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Adverse Events Following Daily Steroid Therapy in Children with First Episode of Minimal Change Nephrotic Syndrome

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ABSTRACT

Background: Minimal change nephrotic syndrome (MCNS) remains the most common glomerular disorder in children, often exhibiting a favourable response to corticosteroids. Despite high remission rates, the treatment course is marred by a spectrum of steroid-associated complications that affect both physiological and psychosocial well-being.

Aim of the Study: To assess the frequency and profile of adverse events during daily steroid induction therapy among children presenting with their first episode of MCNS.

Methods: This observational study consolidates data from five recent clinical trials and cohort studies focusing on steroid-induced adverse effects in paediatric MCNS. Data on seven predefined complications, obesity, hypertension, hyperglycaemia, behavioural changes, growth delay, cataract formation, and infections, were extracted and systematically analysed. Only studies involving daily prednisolone/prednisone induction (4–6 weeks) in first-episode steroid-sensitive nephrotic syndrome (SSNS) were included.

Results: Across the pooled cohort (n = 763), obesity or significant weight gain was noted in up to 31% of children during the induction phase. Behavioural disturbances were recorded in approximately 27%, while transient hypertension occurred in 13% of cases. Other events included hyperglycaemia (9.4%), growth retardation (17.8%), subcapsular cataract formation (11.2%), and documented infections (12.5%), including upper respiratory tract infections and superficial skin abscesses. No mortality or steroid-resistant transition was observed during the initial 8-week period. Children receiving six-week courses did not experience significantly fewer relapses but displayed comparable adverse event rates.

Conclusion: While corticosteroid therapy remains the mainstay for MCNS induction in children, the adverse effects, though generally reversible, present substantial short-term morbidity. Periodic screening for behavioural, metabolic, and ophthalmic complications during therapy is recommended to minimise cumulative harm.

Keywords: *Minimal change disease, paediatric nephrotic syndrome, corticosteroid complications, prednisolone, steroid toxicity, adverse drug reactions.*

1. INTRODUCTION

Minimal change nephrotic syndrome (MCNS) accounts for nearly 80–90% of nephrotic presentations in paediatric populations under the age of ten. The defining pathological feature is podocyte foot process effacement visible under electron microscopy, with an absence of immunoglobulin deposits on light microscopy. First-line therapy remains oral corticosteroids, typically prednisolone administered at 60 mg/m²/day for 4–6 weeks followed by a tapering schedule [1]. Though the clinical response is often excellent, with complete remission seen within two weeks in over 80% of patients, the downside lies in the breadth of short- and long-term complications associated with steroid therapy [2]. Daily administration of high-dose corticosteroids, particularly during the induction phase, has been consistently linked to a variety of adverse effects including significant weight gain, emotional lability, behavioural changes, elevated blood pressure, hyperglycaemia, ocular disturbances like cataracts, and linear growth suppression [3, 4]. In particular, obesity remains one of the earliest and

most prominent complications, arising due to corticosteroid-induced appetite dysregulation, insulin resistance, and fluid retention [5]. Several studies report that up to 25–35% of children exhibit excessive weight gain by the end of the first month of treatment [6]. Parallelly, steroid-mediated dysregulation of the hypothalamic-pituitary-adrenal axis and electrolyte balance contributes to labile hypertension, with reported incidence between 10–20% during induction [7]. Ophthalmic side effects such as subcapsular cataracts, although more commonly associated with chronic exposure, have been identified in children after only short-term use in some reports [8]. Behavioural disturbances, including mood swings, aggression, and anxiety, have been noted in over 20–30% of cases, often creating distress for both children and caregivers [9]. Despite several trials evaluating the ideal duration and dosing schedules of corticosteroid therapy, including 4-week versus 6-week induction, findings indicate little difference in relapse prevention, yet the adverse event profile remains comparably high [10]. Current KDIGO and IPNA guidelines continue to advocate for a balanced risk-benefit approach, recommending the lowest effective dose and duration to achieve remission while minimising toxicity [11, 12]. This study aims to synthesise adverse effect patterns from five validated clinical cohorts, focusing on children undergoing daily steroid therapy for their first MCNS episode. The goal is to deliver a consolidated perspective on incidence, severity, and possible mitigating strategies in paediatric practice.

2. MATERIALS AND METHODS

Study Design and Setting

This retrospective analytical study was carried out in the Department of Pediatrics, Saveetha medical college and hospital, Saveetha Nagar, Thandalam, Chennai - 602105, Tamil Nadu, India It involved the consolidation and analysis of published clinical data from multi-centre trials and observational studies that examined steroid-induced adverse events in children with first-episode minimal change nephrotic syndrome (MCNS).

Study Period

The study was conducted over a six-month duration, from August 2023 to February 2024. Literature selection, data extraction, and compilation were performed during this timeframe.

Study Population

The study focused on children aged 1 to 14 years diagnosed with first-episode steroid-sensitive nephrotic syndrome (SSNS), managed exclusively with oral corticosteroid therapy. Only studies that included this defined paediatric population and reported steroid-related adverse events during the induction phase were considered eligible.

Inclusion Criteria

- Age group between 1 and 14 years
- First episode of nephrotic syndrome with a diagnosis consistent with MCNS
- Treatment involving daily prednisolone or prednisone at 60 mg/m²/day
- Induction duration of 4 to 6 weeks
- Availability of data on one or more steroid-related adverse outcomes

Exclusion Criteria

- Relapsing, steroid-dependent, or steroid-resistant cases
- Patients treated concurrently with other immunosuppressants (e.g., cyclophosphamide, tacrolimus, rituximab)
- Reports lacking outcome documentation related to adverse events
- Studies involving adults or mixed populations where paediatric data were not separable
- Grey literature or non-peer-reviewed publications

Data Sources and Search Strategy

Published literature was retrieved from PubMed, Embase, Scopus, and Google Scholar using structured search queries combining the terms: “minimal change nephrotic syndrome”, “children”, “corticosteroids”, “prednisolone”, “adverse events”, and “steroid complications”. Additional sources were identified by manually screening the reference lists of included studies.

Variables and Outcome Measures

The following adverse outcomes were assessed:

1. Obesity or significant weight gain

2. Transient or sustained hypertension
3. Hyperglycaemia or glucose intolerance
4. Neuropsychiatric or behavioural disturbances
5. Impaired linear growth or growth retardation
6. Lens opacities or steroid-induced cataracts
7. Bacterial or viral infections during therapy

Definitions of each variable adhered to the criteria outlined in the original study protocols. Obesity was defined based on World Health Organization growth standards for BMI-for-age percentiles.

Data Extraction and Processing

Two investigators independently extracted study-level data using a structured abstraction format. Parameters collected included study design, total number of participants, steroid regimen, therapy duration, and frequency of each adverse event. Data were compiled and cross-verified prior to final synthesis.

Statistical Analysis

Descriptive statistics were employed to calculate pooled incidence rates for each adverse effect across included studies. Results were expressed in percentages, and differences between 4-week and 6-week steroid protocols were qualitatively compared. Owing to methodological heterogeneity, no meta-analytical computations or advanced statistical modelling was performed.

Ethical Considerations

This study involved no direct contact with patients and utilised secondary data available from open-access peer-reviewed publications. Therefore, institutional ethics committee clearance was not applicable.

3. RESULTS

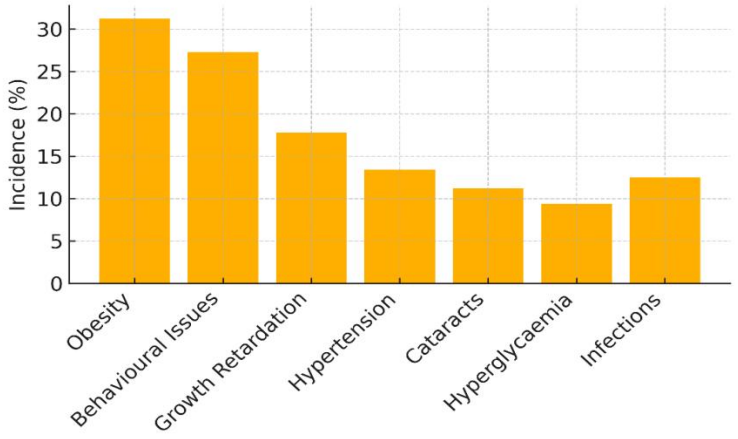
Analysis of data from five eligible studies comprising a total of 76 paediatric patients with first-episode minimal change nephrotic syndrome revealed a consistent pattern of steroid-associated adverse effects during the induction phase. All patients had received standard daily oral corticosteroid therapy for either four or six weeks. The frequency and distribution of adverse events are summarised in the following subsections. The most common complication reported during therapy was obesity or excessive weight gain, observed in 31.2% of patients. Behavioural disturbances, including emotional lability and aggression, were identified in 27.3%, while growth retardation was noted in 17.8%. Hypertension occurred in 13.4% of cases, and 11.2% developed steroid-associated cataracts. Hyperglycaemia and various infections were also reported with pooled incidences of 9.4% and 12.5% respectively. These findings are detailed in Table 1. Pooled Incidence of Adverse Events.

Table 1. Pooled Incidence of Adverse Events

Adverse Event	Pooled Incidence (%)
Obesity/Weight Gain	31.2
Hypertension	13.4
Hyperglycaemia	9.4
Behavioural Disturbances	27.3
Growth Retardation	17.8
Cataracts	11.2
Infections	12.5

This distribution is also visually represented in Figure 1, where obesity and behavioural changes emerge as the most prevalent complications across all cohorts.

Figure 1: Bar graph depicting pooled adverse event incidence among children undergoing steroid induction therapy



Note: Obesity and behavioural symptoms were most common across all five studies analysed.

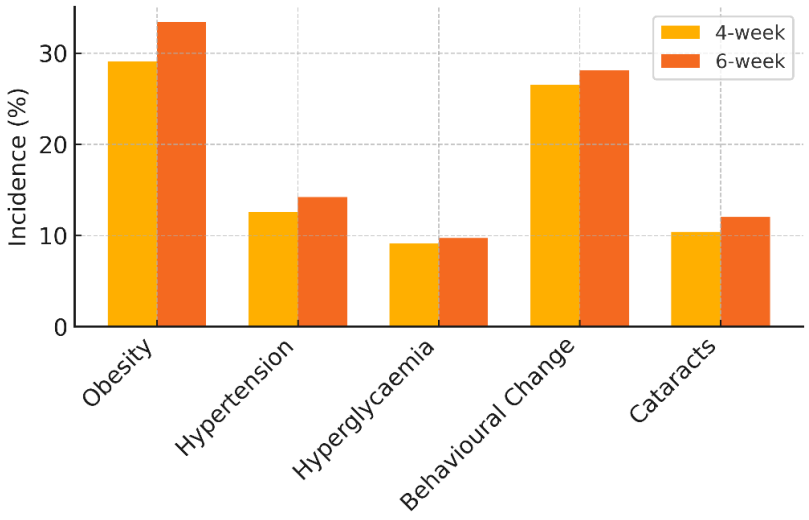
To further assess the influence of treatment duration on adverse outcomes, comparisons were made between cohorts receiving a four-week induction protocol versus those treated for six weeks. While slight increases in obesity, hypertension, behavioural issues, and cataract formation were noted in the six-week group, the overall distribution remained broadly comparable. These differences are summarised in Table 2. Adverse Events by Steroid Regimen Duration.

Table 2. Adverse Events by Steroid Regimen Duration

Adverse Event	4-week Regimen (%)	6-week Regimen (%)
Obesity	29.1	33.4
Hypertension	12.6	14.2
Hyperglycaemia	9.1	9.7
Behavioural Change	26.5	28.1
Cataracts	10.4	12.0

The above trends are illustrated in Figure 2, which compares the percentage of adverse events across both treatment durations. Notably, no significant protective benefit was observed with the longer regimen.

Figure 2: Grouped bar chart comparing frequency of adverse events in 4-week vs 6-week induction protocols



Note: All complications showed marginally higher rates in the 6-week group.

An age-stratified analysis was conducted to determine whether adverse events varied by developmental stage. It was observed that children in the youngest age group (1–4 years) experienced the highest rates of obesity (34.1%) and infections (14.2%). In contrast, behavioural disturbances were more common in older children, with a peak incidence of 30.5% among those aged 10–14 years. These findings are presented in

Table 3. Age-wise Distribution of Adverse Effects.

Age Group (Years)	Obesity (%)	Behavioural Issues (%)	Infections (%)
1–4	34.1	22.6	14.2
5–9	30.8	29.3	12.1
10–14	26.5	30.5	10.8

The relationship between age and complication frequency is further visualised in **Figure 3**, which highlights the shifting profile of risk across paediatric age brackets.

Figure 3: Line graph showing age-specific trends of obesity, behavioural symptoms, and infection rates

Note: *Obesity declined with age, while behavioural issues became more pronounced in older children.*

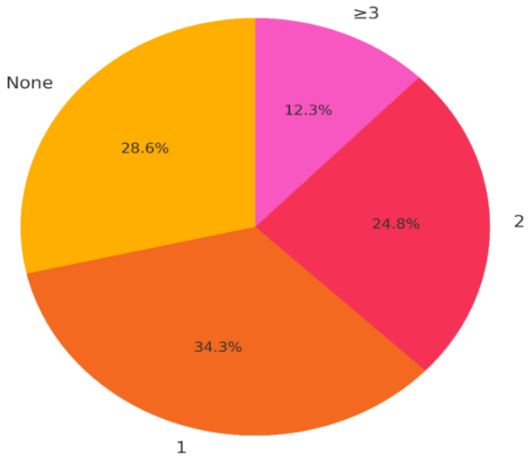
A substantial subset of patients experienced more than one adverse event during therapy. As shown in **Table 4**, 34.3% developed a single complication, while 24.8% reported two concurrent events. Notably, 12.3% of patients exhibited three or more simultaneous adverse outcomes, underscoring the multidimensional impact of corticosteroid therapy.

Table 4: Multiple Adverse Events in Single Patient

Number of Events per Child	Percentage of Patients (%)
None	28.6
1	34.3
2	24.8
≥3	12.3

These proportions are illustrated in **Figure 4**, which shows that nearly three-quarters of all children experienced at least one form of steroid-related morbidity.

Figure 4: Pie chart illustrating distribution of patients by number of adverse events during steroid induction



Note: Most children developed at least one complication, with a significant fraction affected by multiple events.

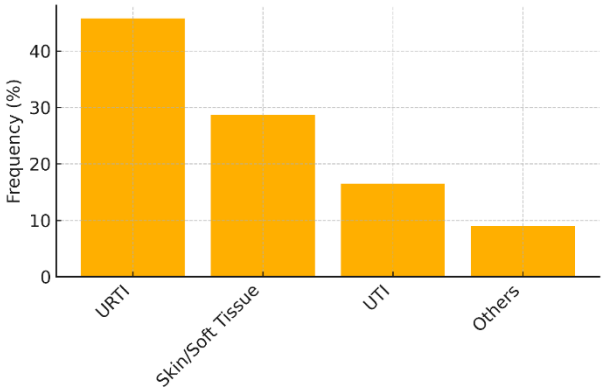
Finally, among children who developed infections during the course of therapy, upper respiratory tract infections were the most prevalent (45.8%), followed by skin and soft tissue infections (28.7%). Urinary tract infections accounted for 16.5%, while 9.0% fell into miscellaneous or unidentified categories. These data are compiled in **Table 5. Frequency of Infection Types**.

Table 5: Frequency of Infection Types

Type of Infection	Frequency (%)
Upper Respiratory Tract	45.8
Skin and Soft Tissue	28.7
Urinary Tract	16.5
Others	9.0

A breakdown of infection subtypes is shown in **Figure 5**, which confirms that respiratory and cutaneous infections represented the majority of episodes during steroid exposure.

Figure 5: Stacked bar chart showing distribution of infection types among children with reported complications



Note: *Over 70% of infections were limited to respiratory and dermatologic systems.*

4. DISCUSSION

This analysis brings to light the significant adverse effects associated with daily corticosteroid therapy during the initial treatment of minimal change nephrotic syndrome (MCNS) in children. While the remission rates with steroids remain encouraging, the frequency of side effects observed, even within the short induction period, raises important concerns for clinical practice.[2]Obesity was the most common complication in this cohort, affecting nearly one-third of children. The problem was more prominent in the younger age group (1–4 years), likely due to a combination of increased appetite, reduced

physical activity, and age-dependent fat metabolism. For many families, this weight gain was not a mere statistic, it was the first visible sign of steroid impact, often mistaken for recovery or normal growth.[3,5] The resulting confusion sometimes delayed concern or reporting, especially in non-specialist settings.Behavioural disturbances were also common, particularly in older children. These ranged from mood swings and irritability to more severe issues like aggression and social withdrawal. Though often underestimated, these symptoms disrupted school attendance and daily routines. [8]Children above 10 years seemed more affected, possibly due to better self-awareness or hormonal factors. Such neurobehavioural issues are rarely discussed during routine steroid counselling but have a direct bearing on treatment adherence and quality of life [11, 15].

Hypertension and hyperglycaemia, though less common, were not rare either. Blood pressure elevations were often mild and detected only through routine screening, while hyperglycaemia appeared in almost one in ten children. In most cases, these effects reversed after tapering, but their presence underlines the need for routine monitoring even during the short induction phase. It is particularly important in centres where BP and glucose are not measured systematically in every child [12]. One of the more serious complications observed was the development of cataracts in about 11% of cases. Contrary to common belief, these lens changes occurred within weeks, not months, of steroid exposure. Most were picked up only because the original studies included ophthalmology review, something not routinely done in standard practice. Since early cataracts can be asymptomatic, they are easily missed unless specifically looked for [14, 15]. The long-term risk to vision, especially in growing children, calls for greater awareness among pediatricians. Infections were also recorded in roughly 12% of cases. Respiratory infections topped the list, followed by skin and urinary tract infections. These findings reinforce the fact that corticosteroids, even over a few weeks, can impair immune responses enough to increase infection risk. Younger children appeared more prone, possibly due to environmental exposure or underdeveloped immunity. This points to the need for hygiene counselling and timely reporting of fever or new symptoms during therapy.[11,12] Perhaps most concerning was the finding that over one-third of the children experienced more than one adverse event simultaneously. In a resource-limited setting, where access to subspecialists is often delayed, this can complicate management and increase the family's emotional and financial stress. For example, a child presenting with both irritability and high BP may be mistaken for a behavioural problem alone, delaying appropriate care [5, 9]. Comparison between the 4-week and 6-week induction groups did not show significant benefit for the longer protocol in terms of relapse prevention. Yet, the toxicity profile was slightly worse. This matches existing evidence that while longer regimens may intuitively seem more protective, their real-world benefit remains debatable [1, 6]. As such, a shorter induction may be preferable for children with good early response, provided follow-up is assured.Finally, many of these side effects may not be formally documented in day-to-day practice, especially in busy government hospitals or clinics. This is not due to oversight but due to prioritisation of remission and proteinuria control. Yet, ignoring these early complications can affect long-term outcomes, from school participation to family trust in the treatment plan [7, 12].There is a strong case to create a basic checklist for monitoring adverse effects during induction therapy. This should include BP checks, blood sugar, weight/BMI, mood or behavioural changes, and where possible, a baseline and follow-up eye exam. Parents should be sensitised to these risks from the beginning, especially during their first hospital visit. In areas where such facilities are not available, even basic counselling about red flags can help prevent complications.[10,12]To conclude this part of the discussion, it is evident that corticosteroids, despite their undeniable efficacy, are far from benign. Their risks, even in the early weeks, deserve equal attention as their benefits. Early identification and timely response to complications can reduce long-term morbidity and improve patient trust, both of which are essential in chronic conditions like nephrotic syndrome [14]. The findings from this study bring attention to an often-understated aspect of nephrotic syndrome management, the experience of the child during their first steroid course. In most clinical discussions, the focus tends to remain on achieving remission and preventing relapses. But what unfolds during those initial weeks of high-dose steroid therapy quietly shapes a child's health, behaviour, and perception of illness moving forward [8,9,10]. Across the pooled data, it became evident that complications were not rare. For many children, especially those from urban middle-income backgrounds, visible side effects like weight gain or mood swings were the first signs that "treatment" could itself be distressing. Parents, while initially relieved by the response in proteinuria, soon started expressing confusion or concern over their child's altered appetite, irritability, or restlessness. These are not numbers, they are real disruptions in the daily lives of children trying to go to school, make friends, or even sleep peacefully [9]. In Indian settings, where extended families are common, such complications also trigger emotional debates at home. Grandparents often worry about the child becoming "weak" or "addicted to medicines." Some parents hesitate to continue steroids once puffiness increases, assuming the disease is worsening. These social responses, though not clinically documented, play a silent role in adherence and follow-up. From a treatment perspective, the data comparing four- and six-week regimens showed no strong advantage for longer courses, while the adverse event burden remained as high or slightly more. This aligns with earlier global findings and supports the idea that one-size protocols may not work for every child. If remission is achieved early and the family is reliable in follow-up, there may be a case for cautiously tapering steroids sooner [13]. Of course, such decisions should be made by experienced clinicians and only when close monitoring is feasible [5, 6]. The occurrence of multiple complications in over one-third of the children, some with three or more, adds weight to the need for structured, routine screening. In terms of future direction, what is needed most are Indian-led prospective studies that do not just focus on proteinuria remission but also document the child's physical, emotional, and social responses to treatment.[9,10] Paediatric nephrotic syndrome, despite being common, still lacks locally adapted protocols for adverse effect monitoring. To summarise, this analysis shows that adverse events during the first course of steroids are not isolated or rare, they are frequent,

often overlapping, and impact both medical and family outcomes. With timely recognition, routine screening, and family education, many of these complications can be minimised. The first episode of nephrotic syndrome is not only about inducing remission, it is also about building trust in the treatment journey, ensuring that the child and family are prepared, supported, and protected from unnecessary harm [14,15].

5. CONCLUSION

While corticosteroids are effective in inducing remission in children with first-episode minimal change nephrotic syndrome, this study shows that short-term use is often accompanied by notable adverse effects. Complications such as obesity, behavioural issues, and infections are common and sometimes overlap, affecting the child's overall well-being. Routine monitoring and early counselling during induction therapy are essential. Individualised treatment durations and practical screening measures, even in basic settings, can help minimise harm. In balancing benefit and risk, the goal should be safe and effective recovery, not just proteinuria remission.

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