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Original Article

Effectiveness of Rituximab in Maintaining Remission Status at One Year in Children with Nephrotic Syndrome in A Tertiary Care Hospital

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ABSTRACT

Introduction: Nephrotic syndrome is a prevalent disorder in children, marked by the abnormal excretion of protein from the bloodstream into the urine due to compromised glomeruli. Conventional treatments such as corticosteroids and immunosuppressive medications, often lead to relapses and may have adverse effects. This study investigated the efficacy of Rituximab in sustaining remission for one year in paediatric patients with nephrotic syndrome at a tertiary care facility. **Objectives:** The study's objective was to assess the effectiveness of Rituximab on remission status in children with steroid-sensitive nephrotic syndrome in a hospital that provides a tertiary care facility as assessed by the number of hospital admissions. **Materials and Methods:** It was a prospective observational study design and children registered in the Paediatric Nephrology unit of SAT hospital since October 2023 were consecutively recruited. In this study, 41 children (2-16 years) diagnosed with steroid-sensitive nephrotic syndrome who are on Rituximab only were observed. Written informed consent was obtained from parents or legal guardians and assent from children over 10. Those with secondary nephrotic syndrome or steroid-resistant nephrotic syndrome were excluded from the study. Two doses of intravenous Rituximab were administered weekly according to the standard infusion protocol. **Results:** Results revealed that 84% of participants achieved complete remission at one-year post-Rituximab treatment. **Conclusion:** The study concluded that Rituximab is a highly effective treatment option that is being utilised more frequently to initiate or extend clinical remission in paediatric patients with nephrotic syndrome. Reducing hospital admissions suggests that Rituximab contributes to more stable disease control and better long-term outcomes in this patient population.

Keywords: Paediatric Nephrotic syndrome, Remission, Rituximab infusion, Steroid-dependent Nephrotic syndrome, Steroid side effects.

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INTRODUCTION

Paediatrics is the branch of medicine that deals with the medical care of infants, children, and adolescents. Paediatric Nephrotic Syndrome (NS) is a common renal disorder in children characterized by heavy proteinuria, hypoalbuminemia, oedema and hyperlipidemia (Korecka *et al*, 2024; Mohkam, 2012). It primarily affects children between the ages of 1 and 6 years, with a peak incidence around 2 to 3 years old (Harambat *et al*., 2012). The syndrome is predominantly caused by glomerular diseases that affect the kidney's filtering units, leading to abnormal protein loss and subsequent clinical manifestations. Clinical features of nephrotic syndrome include proteinuria and hypoalbuminemia, oedema, hyperlipidaemia.

Children with SSNS can have a wide range of outcomes for the remainder of their illness; most of them experiences at least one relapse episode, and up to 50% develop either Frequently Relapsing Nephrotic Syndrome (FRNS) or Steroid-Dependent Nephrotic Syndrome (SDNS), which is characterized by relapses occurring within two months of stopping steroids or the initial stage in the first six months. Children who use steroids may acquire obesity, osteopenia, hypertension, cataracts, and stunted growth as adverse side effects (Gedalia & Shetty, 2004; Seth & Aggarwal, 2004).

The occurrence of side effects remained stable despite an increase in treatment courses or a higher cumulative dose of Rituximab. These results indicate that administering Rituximab therapy multiple times is an effective and relatively safe strategy for the majority of children suffering from FRSDNS.

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MATERIALS AND METHODS

Objectives

To assess the effectiveness of Rituximab on remission status in children with steroid-sensitive nephrotic syndrome in a hospital that provides a tertiary care facility.

Study design

A prospective observational study design was adopted and children registered in the Paediatric Nephrology unit since October 2023 were consecutively recruited.

Study setting

Department of Paediatric Nephrology, SAT Hospital, Government. Medical College, Thiruvananthapuram.

Study population

Children aged 2-16 years diagnosed with steroid-sensitive, including steroid-dependent nephrotic syndrome who were initiated on Rituximab therapy.

Inclusion criteria

Children aged 2-16 years diagnosed with steroid-sensitive nephrotic syndrome who were receiving Rituximab therapy alone were observed.

Written informed consent was obtained from the parents or legal guardians.

Exclusion criteria

Children with secondary nephrotic or steroid-resistant nephrotic syndrome.

Study period

The research study was carried out for 9 months after ethical clearance from the Human Ethics Committee, Government Medical College, Thiruvananthapuram.

Sample size

Sample size was determined based on a study conducted by Gulati *et al.*, (2011) titled "Efficacy and safety of treatment with Rituximab for difficult steroid-resistant and dependent nephrotic syndrome".

The sample size was determined using the formula:

$N= (Z_1- \alpha/_2)^2 \times P \times Q/D^2$.

$= 40.89 \approx 41$

The total sample collected was 50.

Based on hospital statistics, the number of patients diagnosed with Steroid-dependent Nephrotic syndrome over six months was around 12 and it is not possible to get the calculated sample size of 41. Therefore, all individuals who had received a diagnosis of steroid-dependent nephrotic syndrome, who were available during the study period and expressed a willingness to participate were included in the research.

Although 41 patients were ultimately deemed eligible and participated in the study, an initial assessment included 50 patients to account for possible dropouts or screening failures. Nine patients were excluded because of insufficient data.

Remission was either the reduction or disappearance of the signs and symptoms of a disease. The term may also refer to the timeframe in which this decrease takes place.

Sampling technique

All patients meeting the inclusion criteria were consecutively recruited, the process will continue until the sample size is reached.

Study tool

Pre-specified proforma.

Data collection technique

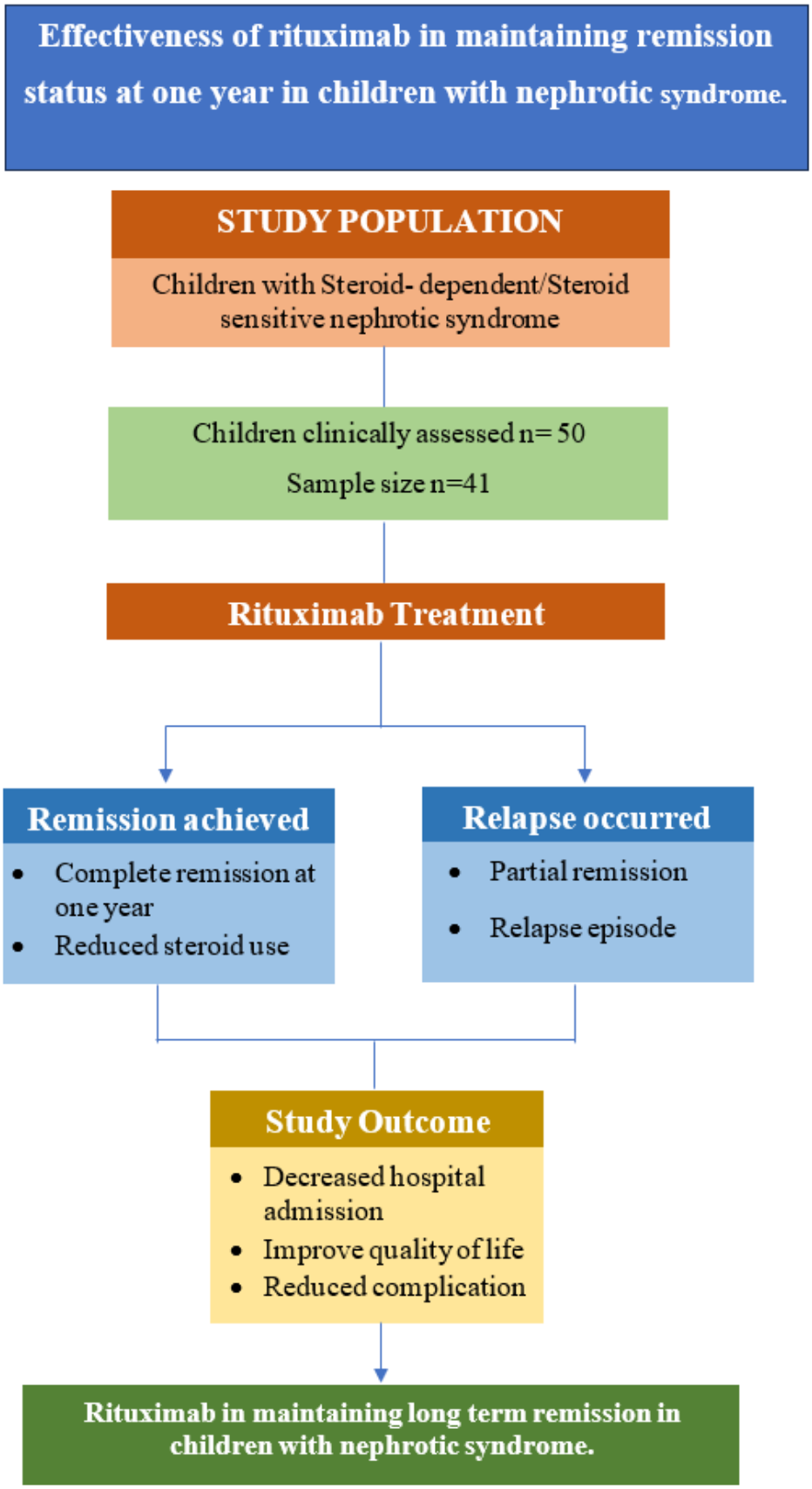
Permission for checking the OP and IP records of patients was obtained from hospital authorities through proper channels and data is being collected from these records.

Study variables

- Demographic information, clinical history, and laboratory parameters at baseline and follow-up.
- Serum IgG levels.
- Remission status.
- Medication dosages and duration.
- Drug side effects, CD 19 Count.
- BMI, pre- and post-rituximab treatment.
- Serum cholesterol at one year, serum albumin at one year.

Study procedure

- The demographic profile of all children who fulfilled the inclusion criteria was recorded in a pre-prepared proforma.
- I.V. Rituximab was given weekly as per the standard infusion protocol.
- Patient was assessed every 6-8 weeks for one year to assess outcomes and adverse events.
- Remission status and immunoglobulin level were checked at one year.


Effectiveness of rituximab in maintaining remission status at one year in children with nephrotic syndrome.
STUDY POPULATION
Children with Steroid- dependent/Steroid sensitive nephrotic syndrome
Children clinically assessed n= 50
Sample size n=41
Rituximab Treatment
Remission achieved
Complete remission at one year
Reduced steroid use
Relapse occurred
Partial remission
Relapse episode
Study Outcome
Decreased hospital admission
Improve quality of life
Reduced complication
Rituximab in maintaining long term remission in children with nephrotic syndrome.

- CD 19 count was checked after 6-8 weeks had been taken from the chart.

Data analysis

- Data was organised into a table format in Microsoft Excel.
- Statistical analysis was conducted utilising IBM SPSS 27.
- Descriptive statistics were used to assess the fundamental attributes of the data.
- Categorical variables can be displayed in numerical and percentage formats.
- Continuous variables following a normal distribution were reported as the mean and standard deviation.
- When continuous variables exhibited skewness, we reported the median and range.
- The MC Neimar test was utilised for paired comparisons and comparison of qualitative parameters.
- Paired T-test/Wilcoxon Signed Rank test was used to compare the paired comparison of quantitative variables according to normality. Additionally, we used repeated measures ANOVA/Friedman test to assess changes in quantitative parameters over time within the study population.
- We considered the confidence interval as 95% and thus the significance level as 5%.
- Bar and pie charts were used to present the percentage distribution.

RESULTS

Age distribution within the study population

The study included children aged 5-16 years, with a mean age of 12.02 ± 3.15 years. Most participants (68%) were in the 11-16-year age group, while 32% were aged 5-10 years, indicating a predominance of older children in the study population.

Distribution of gender among the study population

The study population consisted of 64% males (32 participants) and 36% females (18 participants), comprising a total of 50 children.

The educational background of the parents in the study population shows that a majority, 42% had completed 'Plus Two' education, reflecting a relatively high level of educational attainment. This likely contributed to earlier diagnosis and a better understanding of the treatment protocol. Of the study population, 86% of patients were from rural areas, and the majority (70%) belonged to the Below Poverty Line (BPL) category.

Assessment of the indication for Rituximab

As shown in Figure 1, the primary indication for Rituximab therapy was steroid-related side effects, observed in 90% of participants. Persistent steroid dependence was the second most common indication, reported in 72% of cases. Other indications included non-response to Calcineurin Inhibitors (CNI) in 8%, growth stunting in 4%, and CNI toxicity in 2%.

Assessment of the type of drug side effects among the study population

Figure 2 illustrates the evaluation of steroid-related adverse effects showed that 32% of participants experienced a single type of side effect, while 62% reported multiple types of steroid-related side effects.

Distribution of patients receiving additional medication alongside steroids

A significant majority (96%) of patients were prescribed additional medications along with steroids, underscoring the prevalent use of combination therapy in the management of childhood nephrotic syndrome.

Distribution of additional drugs other than steroids among the study population

Tacrolimus was the most frequently prescribed additional medication, used in 62% of the study participants. This was followed by Mycophenolate Mofetil (MMF), which was administered to 52% of patients. Both Cyclosporine and Cyclophosphamide were prescribed in 26% of cases each. Levamisole was the least commonly utilised agent, with only 14% of patients receiving this medication.

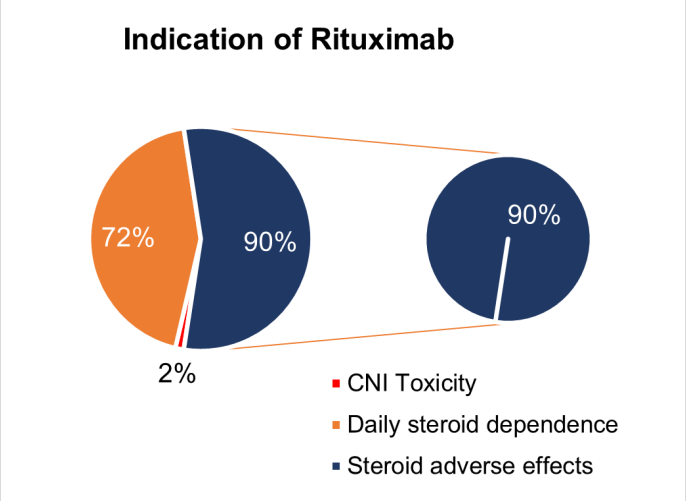


Figure 1: Indication for Rituximab among the study population.

Table 1: Assessment of infection rate before and after Rituximab therapy.

Infection	Before	After
Yes	24(48%)	3(6%)
No	26(52%)	47(94%)
Total	50	100%
M C Neimar Test, $p<0.0001^*$ Significant.		

Assessment of infection rate before and after Rituximab therapy

The data in Table 1 shows, a significant reduction in infection rates following Rituximab therapy. Before treatment, 48% of patients experienced infections, whereas only 6% reported infections after therapy. Correspondingly, the proportion of patients without infections increased from 52% before treatment to 94% after treatment. This reduction was statistically significant ($p < 0.0001$).

Distribution of the number of infections before and after Rituximab therapy

The study demonstrated a significant decline in the frequency of infections per patient following Rituximab therapy. Before treatment, the number of infections ranged from one to five per patient. 29% experienced one infection, 33% experienced two infections, 21% experienced three infections, 13% experienced four infections, and 4% experienced five infections. After Rituximab therapy, the frequency of infections decreased markedly, with 8% of patients experiencing one infection and 4% experiencing two infections. Notably, no patients experienced three or more infections following treatment.

Distribution of site of infection before and after Rituximab therapy among the study population

As shown in Figure 3, a notable change in the pattern of infection sites was observed following Rituximab therapy. Before treatment, respiratory tract infections were predominant, affecting 96% of patients, while septic shock was reported in 4%. After Rituximab therapy, the incidence of respiratory infections declined markedly to 4%. Conversely, new infection types emerged post-therapy, with ear infections and fever with rash each reported in 4% of patients.

Distribution of infection rate before and after Rituximab according to age

The data demonstrated a significant reduction in infection rates among children receiving Rituximab therapy across all age groups analysed. Before treatment, the highest infection rate was observed in the 5-11 years age group, with 16 out of 50 children (32%) affected, followed closely by the 11-16 years age group, with 15 out of 50 children (30%) experiencing infections. After therapy, infection rates dropped substantially, with only 1 child (2%) in the 5-11 years group and 2 children (4%) in the 11-16 years group reporting infections.

Distribution of the number of Rituximab doses among the study population

The majority of patients (92%) received two doses of Rituximab, while only 8% received a single dose. This indicates that most participants adhered to the standard two-dose Rituximab regimen.

Distribution and comparison of weight gain/loss with time

As shown in Table 2, the mean percentage of weight change ranged from 44.09% to 45.42% over the study period, with no statistically significant variation observed ($p = 0.129$). Similarly, the median percentage of weight change remained relatively stable, ranging from 43% to 43.9%.

Distribution and comparison of BMI in the initial and after 1 year

As shown in Table 3, the distribution of Body Mass Index (BMI) was assessed at baseline and after one year of Rituximab therapy. At baseline, BMI values ranged from 11.23 to 35.51, with a mean of 24.36 ± 4.78. After one year, BMI ranged from 13.79 to 34.31, with a mean of 22.61 ± 4.87. The mean reduction in BMI over one year was 1.62 ± 0.568, which was statistically significant ($p = 0.007$).

Distribution and comparison of remission status among the study population

The data summarised in Table 4 indicate that, at 3 months of follow-up, all patients (100%) achieved complete remission with no reported relapses. By 6 months, 96% of patients remained in complete remission, while data were missing for 4%. At 9 months, the complete remission rate declined to 92%, with 2% of patients experiencing relapse and 6% having missing data. At 12 months, 84% of patients remained in complete remission, 10% had relapsed, and 6% had missing data. The Cochran Q test demonstrated a statistically significant change in remission status over time ($p = 0.010$).

Distribution and paired comparison of Cumulative steroid use

As shown in Figure 4, a significant reduction in cumulative steroid use was observed over one year following Rituximab therapy. Among the 50 patients studied, 11 completely discontinued steroid use by the end of the follow-up period. Before treatment, the mean cumulative steroid dose was 453.48 mg (SD = 400.28), with a median of 320 mg and an Interquartile Range (IQR) of 181.75-476 mg. After one year, the mean cumulative steroid dose decreased substantially to 57.87 mg (SD = 132.69), with a median of 26.25 mg and an IQR of 18.15-46.25 mg. This reduction was

Table 2: Distribution and comparison of weight gain/loss with time.

% of weight gain/weight loss	Range	Mean± SD	Median (IQR)
Initial	17-77.8	44.91± 14.3	43(33.38-55.25)
3 Months	17-81	45.42± 14.82	43.5(34.71-56.09)
6 Months	19-79	44.43± 14.56	42.7(33.43-54.4)
9 Months	19.5-77	43.98± 14.03	42.4(33.5-55)
1 Year	20-79	44.09± 13.39	43.9(35-53.5)
Friedman Test, p=0.129, insignificant.			

Table 3: Distribution and comparison of BMI in initial and after 1 year.

BMI	Range	Mean± SD	Mean Difference	Sig.
Pre RTX	11.23- 35.51	24.36± 4.78	1.62± 0.568	0.007*
After 1 Year	13.79- 34.31	22.61± 4.87		
Paired t-test, *p < 0.05 indicates significance.				

Table 4: Distribution and comparison of remission status among the study population.

Time Point	Complete Remission	Relapse	Missing
3 Months	50 (100.0%)	-	-
6 Months	48(96.0%)	-	2 (4.0%)
9 Months	46(92.0%)	1 (2.0%)	3 (6.0%)
12 Months	42 (84.0%)	5 (10.0%)	3 (6.0%
Cochran Q test, p=0.010* Significant.			

statistically significant, as demonstrated by the Wilcoxon Signed Ranks Test ($p < 0.0001$).

Assessment of biochemical markers among the study population

Biochemical and nutritional parameters were assessed one year after Rituximab therapy. Serum cholesterol levels ranged from 137 to 316 mg/dL, with a mean of 188.90 ± 37.16 mg/dL and a median of 183 mg/dL (IQR: 163.7-196). Serum albumin levels were relatively stable, ranging from 3.10 to 4.60 g%, with a mean of 3.92 ± 0.29 g% and a median of 3.9 g% (IQR: 3.87-4.1).

Assessment of disease-specific variables among the study population

The study evaluated key disease-specific variables among children with nephrotic syndrome. The mean age at disease onset was 3.85 years, with most patients diagnosed between 2 and 4.81 years of age.

DISCUSSION

The predominance of older children in this study aligns with findings reported by Chan *et al.*, (2020) who observed an interquartile age range of 6.6-13.5 years at the initiation of Rituximab therapy. This similarity suggests that Rituximab is more commonly initiated in older paediatric patients, possibly reflecting disease course, treatment resistance, or clinical decision-making patterns in this age group.

The observed male predominance in this study indicates that childhood nephrotic syndrome occurs more frequently in males compared to females. This observation aligns with earlier findings by *Agnes S. Garcia* and *Gabriela M. Constantinescu*, who similarly reported a greater prevalence of nephrotic syndrome in male children.

The results indicate that starting Rituximab to address steroid-related toxicity not only helps achieve lasting remission but also leads to fewer disease relapses and hospitalisations. By reducing extended steroid use, Rituximab enhances clinical stability, lowers the necessity for inpatient treatment, and reinforces its effectiveness as a steroid-sparing option for children suffering from nephrotic syndrome.

The high proportion of children experiencing multiple steroid-related adverse effects highlights the severity and complexity of complications associated with prolonged steroid therapy before the initiation of Rituximab. This observation is consistent with findings reported by William E. Smoyer *et al.*, (2019) who demonstrated that the use of Rituximab in children with nephrotic syndrome significantly reduces the burden of steroid-related side effects.

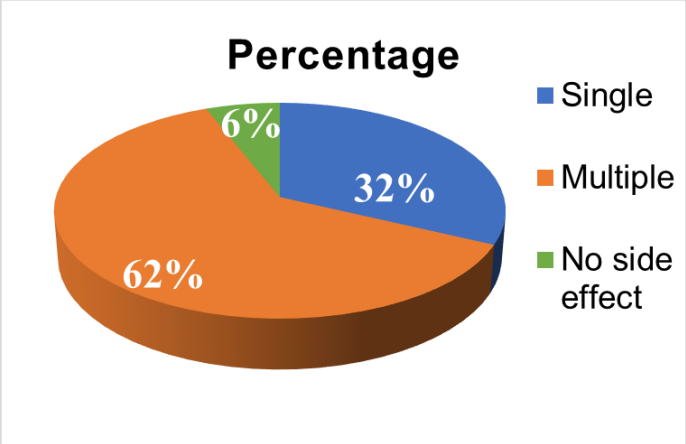


Figure 2: Type of steroid side effects among the individuals participants.

The frequent use of adjunctive therapy observed in this study reflects current treatment practices for childhood nephrotic syndrome. Similar findings were reported by Trautmann *et al.*, (2017) who noted that most patients received additional immunosuppressive agents, such as Tacrolimus or Cyclophosphamide, in combination with corticosteroids.

The findings indicate a clear preference for Tacrolimus and Mycophenolate Mofetil (MMF) as adjunctive immunosuppressive therapies in childhood nephrotic syndrome, likely due to their favourable efficacy and lower toxicity in steroid-dependent or frequently relapsing cases. The limited use of Levamisole may reflect its reduced perceived effectiveness or restricted clinical indications.

These findings align with those of Querfeld *et al.*, (2010) who identified Tacrolimus and MMF as key agents before the widespread adoption of Rituximab. The increasing use of Rituximab for maintaining remission and reducing relapse rates may explain the declining reliance on older immunosuppressive agents such as Cyclophosphamide and Levamisole.

The decrease in infection rates after Rituximab treatment carries significant clinical consequences, as better control of remission and reduced dependence on extended corticosteroid or various immunosuppressive treatments likely lead to fewer disease relapses and hospitalisations. By sustaining remission and minimising infection-related issues, Rituximab could lessen the necessity for inpatient care, boost overall clinical stability, and improve the quality of life for children suffering from nephrotic syndrome.

Rituximab has been shown to significantly decrease both the frequency and severity of infections in childhood nephrotic syndrome. This effect is likely due to enhanced remission and a decreased dependence on long-term corticosteroid or multiple immunosuppressive treatments. These findings underscore its effectiveness as a steroid-sparing agent that reduces morbidity associated with infections.

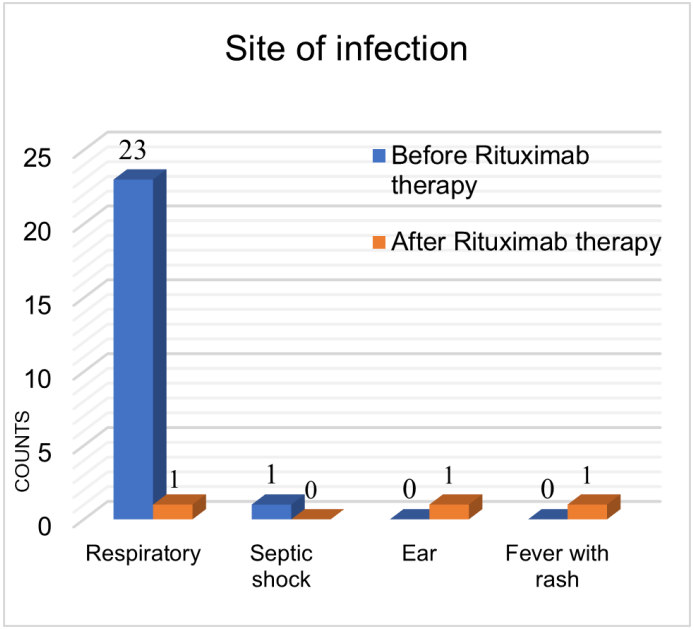


Figure 3: Site of infections before and after Rituximab therapy.

The notable decrease in respiratory tract infections after Rituximab treatment carries important clinical consequences. Enhanced disease management and prolonged remission lead to a reduction in both the frequency and intensity of relapses, subsequently decreasing the necessity for hospitalisation. By reducing the occurrence of severe respiratory infections and their related complications, Rituximab contributes to greater patient stability, lowers healthcare usage, and enhances the overall quality of life for children suffering from nephrotic syndrome.

The prevalence of the two-dose Rituximab regimen indicates compliance with established treatment protocols for childhood nephrotic syndrome and is consistent with the research conducted by *Basu et al.*, (2019). The rare application of a single dose is likely associated with clinical considerations, such as the severity of the disease, the patient's response to treatment, or their tolerance levels. Following established protocols and ensuring optimal dosing contribute to prolonged remission, decrease the frequency of relapses, lower the rate of hospital admissions, and enhance overall results for children suffering from nephrotic syndrome.

The notable reduction in BMI following one year of Rituximab treatment indicates enhanced weight outcomes, probably resulting from improved disease management and decreased corticosteroid use. This observation is consistent with the findings of R. Sinha *et al.*, (2014) which endorse Rituximab's role in sparing steroids and its positive metabolic impacts in paediatric nephrotic syndrome.

The gradual decrease in complete remission over 12 months suggests fluctuations in the disease following Rituximab treatment, although the overall remission rate remained elevated. This notable change indicates relapses in certain patients, which aligns with the relapsing characteristics of childhood nephrotic syndrome and is supported by A. Sinha *et al.*, (2015) highlighting

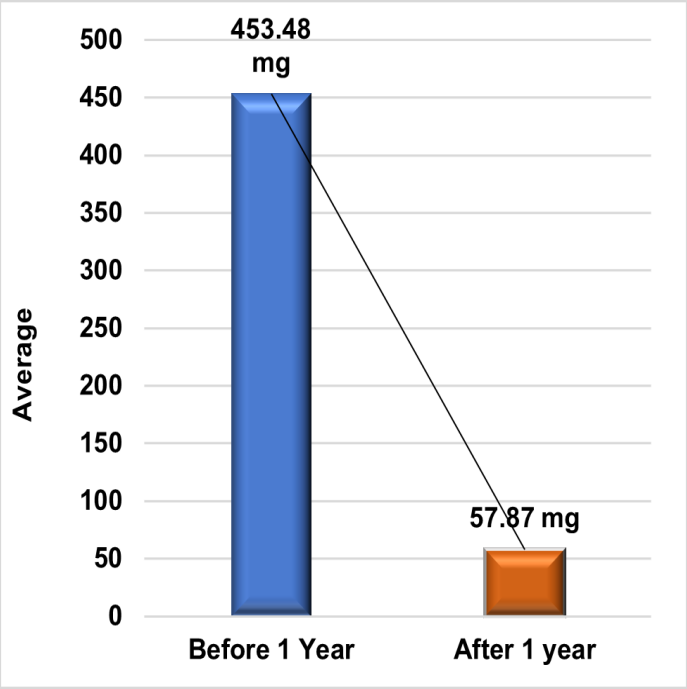


Figure 4: Distribution and paired comparison of Cumulative steroid use.

that sustaining a high remission rate with Rituximab minimises relapses, decreases hospital admissions, and lowers complications, thereby enhancing long-term outcomes and quality of life for children.

The decrease in overall steroid dosage when using Rituximab carries significant clinical consequences: it reduces reliance on steroids and their related side effects, thereby promoting prolonged remission, minimising hospital admissions due to relapses, and enhancing the long-term management and quality of life for children suffering from nephrotic syndrome. This observation is consistent with the findings of Boyer and Niaudet, reinforcing Rituximab's function in diminishing steroid reliance and long-term negative effects in paediatric nephrotic syndrome.

Consistent serum albumin levels signify prolonged remission and enhanced nutritional health following Rituximab treatment, whereas significant fluctuations in cholesterol levels indicate ongoing lipid irregularities in certain patients. These observations are consistent with the work of Strain, Wright, Thacker *et al.*, (2019) emphasising the importance of maintaining sustained remission, which leads to a decrease in relapses and a reduction in hospital admissions. Additionally, monitoring lipid abnormalities aids in preventing long-term metabolic complications, thereby ensuring safer and more effective management of children diagnosed with nephrotic syndrome.

The prevalence of nephrotic syndrome beginning in early childhood underscores the age-related susceptibility and corresponds with the research conducted by Kim, *et al.*, (2017) thereby reinforcing the recognised epidemiological trend in paediatric groups.

SUMMARY

A prospective observational study was carried out in the Paediatric Nephrology Unit at SAT Hospital in Thiruvananthapuram, involving 50 children diagnosed with Steroid-Dependent Nephrotic Syndrome (SDNS) who were treated with Rituximab. The objective of the study was to evaluate the drug's effectiveness in sustaining remission, as indicated by the frequency of hospital admissions. Among the participants, 64% were male, and 68% fell within the age range of 11 to 16 years. The average age at which symptoms began was 3.85 years, with the majority of diagnoses occurring between the ages of 2 and 4.8 years. Rituximab was primarily prescribed due to steroid-related side effects (90%) and steroid dependence. Almost all patients (94%) experienced adverse effects, often multiple in nature. The use of concomitant immunosuppressants was prevalent, particularly Tacrolimus (62%) and MMF (52%). Before treatment, infections were common, particularly respiratory infections, which affected 32% of children aged 5 to 10. The administration of Rituximab led to a significant decrease in infection rates. A majority of patients (92%) received two doses of the medication, with 84% achieving complete remission, alongside notable reductions in BMI and the mean cumulative steroid dose (from 453.48 mg to 57.87 mg), as well as B-cell depletion. Overall body weight remained stable; however, serum albumin levels saw a significant increase, while mean cholesterol levels decreased from 295.5 mg/dL to 185 mg/dL.

CONCLUSION

This study evaluated the efficacy of Rituximab in maintaining remission for one year in paediatric patients suffering from nephrotic syndrome at a tertiary care facility. The findings indicated that Rituximab significantly decreases relapse rates and reduces corticosteroid reliance in children with frequently relapsing or steroid-dependent conditions. A notable percentage of patients sustained remission after one year, reinforcing the potential of Rituximab as a viable option for long-term disease management. The treatment was largely well-tolerated, with minimal adverse effects, highlighting its positive safety profile within the paediatric demographic. However, differences in individual responses emphasise the necessity for tailored treatment strategies. Further extensive, long-term studies are needed to validate the results and to better clarify the role of Rituximab in the treatment of childhood nephrotic syndrome.

LIMITATIONS

The study was conducted with young children, and interactions were primarily carried out with caregivers, typically their parents, who were unable to acquire trustworthy information directly. The study was conducted in a tertiary care government hospital, where the majority of the patients, from low socioeconomic backgrounds, the high cost and limited availability of Rituximab

during certain periods could create a considerable strain on these families, affecting their adherence to treatment, follow-up care, and long-term results.

FUTURE PERSPECTIVES

Standard Treatment Guidelines for treating Nephrotic Syndrome in children should be implemented, which enhance treatment results, decrease unwarranted discrepancies in practice, lessen complications associated with unsuitable or extended therapy, and encourage cost-efficient management. To evaluate the effectiveness of Rituximab on remission status in children with steroid-sensitive nephrotic syndrome findings, we suggest further multicentre (public and private) prospective studies, which include a higher number of patients, longer follow-up periods are recommended to confirm that more authentic data can be collected. Since Rituximab is a relatively expensive drug, future studies should need to evaluate its cost-effectiveness in maintaining remission compared with other therapies.

ABBREVIATIONS

NS: Nephrotic Syndrome; **SSNS:** Steroid Sensitive Nephrotic Syndrome; **FRNS:** Frequently Relapsing Nephrotic Syndrome; **FRSDNS:** Frequently Relapsing Steroid-Steroid-Dependent Nephrotic Syndrome; **SDNS:** Steroid-Steroid-Dependent Nephrotic Syndrome; **CNI:** Calcineurin inhibitors; **MMF:** Mycophenolate mofetil.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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