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Original Research Article

Role of Serum Procalcitonin as a Marker of Bacterial Infection in Relapse Cases of Pediatric Nephrotic Syndrome in a Tertiary Care Hospital in Hyderabad, Telangana

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Conflict of interest: Nil

Abstract

Background: Nephrotic syndrome is one of the most common chronic renal disorders in children and is frequently associated with relapses. During relapse, children are highly susceptible to infections, particularly bacterial infections, which significantly contribute to morbidity and hospitalization. Early identification of bacterial infection is essential for prompt management. Serum Procalcitonin (PCT) has emerged as a promising biomarker for the early detection of bacterial infections.

Objective: To evaluate the role of serum procalcitonin as a marker of bacterial infection in relapse cases of nephrotic syndrome among children admitted to a Tertiary Care Hospital in Hyderabad, Telangana.

Methods: This study was conducted among children diagnosed with relapse of nephrotic syndrome admitted to a tertiary care hospital in Hyderabad. Clinical evaluation and laboratory investigations, including serum procalcitonin levels, complete blood count, C-reactive protein, and relevant cultures, were performed. Serum PCT levels were compared between children with clinically and microbiologically confirmed bacterial infections and those without evidence of bacterial infection.

Results: Serum procalcitonin levels were significantly elevated in children with confirmed bacterial infections compared to those without infection. Higher PCT levels correlated with positive culture findings and increased inflammatory markers. The sensitivity and specificity of serum procalcitonin in detecting bacterial infection were found to be clinically significant.

Conclusion: Serum procalcitonin is a reliable and early biomarker for detecting bacterial infection in relapse cases of nephrotic syndrome among children. Its use may help in early diagnosis, appropriate antibiotic initiation, and reduction of unnecessary antibiotic exposure in non-bacterial cases. Further large-scale studies are recommended to validate these findings.

Keywords Serum Procalcitonin; Nephrotic Syndrome.

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Introduction

Nephrotic syndrome (NS) is the most common glomerular disorder in children, with an annual incidence ranging from 1.2 to 16.9 per 100,000 children. It is characterized by edema, heavy proteinuria (>1 g/m²/day or >40 mg/m²/hour), and hypoalbuminemia (serum albumin <3 g/dL).

Approximately 90% of children with nephrotic syndrome experience at least one relapse during the course of their illness. Nearly 50% of these patients subsequently develop either steroid-dependent nephrotic syndrome (SDNS) or frequent relapsing nephrotic syndrome (FRNS) [1]. Relapse is defined as the presence of urine protein ≥3+ on dipstick testing in three consecutive early morning urine samples (or spot urine protein/creatinine ratio >2 mg/mg) following a period of remission. Frequent relapsing nephrotic syndrome (FRNS) is defined as ≥2 relapses within the first six months of initial therapy, ≥3 relapses in any six-month period, or ≥4 relapses within one year.

Steroid-dependent nephrotic syndrome (SDNS) refers to the occurrence of two or more consecutive relapses during steroid tapering or within 14 days of discontinuing steroids. Steroid-resistant nephrotic syndrome (SRNS) is diagnosed when remission is not achieved after six weeks of

treatment with prednisolone at a dose of 60 mg/m²/day [2]. Although 90–95% of children with steroid-sensitive nephrotic syndrome (SSNS) initially respond to corticosteroid therapy and generally have a favorable prognosis, 60–90% of these initial responders experience relapses. These recurrent episodes contribute to increased morbidity, comorbidities, and reduced quality of life [3].

Relapses are associated with complications such as dyslipidemia, thrombosis, sepsis, and malnutrition. Prolonged and high-dose corticosteroid therapy may result in adverse effects including hypertension, cataracts, impaired glucose tolerance, behavioral disturbances, and avascular necrosis of the hip. To reduce relapse frequency and minimize steroid-related toxicity, various long-term immunosuppressive and steroid-sparing agents are employed, including cyclophosphamide, levamisole, mycophenolate mofetil (MMF), calcineurin inhibitors such as tacrolimus and cyclosporine A (CsA), rituximab, and low-dose alternate-day prednisolone therapy [4].

Relapses frequently occur during periods of immune activation, particularly in association with upper respiratory tract infections (URTIs). Infections represent a major cause of morbidity in children with nephrotic syndrome, especially in developing countries such as India. Children with nephrotic syndrome are particularly susceptible to recurrent bacterial, viral, and fungal infections. Bacterial infections are a significant cause of morbidity and mortality and may also precipitate relapses in these patients. An Indian study reported a 36.6% incidence of severe infections among children with nephrotic syndrome [5].

Diagnosing bacterial infection during relapse can be challenging. Prolonged immunosuppressive therapy may mask classical signs and symptoms of infection, leading to delayed initiation of appropriate antimicrobial treatment. In some cases, relapse may be triggered by an underlying infection without overt clinical features. If infection is not clinically suspected, full-dose corticosteroids may be administered, potentially exacerbating an undetected infection and further compromising immune function.

Conversely, these children are frequently over diagnosed with infection. Corticosteroids can cause neutrophilic leukocytosis, which may be misinterpreted as evidence of bacterial infection, leading to unnecessary antibiotic use. Conventional inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) lack sufficient sensitivity and specificity in this population. Microbiological investigations, including blood cultures, often have limited sensitivity sometimes as low as 25%—and results are not available promptly. Inappropriate antibiotic use poses a significant threat to patient safety and public health by promoting antimicrobial resistance. Therefore, clinical assessment remains the primary method for diagnosing bacterial infections in children with nephrotic syndrome. A rapid and reliable biomarker capable of accurately distinguishing bacterial infection would greatly assist clinicians in decision-making, potentially reducing unnecessary antibiotic exposure, shortening hospital stays, and decreasing healthcare costs.

Among acute-phase reactants, ESR and CRP are widely used in clinical practice. In recent years, procalcitonin (PCT) has gained considerable attention as a promising biomarker for bacterial infection. Increasing evidence supports its utility in improving the diagnostic accuracy of bacterial infections. Compared to traditional markers such as CRP, ESR, and white blood cell count, PCT offers several advantages: it has a short half-life (25–30 hours), remains undetectable in healthy individuals, demonstrates higher specificity for bacterial infections, rises within 6 hours of bacterial stimulation, and declines rapidly with effective infection control.

The present study was undertaken to determine the proportion of children experiencing relapse of nephrotic syndrome who exhibit elevated serum procalcitonin levels suggestive of bacterial infection.

Aim of the Study: To evaluate the role of serum procalcitonin in detecting bacterial infection among children (1–18 years) with relapse of nephrotic syndrome and to assess its association with clinical diagnosis and other inflammatory markers.

Material and Methods

This observational study was conducted in the Department of Tertiary Care Hospital, Hyderabad, from November 2022 to April 2024. Children aged 1 to 18 years diagnosed with relapse of nephrotic syndrome were included.

Based on previous literature reporting infection prevalence of 75% during relapse and major infections in 35% of cases, we hypothesized that 40% of children with relapse would have elevated serum procalcitonin (PCT) levels. With a 95% confidence interval and 8% precision, the calculated sample size was 150.

Inclusion Criteria: Children (1–18 years) with relapse of nephrotic syndrome.

Exclusion Criteria:

1. Children already receiving antibiotic therapy.

Case Definitions:

Nephrotic syndrome was defined as heavy proteinuria (>1 g/m²/day or urine protein/creatinine ratio > 2), hypoalbuminemia (<2.5 g/dL), hyperlipidemia, and edema. Relapse was defined as urine albumin ≥3+ for three consecutive early morning samples or 3+/4+ proteinuria with edema.

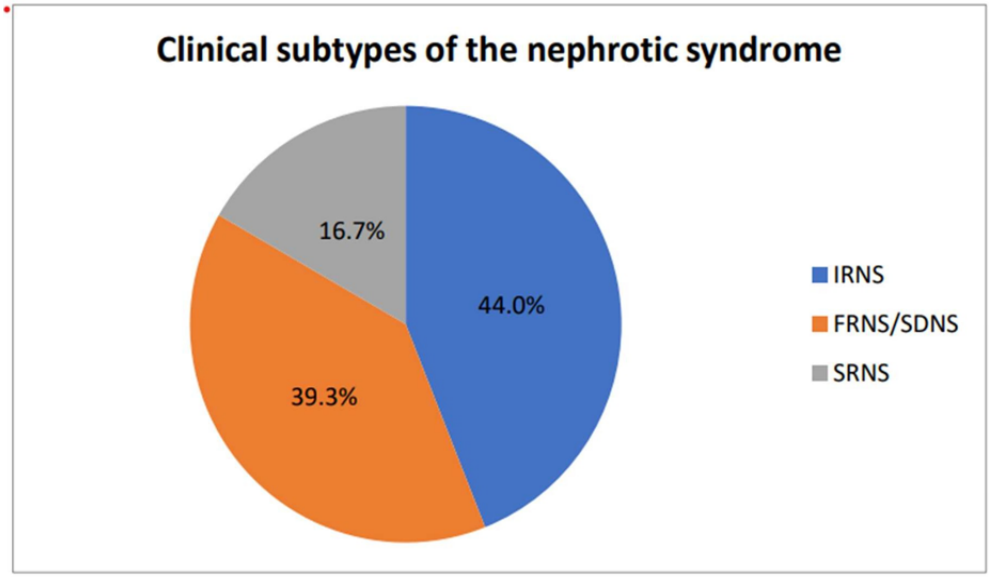
Bacterial infections were diagnosed clinically and confirmed where applicable, including peritonitis, pneumonia, urinary tract infection, cellulitis, and meningitis, based on standard clinical and laboratory criteria.

Statistical Analysis: The raw data were entered into Microsoft Excel and subsequently imported into SPSS statistical software version 22.0 (IBM Corp., Armonk, NY, USA) for analysis. Descriptive statistics were expressed as percentages, mean ± standard deviation (SD), or median with range, as appropriate. The normality of the data distribution was assessed prior to analysis, and appropriate parametric or non-parametric statistical tests were applied accordingly. A p-value <0.05 was considered statistically significant. The agreement between leukocytosis parameters (TLC/DLC), Q-CRP, and serum procalcitonin (PCT) levels was assessed using Cohen's kappa statistic.

Results

Table 1: Basic Demographic parameters of the subjects included in the study

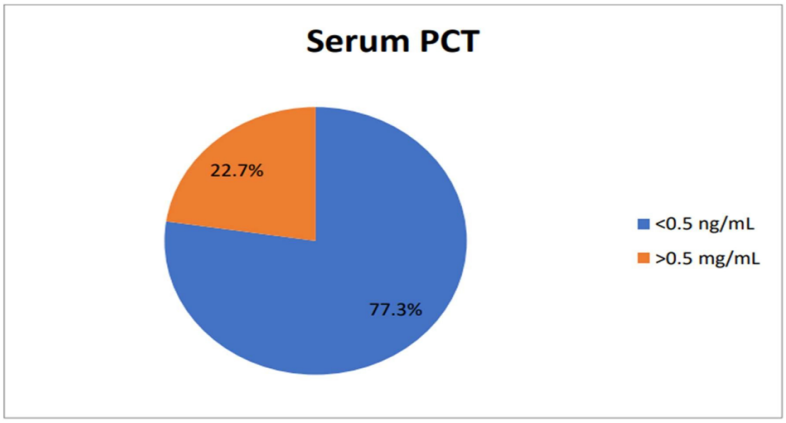
	N	Median	IQR	Range
Age	150	123	124.50	12-216
Weight	150	33.91	27.45	9.16 – 60.18
Height	150	1.24	0.47	0.70-1.65
BMI	150	22.22	1.05	18.18 – 24.47
Age at first episode	150	87.50	86.75	7.0-173.0
Number of previous relapses	150	3.00	3.00	0-7



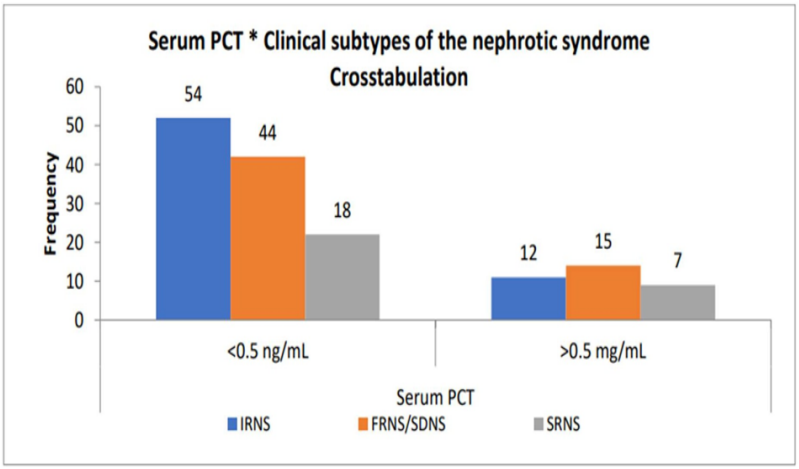
Graph 1: Clinical subtypes of the nephrotic syndrome

Table 2: Descriptive Statistics for Laboratory Parameters

	N	Median	IQR	Range
Hb (gm/dL)	150	11.70	4.68	7.10-15.90
TLC (microliter)	150	17422.00	15694.00	3066-32549
Platelet count (microliter)	150	4.00	3.63	1.50-8.00
Blood urea (mg/dL)	150	149.55	168.85	8.80-318.50
Serum Creatinine (mg/dL)	150	1.09	0.52	0.10-1.49
ANC (microliter)	150	15133.00	10495.75	1055-27670
Serum total protiens (mg/dL)	150	5.10	2.00	3.00-6.40
Serum albumin (mg/dl)	150	2.45	2.00	1.90-12.00
Serum Sodium (mEq/L	150	150.00	20.25	127-169
Serum Pottassium (mEq/L)	150	4.95	1.70	2.90-5.60



Graph 2: Serum PCT * Q-CRP Cross tabulation



Graph 3: Serum PCT * Clinical subtypes of the nephrotic syndrome Crosstabulation

Table 3: univariate logistic regression analysis of subtype of NS with serum PCT positivity status

		B	S.E.	p-value	Exp (B) (Odds Ratio)
Types of NS	IRNS			0.007	
	FRNS /SDNS	0.319	0.516	0.481	1.362
	SRNS	1.264	0.502	0.011	3.431
	Constant	-1.742	0.396	<001	0.271

Table 4: Immunosuppressive therapy * Serum PCT Crosstabulation

Immunosuppressive therapy	Serum PCT		Total
	<0.5 ng/mL	> 0.5 mg/mL	
Intermittent Prednisolone	71	14	85
Lont term alternate day Prednisolone	4	3	7
Mycophenolate mofetil	12	4	16
Calcineurin inhibitor	9	7	16
Cyclophosphamide	2	2	4
> one drug	18	4	22
Total	**116**	**34**	**150**

Table 5: Type of immunosuppressive therapy * Serum PCT Crosstabulation

Immunosuppressive therapy	Serum PCT		Total
	<0.5 ng/mL	> 0.5 mg/mL	
Intermittent Prednisolone	71	14	85
Prolonged immunosuppression	45	20	65
Total	116	34	150

Discussion

This study evaluated the role of serum procalcitonin (PCT) in detecting bacterial infections among children experiencing relapse of nephrotic syndrome (NS). A total of 150 children were included in the study. The median age of the participants was 123 months (range: 12–216 months). The median body weight was 33.91 kg and the median BMI was 22.22 kg/m², indicating that most children were within a relatively healthy anthropometric range. The median age at the first episode of NS was 87.5 months (range: 7–173 months), suggesting variability in disease onset. The median number of previous relapses was three, reflecting the recurrent nature of nephrotic syndrome in pediatric patients.

Previous studies have demonstrated a strong association between infections and relapse in nephrotic syndrome. Mishra et al [6]. reported that among 127 relapse episodes observed in children with a first episode of NS followed for one year, 95 episodes (74.8%) were associated with infection. The authors also observed that infection rates were nearly four times higher during relapse than during remission, suggesting that infections may play an important role in triggering relapses, possibly through immune-mediated mechanisms such as increased interleukin-13 expression.

In the present study, 116 children had serum PCT levels below 0.5 ng/mL, while 34 had levels above this threshold. Among children with PCT levels below 0.5 ng/mL, clinicians diagnosed bacterial infection in 65 cases. Among those with PCT levels above 0.5 ng/mL, 19 were clinically diagnosed with bacterial infection. Among children without clinician-diagnosed bacterial infection, 51 had PCT levels below 0.5 ng/mL and 15 had levels above 0.5 ng/mL. The agreement between clinician-diagnosed bacterial infection and PCT levels was low (Kappa = 0.17), indicating limited concordance between clinical assessment and PCT results.

Several studies from India have reported a high incidence of infections among children with nephrotic syndrome. A study from Chandigarh reported a 50% incidence of major infections, with peritonitis being the most common infection (88.7%), followed by cellulitis. Similarly, Ajayan et al [7]. found that the incidence of major infection was 36.6% among children with NS requiring hospitalization, with peritonitis being the most common infection. While some Indian studies reported urinary tract infections (UTIs) to be relatively uncommon, other studies have observed higher rates of UTIs in children with nephrotic syndrome. International studies also support the association between infections and NS relapse. Lebel et al [8]. Reported their 20-year experience of infections in 239 pediatric NS admissions presenting with fever. Serious bacterial infections (SBI) were identified in 14.6% of cases, most commonly pneumonia, bacteremia/sepsis, and urinary tract infections. Approximately 70% of children with SBI had edema and nephrotic-range proteinuria, suggesting a strong association between infections and relapse. Similarly, a study from Saudi Arabia reported infections in 76% of children admitted with primary childhood nephrotic syndrome, with pneumonia and UTIs accounting for nearly half of the infections.

The inappropriate use of antibiotics remains a significant concern in pediatric practice, particularly in respiratory tract infections. Studies have shown that the implementation of PCT-guided algorithms can reduce antibiotic use by approximately one-third to one-half. In our study, children experiencing relapse with elevated serum PCT levels had slightly longer relapse durations compared with those without elevated PCT levels.

The relationship between immunosuppressive therapy and PCT levels was also evaluated. Among children receiving intermittent prednisolone therapy, the majority had PCT levels below 0.5 ng/mL, whereas a relatively higher proportion of children receiving prolonged immunosuppressive therapy showed elevated PCT levels. This finding may reflect the increased susceptibility to infections in children receiving long-term immunosuppressive treatment.

Our study also examined the agreement between PCT and other inflammatory biomarkers. A strong agreement was observed between PCT and Q-CRP levels (Kappa = 0.584). Among children with PCT levels above 0.5 ng/mL, the majority also had elevated Q-CRP levels (>6 mg/L). In contrast, agreement between PCT and hematological markers such as total leukocyte count (TLC) and absolute neutrophil count (ANC) was weaker, with Kappa values of 0.185 and 0.369, respectively.

Several studies have evaluated the diagnostic performance of PCT in pediatric infections. A prospective study conducted in the United Kingdom involving 213 children presenting to the emergency department with symptoms suggestive of serious bacterial infection reported that PCT and CRP had similar diagnostic performance, with both markers showing an area under the curve (AUC) of 0.70. A meta-analysis by Tsou et al [9]. Demonstrated moderate diagnostic accuracy of PCT for bacterial pneumonia in children, with sensitivity of 0.68 and specificity of 0.60 at a cut-off value of 0.5 ng/mL. Other studies have suggested that lower PCT cut-off values (0.2–0.3 ng/mL) may improve sensitivity without significantly affecting specificity. Additionally, Babenko et al [10]. Proposed a diagnostic decision-tree model using PCT (>0.16 ng/mL) and CRP

(<31.2 mg/L), which demonstrated high sensitivity and specificity for differentiating bacterial from viral meningitis in children.

Overall, our findings indicate that PCT has diagnostic accuracy comparable to Q-CRP and ANC in detecting bacterial infections among children experiencing nephrotic syndrome relapse. PCT may be particularly useful in identifying serious bacterial infections and can serve as a valuable adjunct to clinical evaluation and other laboratory markers.

However, despite its diagnostic utility, routine use of PCT in pediatric nephrology outpatient settings may not be cost-effective. Infection-associated relapses can often be identified using widely available and less expensive biomarkers such as Q-CRP and ANC. Therefore, PCT may be most useful in selected clinical situations where serious bacterial infection is suspected.

The strengths of this study include an adequate sample size and the comparison of multiple commonly used biomarkers for detecting bacterial infections in children with nephrotic syndrome. However, several limitations should be considered. Serial measurement of biomarkers was not performed, preventing evaluation of their kinetic patterns. Furthermore, viral etiologies could not be excluded in cases where bacterial cultures were negative, particularly in respiratory and gastrointestinal infections. This limitation may have resulted in inappropriate antibiotic use in some cases.

Conclusion

1. This study included 150 children with relapse of nephrotic syndrome, enrolled from inpatient wards and outpatient departments over an 18-month period.
2. The median age was 123 months (range: 12–216 months), with male predominance. Infrequent Relapsing Nephrotic Syndrome (IRNS) was the most common subtype, followed by FRNS/SDNS and SRNS.
3. Serum procalcitonin (PCT) levels were <0.5 ng/mL in 77.3% of children and >0.5 ng/mL in 22.7%.
4. Among children with PCT <0.5 ng/mL, a substantial proportion were clinically diagnosed with bacterial infection, while some children with PCT >0.5 ng/mL had no clinical evidence of infection, indicating low agreement between PCT and clinical diagnosis.
5. PCT demonstrated strong agreement with Q-CRP levels, suggesting comparable diagnostic performance for identifying bacterial infections during relapse.
6. Total leukocyte count (TLC) and absolute neutrophil count (ANC) also showed significant association with elevated PCT, supporting their role as additional inflammatory markers.
7. Among nephrotic syndrome subtypes, Steroid-Resistant Nephrotic Syndrome (SRNS) showed a significant association with PCT positivity, indicating a higher likelihood of infection in this group.
8. Overall, PCT may serve as a useful adjunct biomarker for detecting bacterial infections in children with nephrotic syndrome relapse, but widely available markers such as Q-CRP and ANC may be sufficient in routine clinical settings, with PCT being more useful in selected cases of suspected serious bacterial infection.

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