nephrotic syndrome. A significance level of $p < 0.05$ was considered statistically significant.

RESULTS

Table 1: Distribution of participants by sociodemographic characteristics (N=168)

Baseline Characteristics	Frequency	Percentage
Gender		
Male	103	61.31%
Female	65	38.69%
Age		
<4	44	26.19%
4-7	84	50.00%
8-11	24	14.29%
12-15	16	9.52%
Residence		
Slum	4	2.38%
Urban	46	27.38%
Rural	118	70.24%
Socio-economic Status		
Lower class	109	64.88%
Middle class	51	30.36%
Upper class	8	4.76%

The study included 168 participants, with a higher proportion of males (61.31%) compared to females (38.69%). The majority of children (50%) were between the ages of 4 and 7 years, followed by 26.19% under the age of 4, 14.29% aged 8 to 11 years, and 9.52% aged 12 to 15 years. Regarding residence, most participants (70.24%) lived in rural areas, while 27.38% resided in urban areas, and only 2.38% came from slums. In terms of socio-economic status, 64.88% of the participants belonged to the lower class, 30.36% were from the middle class, and only 4.76% were from the upper class.

Table 2: Distribution of participants by recorded risk factors (N=168)

Socio-environmental risk factors	Frequency	Percentage
Early weaning	77	45.83%
Inadequate breast feeding for 2 years	36	21.43%
History of infection	100	59.52%
Malnutrition	55	32.74%
Incomplete immunization	21	12.50%
Family history of kidney disease	12	7.14%
History of atopy	24	14.29%

In terms of socio-environmental risk factors among the 168 participants, 45.83% had a history of early weaning, and 21.43% were inadequately breastfed for at least two years. A notable 59.52% of the children had a recorded history of infections, while 32.74% were affected by malnutrition. Incomplete immunization was reported in 12.50% of participants, and 7.14% had a family history of kidney disease. Additionally, 14.29% of the participants had a history of atopy.

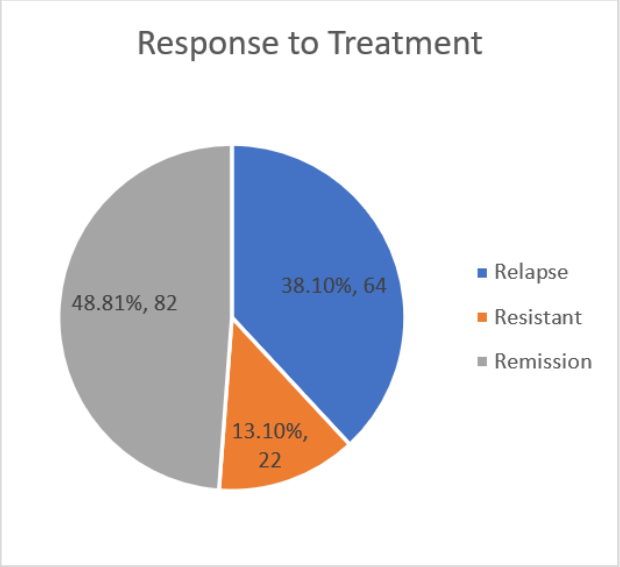

Figure 1: Distribution of participants by response to treatment (N=168)

In terms of treatment response among the 168 participants, nearly half of the children (48.81%) achieved remission, indicating a favorable response to treatment. However, 38.10% of the participants experienced relapse, while 13.10% were resistant to treatment.

Table 3: Relation of treatment response in different sociodemographic factors among nephrotic syndrome cases (N=168)

Variable	Relapse (n=64)		Resistant (n=22)		Remission (n=82)		p-value
	n	%	n	%	n	%	
Gender							
Male	44	68.75%	9	40.91%	50	60.98%	0.069
Female	20	31.25%	13	59.09%	32	39.02%	
Age							
<4	14	21.88%	2	9.09%	28	34.15%	0.235
4-7	34	53.13%	12	54.55%	38	46.34%	
8-11	10	15.63%	4	18.18%	10	12.20%	
12-15	6	9.38%	4	18.18%	6	7.32%	
Socio-economic Status							
Lower class	44	68.75%	16	72.73%	49	59.76%	0.154
Middle class	20	31.25%	5	22.73%	26	31.71%	
Upper class	0	0.00%	1	4.55%	7	8.54%	

The relationship between treatment response and various socio-demographic factors among the 168 nephrotic syndrome cases revealed several important observations. Regarding gender, males constituted the majority of relapse cases (68.75%) and remission cases (60.98%), while females made up the majority of treatment-resistant cases (59.09%). However, this gender difference was not statistically significant (p=0.069). In terms of age distribution, the 4 to 7-year-old age group had the highest proportion of participants in all treatment response categories, with 53.13% in the relapse group, 54.55% in the resistant group, and 46.34% in the remission group. Although the age distribution showed variability across the treatment responses, the differences were not statistically significant (p=0.235). Socio-economic status also influenced treatment outcomes. The majority of relapse (68.75%) and resistant (72.73%) cases came from the lower socio-economic class, while a greater proportion of participants from the upper class achieved remission (8.54%). Despite this trend, the differences in treatment response across socio-economic statuses were not statistically significant (p=0.154).

DISCUSSION

The current study explored the socio-demographic characteristics and clinical outcomes of children with nephrotic syndrome (NS), shedding light on key factors influencing disease progression and treatment response. One of the main findings of this

study was the male predominance (61.31%) among participants, which is consistent with several studies on pediatric nephrotic syndrome. For instance, a study conducted in Bangladesh also reported a higher male-to-female ratio of 2:1 among children experiencing their first NS attack, with males being more prone to frequent relapses [16]. Similar findings were reported by studies from Iran and Saudi Arabia, where males were more frequently affected by NS, supporting the global observation of male predominance in childhood NS [17,18]. This gender distribution could be attributed to potential biological differences in immune response or genetic predisposition, although further research is needed to fully elucidate the underlying mechanisms. In terms of age distribution, this study found that the majority of children (50%) were aged 4 to 7 years, with a significant proportion of relapses and treatment resistance occurring in this age group. This is consistent with findings from Nakanishi *et al.,* who reported that children with idiopathic nephrotic syndrome who experienced frequent relapses had a median age of 5.1 years, indicating that younger children are more susceptible to relapse [19]. Similarly, Kim *et al.,* found that older children were more likely to develop steroid resistance, highlighting the role of age in determining treatment outcomes [20]. The findings from these studies suggest that younger children are more vulnerable to frequent relapses, while older children may face challenges with steroid resistance, making age a critical factor in managing nephrotic syndrome. The study also revealed a significant rural-urban divide in the socio-demographic characteristics of the participants, with 70.24% of children coming from rural areas. This aligns with findings from a study in Ethiopia, which highlighted the role of geographic location in influencing access to healthcare and treatment outcomes for pediatric NS patients [21]. Children in rural areas, often from lower socio-economic backgrounds, may face delays in diagnosis and treatment, which can contribute to higher rates of relapse and poor outcomes. This was further supported by the present study, where most relapse cases (68.75%) and resistant cases (72.73%) were from the lower socio-economic class. Shanta *et al.,* also reported that children from lower socio-economic backgrounds in Bangladesh had a higher risk of relapse due to limited access to consistent healthcare and follow-up [22]. These findings emphasize the importance of addressing socio-economic disparities in the management of nephrotic syndrome, particularly in resource-limited settings like rural Bangladesh. In terms of treatment response, the current study found that 48.81% of participants achieved remission, while 38.10% experienced relapse, and 13.10% were resistant to treatment. These results are comparable to those reported by Kim *et al.,* who observed a 15% rate of initial steroid resistance and an additional 19 patients developing resistance during subsequent relapses [20]. Similarly, a study by Mattoo *et al.,* in Saudi children found that 45% of steroid-sensitive nephrotic syndrome cases experienced frequent relapses, reflecting the challenges of maintaining long-term remission in this population [23]. The high rate of relapse and resistance observed in these studies, including the current one, underscores the need for alternative therapeutic strategies to improve long-term outcomes in children with nephrotic syndrome. In terms of gender-related treatment response, the present study noted that 68.75% of relapse cases were male, while 59.09% of resistant cases were female. This pattern is supported by findings from Mortazavi *et al.,* who observed a higher rate of steroid resistance in female patients, suggesting that gender may play a role in determining response to treatment [17]. The underlying reasons for this gender difference in treatment response remain unclear but could involve genetic or hormonal factors that warrant further investigation. In contrast, studies such as those by Nakanishi *et al.,* and Kim *et al.,* found no significant gender difference in treatment outcomes, indicating that the role of gender in treatment response may vary by population and warrants further study [19,20]. Additionally, early weaning and inadequate breastfeeding were identified as prevalent socio-environmental risk factors in the present study, affecting 45.83% and 21.43% of the children, respectively. These factors have been shown to contribute to poor immune development and increase the susceptibility to infections, which are common complications in nephrotic syndrome. A study by Greer *et al.,* emphasized the protective role of breastfeeding in preventing atopic diseases and infections, highlighting the potential benefits of promoting adequate breastfeeding to mitigate risk factors in children with NS [24]. The high prevalence of infection history (59.52%) and malnutrition (32.74%) in the current study further supports the need for early nutritional interventions to improve disease outcomes, particularly in resource-poor settings where infections can exacerbate NS progression [25]. In conclusion, the findings of this study provide valuable insights into the socio-demographic and clinical factors associated with nephrotic syndrome in children, particularly in Bangladesh. The results highlight the significant role of gender, age, socio-economic status, and geographic location in influencing disease progression and treatment outcomes. Comparative analysis with existing literature supports the need for targeted interventions, particularly in addressing socio-economic disparities and improving access to healthcare for children in rural and low-income populations. Further research is needed to explore the biological mechanisms underlying gender differences in treatment response and to develop more effective therapeutic strategies for managing relapses and steroid resistance in pediatric nephrotic syndrome.

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

The findings from this study underscore the influence of socio-demographic and clinical characteristics on the distribution of nephrotic syndrome cases among children in Bangladesh. Although variations were observed in treatment response across gender, age, residence, and socio-economic status, no statistically significant associations were identified between these socio-demographic factors and treatment outcomes. While trends such as higher relapse rates in male and rural children and resistance in female and younger children were observed, these did not reach statistical significance. This highlights the complexity of nephrotic syndrome in pediatric populations and the need for larger-scale studies to more definitively evaluate the influence of socio-demographic factors. Improved healthcare access and tailored management strategies remain essential for addressing nephrotic syndrome in this context.

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REFERENCES

1. Banh, T. H., Hussain-Shamsy, N., Patel, V., Vasilevska-Ristovska, J., Borges, K., Sibbald, C., ... & Parekh, R. S. (2016). Ethnic differences in incidence and outcomes of childhood nephrotic syndrome. *Clinical Journal of the American Society of Nephrology*, *11*(10), 1760-1768.
2. Yaseen, A., Tresa, V., Lanewala, A. A., Hashmi, S., Ali, I., Khatri, S., & Mubarak, M. (2017). Acute kidney injury in idiopathic nephrotic syndrome of childhood is a major risk factor for the development of chronic kidney disease. *Renal failure*, *39*(1), 323-327.
3. Baek, H. S. (2022). Mechanism, clinical consequences, and management of dyslipidemia in children with nephrotic syndrome. *Childhood Kidney Diseases*, *26*(1), 25-30.
4. Park, E. (2019). Genetic basis of steroid resistant nephrotic syndrome. *Childhood Kidney Diseases*, *23*(2), 86-92.
5. Chanchlani, R., & Parekh, R. S. (2016). Ethnic differences in childhood nephrotic syndrome. *Frontiers in pediatrics*, *4*, 39.
6. Rhodes, R., Christian, M., Imam, H., Sarker, S., Cowper, A., & Day, L. T. (2015). G255 (P) Where there is no specialist–advocating for children with nephrotic syndrome in rural bangladesh.
7. Jahan, I., Hanif, M., Ali, M. A., & Hoque, M. M. (2015). Prediction of Risk Factors of Frequent Relapse Idiopathic Nephrotic Syndrome. *Mymensingh Medical Journal: MMJ*, *24*(4), 735-742.
8. Safaei, A., & Maleknejad, S. (2009). Spectrum of childhood nephrotic syndrome in Iran: A single center study. *Indian journal of nephrology*, *19*(3), 87-90.
9. ÇİÇEK DENİZ, N. E. S. L. İ. H. A. N. (2023). Clinical predictors of steroid resistance in childhood nephrotic syndrome. Available from: https://hdl.handle.net/11424/296050
10. Sarker, M. N., Islam, M. M. S. U., Saad, T., Shoma, F. N., Sharmin, L. S., Khan, H. A., ... & Saha, T. (2012). Risk factor for relapse in childhood nephrotic syndrome-a hospital based retrospective study. *Faridpur Medical College Journal*, *7*(1), 18-22.
11. Antignac, C. (2005). Molecular basis of steroid-resistant nephrotic syndrome. *Nefrologia*, *25*(Suppl 2), 25-28.
12. Jyoti, S. S., Islam, F., Shrabonee, I. I., Sultana, T. N., Chaity, N. I., Nahid, N. A., ... & Apu, M. N. H. (2020). Prevalence of NPHS2 gene R229Q polymorphism in Bangladeshi children with nephrotic syndrome. *Heliyon*, *6*(10). Available from: https://www.cell.com/heliyon/abstract/S2405-8440(20)32160-5
13. Trautmann, A., Schnaidt, S., Lipska-Ziętkiewicz, B. S., Bodria, M., Ozaltin, F., Emma, F., ... & PodoNet Consortium. (2017). Long-term outcome of steroid-resistant nephrotic syndrome in children. *Journal of the American Society of Nephrology*, *28*(10), 3055-3065.
14. Rahman, M., Afroz, S., Ali, R., & Hanif, M. (2016). Health Related Quality of Life in Children with Nephrotic Syndrome in Bangladesh. *Mymensingh medical journal: MMJ*, *25*(4), 703-709.
15. Roy, R. R., Sultana, N., Jesmin, T., Al Mamun, A., Kakon, K. K., Akbar, R., ... & Begum, A. (2023). Steroid-Resistant Nephrotic Syndrome in Children: Clinicohistology and Pattern of Response to Immunosuppressive. *Paediatric Nephrology Journal of Bangladesh*, *8*(1), 7-23.
16. Shanta, S. N., Begum, A., Haque, S. S., Jesmin, T., Mamun, A. A., Sharmim, S., ... & Islam, A. (2023). Demographic Charecterstics of Children with First Attack Idiopathic Nephrotic Syndrome with Relapse-A Hospital-Based Observational Study. *Asian Journal of Pediatric Research*, *13*(4), 140-145.
17. Mortazavi, F., & Khiavi, Y. S. (2011). Steroid response pattern and outcome of pediatric idiopathic nephrotic syndrome: a single-center experience in

northwest Iran. *Therapeutics and clinical risk management*, 167-171.

18. Hacıhamdioğlu, D. Ö., Kalman, S., & Gök, F. (2015). Long-term results of children diagnosed with idiopathic nephrotic syndrome; single center experience. *Turkish Archives of Pediatrics/Türk Pediatri Arşivi*, *50*(1), 37.
19. Nakanishi, K., Iijima, K., Ishikura, K., Hataya, H., Nakazato, H., Sasaki, S., ... & Japanese Study Group of Renal Disease in Children. (2013). Two-year outcome of the ISKDC regimen and frequent-relapsing risk in children with idiopathic nephrotic syndrome. *Clinical Journal of the American Society of Nephrology*, *8*(5), 756-762.
20. Kim, J. S., Bellew, C. A., Silverstein, D. M., Aviles, D. H., Boineau, F. G., & Vehaskari, V. M. (2005). High incidence of initial and late steroid resistance in childhood nephrotic syndrome. *Kidney international*, *68*(3), 1275-1281.
21. 21. Hailu, S. (2018). Predictors of Time to Recovery from a Surgical Repair of Obstetric Fistula at Mekelle Hamlin Fistula Center, Tigray, Ethiopia. *Journal of Pregnancy and Child Health*. *5*(1), 1–8.
22. 22. Beins, N. T., & Dell, K. M. (2015). Long-term outcomes in children with steroid-resistant nephrotic syndrome treated with calcineurin inhibitors. *Frontiers in Pediatrics*, *3*, 104. Available from: https://www.frontiersin.org/journals/pediatrics/articles/10.3389/fped.2015.00104/full
23. 23. Mattoo, T. K., Mahmood, M. A., & Al-Harbi, M. S. (1990). Nephrotic syndrome in Saudi children clinicopathological study of 150 cases. *Pediatric Nephrology*, *4*, 517-519.
24. Greer, F. R., Sicherer, S. H., & Burks, A. W. (2019). COMMITTEE ON NUTRITION. SECTION ON ALLERGY AND IMMUNOLOGY. The Effects of Early Nutritional Interventions on the Development of Atopic Disease in Infants and Children: The Role of Maternal Dietary Restriction, Breastfeeding, Hydrolyzed Formulas, and Timing of Introduction of Allergenic Complementary Foods. *Pediatrics*, *143*(4), e20190281.
25. Gulati, A., Sinha, A., Jordan, S. C., Hari, P., Dinda, A. K., Sharma, S., ... & Bagga, A. (2010). Efficacy and safety of treatment with rituximab for difficult steroid-resistant and-dependent nephrotic syndrome: multicentric report. *Clinical Journal of the American Society of Nephrology*, *5*(12), 2207-2212.