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The quality of life in children with nephrotic syndrome at Prof I.G.N.G Ngoerah Hospital, Denpasar, Bali

Luh Putu Eka Sari Kresnandari[1]*, Gusti Ayu Putu Nilawati[1], I Gusti Ayu Trisna Windiani[1], I Gusti Agung Ngurah Sugitha Adnyana[1], Soetjiningsih[1], Bagus Ngoerah Mahakrishna[1], Ni Luh Sukma Pratiwi Murti[1]

[1]Departement of Child Health, Medical School, Universitas Udayana/ Prof. Dr. IGNG Ngoerah Hospital

*Corresponding to:
Luh Putu Eka Sari Kresnandari; Departement of Child Health, Medical School, Universitas Udayana/ Prof. Dr. IGNG Ngoerah Hospital;
sarikresnandari@gmail.com

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ABSTRACT

Introduction: Nephrotic syndrome (NS) is a common chronic renal disease in children. For chronic illness, the patients requested regular hospital visits and required long term use of steroids or immunosuppressive agents. Besides agents needing therapy, the patients also face the probability of recurrent disease, multiple complications, hospitalization, side effect of treatment and fall into chronic renal disease. The impact could be physical or psychological (emotional, social, school performance). Thus, in this article, we provide the quality of life (QoL) evaluation among children with NS in Prof Dr. I.G.N.G. Ngoerah Hospital, Denpasar, Bali.

Methods: This cross-sectional study was conducted at Prof. Dr. I.G.N.G. Ngoerah Hospital, Denpasar, Bali. The cases included 60 children with NS aged 2–18 years diagnosed as NS based on the medical record and attended a pediatric nephrology clinic from January 2022 until July 2022. The patient's quality of life was assessed using the Pediatric Quality of Life Inventory (PedsQL) generated from 4.0. All the data were analyzed descriptively by using SPSS version 25. The data will be provided in the table.

Result: There were sixty children as study subjects, consisting of 36 (60%) male and 24 (40%) female. The Male gender was more dominant in this study (60% of study subjects). Female patients, lower-income families, duration of illness less than 1 year, group B NS (SRNS, steroid dependence NS), and children not in remission phase and on cyclophosphamide therapy demonstrate a higher proportion of QoL disturbance.

Conclusion: According to this study, we can conclude that most of the NS patients have not disturbed QoL based on the child and the parents' reports.

Keywords: nephrotic syndrome, children, quality of life.

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INTRODUCTION

Children frequently develop the chronic glomerular condition known as nephrotic syndrome (NS). Due to their chronic illness, the patient requested frequent hospital visits and long-term steroid or immunosuppressive drug use.[1] Massive proteinuria (>40 mg/m2/hour or protein/creatinine ratio >2 or dipstick >+2), hypoalbuminemia (2,5 g/dL, edema, and/or hypercholesterolemia (>200 g/dL) are a collection of symptoms that are associated with nephrotic syndrome.[2] With a prevalence of around 16 cases per 100,000 children under the age of 14, idiopathic nephrotic syndrome (INS) is the most prevalent glomerular condition in pediatric nephrology.[3] In Indonesia, the prevalence is about 6 per 100.000 children—3 Incidences of 2 to 7 per 100.000 children per year.[4,5] Most cases of children with nephrotic syndrome (90%) are idiopathic (not associated with systemic disease).[4]

Nephrotic syndrome is linked with significant morbidity; the majority of patients experience repeated episodes. Numerous persons suffer from the steroid-dependent nephrotic syndrome (SDNS), steroid-resistant nephrotic syndrome (SRNS), or the frequently relapsing nephrotic syndrome (FRNS).[2] This illness also has several adverse effects, necessitates hospitalization, and can lead to chronic renal disease stage failure. The quality of life (QoL) will be impacted by each of these conditions.[6]

Nephrotic syndrome has been shown to have a detrimental effect on the quality of life (QoL) of afflicted children.[7,8] Steroid resistance, dependency on steroids, use of cytotoxic treatment, frequent relapses, severe disease, low socioeconomic status, and extended length of illness are all

variables linked to lower scores. The QoL ratings did not substantially change between the various clinical types of NS, according to a study by Agrawal et al.[6] The overall QoL ratings of the children with nephrotic children were not significantly influenced by demographic information. According to this study, children with NS had a higher overall quality of life than kids with other chronic conditions.[6]

Patients seek medical advice for physical or psychological reasons, which may be evaluated using Health-Related Quality of Life (HRQoL) assessments (e.g., emotional, social, or academic performance). The results of those measures' scores may be used to forecast clinical outcomes in terms of morbidity.[2] Pediatric HRQoL is measured using the Pediatric Quality of Life Inventory (PedsQL) assessment methodology, which uses a modular design. The PedsQL may be used effectively with both healthy kids and kids with acute and chronic disorders, according to the available evidence.[7] There is currently a lack of information on the quality of life for children and adolescents in Indonesia who have NS. The current study's objective is to determine the frequency of quality of life (QoL) disruption in children with NS at Prof. I.G.N.G. Ngoerah Hospital.

METHODS

Study design and sampling

This cross-sectional study was conducted at Prof I.G.N.G. Ngoerah Hospital, Denpasar, Bali. The subject was collected by consecutive sampling. The cases included 60 children aged 2–18 years diagnosed as NS based on the medical record, attending a pediatric nephrology clinic from January 2022 until July 2022. Children with physical and cognitive impairment or another systemic disease affecting PedsQL score were ruled out.

Variables

Nephrotic syndrome is a kidney disorder characterized by 4 major clinical characteristics: massive proteinuria, hypoalbuminemia, edema, and hyperlipidemia.[3] In terms of response to steroid therapy, this study divided into two groups, namely: Group A NS include: Steroid sensitive nephrotic syndrome (SNSS) is a remission that occurs after 4 weeks of full-dose prednisone (2mg/kg/day or 60 mg/m^2, with maximum dose 80 mg/day). Frequent relapsing nephrotic syndrome is NS, with two or more relapses within 6 months or four or more relapses within 12 months. Infrequent relapsing nephrotic syndrome if NS has less than two relapses within six months or less than four relapses within 12 months of response. Group B NS includes steroid-resistant nephrotic syndrome is the failure to achieve remission on full-dose prednisone for 4 weeks. Steroid dependence NS is two consecutive relapses within 2 weeks of ceasing therapy. The remission phase is negative or trace proteinuria or proteinuria +1 (proteinuria < 4 mg/m2/hour) for 3 consecutive days in 1 week.

PedsQL Version 4.0 is a screening tool. The quality of life measurement scale on the Peds-QL questionnaire is in the form of closed questions, namely by choosing the already available answers. Assessment is given with a number of 0-4 for each question item. For value 0 = there has never been a problem with the item in question; 1= almost never have a problem with the item in question; 2= sometimes there is a problem with the item in question; 3= there is often a problem with the item in question; 4 = there is always a problem with the question item. Each question answered is converted on a scale of 0-100 for standard interpretation, 0 = 100; 1= 75; 2= 50; 3= 25; 4= 0. The total score is calculated by adding the value of the questions answered divided by the number of questions answered in all fields. Interpretation: The higher the mean score of the answer and the closer to 100, the better the QoL. Scores below 70 (for children aged≥ 8 years old) and below 77 (for children aged < 8 years) show the QoL is disturbed; meanwhile, scores ≥ 70 (for children aged≥ 8 years old) and ≥ 77 (for children age < 8 years) is normal QoL.

Economic status is the cumulative salary of both parents. This study's cut-off is based on Denpasar's minimum regional wage income, Rp 2.500.000/month. Financial status is divided into lower middle income if monthly payroll is below regional minimum wage and upper median income.

Duration of illness is the duration when the diagnosis is established until the time of collecting data. According to the WHO chart, nutritional status is defined by measuring weight per height for children aged 2-5 years and body mass index (BMI) per age for children aged 5-18. The type of medication is the current patient presentation for treating NS.

Research procedure

The study was conducted after the ethical clearance had been approved. The study was approved by the Research Ethics Committee of The Faculty of Medicine Udayana University/ Prof. Dr. I.G.N.G Ngoerah General Hospital Denpasar (275 /UN14.2.2.VII.14/LT/2022). The samples that fit the criteria were then interviewed using a structured questionnaire using PedsQL™4.0 Generic Core Scale. All the data were extracted and coded before being analyzed in SPSS.

Analysis statistic

The data were analyzed by using SPSS for window version 25.0. Descriptive statistical analysis was conducted to describe the general characteristics of the research subjects. Variables with numerical data scales were displayed in median and interquartile ranges because the data was not normally distributed. Variables with categorical data scales were declared relative frequency (amount and percent). The descriptive analysis results were presented using a single distribution table.

RESULTS

There were sixty children as study subjects, consisting of 36 (60%) males and 24 (40%) females. The median and interquartile (IQR) range age was 6-18 years, respectively. The number of subjects between the two groups was similar according to socioeconomic status. Subject's nutritional status in this study was dominantly well nourished (63.3%), followed by obesity in 20% of subjects. A total of 40 (66.7%) subjects were in group A NS (SSNS, infrequent relapsing and frequent relapsing NS), and the remaining (33.3%) were in group B (SRNS and steroid dependence NS). Patients achieved the remission phase when data was collected from around 43 (71.7%) persons and still on relapse or failed to achieve remission

around 17 (28.3%) persons. Based on the child report there was 29,1% of patients had QoL disturbance, and the parents reported 30% QoL disturbance (**Table 1**).

We divided the characteristics of the PedsQL report based on the child report and parents' report (**Tables 2** and **3**). Meanwhile, only 55 samples of pediatric QoL reports were usable. Based on another characteristic, the male gender was more dominant in this study (60% of study subjects). Female patients were known to have a higher percentage of QoL disturbance compared with males in both groups. Regarding the duration of illness, the child report shows a similar number of QoL disturbances. Meanwhile, parent report demonstrates that children whose duration of illness was less than 1 year had a higher percentage of QoL disturbance. Children and parents from upper middle income have a lower proportion of QoL disturbance.

Group B patients have a similar number of QoL disturbances regarding child reports. Still, a higher percentage of QoL disturbance was shown in parent reports. Both children and parents' reports experienced higher QoL disturbance scores when children were not in the remission phase (**Tables 2** and **3**). Various PedsQL scores were demonstrated according to the type of therapy. Children who were using cyclophosphamide showed a higher percentage of disturbance of QoL.

Table 1. Characteristics of study subjects

Characteristics	Total Sample n=60
Gender, n (%)	
Male	36 (60)
Female	24 (40)
Age, median year (IQR)	12 (6-18)
The onset of diagnosis, median year (IQR)	7 (2-17)
Social economy, n (%)	
Lower middle	28 (46.7)
Upper middle	32 (53.3)
Nutrition status, n (%)	
Obesity	12 (20)
Overweight	3 (5)
Well-nourished	38 (63.3)
Mild protein energy malnutrition	4 (6.7)
Moderate protein energy malnutrition	3 (5)
Diagnosis, n (%)	
Group A NS (SNSS, frequent, infrequent relapsing NS)	40 (66.7)
Group B NS (SRNS, steroid dependence NS)	20 (33.3)
Duration of illness,n (%)	
≤1 year	25(4.7)
>1 year	35(58.3)
On Remission Phase, n (%)	
Yes	43 (71.7)
No	17 (28.3)
Type of Therapy	
Full dose prednisone	17 (28.3)
Tapering dose prednisone	22 (36.7)
Cyclophosphamide	10 (16.7)
Not in any medication	11 (18.3)
PedsQL, according to the child report	
Disturbed	16 (29.1%)
Not disturbed	39 (70.9%)
PedsQL, according to the parent's report	
Disturbed	18 (30%)
Not disturbed	42 (70%)

NS: nephrotic syndrome. SNSS: steroid-sensitive nephrotic syndrome. SNRS: steroid-resistant nephrotic syndrome
PEDS QL: The Pediatric Quality of Life Inventory

DISCUSSION

Nephrotic syndrome is a common chronic renal disease in children. As a chronic disease, the patient requested a regular visit to the hospital and required long term use of steroids or an immunosuppressive agent (the immunosuppressive agent commonly used in this hospital for pediatric nephrotic syndrome is intravenous cyclophosphamide, so for administration, patients are expected to be hospitalized monthly). Besides prolonged therapy, the patients also face the probability of recurrent disease; all these conditions negatively impact the quality of life, daily activities, and even social interaction.[2]

In this cross-sectional study, we demonstrate the QoL characteristics of NS children. Prior studies frequently used PedsQL to evaluate four domains of QoL: physical functioning, emotional functioning, social functioning, and school functioning scale. A higher score interprets better QoL.[1] In Table 1, sixty percent (60%) of the subjects were boys. This study has the same result as other studies that showed most NS patients were boys (71 - 80%).[1,11] Female gender in this study has a higher percentage of QoL disturbance. This result is consistent with the previous research in China, which showed significant differences in QoL (particularly in school functioning) between males and females.[1,12] Lower QoL in females approximately due to problems in emotional and social functioning domains, feeling embarrassed with change in appearance, sadness and fear about the treatment.[1]

Duration of illness regarding child report demonstrates children whose condition is less than 1 year has a similar number of QoL disturbances. Still, in parent's report duration of illness, less than 1 year shows a higher percentage of QoL disturbance. We assumed from brief interviews that patients, parents, and caregivers with disease duration of less and more than one year have diverse understandings and coping systems for

Table 2. Quality of life characteristic of NS children based on child reports in several

	QoL disturbed n=16	QoL not disturbed n=39
Gender (n, %)		
Male	7 (20)	28(35)
Female	9 (45)	11(20)
Duration of illness (n, %)		
≤ 1 year	8 (14.5)	14 (25.5)
>1 year	8 (14.5)	25 (45.5)
Socio economic (n, %)		
Lower-income	10 (18)	15 (27)
Upper middle income	6 (11)	24 (44)
Nutrition status (n, %)		
Moderate protein energy malnutrition	3 (5)	0
Mild protein energy malnutrition	1 (1.8)	3 (5)
Well-nourished	6 (11)	28 (51)
Overweight	1(1.8)	3 (5.4)
Obesity	5 (9)	5 (9)
Diagnosis (n, %)		
Group A NS (SNSS, frequent, infrequent relapsing NS)	8 (14.6)	29 (52.7)
Group B NS (SNRS, steroid dependence NS)	8 (14.6)	10 (18.1)
Remission Phase (n,%)		
Yes	6 (11)	17 (31)
No	10 (18)	22 (40)
Type of therapy (n,%)		
Cyclophosphamide	6 (11)	5 (9)
Full dose prednisone	4 (7.2)	13 (24)
Tapering dose prednisone	4 (7.2)	12 (22)
Not in any medication	2 (3.6)	9 (16)

QoL: quality of life. NS: nephrotic syndrome. SNSS: steroid-sensitive nephrotic syndrome. SNRS: steroid-resistant nephrotic syndrome.

managing their illness. There is previous study stated that incomplete acceptance, adaptation to life, medication, and dietary changes relate to disturbance of QoL.[12,13]

Quality of life according to socioeconomic status revealed a higher proportion of QoL disturbance in lower-income families. A similar result was demonstrated either by a child's or a parent's reports. This study aligned with the previous survey; family income per month and type of family had significant differences in QoL among children with chronic disease.[14] According to our findings, we can conclude that even though all our subjects are covered by government health insurance, they still must spend travel expenses to hospital and provide healthy nutrition for their children diet moreover, parents whose occupations were private worker will lose their profit due to absence from work. All these reasons will affect the QoL.

The higher educational level usually affects family income. A study by Pardede et al.[15] divided the academic group of either father or mother, with the result significantly higher value of PedsQL at a higher father educational level. The study by Xiang et al.[16] demonstrates that parents with low academic levels tended to have lower health literacy, usually come from rural areas, and relate to lower income which would probably make poor child health outcomes. All lead to more unintended hospital admission.

Mostly our subjects' nutritional status was well nourished, and this finding is similar to a study by Albar et al.[17] in Wahidin Sudirohusodo Hospital, Makassar, whose nutritional status of pediatric NS dominantly (about 56.3%) was well nourished. The study by Sudihardjo et al.[18] in Surabaya found well-nourished patients were 74.2%, undernourished 1.5%, severely malnourished 11.5% and obesity 2.8%. Factors probably contribute, including early diet intervention and socioeconomic status.[17] Our study found that patients with mild protein-energy malnutrition, well-nourished and overweight still had a lower proportion of QoL disturbance than patients with moderate protein-energy malnutrition and obesity. Different results were found in a previous cross-sectional report in the UK which did not demonstrate lower QoL in obese children with chronic disease, and it was explained because, in the UK, they were not burdened by their body image.[19]

Children diagnosed in group B (SRNS and steroid dependence NS) have a higher proportion of QoL disturbance the group A (SSNS, frequent and infrequent relapsing NS). In correlation with Mbanefo et al. study[2], these finding is consistent. Their study stated that SNRS patients had poorer scores.[2] Most patients who cannot achieve remission after full dose steroid therapy should get intravenous cyclophosphamide monthly regarding protocol for SRNS. Even though all these patients were covered by government health insurance, they still need to make more frequent hospital visits so they will lose several times of school attendants. It also affects their parent or caregiver's life, and parents tend to be more protective, worry and limit their child's activities. Previous studies also indicate that caregiver stress can hurt the child's psychosocial adjustment and QoL.[20]

Patients not in remission also have a higher proportion of QoL disturbance since the condition makes limitations for doing daily activities, feeling discomfort and fear. Moreover, they usually lose engagement with their friend and are absent from formal school because they need to rest. Similar to this finding, a study conducted by Mbanefo et al.[2] explained that children in the relapse phase have poorer physical and school performance scores. They cannot run and carry out routine daily physical activities in the physical domain. They also easily get fatigued related to the disease's severity.[20] Cases with edema are said to be more likely to have impaired emotional and social domain sub-scores.[21]

Table 3. Quality of life characteristic of NS children based on parents' report

	QoL disturbed n=18	QoL not disturbed n=42
Gender (n, %)		
Male	7 (11.7)	29 (48.3)
Female	11 (18.3)	13 (21.7)
Duration of illness (n, %)		
<1 year	10 (16.7)	15 (36)
≥1 year	8 (13.3)	27 (64)
Socio economic (n, %)		
Lower-income	10 (16.7)	18 (30)
Upper middle income	8 (13.3)	24 (40)
Nutrition status (n, %)		
Moderate protein energy malnutrition	3 (5)	0
Mild protein energy malnutrition	1 (1.6)	3 (5)
Well-nourished	8 (13.3)	30 (50)
Overweight	1(1.6)	2 (3.3)
Obesity	5 (8.4)	7 (11.7)
Diagnosis (n, %)		
Group A NS (SNSS, frequent, infrequent relapsing NS)	8 (13.3)	32 (53.3)
Group B NS (SNRS, steroid dependence NS)	10 (16.7)	10 (16.7)
Remission Phase (n, %)		
Yes	4 (6.7)	22 (36.7)
No	14 (23.3)	20 (33.3)
Type of therapy (n, %)		
Cyclophosphamide	4 (6.7)	6 (10)
Full dose prednisone	6 (10)	11(18.3)
Tapering dose prednisone	7 (11.7)	15(25)
Not in any medication	1 (1.7)	10(16.6)

QoL: quality of life. NS: nephrotic syndrome. SNSS: steroid-sensitive nephrotic syndrome. SNRS: steroid-resistant nephrotic syndrome.

Children in cyclophosphamide had the highest proportion of QoL disturbance compared to other groups. Patients on tapering dose prednisone who had already stopped medication had a lower ratio of QoL disturbance. All are related to the remission phase itself. This result was in line with the study by Roussel,[9] patients who were still on relapse or grouped as SRNS or dependent steroid NS tend to have worsened clinical conditions and need to do frequent hospital visits.[22] It must be considered that QoL can be different during relapse.

Varni et al.[23] established Peds-QL cut-off values for children < 8 years old, namely 83 for healthy children, moderately ill 79, and chronic diseases 77. For children aged ≥8 years, the score for healthy children is 78. For rather poorly, it is 76, and for chronic diseases is 70.[23] In our study, we use cut-off points for chronic disease. Based on child report there was 29,1% of patients had QoL disturbance, and parents reported that 30% had QoL disturbance. Our study has a relatively similar result compared with Pardede et al.[15] which the percentage of QoL disturbance based on child reports counted as around 29.7%—based on the parent's information, disruption of QoL calculated as about 24.3%.

This initial study evaluates QoL in our hospital pediatric patients with nephrotic syndrome. This was only done in a single-center study, leading to variations between other centers might occur. Another area for improvement of this study is cross sectional design, which cannot strongly conclude the relation of each characteristic to PedsQL value. We recommend for longitudinal cohort study with a larger sample that can observe initial QoL when diagnosed with NS until they complete treatment.

CONCLUSION

According to this study, we can conclude that most of the NS patients have not disturbed QoL based on the child and the parents' reports.

CONFLICT OF INTEREST

The author reports no conflicts of interest in this work.

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AUTHOR CONTRIBUTIONS

Study design, data collection, statistical analysis, result interpretation, and manuscript preparation: LPESK. Study design, result interpretation, and manuscript preparation: GAPN, IGATW, IGANSA, S. Study design and manuscript preparation: BGM, LSPM. All authors reviewed and approved the final manuscript.

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