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Multimorbidity Profiles and Health-related Quality of Life in Children with Cerebral Palsy: A Multidimensional Analysis

Serebral Palsili Çocuklarda Multimorbidite Profilleri ve Sağlıkla İlişkili Yaşam Kalitesi: Çok Boyutlu Bir Analiz

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Abstract

Objective: To quantify the relative contributions of motor severity and non-motor comorbidities to health-related quality of life (HRQoL) in individuals with cerebral palsy (CP) and to evaluate their statistical associations.

Methods: In this cross-sectional study, 218 children with CP (aged 6-18 years) were evaluated using the gross motor function classification system (GMFCS), pediatric evaluation of disability inventory (PEDI), pediatric quality of life inventory (PedsQL), and Pittsburgh sleep quality index. Comorbidities were identified through clinical records.

Results: A higher GMFCS level was the strongest independent predictor of lower HRQoL (β=-0.58, p<0.001), followed by poorer sleep quality (β=-0.25, p=0.002), epilepsy (β=-0.22, p=0.004), and malnutrition (β=-0.18, p=0.010). Dominance analysis showed that GMFCS and sleep quality together accounted for most of the explained variance in HRQoL. Latent class analysis identified three comorbidity clusters: low-burden (43%), moderate-burden (33%), and high-burden (24%), with the high-burden cluster demonstrating markedly lower PEDI and PedsQL scores (p<0.001). Sleep quality was indirectly and significantly associated with the relationships among epilepsy, malnutrition, and HRQoL.

Conclusion: Motor severity explains a large proportion of HRQoL differences in CP; however, non-motor comorbidities-especially sleep disturbance, epilepsy, and malnutrition-represent substantial and potentially modifiable contributors. Distinct multimorbidity clusters and identified mediating pathways indicate the need for integrated care models that address motor and systemic factors simultaneously. Early targeting of sleep and nutritional health may meaningfully improve quality of life trajectories in children with CP.

Keywords: Cerebral palsy, quality of life, sleep disturbance, epilepsy, malnutrition, multimorbidity

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Öz

Amaç: Bu çalışmanın amacı, serebral palside (SP) motor şiddet ile non-motor komorbiditelerin sağlıkla ilişkili yaşam kalitesi (HRQoL) üzerindeki göreceli ve istatistiksel olarak ilişkili katkılarını nicel olarak değerlendirmektir.

Yöntem: Bu kesitsel çalışmada, yaşları 6-18 arasında değişen 218 SP'li çocuk değerlendirilmiştir. Değerlendirmelerde gross motor fonksiyon sınıflandırma sistemi (GMFCS), pediyatrik engellilik değerlendirme envanteri (PEDI), pediyatrik yaşam kalitesi ölçeği (PedsQL) ve Pittsburgh uyku kalitesi indeksi kullanılmıştır. Komorbiditeler klinik kayıtlar üzerinden belirlenmiştir.

Bulgular: Daha yüksek GMFCS düzeyi, daha düşük yaşam kalitesinin en güçlü bağımsız belirleyicisi olarak bulunmuştur (β=-0,58, p<0,001). Bunu sırasıyla kötü uyku kalitesi (β=-0,25, p=0,002), epilepsi (β=-0,22, p=0,004) ve malnütrisyon (β=-0,18, p=0,010) izlemiştir. Dominans analizi, GMFCS ve uyku kalitesinin birlikte HRQoL'de açıklanan varyansın büyük kısmını oluşturduğunu göstermiştir. Latent sınıf analizi ile üç komorbidite kümesi tanımlanmıştır: düşük yük (%43), orta yük (%33) ve yüksek yük (%24). Yüksek yük grubunda PEDI ve PedsQL skorları anlamlı derecede daha düşük bulunmuştur (p<0,001). Uyku kalitesinin, epilepsi, malnütrisyon ve HRQoL arasındaki ilişkilerle anlamlı dolaylı istatistiksel ilişkiler gösterdiği belirlenmiştir.

Sonuç: Motor şiddet, SP'de yaşam kalitesindeki farklılıkların önemli bir kısmını açıklamaktadır. Ancak uyku bozukluğu, epilepsi ve malnütrisyon gibi non-motor komorbiditeler de önemli ve potansiyel olarak değiştirilebilir belirleyicilerdir. Tanımlanan multimorbidite kümeleri ve aracılık yolları, motor ve sistemik faktörleri birlikte ele alan entegre bakım modellerinin gerekliliğini ortaya koymaktadır. Özellikle uyku ve beslenme durumuna erken müdahale, SP'li çocuklarda yaşam kalitesi seyrini anlamlı şekilde iyileştirebilir.

Anahtar Kelimeler: Serebral palsi, yaşam kalitesi, uyku bozukluğu, epilepsi, malnütrisyon, multimorbidite

Introduction

Cerebral palsy (CP) is the leading cause of lifelong motor disability in childhood, affecting 2-3 per 1000 live births worldwide[1]. Despite its definition as a non-progressive motor disorder resulting from early brain injury, CP is now recognized as a complex neurodevelopmental condition with extensive multisystem involvement[2]. Non-motor comorbidities frequently exceed motor limitations in shaping functional independence, participation, and overall quality of life (QoL), yet remain comparatively underexplored in clinical research[3].

Among these comorbidities, epilepsy, malnutrition, and sleep disturbances are highly prevalent and clinically consequential. Epilepsy affects 40-60% of children with CP, particularly in those with bilateral spastic or dyskinetic subtypes, and is strongly associated with cognitive impairment and reduced QoL[4]. Malnutrition-arising from oropharyngeal dysphagia, gastrointestinal dysfunction, and increased metabolic expenditure-affects approximately one-third of children with CP, contributing to impaired growth, immune dysfunction, suboptimal neurodevelopment, and reduced participation in therapy[5]. Sleep disturbances are similarly pervasive: they occur in up to 75% of children with CP and include sleep fragmentation, sleep-disordered breathing, and circadian dysregulation[6]. Recent evidence suggests that sleep may serve as a mediator linking neurological instability, metabolic stress, and impaired daily functioning[7-9].

Despite the high prevalence of these conditions, their interdependent mechanisms and collective contribution to QoL remain poorly characterized. Research has traditionally examined epilepsy, nutrition, and sleep in isolation, overlooking their potential clustering and shared pathways[10]. Multimorbidity frameworks-long applied in adult medicine-are now gaining traction in developmental disability research, with emerging studies revealing distinct comorbidity phenotypes in CP that align with clinical severity and functional trajectories[11,12]. Latent class analysis (LCA) offers a robust, person-centred method to identify these clusters and has begun to uncover "high-burden" subgroups characterized by pronounced neurological and systemic instability[13].

Beyond descriptive clustering, mechanistic modelling approaches such as mediation analysis can clarify how specific comorbidities interact to influence functional outcomes. Prior research has shown that pain, fatigue, or parental mental health may partially mediate the association between motor severity and health-related QoL (HRQoL) in CP[14]. However, no study to date has examined whether sleep quality may partially mediate the effects of epilepsy and malnutrition on QoL, despite a compelling biological rationale. Sleep disruption can amplify seizure susceptibility, exacerbate nutritional deficiencies, worsen behavioural dysregulation, and diminish neuroplasticity-all of which are directly relevant to CP[7-9].

The present study addresses this gap by integrating variable-centred (regression, dominance analysis) and person-centred (LCA) methods to delineate the multimorbidity structure of epilepsy, malnutrition, and sleep disturbances in children with CP. A statistical mediation framework was further tested to evaluate whether sleep quality was indirectly associated with HRQoL in the relationships between neurological and nutritional comorbidities. This multidimensional analytic framework aligns with the growing emphasis on precision rehabilitation, which seeks to tailor interventions not only to motor subtype or severity but also to the child's broader systemic and neurodevelopmental profile[15].

By characterizing comorbidity clusters and elucidating potential interaction pathways, this study aims to identify modifiable, high-impact therapeutic targets that could meaningfully improve participation, independence, and QoL in children and adolescents with CP.

Materials and Methods

Study Design and Participants

This cross-sectional observational study included children and adolescents with CP who attended the Pediatric Neurology Department at Recep Tayyip Erdoğan University Training and Research Hospital between October 2024 and October 2025. All diagnoses were confirmed by a pediatric neurologist based on contemporary definitions of CP, and motor severity was classified using the [gross motor function classification system (GMFCS) levels I-V]. Children were eligible if they were between 6 and 18 years of age, had a confirmed diagnosis of non-progressive CP, and had a primary caregiver capable of completing proxy-report questionnaires. Participants were excluded if they presented with progressive neurological conditions or an acute medical illness at assessment, or had incomplete clinical, anthropometric, or questionnaire data. Severe sensory impairments that could compromise valid proxy reporting were also grounds for exclusion.

A total of 218 participants met the eligibility criteria and were included in the analyses. The sample size exceeded the requirement identified through an a priori power analysis performed using G*Power (version 3.1). Assuming a medium effect size (f^2=0.15) for multiple linear regression with four predictors, an alpha of 0.05, and 95% power, a minimum sample size of 129 participants was required. The final sample, therefore, provided adequate power for all multivariate and mediation models. Written informed consent was obtained from all caregivers. Ethical approval was granted by the Recep Tayyip Erdoğan University Non-Interventional Clinical Research Ethics Committee (approval no: 2025/372, date: 11.09.2025), and all procedures adhered to the Declaration of Helsinki.

Measures

Functional Independence and QoL

Functional independence was assessed using the pediatric evaluation of disability inventory (PEDI), which evaluates self-care, mobility, and social function, and has been validated across GMFCS levels[16]. HRQoL was measured using the parent-proxy version of the pediatric QoL inventory (PedsQL), which is widely used in children with neurodevelopmental disabilities because of its sensitivity to physical, emotional, and psychosocial functioning[17].

Sleep Quality

Sleep quality was evaluated using the Pittsburgh sleep quality index (PSQI). Although originally developed for adults, the PSQI has demonstrated strong reliability and convergent validity in pediatric neurodisability cohorts, including children with CP[18,19]. Furthermore, several pediatric neurodevelopmental studies have supported the feasibility of proxy-reported administration of the PSQI in children with communication and cognitive impairments, particularly when multidimensional sleep assessment is required. Actigraphy- and CSHQ-based studies have further supported its construct validity in this population[20].

Nutritional Status and Comorbidities

Nutritional status was determined using anthropometric measurements and clinical assessment for malnutrition [body mass index (BMI)-for-age <-2 standard deviation or clinician-confirmed nutritional deficiency], in accordance with recent guidelines for children with severe neurological impairment[21]. Comorbidities-including epilepsy, orthopedic complications, feeding difficulty, pain, gastroesophageal reflux, behavioral problems, communication deficits, and intellectual disability-were extracted from clinical and neurophysiological records. Operational definitions and full distributions are provided in Supplementary Table 1.

Statistical Analysis

Descriptive statistics were calculated to summarize demographic and clinical characteristics. Group differences

across GMFCS levels were assessed using one-way analysis of variance for continuous variables and chi-square tests for categorical variables. Pearson correlation coefficients were used to explore bivariate associations. All preliminary analyses were conducted in SPSS (version 28.0; IBM Corp.).

A multiple linear regression model was constructed to identify independent predictors of HRQoL (PedsQL total score), including GMFCS level, sleep quality (PSQI), epilepsy, and malnutrition. Model adequacy was evaluated using adjusted R^2, standardized β coefficients, 95% confidence intervals (CIs), and [variance inflation factors (VIF) <2.0]. Relative predictor importance was quantified by dominance analysis implemented in the relaimpo package in R (version 4.3.1), using 1000 bootstrap samples.

LCA was performed in Mplus version 8.9, using maximum likelihood estimation with robust standard errors. Competing models were evaluated using Akaike information criterion, Bayesian information criterion (BIC), adjusted BIC, entropy, and the bootstrap likelihood ratio test. A three-class solution was selected as optimal.

Mediation analysis was conducted using the PROCESS macro (model 4) in SPSS with 5000 bias-corrected bootstrap samples to test whether sleep quality was statistically associated with the relationships between epilepsy and HRQoL and between malnutrition and HRQoL. Indirect effects were considered significant when the 95% CI did not include zero.

Results

A total of 218 children and adolescents with CP were included. The mean age was 11.9±4.6 years (range: 6-18), and 44% were female. According to the GMFCS, 37% of participants were classified as mild (levels I-II), 28% as moderate (level III), and 35% as severe (levels IV-V). Gestational age (mean 35.4±3.6 weeks) and birth weight (mean 2520±710 g) did not differ significantly across GMFCS groups (p>0.05). Sex distribution and perinatal history also did not differ significantly between groups. Accordingly, these variables were not included as covariates in subsequent multivariable analyses. The prevalence of comorbidities increased consistently as motor severity increased, including epilepsy, malnutrition, intellectual disability, and visual and hearing impairments (all p<0.001; Table 1).

Comorbidities were common and showed pronounced gradients across the severity spectrum. Epilepsy was diagnosed in 40.4% of participants, rising from 15.2% in mild CP to 65.4% in severe CP. Malnutrition was identified in 43.6% of the cohort, with stepwise increases by CP severity (11.3% in mild CP, 35.0% in moderate CP, and 70.5% in severe CP). Feeding difficulties (32.1%), gastroesophageal reflux (19.2%), hip displacement (24.3%), scoliosis (18.8%), and joint contractures (30.3%) also increased markedly with higher GMFCS levels (all p<0.001). Intellectual disability and sensory impairments showed the same pattern (Table 2).

Functional and QoL measures demonstrated clear differences between GMFCS groups. The mean PEDI score was 54.2±18.7, with significantly lower scores in children with severe CP compared with other groups (p<0.001). Sleep quality, assessed by the PSQI, was impaired in most participants (mean 8.7±3.5), and scores increased with motor severity (p<0.001). The mean PedsQL total score was 61.4±17.6 and showed a marked gradient across GMFCS levels: higher motor severity was associated with

Table 1. Demographic and clinical characteristics of participants

Characteristic	Total (n=218)	Mild CP (I-II, n=80)	Moderate CP (III, n=60)	Severe CP (IV-V, n=78)	p-value
Age (years, mean ± SD)	11.9±4.6	10.4±3.8	11.8±4.2	13.6±4.5	0.004*
Female sex (%)	44	46	43	41	0.82
Gestational age (weeks, mean ± SD)	35.4±3.6	36.2±2.9	35.1±3.3	34.8±4.2	0.07
Birth weight (g, mean ± SD)	2520±710	2680±680	2490±700	2380±720	0.09
Presence of epilepsy (%)	40.4	15.2	41.7	65.4	<0.001**
Malnutrition (%)	43.6	11.3	35.0	70.5	<0.001**
Visual and/or hearing impairment (%)	28.8	9.0	24.0	48.7	<0.001**
Intellectual disability ≥ mild (%)	33.9	10.5	32.5	57.7	<0.001**

Continuous variables were analyzed using one-way analysis of variance, and categorical variables were analyzed using the chi-square test. A single asterisk (*) indicates p<0.05, and a double asterisk (**) indicates p<0.001; both denote statistically significant differences

SD: Standard deviation, CP: Cerebral palsy

substantially lower HRQoL (p<0.001). Physical and emotional functioning subdomains demonstrated comparable patterns (Table 3).

Correlation analyses showed strong associations between GMFCS level and both functional independence (PEDI; r=-0.75, p<0.001) and HRQoL (PedsQL; r=-0.72, p<0.001). Poorer sleep quality was moderately correlated with higher GMFCS levels (r=0.48, p<0.001), lower PedsQL scores (r=-0.56, p<0.001), and lower PEDI scores (r=-0.39, p<0.001). Epilepsy was significantly positively correlated with PSQI (r=0.34, p<0.001) and negatively correlated with functional and HRQoL measures. Malnutrition was also associated with lower PedsQL and PEDI scores (p<0.001) (Table 4).

Multivariate regression analysis identified four independent predictors of HRQoL: GMFCS level (β=-0.58, p<0.001), PSQI score (β=-0.25, p=0.002), epilepsy (β=-0.22, p=0.004), and malnutrition (β=-0.18, p=0.010). The model demonstrated good explanatory capacity (adjusted R^2=0.62), and no multicollinearity was detected (VIF <2.0). These findings indicate that motor severity, sleep disturbance, seizure disorder, and nutritional status each contribute uniquely to HRQoL (Table 5).

LCA revealed three comorbidity clusters as the optimal solution (BIC=4615.8; entropy=0.86). The low-burden class (43%) was characterized by minimal comorbidities and predominantly mild motor impairment. The moderate-burden class (33%) demonstrated intermediate rates of epilepsy, feeding problems, and malnutrition, with most children classified as GMFCS III. The high-burden class (24%) exhibited elevated probabilities of epilepsy, malnutrition, orthopedic complications, sleep disturbance, and intellectual disability, with a predominance of severe motor impairment. HRQoL and functional outcomes differed significantly between classes, with the lowest scores observed consistently in the high-burden group (p<0.001) (Supplementary Table 2, Figure 1).

Table 2. Prevalence of comorbidities across GMFCS severity levels

Comorbidity	Total (n=218)	Mild CP (I-II, n=80)	Moderate CP (III, n=60)	Severe CP (IV-V, n=78)	p-value
Epilepsy (%)	40.4	15.2	41.7	65.4	<0.001**
Nutritional difficulties (%)	38.5	10.0	32.0	69.2	<0.001**
Malnutrition (%)	43.6	11.3	35.0	70.5	<0.001**
Dysphagia (%)	32.1	9.1	29.0	61.5	<0.001**
Gastroesophageal reflux (%)	19.2	5.6	15.0	38.5	<0.001**
Hip dislocation (%)	24.3	6.3	19.0	46.2	<0.001**
Scoliosis (%)	18.8	3.8	14.5	39.7	<0.001**
Contractures (%)	30.3	8.9	26.5	55.1	<0.001**
Visual and/or hearing impairment (%)	28.8	9.0	24.0	48.7	<0.001**
Intellectual disability ≥ mild (%)	33.9	10.5	32.5	57.7	<0.001**

Comparisons among GMFCS groups were performed using the chi-square test for categorical variables

**: p<0.001 indicates statistically significant group differences, CP: Cerebral palsy, GMFCS: Gross motor function classification system

Table 3. Functional and quality of life measures across GMFCS levels

Measure	Total (n=218)	Mild CP (I-II, n=80)	Moderate CP (III, n=60)	Severe CP (IV-V, n=78)	p-value
PEDI total score (mean ± SD)	54.2±18.7	72.1±14.2	56.3±13.9	32.9±12.8	<0.001**
PSQI total score (mean ± SD)	8.7±3.5	6.0±2.8	8.5±3.1	11.0±3.2	<0.001**
PedsQL total score (mean ± SD)	61.4±17.6	80.2±12.5	62.8±13.8	42.9±11.7	<0.001**
Physical functioning subscale	58.3±19.2	79.5±14.1	60.7±13.5	37.6±12.9	<0.001**
Emotional functioning subscale	64.8±18.1	82.1±13.7	67.2±15.3	45.9±14.5	<0.001**

Group comparisons were conducted using one-way analysis of variance followed by Bonferroni-adjusted post-hoc tests **: p<0.001 indicates statistically significant group differences. Higher PSQI scores indicate poorer sleep quality, CP: Cerebral palsy, GMFCS: Gross motor function classification system, PSQI: Pittsburgh sleep quality index, PEDI: Pediatric evaluation of disability inventory, PedsQL: Pediatric quality of life inventory, SD: Standard deviation

Table 4. Correlation coefficients between functional, quality of life, and clinical variables

Variables	PedsQL	PEDI	PSQI	Epilepsy	Malnutrition	GMFCS
PedsQL	-	0.68**	-0.56**	-0.29**	-0.41**	-0.72**
PEDI	0.68**	-	-0.39**	-0.25**	-0.35**	-0.75**
PSQI	-0.56**	-0.39**	-	0.34**	0.28**	0.48**
Epilepsy	-0.29**	-0.25**	0.34**	-	0.22*	0.44**
Malnutrition	-0.41**	-0.35**	0.28**	0.22*	-	0.46**
GMFCS	-0.72**	-0.75**	0.48**	0.44**	0.46**	-

All correlations were calculated using Pearson's correlation coefficients

*: p<0.05, and **: p<0.001 indicate statistically significant relationships, GMFCS: Gross motor function classification system, PSQI: Pittsburgh sleep quality index, PEDI: Pediatric evaluation of disability inventory, PedsQL: Pediatric quality of life inventory

Table 5. Multivariate linear regression predicting health-related quality of life (PedsQL total score)

Predictor	Standardized β	95% confidence interval	p-value
GMFCS level	-0.58	-0.64 to -0.47	<0.001***
PSQI total score	-0.25	-0.39 to -0.12	0.002**
Epilepsy (yes)	-0.22	-0.33 to -0.09	0.004**
Malnutrition (yes)	-0.18	-0.29 to -0.06	0.010*

Model statistics, adjusted R^2=0.62, F (4, 213) =47.8, p<0.001; no multicollinearity detected (variance inflation factor <2.0)

*: p<0.05, **: p<0.01, ***: p<0.001 indicate statistical significance, GMFCS: Gross motor function classification system, PSQI: Pittsburgh sleep quality index, PedsQL: Pediatric quality of life inventory

Mediation analyses indicated that sleep quality was indirectly and significantly associated with the relationships between epilepsy and HRQoL and between malnutrition and HRQoL. The indirect effect was significant for epilepsy (β_indirect=-0.07; 95% CI: -0.12 to -0.03) and for malnutrition (β_indirect=-0.05; 95% CI: -0.10 to -0.02). Sleep quality accounted for 28% of the total effect of epilepsy on PedsQL and 25% of the total effect of malnutrition on PedsQL.

The mediation model demonstrated acceptable overall fit indices (comparative fit index=0.97, root mean square error of approximation=0.04) (Supplementary Table 3). Figure 2 shows the standardized mediation pathways linking epilepsy and malnutrition to HRQoL through sleep quality.

Dominance analysis demonstrated that GMFCS level contributed the largest proportion of explained variance in

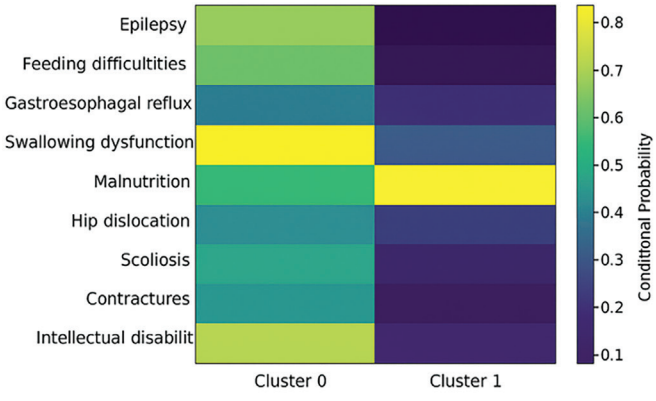

Figure 1. Latent class analysis identifying three comorbidity clusters among children with cerebral palsy. Class proportions are posterior probability-weighted estimates (43%, 33%, and 24%)

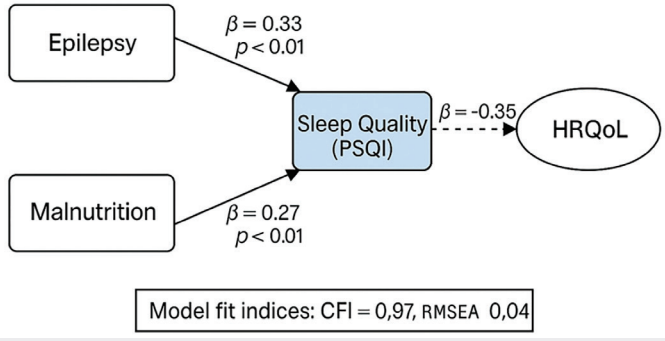

Figure 2. Standardized mediation model illustrating the statistically derived indirect associations of epilepsy and malnutrition with HRQoL through sleep quality in children with CP

CP: Cerebral palsy, PSQI: Pittsburgh sleep quality index, HRQoL: Health-related quality of life, CFI: Comparative fit index, RMSEA: Root mean square error of approximation

HRQoL (≈42%), followed by sleep quality (≈28%), epilepsy (≈18%), and malnutrition (≈12%) (Figure 3). Orthopedic variables and BMI contributed minimally.

These findings were consistent with the regression results. All variable definitions and descriptive statistics are provided in Supplementary Table 1; LCA model parameters are provided in Supplementary Table 2; and mediation coefficients are provided in Supplementary Table 3.

Discussion

This study provides a comprehensive multidimensional analysis of the determinants of HRQoL in children and adolescents with CP. The findings demonstrate that, although gross motor function remains the dominant predictor of HRQoL, sleep disturbances, epilepsy, and malnutrition exert substantial, independent effects on HRQoL. These results reinforce the contemporary understanding of CP as a multisystem neurodevelopmental condition in which functional outcomes arise from interactions among motor impairment, neurological comorbidities, and broader biopsychosocial factors[22,23].

The strong negative association between GMFCS level and HRQoL is consistent with extensive evidence linking motor severity with reduced participation, greater dependence, and limitations in daily functioning[24]. However, the regression and dominance analyses collectively indicate that motor impairment explains only part of the outcome variance.

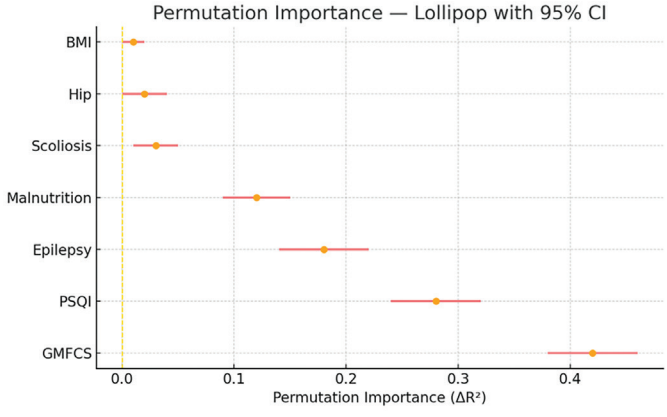

Figure 3. Relative importance (dominance weights) of predictors of health-related quality of life in children with cerebral palsy

BMI: Body mass index, CI: Confidence interval, GMFCS: Gross motor function classification system, PSQI: Pittsburgh sleep quality index

Sleep quality and nutritional status together accounted for nearly 40% of the overall explained variance, indicating that two children of the same GMFCS level may have markedly different QoL profiles depending on these modifiable factors. This supports emerging conceptual models proposing that comorbidities in CP are not merely consequences of motor dysfunction but also co-determinants of developmental, psychosocial, and functional trajectories[25].

A key contribution of the present study is the identification of sleep quality as both an independent determinant and a mediator of HRQoL. The mediation model revealed that sleep partially accounted for the associations among epilepsy, malnutrition, and HRQoL, suggesting that sleep disruption functions as an active mechanism-rather than a passive symptom-within the broader multimorbidity network in CP. Evidence from pediatric neurology increasingly demonstrates that fragmented or nonrestorative sleep is associated with cognitive impairment, behavioral dysregulation, and emotional difficulties in CP[26-28]. Longitudinal studies have shown that reduced sleep efficiency predicts poorer executive functioning and lower adaptive behavior scores over time[29]. Given its bidirectional relationship with seizures-where sleep deprivation increases epileptiform activity and nocturnal seizures degrade sleep continuity-addressing sleep disturbance may yield downstream improvements in cognitive, behavioral, and psychosocial domains[30]. Importantly, the finding that sleep quality accounted for 28% of the association between epilepsy and HRQoL suggests that therapeutic strategies for children with CP and epilepsy should extend beyond seizure control alone. Sleep-focused assessment and interventions, including sleep hygiene optimization and targeted nocturnal management, may represent important parallel components of comprehensive care in this population.

The independent contribution of malnutrition to reduced HRQoL further underscores the importance of nutritional assessment in CP. Prior research has shown that children with CP face an elevated risk of undernutrition due to dysphagia, reflux, and feeding inefficiency, but recent work also emphasizes the neurodevelopmental consequences of chronic undernutrition, including impaired cortical maturation, elevated inflammatory cytokines, and reduced neuroplastic potential[31]. The association between malnutrition and poorer sleep, observed in the mediation analysis, aligns with studies indicating shared metabolic and neuroendocrine pathways linking dietary insufficiency, disrupted circadian regulation, and increased fatigue[32]. These mechanisms offer biologically plausible explanations for the observed indirect effects on HRQoL.

The LCA expanded these findings by identifying three distinct comorbidity profiles-low-burden, moderate burden, and high burden. Children in the high-burden class exhibited markedly lower levels of HRQoL and functional independence, consistent with studies demonstrating that multimorbidity patterns in CP are structured rather than random[33,34]. Notably, the comorbidity patterns characterized here during childhood parallel those reported in adults with CP, in which neurological, musculoskeletal, and cardiometabolic multimorbidity clusters predict reduced life expectancy and increased healthcare utilization[35]. This developmental continuity suggests that early identification of high-burden profiles may enable proactive, preventive intervention to alter long-term trajectories.

Methodologically, this study contributes to the CP literature by integrating complementary statistical approaches-multivariate regression, dominance analysis, and mediation modelling-within a unified analytical framework. The regression model identified independent predictors; the dominance analysis quantified each variable's overall explanatory contribution; and the mediation analysis elucidated the statistical pathways linking comorbidities to HRQoL. Rather than conflicting, these methods converged on a coherent hierarchy: GMFCS level formed the structural basis of HRQoL, sleep quality acted as both a parallel determinant and a pathway through which epilepsy and malnutrition exert their influence, and epilepsy and malnutrition emerged as clinically meaningful comorbidities whose effects are partly modifiable. This triangulation supports a systems-level conceptualization of CP, consistent with modern models of precision rehabilitation[36,37].

The clinical implications of these findings are substantial. Routine assessment of sleep quality and nutritional status should be integrated into standard CP care pathways, alongside motor evaluation. Screening tools, such as the PSQI and structured feeding and nutrition assessments, may facilitate early detection of risk, although future work incorporating pediatric-specific sleep measures, such as the children's sleep habits questionnaire, may enhance behavioral granularity[38]. Interventions targeting sleep hygiene, nocturnal positioning, seizure optimization, and feeding rehabilitation may meaningfully improve HRQoL, potentially exceeding the effect size achievable through motor-focused therapy alone[38,39]. These results also underscore the role of interdisciplinary care models in which neurology, physiotherapy, gastroenterology, sleep medicine, and nutrition services collaborate to address the interconnected determinants of child health.

Study Limitations

Several limitations warrant consideration. The cross-sectional design precludes causal inference; it is plausible that lower HRQoL could exacerbate sleep or nutritional difficulties via reduced activity or caregiver strain. The single-center, tertiary-care sample may overrepresent children with more severe CP. A lthough PSQI demonstrates strong validity in pediatric neurodisability populations, its original development for adults should still be considered when interpreting sleep-related findings. Longitudinal, multi-center studies employing objective sleep measures, standardized nutritional assessments, and external validation of comorbidity clusters would strengthen generalizability. Although advanced statistical techniques were used, all analyses were derived from the same dataset; thus, predictive estimates require replication.

This study demonstrates that sleep quality, epilepsy, and malnutrition significantly and independently influence HRQoL in children with CP, beyond the contribution of motor severity. These findings show the importance of integrating sleep and nutritional interventions with traditional motor-based rehabilitation strategies. Recognizing CP as a multisystem condition-with modifiable comorbidities that jointly shape developmental and psychosocial outcomes-provides a strong rationale for comprehensive, interdisciplinary, and precision-oriented care models aimed at improving participation and long-term well-being for children with CP.

Conclusion

In this large cross-sectional study of children with CP, HRQoL was shaped not only by gross motor severity but also by a constellation of modifiable non-motor comorbidities. Sleep disturbance, epilepsy, and malnutrition emerged as independent and interacting determinants of well-being, with sleep quality acting as a potential explanatory factor linking neurological and nutritional burden to reduced daily functioning. The identification of distinct multimorbidity clusters and the quantification of the relative importance of predictors suggest that the cumulative impact of comorbidities is structured rather than incidental.

These findings underscore the need to reframe CP as a multisystem condition in which early recognition and management of sleep dysfunction, nutritional deficits,

and seizure instability are essential components of care. Incorporating systematic screening for these factors into routine clinical practice may meaningfully improve participation, emotional health, and long-term developmental trajectories. Future longitudinal and interventional studies are warranted to determine whether targeted, multidisciplinary approaches can modify life-course risks associated with high-burden comorbidity profiles.

Ethics

Ethics Committee Approval: Ethical approval was granted by the Recep Tayyip Erdoğan University Non-Interventional Clinical Research Ethics Committee (approval no: 2025/372, date: 11.09.2025), and all procedures adhered to the Declaration of Helsinki.

Informed Consent: Written informed consent was obtained from all caregivers.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: M.B., Concept: M.B., Ö.B.Ç., Design: M.B., Ö.B.Ç., Data Collection or Processing: M.B., Analysis or Interpretation: M.B., Ö.B.Ç., Literature Search: M.B., Ö.B.Ç., Writing: M.B., Ö.B.Ç.

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