ORIGINAL ARTICLE

Behavior Problems Associated with Corticosteroid Use in Children with Nephrotic Syndrome

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ABSTRACT
Background: *Chronic conditions, notably nephrotic syndrome (NS), are related to psychological problems. Corticosteroid therapy in children with NS may cause a variety of side effects including behavioral issues.* ***Aim:*** *The current study was conducted to investigate the association between various behavioral disorders in children and cumulative doses of steroid. Methods & Materials: From June 2017 to May 2018, this prospective case-control study was conducted at various institutes and medical college hospitals in Dhaka as well as Bogura. One hundred cases of NS aged 4-17 years from a purposive sampling approach, as well as 100 age and gender-matched control subjects were enrolled. The behavior of children with NS and controls was assessed using SDQ grading. A data collection sheet was developed, and the Bengali version of the SDQ format was used. Variables were measured using various methods. SDQ was compared to these variables, and data were analyzed using SPSS (version 22).* ***Results:*** *In both case and control, males were predominant though not significant statistically. The case and control groups had mean age of 7.86 ± 2.98 and 7.19 ± 2.77 years respectively which was also not statistically significant. Most of the study subjects were from rural area in both groups. The emotional symptoms scale, conduct difficulties scale, and peer relationship problems were significantly higher in cases than in control group, whereas the pro-social behavior scale was significantly lower. SDQ score had no correlation with cumulative doses of steroid.* ***Conclusion:*** *Children with NS experience much greater psychological issues than the control group, unrelated to cumulative doses of steroid. So, they should be assessed for behavioral abnormalities during and after treatment of the original problem.*

Keywords: *Corticosteroid therapy, psychological problems, Nephrotic syndrome, Behavioral issues*

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INTRODUCTION

Nephrotic syndrome (NS) is mostly a pediatric illness, occurring more frequently in children than adults. The majority of children with NS have steroid-sensitive minimal change disease, which is generally mild. Teeninga et al. (2012) observed that the condition leads to recurrent relapses, which are commonly associated with steroid dependence in 20 to 60% of patients [1]. Bagga et al. (2005) showed that minimum change NS is more common in boys than in girls (2:1) and usually develops between the ages of 2 and 6 years [2]. Childhood peer interactions are highly linked to emotional, behavioral, and adjustment challenges. Thus, strong peer interactions are essential to live a tranquil and healthy life. Kim et al. (2001) and Newcomb et al. (1993) emphasized the importance of good mental health and family interaction in coping with peers. Coie et al. (1992) demonstrated that childhood peer social status can be predicted by both parent-reported externalized and self-reported internalized illnesses [3-5]. The authors also stressed the importance of the information source in synchronizing patterns of predictor-outcome relationships. Any chronic physical illness, especially in children, has biological, behavioral, and social aspects that affect the child's mental health, social and personality development, and family [6]. Ozkaya et al. (2004) found that this would naturally apply to children with NS due to its protracted relapsing and remitting history [7]. Ridder et al. (2008) observed that chronic diseases frequently produce exhaustion and lethargy [8], reducing a person's vitality for physical, emotional, and social pursuits. Infections and inflammatory processes can cause psychosomatic symptoms such as depression [9]. Kivimäki et al. (2014) described sleeping problems [10], and Cho et al. (2013) found tiredness problems [11]. Prolonged corticosteroid use may also contribute to behavioral issues in this particularly sensitive population. Steroid 'psychosis' is a well-known side consequence of high-dose glucocorticoid treatment Neurobiological research has revealed strong evidence for steroid’s direct influence on the regulation of behavioral patterns. Zhao et al. (2008) mentioned that recurrent corticosteroid injections cause depressive behavior in specific

mouse models [12]. Fitzgerald and Beggs (2001) concluded that pain from both medical problems and treatment can cause anxiety and have an impact on future pain sensitivity and neurological development [13]. NS is a condition that should be treated carefully to decrease morbidity and mortality. If behavioral difficulties persist, they will place a significant load on the patient and family. As a result, these individuals should be given special treatment early in the course of the disease to avoid behavioral issues.

METHODS & MATERIALS

A prospective case-control study was conducted in the Department of Pediatric Nephrology, National Institute of Kidney Diseases and Urology, Dhaka; Dhaka Medical College Hospital, Dhaka; Sir Salimullah Medical College & Mitford Hospital, Dhaka; Shaheed Suhrawardy Medical College Hospital, Dhaka;Institute of Child and Mother Health (ICMH), Dhaka and Shaheed Ziaur Medical College Hospital, Bogura between June 2017 and May 2018. Ethical clearance was taken from the respective authorities of different institutions. Written consent was taken from each parent/guardian of patients/controls. Using a purposive sample strategy, this study included 100 cases of NS aged 4-17 years, as well as 100 age and gender-matched controls. The Strengths and Difficulties Questionnaire (SDQ) scoring was used to analyze children's behavior patterns with NS. A data collection sheet was developed, and the Bengali version of the SDQ format was used. Several variables were measured. The SDQ was compared to these factors, and the data was analyzed using SPSS (version 22). A p value of ≤ 0.05 was considered statistically significant.

SDQ: A brief behavioral screening questionnaire for child and adolescent mental
health problem which was developed, adopted and validated by Goodman et al. in 1995. All the five scales were used in this study (Emotional symptoms, Conduct problems, Hyperactivity/inattention, Peer relationship problems and Pro-social behavior).

RESULTS

A total of 200 children were studied, including 100 cases and 100 controls. The mean age of cases was 7.86 ± 2.98 years, and 54% were male; most (88%) were from rural areas. Clinically, 62% of cases had mild edema. Cases had higher SDQ scores for emotional symptoms (1.20 ± 1.33 vs. 0.47 ± 0.87, p < 0.001), conduct problems (0.45 ± 0.88 vs. 0.12 ± 0.56, p < 0.001), and peer relationship problems (1.40 ± 1.22 vs. 1.03 ± 0.88, p < 0.001) compared to controls, while hyperactivity scores were similar (1.23 ± 1.49 vs. 1.10 ± 1.33, p = 0.601).

Table I shows the gender distribution of the study subjects. Males were slightly more predominant in both groups, comprising 54% of cases and 57% of controls. The difference in gender distribution between cases and controls was not statistically significant (p = 0.669), indicating that the two groups were comparable in terms of sex.

Table – I: Sex of the study subjects (*n*=200)

Parameters	Group		P value
	Case (n=100)	Control (n=100)	
Gender			
Male	54 (54.0)	57 (57.0)	0.669**
Female	46 (46.0)	43 (43.0)	

Table II shows the age distribution of the study subjects. In both groups, the majority of children were aged 4–10 years (cases: 80%, controls: 86%). The mean age was 7.86 ± 2.98 years in cases and 7.19 ± 2.77 years in controls. There was no statistically significant difference in age between the two groups, indicating that cases and controls were comparable in terms of age.

Table – II: Age of the study subjects (*n*=200)

Parameters	Group		P value
	Case (n=100)	Control (n=100)	
Age (years)			
4-10	80 (80.0)	86 (86.0)	0.094*
11-17	20 (20.0)	14 (14.0)	
Mean ± SD	7.86 ± 2.98	7.19 ± 2.77	

Table III shows the SDQ scores between cases and controls. Cases had significantly higher scores than controls in emotional symptoms (1.20 ± 1.33 vs. 0.47 ± 0.87, p < 0.001), conduct problems (0.45 ± 0.88 vs. 0.12 ± 0.56, p < 0.001), and peer relationship problems (1.40 ± 1.22 vs. 1.03 ± 0.88), indicating greater emotional and behavioral difficulties. In contrast, the pro-social behavior score was lower in cases than controls (9.52 ± 1.02 vs. 9.85 ± 0.48), suggesting reduced positive social behavior among cases. Hyperactivity scores were similar between the groups (1.23 ± 1.49 vs. 1.10 ± 1.33, p = 0.601). Overall, the total SDQ score was higher in cases (4.28 ± 2.59) than in controls (2.72 ± 1.95), reflecting increased psychosocial difficulties in the case group.

Table – III: SDQ level of different psychiatric scales in case and control (*n*=200)

SDQ scales	Group		P value
	Case (n=100) [mean ± SD]	Control (n=100) [mean ± SD]	
Emotional symptoms scale	1.20 ± 1.33	0.47 ± 0.87	<0.001
Conduct problem scale	o.45 ± 0.88	0.12 ± 0.56	<0.001
Hyperactivity scale	1.23 ± 1.49	1.10 ± 1.33	0.601
Peer relationship problem scale	1.40 ± 1.22	1.03 ± 0.88	0.023
Pro-social behavior scale	9.52 ± 1.02	9.85 ± 0.48	0.014

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Total scale	4.28 ± 2.59	2.72 ± 1.95	<0.001

Table IV shows the correlation between SDQ score and cumulative dose of steroid among cases. The correlation was very weak and not statistically significant (r = 0.059, p = 0.569), indicating that the SDQ score was not associated with the cumulative steroid dose in these children.

Table – IV: Correlation of SDQ score with cumulative dose of steroid in cases (*n*=100)

	r value	P value
Cumulative dose of steroid	0.059	0.569

Table V shows the correlation between SDQ score and cumulative steroid dose across different clinical types of nephrotic syndrome. In all subtypes—first attack (r = 0.031, p = 0.898), FRNS (r = 0.312, p = 0.239), IFRNS (r = 0.217, p = 0.119), and SDNS (r = -0.138, p = 0.767)—the correlations were weak and not statistically significant. This indicates that SDQ scores were not related to the cumulative steroid dose in any clinical type of nephrotic syndrome.

Table – V: Correlation of SDQ score with cumulative dose of steroid in different clinical types of NS (*n*=100)

Clinical types of nephrotic syndrome	r value	P-value
First Attack	0.031	0.898
FRNS	0.312	0.239
IFRNS	0.217	0.119
SDNS	-0.138	0.767

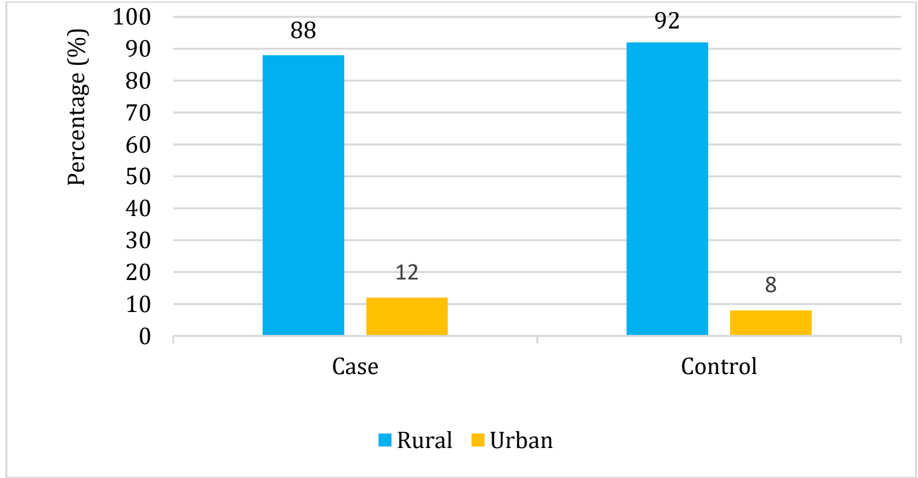

Figure – 1: Residence of the study subjects

Figure 1 illustrates the residence of the study participants. The majority of both cases (88%) and controls (92%) were from rural areas, indicating that most study subjects in this population resided in rural settings.

DISCUSSION

In the present study, males outnumbered females in both the case and control groups. Rodriguez et al. (2003) and Guha et al. (2009) also found similar findings [14, 15]. However, Agrawal et al. (2017) included a comparable number of males and females in their study [16].

The average age of the patients and controls was nearly comparable in this study. The patients' mean age was similar to that of Guha et al. (2009) and Ghobrial et al. (2013) [15, 17]. Rodriguez et al. (2003) enrolled older children, with an average age of 9.48±3.06 years in cases and 9.28±2.85 years in controls [14].

In the current study, 88% of cases were from rural regions. Guha et al. (2009) identified 72% from rural populations which is nearly identical to this study [15].

This study revealed that children with NS had much higher levels of emotional symptoms, behavioral problems, and peer interaction concerns than healthy children, whereas pro-social behavior was significantly lower. Overall, children with NS experienced much greater psychological issues than the control group. Rodriguez et al. (2003) noted that children with NS experienced more emotional symptoms, peer problems, and overall psychological challenges [14]. Ghobrial et al. (2013) found no significant differences [17]. Agrawal et al. (2017) assessed the quality of life for children with NS [16]. They used PedsQL 4.0, which is a generic core scale. Children with NS received considerably higher scores on both physical and emotional dimensions. They also found that children with NS had a much worse social score than their healthy counterpart. Boraey and El-Sonbaty (2011) mentioned that children with NS exhibit significantly more behavioral problems than healthy children [18]. Manti et al. (2013) found that children with NS had significantly higher total psychosocial scores measured by the Child Behavior Checklist (CBCL) [19]. Mehta et al. (1995) also used the CBCL to assess behavioral and social skills in children with NS [20]. When comparing children with NS to healthy children, they observed a significantly higher CBCL score in behavioral issues and a significantly lower score in social competence. Guha et al. (2009) concluded that hyperkinesia was the most common behavioral abnormality, followed by conduct disorder, learning difficulties, and obsessive-compulsive neurosis [15].

In this study, a large cumulative dose of steroid was found to have no effect on SDQ levels. The cumulative dose of steroid for various clinical forms of NS demonstrated no link with SDQ. However, Mishra et al. (2015) observed a favorable correlation with cumulative steroid dose [21]. This could be related to the difference in sample size (n=45) and type of questionnaire (CBCL). Steroid is not the primary contributor to behavioral change. Family environment, maternal stress, and illness-related variables may all play an impact. High-dose short-term steroid might have a deleterious impact on behavior, as mentioned by Hall et al. (2003) and Soliday et al. (1999) [22, 23].

LIMITATIONS

This was a cross-sectional study with purposive sampling. So, these patients were not evaluated further and it was not possible to know how long it took for symptoms to resolve after cessation of steroid.

CONCLUSION & RECOMMENDATION

Children with NS experience much higher levels of psychological issues including emotional symptoms, behavioral problems, and peer interaction concerns than their healthy counterpart, whereas pro-social behavior is significantly lower. Though no significant relationship was found with cumulative dose of steroid, these problems should not be overlooked during treatment of the original disease and thereafter. A longitudinal study with larger sample size should be conducted for further understanding of the condition.

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