Global Academic Journal of Medical Sciences

Available online at www.gajrc.com
DOI: 10.36348/gajms.2023.v05i03.003

OPEN ACCESS

ISSN: 2706-9036 (P)
ISSN: 2707-2533 (O)

Original Research Article

Quality of Life in Children with Minimal Change Nephrotic Syndrome

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Article History
Received: 15.04.2023
Accepted: 19.05.2023
Published: 24.05.2023

Abstract: ***Introduction*:** Nephrotic syndrome (NS) in children is a common, yet challenging, relapsing, and remitting renal disorder and exhibits a heterogeneous clinical phenotype ranging from a single episode, infrequently relapsing, frequently relapsing to steroid-resistant disease. Although 80% of these children are corticosteroid responsive, nearly half of them demonstrate a frequently relapsing or steroid-dependent course, often resulting in multiple complications, hospitalizations, or even chronic renal failure. ***Objective*:** To assess the quality of life in patients with minimal change nephrotic syndrome. ***Methods*:** This cross-sectional, comparative, questionnaire-based study was conducted in Dhaka Shishu Hospital, Dhaka, Bangladesh July to December 2022. The cases included children with MCD, attending the pediatric nephrology unit and outpatient clinic of nephrology unit. 100 children were selected then they were randomly subdivided into 2 groups, group 1 included 50 known cases of MCD aged 2–18 years and group 2 included 50 age matched children attending the general pediatric outpatient clinic and other pediatric subspecialty clinics. We distributed two questionnaires to 32 outpatients with MCNS. We also used the Self-Care Behavior Scale for patients with chronic kidney disease (CKD), which consists of 31 questions with 4 subscales. ***Results*:** Total of one hundred studied nephrotic patients with MCD and an equal number of controls with other chronic diseases aged 2.2–15 year and 3.5–13 years, respectively, were included in the study. Table 1 illustrated the demographic details of the studied cases and controls. Among children with MCD, 32% had first attack or infrequently relapsing variant while 68% had difficult to treat clinical phenotypes (frequently relapsing, steroid– dependent and steroid-resistant varieties). The SF-36v2 social functioning subscale was most impaired and bodily pain was least affected in patients with MCNS. The self-care subscales of information/communication and positive behavior had positive correlations with the QOL subscales of mental health (< 0.05) and vitality ($p<0.05$). The correlation between social functioning and information/communication was close to significant (= 0.051). ***Conclusion*:** In conclusion, our findings suggest that patients with MCNS have lower QOL based on low social functioning and that QOL is related to the positive behavior and thoughts of the patients. These results also show that healthcare professionals should be conscious of the QOL of children with MCNS.

Keywords: Quality of Life, Minimal Change, Nephrotic Syndrome.

INTRODUCTION

Nephrotic syndrome (NS) in children is a common, yet challenging, relapsing, and remitting renal disorder and exhibits a heterogeneous clinical phenotype ranging from a single episode, infrequently relapsing, frequently relapsing to steroid-resistant disease [1]. Although 80% of these children are corticosteroid responsive, nearly half of

them demonstrate a frequently relapsing or steroid-dependent course, often resulting in multiple complications, hospitalizations, or even chronic renal failure [2]. Not infrequently, NS spans a significant portion of a child's formative years. For these reasons, quality of life (QOL) is an increasingly important issue in healthcare for chronic diseases. We have an interest in studying QOL of patients with renal diseases, as a typical example of chronic disease. The daily life of patients with renal disease is often limited by factors that are common to other chronic diseases, and these factors can easily decrease QOL [3, 4, 5]. The onset of minimal change nephrotic syndrome (MCNS) is usually sudden and many patients experience repeated relapses and have to take regular medications that cause various side effects [6]. This is the most widely used health-related QOL scale, and many previous studies have examined QOL of patients with renal diseases using this scale. Several studies have also shown a relationship between self- care and QOL in hemodialysis patients, and other studies have examined the relationship between self-efficacy and QOL [7-9]. Hence, a formal evaluation of the impact of the disease on physical, emotional, social, and school performance and health-related QOL (HRQOL) is imperative to provide comprehensive and holistic patient care.

MATERIALS & METHODS

This cross-sectional, comparative, questionnaire-based study was conducted in Dhaka Shishu Hospital, Dhaka, Bangladesh July to December 2022. The cases included children with MCD, attending pediatric nephrology unit and outpatient department. 100 children were selected then they were randomly subdivided into 2 groups, group 1 included 50 known cases of MCD aged 2–18 years and group 2 included 50 age matched children attending the general pediatric outpatient clinic and other pediatric subspecialty clinics.

Inclusion Criteria

All children of both sexes with INS who fulfilled clinical and or histopathological criteria of MCD. NS was defined by the International Study for Kidney Diseases in Children (ISKDC) criteria which included heavy proteinuria, hypoalbuminemia (serum albumin < 2.5 g/dL), hyperlipidemia (serum cholesterol > 200 mg/dL), and edema [4]. Nephrotic range proteinuria was defined as early morning urine protein 3+/4+ (on dipstick) and spot protein: creatinine ratio > 2 mg/mg. INS was pheotypically classified according to Bagga and Strivastava [5]. The cases group was managed by the routine protocol of management of nephrotic syndrome [5].

Exclusion Criteria

Children less than 2 years of age, as they mostly could not MCD or NS secondary to systemic diseases. The controls were required to have not any clinical or biochemical features of INS.

All the parents of included subjects were explained about the purpose of the study, and confidentiality of data collected was ensured. History included personal data (name, age, sex, address, telephone,) history of diseases or developmental disorders, socioeconomic level, age of 1st presentation, duration of disease, frequency of relapses was measured in studied cases group.

Subtype of Steroid Sensitive Nephrotic Syndromes which were:

a) Frequent relapsing nephrotic syndrome: This was defined as relapse ≥ 4 times per year or ≥ 2 times per 6 months. Relapse was defined as recurrence of proteinuria [urine albumin dipstick ≥ 2+ on 3 consecutive days, most often in association with recurrence of edema
b) Infrequent relapsing nephrotic syndrome: This was defined as relapse < 4 times per year or < 2 times per 6 months.
c) Steroid dependent nephrotic syndrome: This was defined as relapse every time with the withdrawal of steroids from every day to every other day therapy [5].

Clinical Examination

Included anthropometric measurements and vital signs especially arterial blood pressure which was measured by auscultatory method using a mercury sphygmomanometer , in the semi setting position after 10 minutes of rest, using an appropriate sized cuff and was taken as the mean value of 3 successive readings in 3 different days, presence of edema or presence of any complication either of the disease or for immunosuppressant agents used for treatment (e.g. prednisolone, Cyclosporin A, Cyclophosphamide, Mycophenolate moefetyl or others).

Laboratory Investigations (in the 1st visit only) including

Boiling test for urine sample, complete urine analysis, 24 hr. urinary proteins, complete blood count (CBC), erythrocyte sedimentation rate (ESR), serum albumin, total serum cholesterol and kidney function tests (BUN, serum creatinne).

QOL Assessment

Validity and reliability of used questionnaire- Data were collected using a validated Bangla version of structured questionnaire. It took

approximately 30 min to gather the required information from the parents of included subjects. The tool was piloted on 20 parents before initiation of the study. The tool evaluates the QOL in five domains: physical functioning (Eight Items), psychosocial functioning including emotional functioning (five items), social functioning (five items), and school functioning (5 items). The PedsQL scores range from 0 to 100 points. Recall time was one month and a 5-point response scale was used from 0 (never a problem) to 4 (almost always a problem). The scores of each item were then reversed and linearly transformed into a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0), with higher PedsQL scores indicating a better QOL. Parameters studied were QOL total score, QOL in social, emotional, physical, and school domains [4]. The questionnaires were filled through an interview with the child and the Caregiver, the questions were asked in lay language to the child if he was older than 6 years and to the caregiver if the child was ≤ 6 years [4].

Statistical Analysis

Continuous variables with normal distribution were expressed as mean values and standard deviation and compared using Student's t-test, whereas those not normally distributed were expressed as median and range and analyzed using Mann–Whitney U-test. Categorical variables were compared using Chi-square test or Fisher's exact test. One-way analyses of variance or Kruskal - Wallis tests were used to analyze statistical differences between three or more groups for parametric and nonparametric data, respectively. P < 0.05 was considered statistically significant. Data were evaluated using Statistical Package for the Social Science (SPSS) software version 16.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Total of one hundred studied nephrotic patients with MCD and an equal number of controls with other chronic diseases aged 2.2–15 year and 3.5–13 years, respectively, were included in the study. Table 1 illustrated the demographic details of the studied cases and controls. Among children with MCD, 32% had first attack or infrequently relapsing variant while 68% had difficult to treat clinical phenotypes (frequently relapsing, steroid–dependent and steroid-resistant varieties). The median duration of the disease was 33 months. The disease profile among the control children included chronic diseases, idiopathic epilepsy (15 cases), persistant asthma (8 cases), hemophilia (1 cases), beta thalassemia major (2 cases), hyperthyroidism (4 cases), hypothyroidism (7 cases), congenital heart disease (3 cases), chronic rheumatic heart disease (4 cases), attention deficit hyperactivity disorder (2 cases), autoimmune hemolytic anemia (2 cases), congenital dyserythro-poietic anemia (1 cases), and hypereosinophilic syndrome (1 case). Comparison of baseline characteristics of cases and controls revealed no statistical difference (p > 0.05) (Table 1).

Table 2 compared between the cases and controls according to the median PedsQL™ 4.0 Generic Core Scale scores. It was found that the median PedsQL™ 4.0 Generic Core Scale scores were higher in cases when compared to controls. There were significantly better scores in physical (P = 0.004), emotional (P = 0.03), and social functioning (P = 0.01) among the former. However, the school performance scores in cases versus controls were not significantly different from each other (p = 0.75).

Table 3 summarized comparison between QOL in different clinical phenotypes of the studied MCD and concluded no statistically significant differences between different clinical phenotypes regarding QOL (p>0.05). Univariate analysis for poor total QOL scores was performed for this study. Poor scores were defined as scores below the 25th percentile of the median total QOL score of cases. Demographic details such as age [OR: 0.5 (95% CI: 0.1-2.3)], gender [OR: 0.38(95% CI: 0.07-2.1)], duration of illness [OR: 0.86 (95% CI: 0.2-4)], steroid resistance [OR: 3.3 (95% CI: 0.36-30.1)], complications related to therapy [OR: 1.8 (95% CI: 0.2-17.6)], and per capita income and history of peritonitis [OR: 1.4 (95% CI: 0.14-14.1)] did not significantly influence the total QOL scores among our studied nephrotic children (P > 0.05). Similarly, univariate analysis for predictors of poor school performance QOL scores did not reveal the fore mentioned variables to be significant.

Table 1: Demographic and social data of studied groups (N=100)

	MCD Group (N=50)		Control group(N=50)		P value
	N	%	N	%	
Age (years)					
2-4	12	24	3	6	0.1
5-7	15	30	15	30	
8-12	16	32	27	54	
13-18	7	14	5	10	

Age at enrollement (years) range	2.2-15	7	3.5-13	8.5	0.1
Sex:					
Males	30	60	26	52	0.4
Females	20	40	24	48	0.6
Disease Duration (months) range	0.5-132	33	1-132	36	0.22
Relapse number range	1-16	4	-	-	-
Family income(Egyptian pound/month) range	400-1.250	800	285-3750	1000	0.8
Serum Albumin(g/dl) range	1.3-4.6	2.5	-	-	-
Serum cholesterol(mg/dl) range	151-450	323.3	-	-	-
Clinical types:					
Infrequently relapsing.	16	32	-	-	
Frequently relapsing.	15	30	-	-	
Steroid Dependent	9	18	-	-	
Steroid Resistant	10	20	-	-	-
Clinical picture:					
Edema	11	22	-	-	
Hypertension	20	40	-	-	

Table 2: Both group medications anf complications (N=100)

	MCD Group (N=50)		Control group(N=50)		P value
	N	%	N	%	
Prior Medications:					
Prednisolone	41	82	-		
Levamisol	20	40	-		
Cyclophoshamide	8	16	-		
Cyclosporin A	13	26	-		
Mycophenolate Mofetil	8	16	-		
Pnumococcal vaccine	15	30			
Complications:					
Peritonitis	4	8			
Complications of treatment:					
Cushinoid facies.	2	4			
Cataract.	3	6			

Table 3: PedsQL™ 4.0 Generic Core Scale Quality of Life scores in cases and controls.

	Cases		Controls		
	No (%)	Range (Median)	No (%)	Range (Median)	P value
Physical scores: Range (Median)	50(100%)	58.6-75(71.9)	50(100%)	58.6-68.8(63)	0.004*
Emotional scores: Range (Median)	50(100%)	55-65(65)	50(100%)	55-65(60)	0.03*
Social scores Range (Median)	50(100%)	63.8-75(70)	50(100%)	60-70(65)	0.01*
School scores Range (Median)	40(80%)	56.3-65(63)	48(98%)	53-65(65)	0.75
Total score	40(80%)	59-68.8(65)	48(98%)	58-65.8 (62.2)	0.01*
**P* value significant (<0.05).					

Table 4: Comparison of PedsQL™ 4.0 Generic Core Scale quality of life in different clinical phenotypes of studied MCD.

	Steroid dependent and frequently relapsing (SDNS/FRNS) (N=24)	Steroid resistant (SRNS)(N=10)	Infrequently relapsing and first episode (N=16)	P value
Physical scores: Range(Median)	56.3-75(68.8)	65.6-75(71.9)	65.6-75(71.9)	0.72
Emotional scores Range (Median)	51.3-70(63)	60-71.3(60)	56.3-75(63)	0.3
Social scores Range (Median)	65-75(70)	63.8-75(73)	60-75(70)	0.66
School scores Range (Median)	58.8-65(60)	60-65(65)	55-65(60)	0.53
p value is significant <= 0.05				

DISCUSSION

In pediatric age, patients with chronic diseases as NS. Most of publications and clinical articles focus on the effects of disease activity itself more than long term sequlae. Recently, it is increasingly identified that the impacts on HRQOL is not related to disease activity and therapy but also affected by the cumulative psychological, emotional, behavioural and social effects of the illness as well as drug intake [10, 11]. Among the self-care subscales, scores for information/communication and positive behavior had positive correlations with the QOL subscales of mental health and vitality. In the United States, it has been shown that hemodialysis patients have lower QOL scores than CKD patients and that CKD patients have lower QOL scores than the general population for all items except mental health [9]. Ru¨th *et al.,* found that pediatric patients with nephrotic syndrome had lower scores for social functioning compared with healthy children using another QOL scale [2]. The lower scores for social functioning were significantly related to steroid dependency and cyclophosphamide therapy among illness-related variables and were also related to the number of relapses, although without a significant association [1, 3, 12]. A better understanding of HRQOL in such pediatric patients could help to improve the prognosis of the disease. The flexibility, reliability, and validity of PedsQL core and modular design made it a simple famous tool in a variety of research publications and clinical applications for chronic health hazards in children and adolescents. PedsQL™ 4.0 Generic Core Scale is a previously well used legacy tool that evaluates the body (physical), feelings (emotional), social, and school achivements [8, 9]. There were few research studies regarding QOL in children with NS [10, 13]. Most of published articles have included adult patients or have included patients from Western countries with relatively high socioeconomic standars [12]. So, their occlusions cannot be generalized to other communities. The present study concluded a better QOL in pediatric patients with MCD when compared with other chronic pediatric diseases. More interestingly, we concluded that the assessment of physical, affective, and social performance was better than pediatric patients with other chronic pediatric diseases. This led to a good compliance and a good follow-up of included patients. However, an important conclusion was that the school achievement scores in our nephrotic patients were not different from diseased controls in contrast to the other domains in HRQOL. An analysis of the PedsQL Inventory questionnaire results revealed that all school-going children with INS enrolled in the study, “missed some school days to go to the doctor or hospital” or “missed some school days because of not feeling well.” The recurrent or relapsing sequlae nature of disease in INS in pediatric age caused irregular school attendance and children may found it was difficult for them to adapt with the burden of missed lessons in addition to interrupted teachers interactions. Moreover, the integration of nephrotic school children into the classroom situation might be disturbed secondary to inadequate school environment included lack of health education of teachers who had insufficient knowledge about the nephrotic syndrome and inability to spend adequate compensatory times with these patients [13]. There are few available publications as regard the evaluation of HRQOL in pediatric patients with MCD, especially from developing countries like Asian and Arab countries. Ruth *et al.,* evaluated QOL, psychological and social adjustment by standardized questionnaire in 45 European pediatric patients with steroid-sensitive NS from the Netherlands. Only the QOL subscale “social function” was impaired while other domains were not affected [10]. In USA, an evaluation of QOL using PedsQL Inventory in 127 American children with prevalent NS as compared to incident NS showed poor scores in social and school performances [12]. In contrast, most Asian studies from India have described the behavioral profile of children with INS, but data regarding QOL in pediatric nephrotic patients was seldom. The emotional and social domains of HRQOL in children with chronic diseases have been assumed to be markedly attributed to ethnic, sociocultural, and socioeconomic status [13]. So the situation different from children in the Western world and could explain the differences in results of our study in comparison to Western countries. This is the first study evaluating HRQOL in acohort of pediatric NS in South India using a validated and flexible measurement model, namely PedsQL™ 4.0 Generic Core Scale and is particularly consistent with the paltriness of information in QOL in this patient population. The recruitment of controls with chronic ailments involving other systems provides a reasonable comparative assessment of QOL that has been performed in earlier studies as well [12,13]. Our results suggest that nephrotic syndrome has an impact on social functioning of patients with MCNS, and previous findings suggest that QOL may also be influenced by steroid dependency, method of treatment, and depression. However, MCNS has a benign prognosis, and QOL of patients with MCNS may be better than that of CKD patients. We suggest that healthcare professionals should consider improving self-care not only to improve chronic diseases but also to improve self-efficacy for better QOL in these patients. The present study has some limitations. Although factors such as age, gender, duration of illness, clinical type of NS, per capita income, and the immunosuppressive drugs provided

for the patients were evaluated for their possible contribution to poor QOL scores, the study could not demonstrate any statistically significant influence. This could be due to a relatively small sample size which was inconsonance with the short duration of study. The study is also limited by its cross-sectional nature as a result of which a long-term follow up of this cohort was not undertaken.

CONCLUSIONS

The overall QOL in children with NS was better when compared with other chronic pediatric illnesses. Clinical phenotypes of NS and demographic parameters did not affect the QOL. Although further studies are needed to confirm the findings of this study and explore the underlying cause of school absences, it is suggested that school level interventions, especially in schools with a larger number of low- income students should be explored as a strategy to reduce school absenteeism due to NS. Improving attendance in these children requires a multifaceted approach directed toward psychosocial interventions.

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