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# Assessment of health-related quality of life of children with idiopathic nephrotic syndrome and their caregivers in China

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## Abstract

**Aims** The primary aim of this study was to characterize the health-related quality of life (HRQoL) and identify the associated factors among children aged 2 to 18 in China diagnosed with idiopathic nephrotic syndrome (INS). Additionally, the study aimed to evaluate the HRQoL and caregiving burden of their caregivers and investigate the correlation between the HRQoL of the children and that of their caregivers.

**Methods** This study recruited 181 children diagnosed with INS from Children's Hospital, Zhejiang University School of Medicine in China. The proxy-reported PedsQL Generic Core Module (PedsQL™ 4.0 GCM) was used to measure the HRQoL of children, and the EuroQol five-dimensional questionnaire, five-level version (EQ-5D-5L) was applied to measure caregivers' HRQoL. Differences in scale scores and total scores of PedsQL™ 4.0 GCM were assessed using t-tests and one-way ANOVA. Multivariate linear regression analysis was used to identify the factors associated with children's HRQoL. Pearson correlation analysis evaluated the correlation between children's HRQoL and caregiver's HRQoL.

**Results** HRQoL of Children with INS declines with increasing age, and children aged 5-18 had lower scores in physical functioning, emotional functioning, school functioning, psychosocial health summary score, and total PedsQL™ 4.0 GCM score compared to healthy children. Various factors, including the mother filling out the questionnaire, the father being unemployed, and the use of other medications except for steroids, were associated with worse HRQoL of children ( $p$  values < 0.05). Additionally, a correlation exists between children's HRQoL and their caregivers' HRQoL.

**Conclusion** This study evaluated the HRQoL of children aged 2-18 years diagnosed with INS in China, along with the HRQoL of their caregivers. Multiple factors potentially influence the HRQoL of children. A significant correlation

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was observed between the HRQoL of children and their caregivers, who frequently experienced varying levels of caregiving burden. Therefore, it is recommended that healthcare professionals prioritize optimizing HRQoL for children with INS and their caregivers.

**Keywords** Quality of life, Idiopathic nephrotic syndrome, Burden of disease, Children, Caregiver

## Background

Numerous glomerular disorders in pediatric populations present as nephrotic syndrome, with a majority being idiopathic in origin. Idiopathic Nephrotic Syndrome (INS), a common manifestation of chronic kidney disease, represents a major cause of morbidity and mortality globally among children and young adults [1, 2]. INS is clinically defined by the triad of proteinuria, hypoalbuminemia, and edema [3, 4]. The incidence of INS ranges from 1.15 to 16.9 per 100,000 children, with variations observed across different races and geographical regions [5]. Clinical manifestations in children can range from mild to severe, with unpredictable patterns of relapse and remission [4, 6]. The standard initial therapeutic intervention generally entails the administration of glucocorticoids. INS is frequently categorized based on the clinical response to steroid treatment into steroid-sensitive (SS) and steroid-resistant (SR) forms. In instances where the disease is categorized as SR or in cases of relapse, the utilization of oral immunosuppressive drugs (OID) may be necessary for select pediatric patients [5, 7, 8]. The prolonged treatment duration and the propensity for relapse in INS have substantial implications for the health-related quality of life of affected children and their families [8].

Health-related quality of life (HRQoL) encompasses multiple dimensions, including physical, psychological, and social aspects related to health. This concept serves as a critical indicator, complementing traditional health outcomes such as morbidity and mortality [9, 10]. HRQoL is influenced by both individual and environmental characteristics [11]. Impaired HRQoL in children with INS has been well-documented in previous studies [11–15]. Factors associated with HRQoL include the duration of INS, gender, race, socioeconomic status, frequency of relapse, steroid resistance, and the use of calcineurin inhibitors (CNI) [6, 7, 9, 11, 14, 16–19]. However, the majority of these studies have been conducted in developed countries, with limited data available from developing countries. A review of the literature reveals studies on the HRQoL of children with INS from Sudan, Egypt, India, and Iran, and one study from China [9, 11, 17, 20–22]. Moreover, previous studies have been limited by relatively small sample sizes, particularly among younger children, resulting in an incomplete understanding of the current status and determinants affecting the

quality of life of Chinese children with INS. Additionally, there is a notable lack of data regarding the quality of life of caregivers of pediatric patients with INS.

Therefore, we conducted this study to assess the HRQoL of pediatric patients diagnosed with INS and their caregivers. The primary objective was to evaluate the HRQoL and identify the associated factors among children aged 2 to 18 years in China with INS. Furthermore, we aimed to assess the HRQoL of caregivers and investigate the correlation between the HRQoL of children and that of their caregivers.

## Methods

### Study design and participants

This was a cross-sectional, questionnaire-based survey that was led by the Department of Child Health Care and the Department of Nephrology at Children's Hospital, Zhejiang University School of Medicine. Participants were recruited from both outpatient and inpatient populations within the hospital, as well as from an online community facilitated through a WeChat group specifically designed for clinician-patient communication. WeChat, a multifunctional Chinese application, supports instant messaging, social media interaction, and payment services. The WeChat group served as a crucial adjunct to healthcare by disseminating disease-related knowledge and family care skills to caregivers, thereby offering them both professional and peer support.

The inclusion criteria for the study encompassed children who (1) had been diagnosed with INS; and (2) were under 18 years of age. The exclusion criteria comprised children who (1) had other severe physical or psychiatric disorders; and (2) whose caregivers were unable to comprehend and complete the questionnaire. Primary caregivers who were very familiar with the children's health status were invited to participate in the survey. The online survey was administered from January to August 2024. Ultimately, caregivers of 181 patients diagnosed with INS completed the questionnaire.

### Ethical approval statements

This study was conducted according to the Declaration of Helsinki [23], and was approved by the Medical Ethics Committee of the Children's Hospital, Zhejiang

University School of Medicine (2024-IRB-0294-P-01). All caregivers gave their consent to participate in the study.

### Data collection

An expert panel was convened to develop the questionnaire, comprising three senior clinicians (XW, JW, and JM) and one clinical epidemiologist (GB). The questionnaire was drafted following two rounds of discussion, informed by a review of the literature and expert opinions. Subsequently, a pre-test pilot was conducted within 20 caregivers of children with INS. Additionally, brief face-to-face interviews were conducted with eight caregivers post-pilot to gather their feedback and suggestions. A revised version of the electronic questionnaire was ultimately employed for this study, comprising four sections: general characteristics, disease- and treatment-related characteristics, HRQoL of children, and HRQoL of caregivers. The electronic questionnaire was developed and visualized by two research assistants (LG and YS) utilizing Wenjuanxing (<https://www.wjx.cn/>), a widely used online platform for creating survey questionnaires. We produced and distributed the poster featuring the QR code throughout the clinics and wards of the Department of Nephrology at the hospital where the study was conducted. Additionally, the QR code was distributed through the WeChat group. Clinicians participating in this study provided detailed explanations of its objectives to caregivers, ensuring comprehensive understanding prior to obtaining their informed consent for participation.

General characteristics encompass socio-demographic factors, such as children's age and gender, parental education, household income, marital status, and employment status, as well as medical insurance. Clinical characteristics include the onset time of INS, the time of diagnosis patient type (i.e., inpatient or outpatient), complications (e.g., hematuria, hypertension), and prescribed medications.

Children's HRQoL was assessed using the proxy-reported PedsQL™ 4.0 Generic Core Module (PedsQL™ 4.0 GCM). Prior to data collection, authorization to use this instrument was obtained through a request on the Mapi Research Trust website (<https://eprovide.mapi-trust.org/instruments/pediatric-quality-of-life-inventory>), which allowed us to download the PedsQL™ 4.0 GCM without a license fee for unfunded research. The proxy-reported PedsQL™ 4.0 GCM is administered to evaluate HRQoL in children and adolescents aged 2–18 years. For children aged 2 to 4 years, the instrument comprises 21 items distributed across four scales: physical functioning (eight items), emotional functioning (five items), social functioning (five items), and school functioning (three items). The instrument designed for

children aged 5 to 18 years includes 23 items, also organized into four scales: physical functioning (eight items), emotional functioning (five items), social functioning (five items), and school functioning (five items). Each item is presented with five response options on a scale ranging from 0 to 4, where 0 indicates "never a problem," 1 indicates "seldom a problem", 2 indicates "sometimes a problem", 3 indicates "often a problem", and 4 indicates "always a problem". To standardize these items on a 0–100 scale, a linear transformation is applied as follows: 0 is transformed to 0, 1 to 25, 2 to 50, 3 to 75, and 4 to 100. Scale scores and total scores are computed by summing the item scores and dividing by the number of items responded to. A higher score indicates a better HRQoL. The instrument was previously validated in China, demonstrating satisfactory reliability and validity [24, 25]. In the current study, we computed Cronbach's alpha coefficients, with the results detailed in Supplementary Table S1.

The health-related quality of life of caregivers was assessed utilizing the five-level EuroQol five-dimensional questionnaire, five-level version (EQ-5D-5L). The EQ-5D descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each rated on a five-level scale ranging from no problems to extreme problems. Furthermore, the EQ visual analogue scale (EQ-VAS), which spans from 0 (indicating the worst health you can imagine) to 100 (indicating the best health you can imagine), was employed to evaluate the overall health perception of the respondent. In addition, we selected five question items from Zarit Caregiver Burden Interview (ZBI) [26] to measure specific caregiver's burdens due to taking care of children with INS. The five questions are (1) "Do you feel that because of the time you spend with your child that you do not have enough time for yourself?", (2) "Do you feel stressed between caring for your child and trying to meet other responsibilities (work, home)", (3) "Do you feel your health has suffered because of your involvement with your child?", (4) "Do you feel that you do not have enough money to care for your child in addition to the rest of your expenses", and (5) "Overall, how burdened do you feel in caring for your child".

### Statistical analysis

Firstly, descriptive analysis was conducted to compute means and standard deviations (SDs) for continuous variables exhibiting a normal distribution, and medians with interquartile ranges for continuous variables with a non-normal distribution. For categorical variables, frequencies and percentages were calculated. Subsequently, the mean scores of the scales and the overall score of the PedsQL™ 4.0 GCM were compared with the corresponding

scores of age-matched healthy children as reported in the extant literatures [24, 25]. Next, we employed two independent samples t-tests and one-way Analysis of Variance (ANOVA) to evaluate the differences in mean scores of the scales and the overall score of the PedsQL™ 4.0 GCM across various subgroups. Despite achieving statistical significance, we additionally calculated effect sizes, i.e., Cohen's  $d$  and partial eta squared ( $\eta_p^2$ ), to evaluate the clinical relevance of our findings. Cohen's  $d$  is calculated as the absolute value of the difference in mean scores between two groups divided by the largest standard deviation. The interpretation of Cohen's  $d$  is as follows:  $0.2 \leq d < 0.5$  indicates a small effect size,  $0.5 \leq d < 0.8$  indicates a moderate effect size, and  $d \geq 0.8$  indicates a large effect size [27].  $\eta_p^2$  was calculated to estimate the effect size of a difference across three or more subgroups. Effect sizes are indicated as  $0.01 \leq \eta_p^2 < 0.06$  indicates a small difference,  $0.06 \leq \eta_p^2 < 0.14$  indicates a moderate difference, and  $\eta_p^2 \geq 0.14$  indicates a large difference. Finally, variables that demonstrated a statistical significance were subsequently incorporated into the multivariate linear regression models to assess the independent associated factors of HRQoL of INS children.

Regarding the caregiver's HRQoL, we calculated the proportions of the five dimensions and the utility score of the EQ-5D-5L based on the value set of the Chinese adult population [28]. The means and standard deviations (SD) of the utility score and EQ-VAS scores were utilized to evaluate overall HRQoL. The relationships between the scale scores and total scores of the PedsQL™ 4.0 GCM with the utility score and EQ-VAS score were analyzed using Pearson correlation analysis. In addition, we calculated the proportions of reported caregiver's burden across five questions extracted from the instrument ZBI.

All the statistical analyses were conducted by using SPSS version 27.0 (SPSS Inc., Chicago, USA). The statistical significance was indicated when  $p$  value  $< 0.05$ .

## Results

### General characteristics of the study population

Table 1 presents the general characteristics of the study population. The median age of children was 4.0 years, and 68.5% were boys. Mothers filled out 76.2% of the questionnaires. 37.6% of mothers and 42.5% of fathers had a high educational level, i.e., a bachelor's degree or above. 37.6% of families lived in urban areas. Additionally, 82.9% of the parents had someone at home to take care of the sick child. 81.8% of children had a health insurance.

### Clinical characteristics of the study population

Table 2 provides a comprehensive summary of the clinical characteristics of the study population. The median age at disease onset and at diagnosis of INS was 3.7 years.

**Table 1** General and clinical characteristics of children with idiopathic nephrotic syndrome ( $n=181$ )

Characteristic	Values <sup>a</sup>
Age of the child, year	4.0 [4.0, 5.0]
Age groups	
2-4 years old	35 (19.3)
5-7 years old	59 (32.6)
8-12 years old	50 (27.6)
13-18 years old	37 (20.4)
Gender	
Boy	124 (68.5)
Girl	57 (31.5)
Current weight of the child, kilogram (kg)	25.00 [18.05, 43.00]
Current Height, centimeter (cm)	122.00 [108.00, 149.50]
BMI (kg/m <sup>2</sup> )	16.41 [14.79, 20.20]
Caregiver who filled out the questionnaire	
Mother	138 (76.2)
Father or others	43 (23.7)
Maternal educational level	
Middle school or lower	65 (35.9)
High school or equivalent	48 (26.5)
Bachelor degree or higher	68 (37.6)
Paternal educational level	
Middle school or lower	56 (31.0)
High school or equivalent	48 (26.5)
Bachelor degree or higher	77 (42.5)
Employment of mother	
Yes	130 (71.8)
No	51 (28.2)
Employment of father	
Yes	172 (95.0)
No	9 (5.0)
Annual household income (RMB)	
Less than 100,000	95 (52.5)
100,000 to 200,000	35 (19.3)
More than 200,000	51 (28.2)
Parental marital status	
Married	175 (96.7)
Divorced	6 (3.3)
Residence	
Urban	68 (37.6)
Rural	113 (62.4)
Having a health insurance	
No	33 (18.2)
Yes	148 (81.8)
Having someone at home to take care of the sick child	
Yes	150 (82.9)
No	31 (17.1)
Having a sibling or siblings	
Yes	110 (60.8)
No	71 (39.2)

<sup>a</sup> Values presented in this table presents medians, interquartile ranges, numbers, and percentages

**Table 2** Clinical characteristics of children with idiopathic nephrotic syndrome (INS) ( $n = 181$ )

Characteristic	Values <sup>a</sup>
Age of onset of INS (year)	3.7 [2.3, 8.0]
Age of diagnosis of INS (year)	3.7 [2.3, 7.7]
First-time visit of the hospital, yes	54 (29.8)
Number of visiting tertiary hospitals in the last 6 months	2 (1, 3)
Presence of hematuria, yes	9 (5.0)
Renal insufficiency, yes	18 (9.9)
Presence of hypertension, yes	11 (6.1)
Only using the steroid, yes	50 (27.6)
Medications used for treatment except for steroid	
Oral immunosuppressive drug	88 (48.6)
Rituximab	51 (28.2)
Other medications	51 (28.2)
Immunosuppressive medications used for treatment	
Levamisole	1 (0.6)
Mycophenolate mofetil	41 (22.7)
Cyclophosphamide	5 (2.8)
Tacrolimus	58 (32.0)
Cyclosporine A	7 (3.9)
Other	5 (2.8)
Primary concern regarding illness perceived by parents	
Nephrotic syndrome cannot be cured	129 (71.3)
The physical discomforts caused by INS	11 (6.1)
Psychological problems caused by INS	8 (4.4)
Concerns about adverse effects of medications	12 (6.6)
Concerns about sequelae	9 (5.0)
The negative impact of illness on children's education	3 (1.7)
Psychological problems of caregivers	1 (0.6)
The financial burden due to the disease	7 (3.9)
Other concerns	1 (0.6)

<sup>a</sup> Values presented in this table are medians, interquartile ranges, numbers, and percentages

At the time of this study, 29.8% of the children were making their initial hospital visit. Over the past six months, the median number of visits to a tertiary hospital was 2. The proportions of hematuria, renal insufficiency, and hypertension among the participants were 5.0%, 9.9%, and 6.1%, respectively. Additionally, 27.6% of the children were treated only with steroids. Additionally, 48.6% used oral immunosuppressive drugs, 28.2% received rituximab, and 28.2% took other medications. Notably, 71.3% of caregivers were primarily concerned about the incurability of INS.

#### Scales scores and total scores of PedsQL™ 4.0 GCM in INS children at different age groups

Table 3 presents the means and standard deviations of scale scores and total scores of PedsQL™ 4.0 GCM in INS children at different age groups in our study. Children

aged 13–18 years had significantly lower scores in all scales as well as lower total scores compared with scores at other age groups ( $p$  values < 0.05). The effect sizes ranged from 0.044 to 0.338.

In addition, we compared the mean scores of PedsQL™ 4.0 GCM in our study population with the published scores from healthy children of the same age [24, 25]. The results are presented in the Supplementary Table S2. For children aged 2 to 4 years, both the total score and the average of scale scores were significantly higher than the averages of the healthy controls ( $p$  values < 0.05) except for the mean score of school functioning ( $p = 0.121$ ). For children aged 5 to 18 years, the averages of scale scores and the total score were significantly lower than the averages of the healthy controls ( $p$  values < 0.05) except for the mean score of the social functioning scale ( $p = 0.171$ ).

#### Differences in average scores of PedsQL™ 4.0 GCM scales and total score

Table 4 presents differences in the mean values of PedsQL™ 4.0 GCM scales and total scores in the study population. We showed the variables with at least one statistically significant difference (i.e., when  $p$  value < 0.05) regarding the average scores of PedsQL™ 4.0 GCM scales and total scores, and the remaining results are presented in Supplementary Table S3. Notably, when mothers filled out the questionnaire, children had lower average scores on the scale of emotional functioning ( $p = 0.004$ ), school functioning ( $p = 0.045$ ), psychosocial health summary score ( $p = 0.010$ ), and total score ( $p = 0.023$ ) compared to those scores when fathers or others filled out the questionnaire. The average scores were significantly higher in social functioning ( $p < 0.001$ ), school functioning ( $p = 0.017$ ), psychosocial health summary score ( $p = 0.013$ ) as well as total scores ( $p = 0.016$ ) in children whose mothers had a high education compared to their counterparts. Children who visited the hospital for the first time had higher average scores in social functioning ( $p = 0.005$ ), psychosocial health summary score ( $p = 0.016$ ), and total scores ( $p = 0.023$ ). Children on steroid-exclusive regimens had relatively higher mean scores in all scales and total scores ( $p$  values < 0.05). More specifically, in terms of medical treatments, we also compared the scores of PedsQL™ 4.0 GCM in children who only used steroids with those using two or more medications. Results are shown in the Supplementary Table S4. Children had the highest mean scores in all scales and total score compared to patients using oral immunosuppressive drugs (OID) and/or rituximab (RTX). Children using both OID and RTX had the lowest mean scores in all scales and the total score. Furthermore, we applied the Post hoc comparisons and found that there were only significant differences in averages of total score when only

**Table 3** Means and standard deviations of scales and total scores of PedsQL™ 4.0 GCM among children with idiopathic nephrotic syndrome at different age groups ( $n = 181$ )

	2-4 years ( $n = 35$ )	5-7 years ( $n = 59$ )	8-12 years ( $n = 50$ )	13-18 years ( $n = 37$ )	$p$ value	Effect size ( $\eta_p^2$ ) <sup>a</sup>
Physical functioning	89.20 ± 14.57	75.37 ± 17.60	53.64 ± 15.84	70.61 ± 21.64	< 0.001	0.338
Emotional functioning	82.29 ± 20.98	72.80 ± 18.06	74.50 ± 21.62	68.11 ± 27.01	0.048	0.044
Social functioning	90.86 ± 12.57	83.56 ± 19.41	84.70 ± 15.76	62.25 ± 18.08	< 0.001	0.255
School functioning	84.13 ± 24.42	69.75 ± 16.98	73.30 ± 18.51	65.27 ± 26.77	0.010	0.067
Psychosocial Health Summary Score	86.72 ± 18.03	75.17 ± 14.93	77.47 ± 15.19	65.35 ± 21.05	< 0.001	0.124
Total score	87.93 ± 16.46	75.24 ± 14.08	69.18 ± 14.41	67.18 ± 20.48	< 0.001	0.141

Values presented in this table are means and standard deviations

<sup>a</sup> In this table, we presented partial eta squared ( $\eta_p^2$ ) for ANOVAs to estimate the effect size. Effect sizes are indicated as small ( $\eta_p^2 = 0.01$ ), medium ( $\eta_p^2 = 0.06$ ), and large ( $\eta_p^2 = 0.14$ ) effects

using steroids vs. only using OID, as well as only using steroid vs. using both OID and RTX (see Supplementary Table S5).

#### Associated factors of the total PedsQL™ 4.0 GCM score

Table 5 shows the results of multivariate linear regression analyses to assess associated factors of the HRQoL in children with INS measured by PedsQL™ 4.0 GCM. Factors significantly associated with children's HRQoL include mothers filling out the questionnaire ( $\beta = 6.20$ ; 95% CI: 0.12, 12.27;  $p = 0.046$ ), the non-employment status of fathers ( $\beta = -12.12$ ; 95% CI: -23.42, -0.82;  $p = 0.036$ ) and using non-steroid treatment ( $\beta = -6.60$ ; 95% CI: -12.62, -0.58;  $p = 0.032$ ). The adjusted  $R^2$  is 0.132.

#### Caregiver's health-related quality of life and caregiver's burden

The caregiver's HRQoL profile, composed of the five health dimensions, is shown in Fig. 1. The percentage of reporting "no problem" in mobility, looking after themselves, doing usual activities, pains and discomforts, and feeling worried, sad or unhappy was 52.41%, 76.47%, 93.58%, 95.19% and 94.12%, respectively. Notably, 38.50% of caregivers reported slight problems in the dimension 'feeling worried, sad or unhappy', 8.02% moderate problems, 0.53% severe problems and 0.53% extreme problems. As shown in Supplementary Table S6, the mean of EQ-5D-5L utility score is 0.94 with a standard deviation of 0.08, and the median of EQ-5D-5L VAS score is 89 (interquartile range: 79, 100). Furthermore, Table 6 shows that the scale scores and total score of PedsQL™ 4.0 GCM are statistically significantly correlated to EQ-5D-5L utility score and VAS score ( $p$  values < 0.05). In addition, Fig. 2 demonstrates the specific caregiver's burden due to taking care of children with INS. 31.6% of parents reported that they sometimes don't have enough time for themselves, 5.4% reported quite frequently, and

7.9% nearly always. 49.7% of parents reported that they felt sometimes stressed to take care of the child with INS and striving to balance other family or work responsibilities, 9.6% reported quite frequently, and 8.0% nearly always. 26.7% of parents reported that they felt sometimes their own health being affected due to taking care of the INS child, 3.2% reported quite frequently, and 2.7% reported nearly always. 29.4% of parents reported that sometimes they felt financial burden to take care of the sick child, 2.1% reported quite frequently, and 11.2% nearly always. Overall, the frequency of rating of caregiver's burden as 'not at all', 'a little', 'moderately', 'quite a bit' and 'extremely' are 30.0%, 42.2%, 13.4%, 10.7% and 3.7%, respectively.

#### Discussion

In the present study, we have conducted an assessment of the HRQoL among children aged 2 to 18 years diagnosed with INS in China, as well as the HRQoL of their caregivers and the burden experienced by caregivers in managing children with INS. Our findings indicate that children's HRQoL declines with increasing age. Various factors, including parental educational level, father's employment status, and medication treatment plans, may be associated with children's HRQoL. Additionally, there is a correlation between children's HRQoL and their caregivers' HRQoL. Nearly 70% of caregivers reported experiencing a burden to some extent due to the responsibilities of caring for children with INS.

Our findings indicated that the HRQoL score of children aged 2 to 4 years in our study was superior to that reported for healthy children in the existing literature [25]. This finding potentially attributed to factors such as the young age of the children, the brief duration of INS, not attending schools, and the absence of perceived symptoms. Consequently, these children may not present many changes in functioning, and their caregivers may

**Table 4** Comparing the average scale and total scores of PedsQL™ 4.0 GCM across groups in children with idiopathic nephrotic syndrome ( $n = 181$ )

Characteristics	Physical functioning	Emotional functioning	Social functioning	School functioning	Psychosocial health summary score	Total score
Gender						
Boy	73.26 ± 20.36	74.88 ± 20.95	82.06 ± 18.83	72.63 ± 21.15	76.09 ± 16.64	74.56 ± 15.97
Girl	66.31 ± 22.86	72.54 ± 24.15	78.47 ± 20.93	69.58 ± 22.09	73.18 ± 20.32	70.53 ± 19.35
<i>p</i> value	0.042	0.508	0.251	0.388	0.325	0.155
Effect size <sup>a</sup>	0.32	0.10	0.18	0.14	0.16	0.23
Caregiver who filled out the questionnaire						
Mother	69.82 ± 21.29	71.52 ± 22.46	79.90 ± 20.21	69.89 ± 20.99	73.28 ± 17.66	71.65 ± 16.88
Father or others	75.06 ± 21.36	82.56 ± 18.07	84.24 ± 16.94	77.96 ± 22.19	81.89 ± 17.48	78.99 ± 17.38
<i>p</i> value	0.161	0.004	0.204	0.045	0.010	0.023
Effect size	0.25	0.54	0.23	0.37	0.49	0.43
Maternal educational level						
Middle school or lower	68.08 ± 22.58	71.85 ± 23.64	74.20 ± 21.37	65.52 ± 26.89	70.34 ± 21.10	69.12 ± 20.16
High school or equivalent	69.08 ± 23.21	75.00 ± 22.41	79.88 ± 20.80	74.00 ± 17.31	75.24 ± 16.76	72.40 ± 16.24
College or above	75.33 ± 18.19	75.74 ± 20.04	88.10 ± 13.71	75.98 ± 16.39	79.85 ± 13.85	77.96 ± 13.38
<i>p</i> value	0.111	0.568	< .001	0.017	0.013	0.016
Effect size	0.03	0.01	0.10	0.05	0.05	0.05
Paternal educational level						
Middle school or lower	65.80 ± 23.42	71.07 ± 24.38	73.28 ± 21.72	67.31 ± 23.76	70.24 ± 20.73	68.12 ± 19.86
High school or equivalent	74.40 ± 23.59	78.33 ± 22.30	83.80 ± 16.66	73.93 ± 23.05	78.07 ± 16.91	76.23 ± 17.52
College or above	72.82 ± 17.58	73.77 ± 19.67	84.71 ± 18.09	73.36 ± 18.16	76.88 ± 15.69	75.10 ± 14.00
<i>p</i> value	0.078	0.240	0.002	0.215	0.056	0.033
Effect size	0.05	0.03	0.11	0.02	0.04	0.04
Employment status of father						
Yes	71.69 ± 21.48	75.44 ± 20.89	82.04 ± 18.73	72.71 ± 20.76	76.31 ± 17.23	74.21 ± 16.77
No	59.12 ± 15.47	49.44 ± 28.33	59.80 ± 23.49	52.59 ± 25.62	54.55 ± 18.29	56.14 ± 16.64
<i>p</i> value	0.085	< 0.001	< 0.001	0.006	< 0.001	0.002
Effect size	0.67	1.05	1.05	0.86	1.22	1.08
First visit to the hospital for the diagnosis of INS						
Yes	75.24 ± 21.13	77.78 ± 21.69	87.17 ± 15.96	76.81 ± 20.28	80.52 ± 16.55	78.13 ± 16.69
No	69.29 ± 21.30	72.60 ± 21.98	78.28 ± 20.34	69.66 ± 21.63	73.08 ± 18.07	71.37 ± 17.10
<i>p</i> value	0.086	0.147	0.005	0.054	0.016	0.023
Effect size	0.28	0.24	0.49	0.34	0.43	0.40
Presence of renal insufficiency						
Yes	61.43 ± 19.73	71.39 ± 23.57	70.41 ± 22.75	68.44 ± 20.87	68.90 ± 20.34	65.38 ± 17.27
No	72.13 ± 21.32	74.45 ± 21.84	82.09 ± 18.86	71.96 ± 21.55	75.79 ± 17.60	74.07 ± 17.04
<i>p</i> value	0.043	0.576	0.016	0.533	0.144	0.054
Effect size	0.52	0.14	0.56	0.17	0.36	0.51
Presence of hypertension						
Yes	60.34 ± 20.16	67.73 ± 24.94	67.84 ± 19.50	64.50 ± 19.92	65.80 ± 17.96	63.42 ± 17.48
No	71.76 ± 21.31	74.56 ± 21.78	81.78 ± 19.28	72.08 ± 21.52	75.73 ± 17.81	73.86 ± 17.05
<i>p</i> value	0.086	0.319	0.021	0.280	0.089	0.063
Effect size	0.55	0.29	0.72	0.37	0.56	0.60
Only using steroid treatment						
Yes	77.04 ± 19.97	80.70 ± 21.92	87.43 ± 15.22	80.61 ± 21.38	82.81 ± 17.08	80.41 ± 16.76
No	68.79 ± 21.51	71.64 ± 21.54	78.45 ± 20.45	68.41 ± 20.62	72.39 ± 17.48	70.66 ± 16.69
<i>p</i> value	0.020	0.013	0.005	0.001	< 0.001	0.001
Effect size	0.40	0.42	0.50	0.58	0.60	0.58

Values presented in this table are means and standard deviations

<sup>a</sup> Effect size was calculated as Cohen's  $d$  and partial eta squared ( $\eta_p^2$ ) to estimate clinical relevance. Effect sizes are indicated as small ( $d = 0.2$ ,  $\eta_p^2 = 0.01$ ), medium ( $d = 0.5$ ,  $\eta_p^2 = 0.06$ ), and large ( $d = 0.8$ ,  $\eta_p^2 = 0.14$ ) difference

**Table 5** Associated factors of total PedsQL™ 4.0 GCM score in the multivariate linear regression analyses

	PedsQL™ 4.0 GCM total score	
	β (95% confident interval)	P value
<b>Caregiver who filled the questionnaire</b>		
Mother (n = 138)	Reference	
Father and others (n = 43)	6.20 (0.12, 12.27)	0.046
<b>Maternal educational level</b>		
University or higher (n = 68)	Reference	
High school or equivalent (n = 48)	-5.75 (-13.82, 2.32)	0.161
Middle school or lower (n = 65)	-6.13 (-16.21, 3.95)	0.232
<b>Paternal educational level</b>		
University or higher (n = 77)	Reference	
High school or equivalent (n = 48)	3.41 (-4.86, 11.68)	0.417
Middle school or lower (n = 56)	-1.29 (-11.11, 8.53)	0.796
<b>Employment of father</b>		
Yes (n = 172)	Reference	
No (n = 9)	-12.12 (-23.42, -0.82)	0.036
<b>First onset of symptoms</b>		
Yes (n = 54)	Reference	
No (n = 127)	-3.27 (-9.32, 2.77)	0.286
<b>Steroid</b>		
Yes (n = 50)	Reference	
No (n = 131)	-6.60 (-12.62, -0.58)	0.032
<b>Adjusted R<sup>2</sup></b>	0.132	

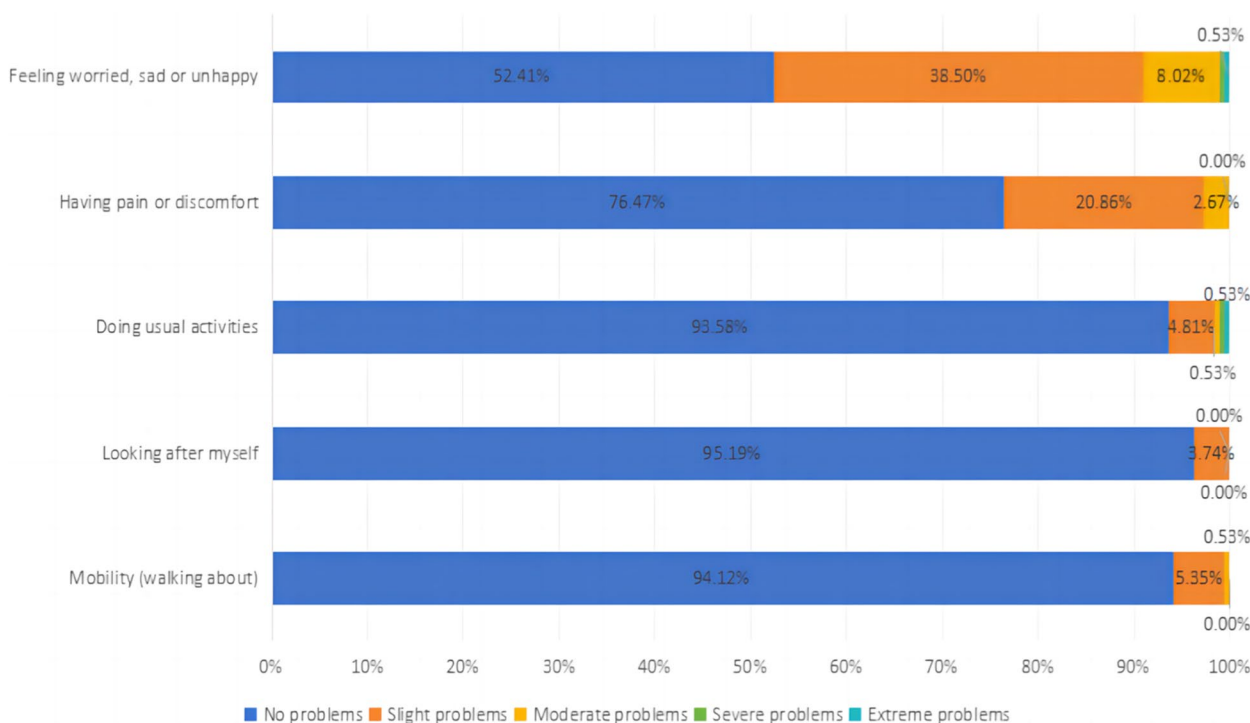
not regard this health condition as impactful to children's lives, as it does not interfere with their schooling or other activities. In addition, this observed discrepancy may be due to the relatively small sample sizes in both our study ( $n = 35$ ) and the referenced study ( $n = 36$ ) [25]. The referenced study was conducted in 2005, which may not accurately represent the current HRQoL profile of Chinese children aged 2 to 4 years [25]. Moreover, the clinical stage and duration of INS can affect children's HRQoL. Roussel et al. found that children with steroid-dependent or steroid-resistant nephrotic syndrome had HRQoL scores similar to those of healthy children [8], likely because the study participants were in stable remission. Similarly, children aged 2 to 4 years exhibited a relatively brief disease duration and a lower incidence of relapse, which may contribute to a quality of life comparable to that of the general population.

Our study revealed that INS children's HRQoL aged 5 to 18 years was inferior to that reported for healthy children in the existing literature [25], a finding that aligned with previous research [4, 9, 11, 17, 29]. Selewski et al. found that children with INS demonstrated lower scores on assessments of social and school functioning. In a similar vein, a study conducted in India involving 102 participants indicated that these children scored

significantly lower in physical, social, and school functioning compared to their healthy counterparts, with school functioning being the most severely impacted [4, 17]. Furthermore, a recent study conducted in the Netherlands revealed that children aged 8 to 18 years exhibited a significant decline in scores related to physical and emotional functioning, as well as overall HRQoL [29]. These disparities may be attributed to differences in cultural contexts, healthcare systems across various countries, and the stage and relapse frequency of the disease among patients [7, 11, 20].

In our study, the scores for emotional functioning, school functioning, psychosocial health summary, and the total score were higher when fathers or others completed the questionnaire compared to mothers. This discrepancy may be attributed to fathers' lower emotional sensitivity, potentially resulting in a relatively more optimistic outlook and reduced anxiety. Notably, the score for physical functioning did not reach statistical significance, which may be due to the objective nature of the physical functioning questions measured by the PedsQL™ 4.0 GCM-Physical Functioning Scale. Our findings align with previous research, which also indicated that caregivers who completed the questionnaire reported similar physical health related outcomes [30]. Our findings





**Fig. 1** Caregiver's HRQoL profile composed of the five health dimensions of EQ-5D-5L

suggest that children's HRQoL is significantly better, both at the scale level and overall level, when their parents possess higher educational attainment and are employed. This observation aligns with the earlier study [31], which demonstrated a positive correlation between paternal education and proxy-reported HRQoL. It is plausible that families with relatively higher socioeconomic status are better positioned to provide the necessary support for managing the care of ill children, thereby contributing to an enhanced HRQoL. Our findings indicate that paternal unemployment is associated with a significant impairment in children's HRQoL across all scales and at the overall level, with effect sizes suggesting moderate

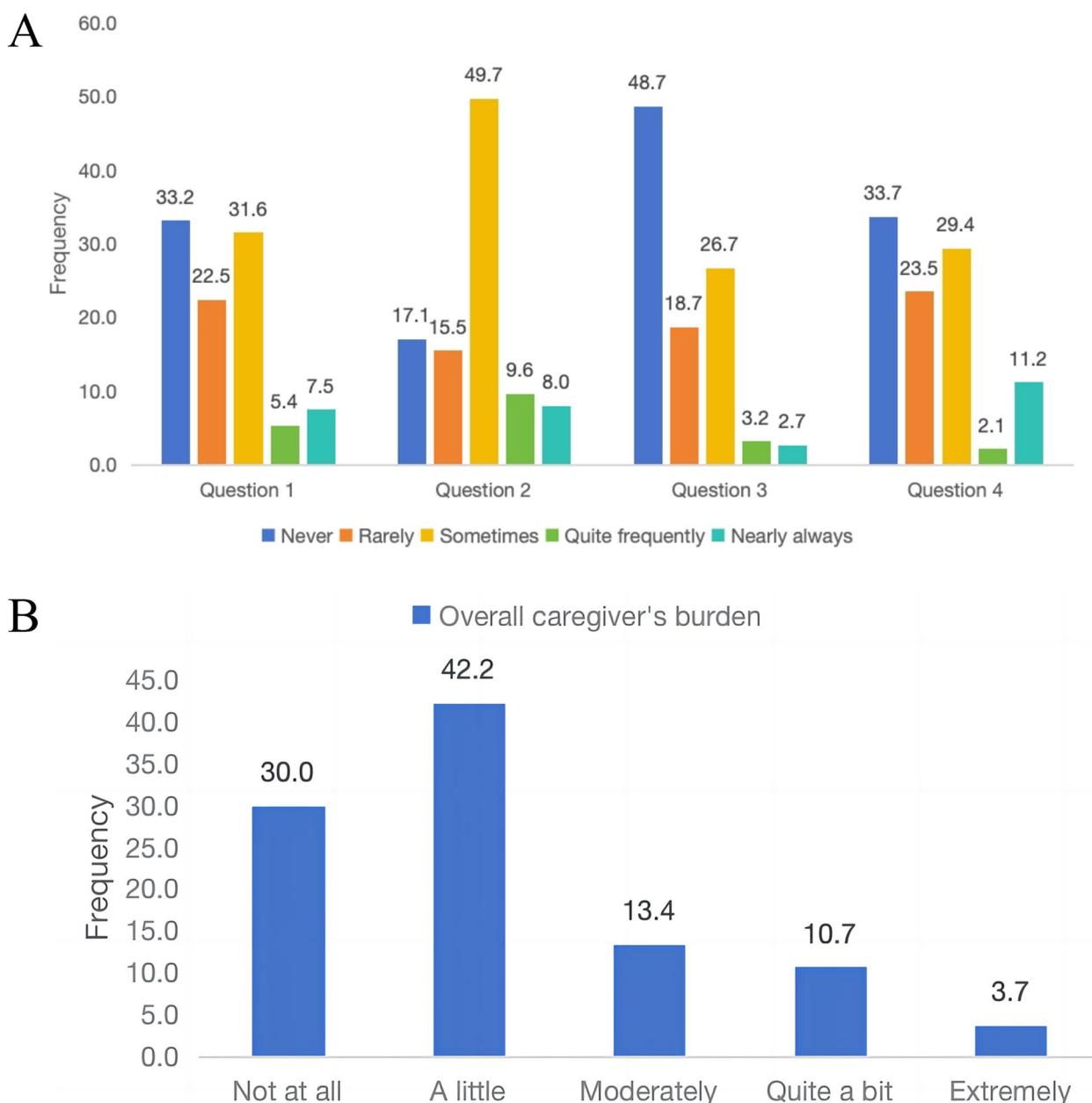
to large differences. This variable remained statistically significant in the regression model even after adjusting for other covariates. In the context of Chinese social and cultural norms, paternal unemployment may exert a substantial influence on family dynamics, particularly in the realm of medical decision-making.

In this study, children with newly diagnosed INS exhibited elevated scores in social functioning, psychosocial health summary, and overall PedsQL™ 4.0 GCM scores. This observation can be attributed to the early stage of the disease, during which they experienced relatively minimal adverse effects from treatment and pain. In contrast, patients with recurrent disease and prolonged duration demonstrated a significantly diminished quality of life compared to those with initial onset, with the effect size nearing a moderate level. Our findings are consistent with previous studies that have documented the adverse effects of relapse on HRQoL [4, 9, 11, 17, 29]. Additionally, our study reveals that social and psychosocial functioning are notably affected by relapse. This phenomenon may be attributed to the necessity for frequent hospital visits, diminished social interactions, the cumulative psychological impact of complications such as edema, obesity, and hirsutism, and the resultant isolation from peers [11, 17, 20].

Regarding pharmacological interventions, our study found that patients on a steroid-exclusive regimen

**Table 6** The correlation between PedsQL™ 4.0 GCM scale/total scores and EQ-5D-5L utility and VAS score

	Utility score		VAS	
	Pearson r	P value	Pearson r	P value
Physical functioning	0.299	<0.001	0.285	<0.001
Emotional functioning	0.338	<0.001	0.270	<0.001
Social functioning	0.223	0.003	0.246	<0.001
School functioning	0.338	<0.001	0.241	0.002
Psychosocial Health Summary Score	0.352	<0.001	0.302	<0.001
Total score	0.374	<0.001	0.337	<0.001



**Fig. 2** Specific Caregiver's burden due to taking care of children with INS. **A** Frequency of four specific caregiver's burden. Question 1: "Do you feel that because of the time you spend with your child that you do not have enough time for yourself?", Question 2: "Do you feel stressed between caring for your child and trying to meet other responsibilities (work, home)?", Question 3: "Do you feel your health has suffered because of your involvement with your child?", Question 4: "Do you feel that you do not have enough money to care for your child in addition to the rest of your expenses?"; **B** Frequency of overall rating of caregiver's burden

reported a higher quality of life compared to those who used oral immunosuppressive drugs (OID) and/or rituximab (RTX). This association remained statistically significant even after adjusting for covariates. This finding is plausible, as children treated with only steroids were likely in the initial stages of the disease, experiencing less disease-related pain and fewer complications. Children

receiving treatment with OID or RTX required frequent hospital admissions and endured discomforts associated with RTX infusions. These factors negatively affected their emotional well-being and diminished their opportunities for social interactions and participation in school activities.

Caregivers are essential to the long-term management of children with INS, a chronic condition necessitating prolonged treatment. Over time, caregivers are responsible for ongoing proteinuria monitoring, medication administration, management of specialized diets, coordination of frequent hospital follow-up visits, addressing the emotional well-being of the children, and making critical decisions. Consequently, the role of a caregiver for a child with INS is both stressful and demanding. Our study revealed that approximately 30% of caregivers assessed their caregiving burden as moderate or higher. The demands of caring for a sick child often result in insufficient personal time, challenges in balancing work and life responsibilities, perceived financial strain, and deteriorating health. These negative effect may accumulate over time and adversely affect their HRQoL [32]. Liu et al. reported that anxiety was present in 63.4% of caregivers of children with INS, and depression was observed in 68.4% of parental caregivers [33]. Understanding the correlation between the HRQoL of both children and their caregivers may aid in the development of targeted and personalized health education strategies. Such strategies can assist caregivers in adapting to their roles and achieving optimal health outcomes for the children.

### Strengths and limitations

This study demonstrates several notable strengths. Firstly, it examines the HRQoL of children with INS in China, utilizing a relatively large sample size of patients aged 2 to 18 years. Importantly, the study incorporates specialized instrument PedsQL™ 4.0 GCM for children aged 2 to 4 years, thereby improving the assessment of quality of life within this younger demographic. Secondly, a comprehensive evaluation of a broad spectrum of potential influencing factors was conducted to enhance the understanding of health status and medical care among children with INS. Furthermore, effect size metrics, specifically Cohen's  $d$  and  $\eta_p^2$ , were utilized to offer a more nuanced analysis of the findings and to assess the clinical relevance of differences in HRQoL scores across subgroups. This methodological approach addresses the limitations inherent in relying solely on statistical significance.

However, the study presents several limitations that warrant attention. Firstly, it is a single-center study that lacks a large-sample standard dataset of Chinese children to serve as a healthy control group. Secondly, the cross-sectional design precludes longitudinal HRQoL assessments over time, thereby limiting the ability to establish causality. Additionally, it is imperative to monitor these children longitudinally to assess the development of

their quality of life (QOL) over time. This approach will enable health professionals, patients, and caregivers to comprehend the impact of INS and to implement timely, targeted interventions aimed at enhancing patient well-being. Consequently, we recommend that future research adopt a longitudinal study design or incorporate follow-up assessments of HRQoL. Thirdly, even though the previous study showed strong agreement that the proxy-reported questionnaire is reliable [17], incorporating both proxy- and self-reported outcomes may provide more comprehensive insights. Fourthly, the present study exclusively utilized a quantitative approach, which yielded a comprehensive dataset elucidating the HRQoL profile of children with INS in China. Although a range of associated factors influencing children's HRQoL has been identified, this approach only partially explains the HRQoL outcomes observed in children with INS. To obtain a more profound understanding of this issue, we recommend incorporating qualitative investigations alongside quantitative methods in future research, thereby adopting a mixed-methods study design.

### Conclusion

This study evaluated the HRQoL of children aged 2-18 years diagnosed with INS in China, as well as the HRQoL and caregiving burden of their caregivers. The findings reveal a decline in children's HRQoL with increasing age, potentially influenced by variables such as parental education, paternal employment status, and medication regimens. A significant correlation was identified between the HRQoL of the children and that of their caregivers, who frequently experience varying levels of caregiving burden. Consequently, it is recommended that healthcare professionals prioritize the optimization of HRQoL for both children with INS and their caregivers.

### Abbreviations

HRQoL	Health-related Quality of Life
INS	Idiopathic Nephrotic Syndrome
PedsQL™ 4.0 GCM	Pediatric Quality of Life Inventory Generic Core Module
EQ-5D-5L	EuroQol five-dimensional questionnaire, five-level version
OID	Oral Immunosuppressive Drugs
RTX	Rituximab
SS	Steroid-Sensitive
SR	Steroid-Resistant
CNI	Calcineurin Inhibitors
BMI	Body Mass Index
ZBI	Zarit Burden Interview
VAS	Visual Analogue Scale
SPSS	Statistical Package for the Social Sciences
SD	Standard Deviation
ANOVA	Analysis of Variance
CI	Confidence Interval
RMB	Renminbi (Chinese currency)

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12955-024-02310-6>.

Supplementary Material 1.  
Supplementary Material 2.  
Supplementary Material 3.  
Supplementary Material 4.  
Supplementary Material 5.  
Supplementary Material 6.

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### Authors' contributions

Xia Wang, Jianhua Mao and Guannan Bai were involved in the study conceptualization and design. Xia Wang, Jingjing Wang, Chunyue Feng, Haidong Fu, Huijun Shen, and Xiujuan Zhu collected data. Leijing Guan and Yifei Shao carried out statistical analyses and prepared all the tables/figures. Xia Wang and Guannan Bai wrote the main manuscript texts. Abdul Rafay prepared the supplementary tables. Xia Wang, Danny Junyi Tan and Guannan Bai wrote the first draft of this manuscript. Jianhua Mao and Guannan Bai supervised the whole project. All authors reviewed the manuscript and provided critical revisions of the article for important intellectual content. All the authors contributed to the interpretation of the data and approved the article's final version.

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### Data availability

No datasets were generated or analysed during the current study.

### Declarations

#### Ethics approval and consent to participate

The study protocol was conducted according to the Declaration of Helsinki, and was approved by the Medical Ethics Committee of the Children's Hospital, Zhejiang University School of Medicine (2024-IRB-0294-P-01). All caregivers gave their consents and voluntarily participated in the study.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare no competing interests.

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