

ORIGINAL RESEARCH

Psychological Abnormalities in Children with Minimal Change Nephrotic Syndrome

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ABSTRACT

Introduction: Children with chronic physical illnesses are generally considered at increased risk for behavior difficulties.

Aim: To assess the psychological abnormalities in children with minimal change nephrotic syndrome.

Methods: A cross sectional observational study on 150 patients clinically diagnosed with minimal change nephrotic syndrome and fulfilling inclusion (for cases) and exclusion criteria and 150 controls, conducted in the Pediatric department of a tertiary care hospital for 12 months i.e from September 2020 to august 2021. Data of study and control group were collected, compared and inferences were drawn after proper statistical analysis.

Results: Prevalence of psychosocial illness in children suffering from minimal change nephrotic syndrome for at least a duration of six months was seen significantly more in cases (62%) of cases as compared with healthy controls (20%). psychosocial illness was not significantly affected by sociodemographic parameters. The most common psychosocial illness found was inattention (40%), followed by somatic symptoms (32%). Duration of Steroid therapy, Steroid dependence and Number of relapses significantly affected the prevalence of psychosocial illness.

Conclusion: Children with nephrotic syndrome should be routinely screened for psychological and behavioral abnormalities so as to enable early intervention.

Keywords: Minimal Change Nephrotic Syndrome, Psychological.

INTRODUCTION

Children with chronic physical illnesses are associated with increased psychopathologies problems in children. These children are at high risk of developing emotional and behavioral problems and are twice likely to develop psychiatric disorders.¹Nephrotic syndrome is one of the common chronic diseases affecting children world-wide, with a higher incidence in South Asian children. The prevalence of kidney disease is 15-74 cases per one million children.² Nephrotic syndrome, with its relapsing and remitting course has biological, behavioral, and social manifestations that have implications on the mental health, social and personality development of the child.³Prolonged steroid treatment may also contribute to behavioral

disturbances in this especially vulnerable population.⁴The effects of steroid therapy on emotional disturbances, such as anxiety, have been acknowledged.⁵It has been suggested that children with nephrotic syndrome may be particularly susceptible to the side effects of steroids because of the increased free serum prednisolone levels measured during periods of hypoalbuminemia.⁶ However, in busy clinical practice the psychosocial aspect of care may be overlooked in the pressure to treat and control disease processes, unless their importance is stressed by appropriate evidence.⁷This prolonged need of taking medications, frequent contact with medical professionals, and interruptions in schooling and everyday activities may be mechanisms through which the illness increases affected children's psychological problems.⁸The consequences of these disorders include the impact during childhood and the persistence of mental ill health into adult life. Present study envisages to investigate possible differences in psychosocial problems in children with nephrotic syndrome compared to healthy controls and to examine the effect of disease-specific and treatment-specific characteristics.

AIM

To assess the psychological abnormalities and risk factors associated in children with minimal change nephrotic syndrome.

METHODS

A cross sectional observational study on 150 patients clinically diagnosed with minimal change nephrotic syndrome and fulfilling inclusion (for cases) and exclusion criteria and 150 controls, conducted in the Pediatric department of a tertiary care hospital for 12 months i.e from September 2020 to August 2021. Ethical clearance was obtained from the Institutional Review Board. The prevalence of cognitive and psychosocial abnormalities in children with nephrotic syndrome is found to be 30-50% in previous studies. Taking an average of 40%, sample size is calculated to be 150. A study group of 150 patients who presented to our hospital in the study period, clinically diagnosed with minimal change nephrotic syndrome at least 6 months and 6-14 yr age were enrolled in the study group. A control group of 150 children of 6-14 yrs were selected from healthy individuals attending the immunisation clinic. Children with secondary nephrotic syndrome, any other chronic illnesses, taking drugs affecting central nervous system such as anti-epileptics, anti-depressants, anti-psychotics, stimulants etc, under treatment for ADHD, autism and other behavioral disorders prior to diagnosis of nephrotic syndrome and Patients who denied consent were excluded. Patients' parents were explained about the study and were asked to sign a written informed consent form. All the parents of the patients in the study group were subjected to the detailed history taking using a self-designed pro-forma regarding their socio-demographic details (age, gender, caste, residence etc), onset and duration of disease and duration of steroid medication. Routine investigations were done to assess laboratory parameters such as CBC, serum albumin, serum cholesterol, renal function, serum electrolytes etc.

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). For psychosocial impairments, "DSM-5 parent/guardian-Rated Level 1 Cross-Cutting Symptom Measure-Child aged 6-17 was used to assess mental health domains that are affected. This is a measure offered by American Psychiatric Association (APA), containing 12 domains named Somatic symptoms, Sleep problems, Inattention, Depression, Anger, Irritability, Mania, Anxiety, Psychosis, Repetitive thoughts and behaviors, Substance use, Suicidal ideation/ suicide attempts. After interviewing the parent/guardian, each item of the domain is showed on a 5-point scale. If the highest score for the domain exceeds the threshold score, then the DSM-5 level 2 cross-cutting symptom measure is applied, which categorizes the case into mild, moderate and severe.

Data of study and control group were collected, compared and inferences were drawn after proper statistical analysis. Chi square test (with or without Yates' correction), Fisher's exact test and student t test were applied as appropriate to compare the variables. Difference was considered significant when p value was <0.05 .

RESULTS

Majority of cases were between 6-8 years of age (66%) with mean value of 8.10 ± 1.19 years. Majority of control were in group 6-8 years (67.33 %) with mean age of 8.04 ± 1.02 yr. In study group there were 67.33% males and in controls there were 64% males, majority of cases presented with decrease urine output (87%), followed by edema (70%), abdominal distension (28%), vomiting (6%), and hypertension (6%). In cases, majority had duration of illness between $>2-4$ years (36.67%) followed by 32.67% had duration of illness ≤ 2 years. The mean duration of disease was 3.54 years. Majority of cases of nephrotic syndrome were Steroid responsive (62.7%), followed by 27.3% had Frequent relapsing nephrotic syndrome (FRNS) and 10% had Steroid dependent nephrotic syndrome (SDNS).

In children with nephrotic syndrome, the prevalence of psychosocial illness was found to be 62%, as 94 out of 150 cases had problem in at least one of the 12 domains of dsm-5. In contrast, only 20% of the control group had any psychosocial illness. The difference was statistically very highly significant as P value was <0.00001 .

Among Cases having somatic symptoms, 66.67% had mild, 25% had moderate, and 8.33% had severe symptoms. Cases having inattention 80% had mild, 15% had moderate, and 5% had severe symptoms, Cases having Depression 73.3 % had mild, 20% moderate and 6.7% had severe symptoms, Cases having Anger 62.5% had mild and 25% had moderate and 12.5% had severe symptoms, Cases having Irritability 64% had mild and 24 % had moderate and 12% had severe symptoms, and Cases having Anxiety 76.7% had mild and 16.67% had moderate and 6.7% had severe symptoms.

In males, most common psychosocial illness was inattention (38.6%), followed by somatic symptoms (27.2 %) and anxiety (21.7%) while in females it was inattention (42.8%), followed by somatic symptoms (40.8 %). No significant relation was observed in different domains of psychosocial illness with gender and age groups.

The psychosocial illness was more prevalent in patients whose parents had low education status. We found that among illiterate group, 75.5% of the patients had psychosocial illness. Among children whose parent's literacy was of 5th standard or less, psychosocial illness was present in 64.79%, prevalence was more in patients who belonged to upper lower (69.57%), lower (67.57%) and lower middle (61.29%) classes of socioeconomic status as per Modified Kuppuswami scale, as compared to upper (50%) and upper middle (50%) and more prevalent in those living in rural area (66.09%), as compared to those living in urban area (51.43%). Though statistically non-significant, a close association was observed.

Higher number of cases who had the diagnosis of steroid dependent nephrotic syndrome and frequently relapsing nephrotic syndrome were found to be suffering from psychosocial illness, as compared with steroid responsive group. Highest prevalence (86%) was found in steroid dependent cases. The difference was statistically significant as chi-square statistic was 7.002 and the p-value was 0.0301.

Psychosocial Illness was more prevalent in cases who were on steroid medication for a longer duration of time. Highest prevalence (72.7%) was observed in patients who had steroid therapy for 31-40 weeks. A statistically significant difference was found p-value 0.029.

There was no statistically significant difference found between serum albumin levels and psychosocial illness. Chi-square statistic is 0.6814 and the p-value was 0.4091.

In nephrotic syndrome cases having psychosocial illness, those having duration of disease of >4 years, 67.39% were affected and 59.18% of those having ≤ 2 years of disease were

affected. There is statistically no significant difference between Psychosocial illness with duration of disease (P-value 0.0.6065).

Here, psychosocial illness was higher in cases who had higher number of relapses. 77.38% of cases having relapse of ≥ 4 had psychosocial illness and there is statistically very highly significant difference between Psychosocial illness with number of relapse (P-value 0.00002).

Table 1: Prevalence of Psychosocial Illness in Study and Control Groups (as per DSM-5)

Group	Psychosocial illness				
	Present		Absent		Total
	N	%	N	%	N
Study	94	62	56	38	150
Control	30	20	120	80	150
P-value	Chi-square statistic is 61.6278. The p-value is < 0.00001				

Fig 1: Psychosocial Illness According to Severity Gradings as per DSM-5

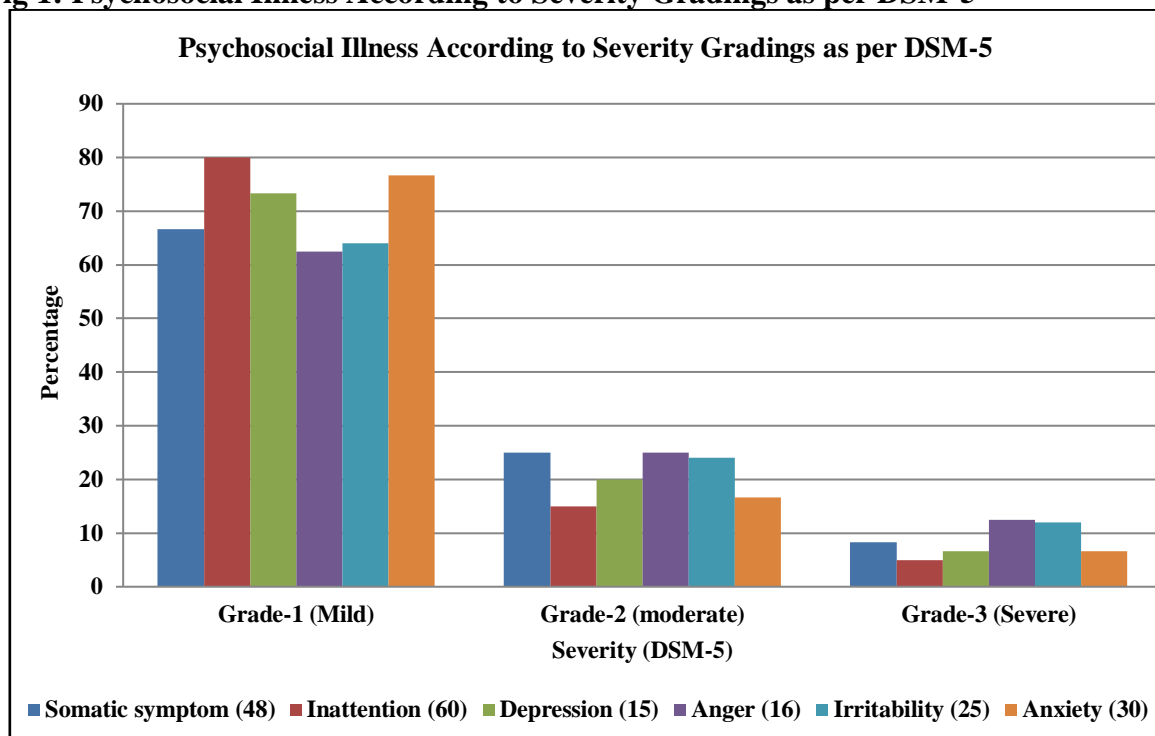


Table 2: Distribution of Psychosocial Illness according to age and sex of case

Psychosocial Illness	Somatic symptom (48)	Inattention (60)	Depression (15)	Anger (16)	Irritability (25)	Anxiety (30)
Male (101)	28 (27.72)	39 (38.61)	10 (9.90)	12 (11.88)	17 (16.83)	22 (21.78)
Female (49)	20 (40.82)	21 (42.86)	5 (10.20)	4 (8.16)	8 (16.33)	8 (16.33)
P-value	0.1049	0.6194	0.9543	0.4902	0.9833	0.4354
6-8 Years(99)	31 (31.31)	38 (38.3)	11 (11.11)	10 (10.10)	20 (20.20)	18 (18.18)
9-11Years(51)	17 (33.3)	22 (43.1)	4 (7.84)	6 (11.76)	5 (9.80)	12 (23.53)
P-value	0.99	0.50	0.48	0.75	0.10	0.43

Table: 3 Distribution of Psychosocial Illness According to Parent's Education Status.

Parent's education status (N)	Psychosocial Illness				Total
	Present		Absent		
	N	%	N	%	
7	24.14	75.86			0.18
≤5th standard (71)	46	64.79	25	35.21	
6th-12th standard (34)	18	52.94	16	47.06	
Graduate/ Post Graduate (16)	8	50.00	8	50.00	
Socio-Economic Status					
Upper (16)	8	50.00	8	50.00	0.204
Upper middle (20)	10	50.00	10	50.00	
Lower middle (31)	19	61.29	12	38.71	
Upper lower (42)	32	69.57	10	21.74	
Lower (41)	25	67.57	16	43.24	
AREA					
Rural (115)	76	66.09	39	33.91	0.116
Urban (35)	18	51.43	17	48.57	

Table: 4 Association between Duration of steroid therapy and Psychosocial Illness

Type	Psychosocial Illness				P value
	Present		Absent		
	NO.	%	No.	%	
FRNS (41)	29	70.7	12	29.3	0.030*
Steroid responsive (94)	52	55.3	42	44.7	
SDNS (15)	13	86	2	14	
Duration of steroid therapy					
11-20 weeks (42)	18	42.84	24	57.14	0.029*
21-30 weeks (72)	50	69.44	22	30.55	
31-40 weeks (33)	24	72.73	9	27.27	
≥41 (3)	2	66.67	1	33.33	
Serum Albumin					
<2.0 (101)	61	60.40	40	39.60	0.40
≥2 (49)	33	67.35	16	32.65	

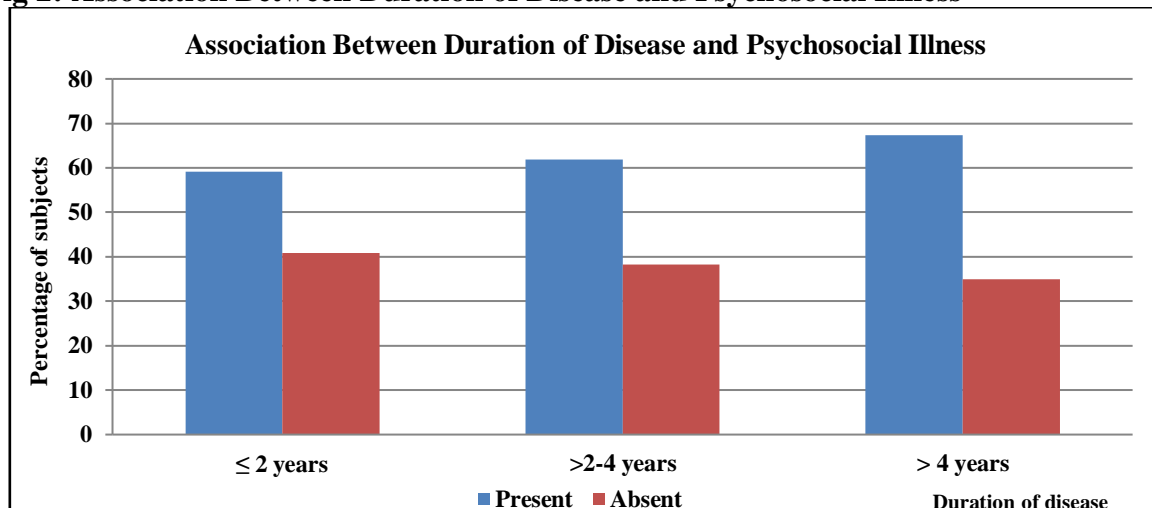
Fig 2: Association Between Duration of Disease and Psychosocial Illness

Table: 5 Association between No. of Relapses with Psychosocial illness

No. of Relapses	Psychosocial illness				P value
	PRESENT		Absent		
	N	%	N	%	
<4 (66)	29	43.94	37	56.06	0.00002*
≥4 (84)	65	77.38	19	22.62	

DISCUSSION

Children with chronic physical illnesses are generally considered at increased risk for behavior difficulties. Illnesses not only affect their psychosocial development but also increase behavior problems in siblings, with an added burden of the disease on family life.⁹ Our findings suggest that children with nephrotic syndrome may experience higher levels of emotional/ behavioral problems related to disease- and treatment- specific variables. Based on the responses of the CBCL, the patients presented with more internalizing problems, such as withdrawal and somatic complaints than healthy controls. It is quite difficult to differentiate the effects of treatment vs. the disease itself on behavior. When in remission, the child with nephrotic syndrome may appear physically well, but medical insistence on regular monitoring for proteinuria is an ever-present reminder that there is an underlying chronic medical condition, which may potentially relapse.

Among study group, majority of cases were between 6-8 years of age (66%) with (mean value of 8.10 ± 1.19 years). 67.33% of cases were males and 32.67% females. Among controls, majority were in group 6-8 years (67.33 %) with 64% males and 36% females. There was statistically no significant difference in age groups (P-value 0.4182) and gender (P-value 0.54) between the two groups. Zyada et al⁹ found mean age of children with nephrotic syndrome was 8.8 years. Male sex was predominant in the sample studied. Mehta et al⁴ found mean age at evaluation was 7.2 ± 3.2 years and mean age at of the controls was 6.5 ± 3.2 years.

Majority of cases of nephrotic syndrome were Steroid responsive (62.7%) followed by 27.3% had Frequent relapsing nephrotic syndrome (FRNS) and 10% had Steroid dependent nephrotic syndrome (SDNS). Mishra et al¹⁰ found that 52 cases had FRNS, 28 cases were steroid responsive and 31 cases in steroid dependent.

In our study, the psychosocial illness was more prevalent in patients whose parents had low education status but not statistically significant. We found that among illiterate group, 75.5% of the patients had psychosocial illness. Among children whose parent's literacy was of 5th standard or less, psychosocial illness was present in 64.79%. Manti et al¹¹ reported that Almost 1 in 5 parents (19.5%) of children with nephrotic syndrome had a low educational level while all parents of the children in the control group had at least a medium educational level ($P < 0.001$).

In our study, inattention (40%) was the most common psychosocial illness followed by Somatic symptom (32%), Anxiety (20%), Irritability (19.3%), Anger (10.67%), Depression (10%), Sleep Problems, mania, Psychosis, repeated thoughts, Substance abuse and Suicide ideation was absent in cases. Manti et al¹¹ noticed abnormalities in withdrawn, somatic complaints, thought, internalizing, and total problems. Significantly higher frequency of abnormality (T-score > 69) was noticed in the patient rather than in the control group in the aforementioned variables (9.8% vs. 0%, 12.8% vs. 0%, 23.1% vs. 2.4%, 25.0% vs. 2.5%, 32.1% vs. 7.7%, respectively). Thus, Manti et al¹¹ observed that severe disease seemed to present more somatic complaints and externalizing problems than did those with mild or moderate disease. Zyada et al⁹ reported that abnormalities in subscale anxiety, depression, and withdrawal were higher than those in aggressiveness and delinquency. There was a

statistically significant difference between both group as regards withdrawal, anxiety/depression, and thought and attention problems.

Solidayet al¹² study concluded that the most common symptoms were depression, anxiety, somatic complaints, and social withdrawal. As many as 29% of children who have kidney disease experience these problems.

Mehta et al⁴ reported lower scores for children with nephrotic syndrome than the controls. Behavior problems related to depressed, hyperactive or aggressive behavior, somatic complaints (body aches, pain) and social withdrawal were more frequent amongst children with nephrotic syndrome.

In our study, Psychosocial Illness was more prevalent in cases who were on steroid medication for a longer duration of time. A statistically significant difference was found as chi-square statistic is 8.972 and p-value is 0.029.

In Manti et al¹¹ study Duration of steroid medication differed among the T-score categories of anxiety/depression (< 65: 31.0 ± 51.0, 65–69: 12.0 ± 2.0, > 69: 94.0±51.0, P=0.011) and among those of externalizing problems (< 65: 31.0 ± 51.0, 65–69: 12.0 ± 2.0, > 69: 94.0 ± 51.0, P = 0.039). Manti et al¹¹ observed that duration of steroid treatment was found to be significantly related to children's anxiety/ depression and externalizing problems. This finding may reflect the effect of the extended exposure to steroids on the children's physical appearance and fitness, as it was reflected in the significant differences in the BMI, height, and WHR between patients and controls in the present sample. Changes in these crucial dimensions of children's self-image can affect their self-esteem and their peer relationships (e.g. facing social exclusion or bullying) leading to anxiety/depression and behavior problems. Similarly, many other study^{12,13} studies indicate that insomnia, tearfulness, irritability, argumentative behavior, and tiredness are more common in children on steroids than controls.

In our study, higher number of cases who had the diagnosis of steroid dependent nephrotic syndrome and frequently relapsing nephrotic syndrome were found to be suffering from psychosocial illness, as compared with steroid responsive group. The difference was statistically significant as chi-square statistic is 7.002 and the p-value is 0.0301.

Heiniger et al¹⁴ found that children with nephrotic syndrome showed features of depressed, hyperactive, or aggressive behavior. Somatic complaints, social withdrawal, and poor school performance were also observed. This might be, in part, related to steroid-induced psychosis, which is one of the serious adverse effects of corticosteroid therapy. Neuhaus et al¹⁵ observed that psychosocial adjustments are impaired in children with steroid-sensitive idiopathic nephrotic syndrome (SSNS). Steroid treatment, both short-term and long-term, is an important contributor among other determinants. The exact mechanisms by which steroids lead to behavioral alterations in humans are unclear. Solidayet al¹² found abnormal scores in relation to anxiety/depression and aggressive behavior developing during treatment in five out of seven children with nephrotic syndrome.

In our study, in nephrotic syndrome cases having psychosocial illness, those having duration of disease of >4 years, 63.04% were affected and 53.06% of those having ≤2 years of disease were affected. There is statistically no significant difference between Psychosocial illness with duration of disease (P-value 0.06065). In Manti et al¹¹ study the duration of the illness was associated with more anxiety/depression symptoms.

In our study, psychosocial illness was higher in cases who had higher number of relapses and there is statistically significant difference between Psychosocial illness with number of relapse (P-value 0.00002). Manti et al¹¹ observed that frequent relapses being associated with somatic complaints and externalizing/ aggressive behavior. Guha and colleagues¹⁶ demonstrated a significant association between behavioral problems and frequency of relapse. On the contrary to our results Ghobrial et al¹⁷ found that steroid dose, number of

relapses, or frequent use of immunosuppressant's did not affect psychological scores of the patients.

CONCLUSION

Nephrotic syndrome being the commonest chronic renal disease affecting the children was found to be significantly associated with higher prevalence of psychological abnormalities. The variables significantly increasing the risk of psychological abnormalities in our study were, longer duration of disease and steroid usage, FRNS and SDNS types of nephrotic syndrome and greater number of relapses. Children with nephrotic syndrome should be routinely screened for psychological and behavioral abnormalities so as to enable early intervention.

REFERENCES

1. Vogt BA, Avner ED. Conditions particularly associated with proteinuria: nephrotic syndrome. In: Behrman RE, Kliegman RM, Jenson HB, editors. Nelson textbook of pediatrics. 17 ed. New Delhi, India: Elsevier; 2004. pp. 1753–1757.
2. Warady BA, Chadha V. Chronic kidney disease in children: the global perspective. *Pediatr Nephrol* 2007;22:1999-2009.
3. Hall AS, Thorley G, Houtman PN: The effects of corticosteroids on behavior in children with nephrotic syndrome. *Pediatr Nephrol* 2003, 18(12):1220–1223.
4. Mehta M, Bagga A, Pande P, Bajaj G, Srivastava RN: Behavior problems in nephrotic syndrome. *Indian Pediatr* 1995, 32(12):1281–1286.
5. Belfer M L, Saxena S. 2006a. The Treatment of Child and Adolescent Mental Health Problems in Primary Care: A Systematic Review. *Family Practice* 18: 373–82.
6. Vance JC, Pless IB. The effect of chronic nephrotic syndrome on the affected child. *J Dev Behav Pediatr* 1983; 4:159–162.
7. Benner-Davis S, Heaton P C. Attention Deficit and Hyperactivity Disorder: Controversies of Diagnosis and Safety of Pharmacological and Nonpharmacological Treatment. *Current Drug Safety* 2007; 2: 33–42.
8. Chersich M F, Urban M, Olivier L, Davies L A, Chetty C. others. Universal Prevention Is Associated with Lower Prevalence of Fetal Alcohol Spectrum Disorders in Northern Cape, South Africa: A Multicentre Before-After Study. *Alcohol and Alcoholism* 2012; 47: 67–74.
9. Zyada F, Elbatrawy A, Khalifa D, Waly SG, Mouawad EM, Ahmed D. Psychosocial aspects of nephrotic syndrome among children and their caregivers: Middle East Current Psychiatry. 2013 Jul;20(3):164–71.
10. Mishra OP, Basu B, Upadhyay SK, Prasad R, Schaefer F. Behavioral abnormalities in children with nephrotic syndrome. *Nephrology Dialysis Transplantation*. 2010 Aug 1;25(8):2537–41.
11. Manti P, Giannakopoulos G, Giouroukou E, Georgaki-Angelaki H, Stefanidis CJ, Mitsioni A, et al. Psychosocial and cognitive function in children with nephrotic syndrome: association with disease and treatment variables. *BioPsychoSocial Med*. 2013 Dec;7(1):10.
12. Soliday E, Grey S, Lande MB. Behavioral effects of corticosteroids in steroid-sensitive nephrotic syndrome. *Pediatrics*. 1999 Oct;104(4):e51.
13. Stuart FA, Segal TY, Keady S: Adverse psychological effects of corticosteroids in children and adolescents. *Arch Dis Child* 2005, 90:500–506.
14. Heiniger N, Spaniol V, Troller R, Vischer M, Aebi C. A reservoir of *Moraxella catarrhalis* in human pharyngeal lymphoid tissue. *J Infect Dis* 2006; 196:1080–1087.

15. Neuhaus TJ, Langlois V, Licht C. Behavioral abnormalities in children with nephrotic syndrome—an underappreciated complication of a standard treatment? *Nephrol Dial Transplant* 2010;25:2397– 2399.
16. Guha P, Deaghosal M. Behavior profile of children with nephrotic syndrome. *Indian J Psychiatry* 2009; 51:122–126.
17. Ghobrial EE, Fahmey SS, Ahmed ME, Botrous OE. Behavioral Changes in Egyptian Children With Nephrotic Syndrome. 2013;7(2):9.