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Associations between Infant and Parent Characteristics and Measures of Family Well-Being in Neonates with Seizures: A cohort study

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Abstract

Objective—To characterize and determine risk factors for key dimensions of well-being at hospital discharge in families of neonates with acute symptomatic seizures.

Study Design—This prospective, observational cohort study enrolled 144 parent-infant dyads among neonates with acute symptomatic seizures from nine pediatric hospitals of the *Neonatal Seizure Registry*. One parent per family completed discharge surveys, which included measures of anxiety and depression, health related quality of life, and impact on the family. Multivariable regression analyses adjusted for site were constructed to examine parent and infant characteristics associated with well-being.

Results—At discharge, 54% of parents reported symptoms of anxiety and 32% reported symptoms of depression. Parents of infants with hypoxic-ischemic encephalopathy reported more depression and worse quality of life (QOL) than parents of infants with other seizure etiologies. Parental QOL was also lower with greater infant age at discharge. A higher level of maternal education was associated with greater impact on the family. All of these differences were medium to large effect sizes, ranging from 0.52 to 0.78.

Conclusions—Symptoms of anxiety and depression are common in parents of infants with neonatal seizures and several parent and infant characteristics are associated with poorer parental quality of life and family well-being. These findings are a call to action to improve mental health screening and services for parents of infants with neonatal seizures.

Keywords

anxiety; depression; quality of life; family impact; hypoxic-ischemic encephalopathy; perinatal ischemic stroke; intracranial hemorrhage

Introduction

The early parent-infant relationship is a key influencer of child health and developmental outcomes (1,2). Threats to parent well-being such as anxiety, depression, poor quality of life (QOL) and difficulties in family coping, may have long-lasting adverse effects on the parent-infant relationship, as well as child health and developmental outcomes (3–6). Parents of infants who require a neonatal intensive care unit (NICU) admission at birth for conditions

such as prematurity or congenital heart disease often experience threats to family well-being (7,8) that compound their child's risk for physical and developmental problems in later life (9–13).

Neonatal seizures most often reflect acute brain injury (e.g., most commonly hypoxic-ischemic encephalopathy [HIE], perinatal ischemic stroke, or intracranial hemorrhage [ICH]), and are frequently associated with short and long-term neurological disorders (14). However, parent and family well-being has not been characterized for infants with neonatal seizures and it is not known if their experiences are similar to, or different from those of infants with other neonatal conditions. Routine postpartum mental health screening has been adopted in only a few states (15) and there is no widely adopted standard for parental mental health screening in the NICU setting. Characterization of anxiety, depression, health related quality of life, and family impact for parents of infants with neonatal seizures is necessary to design effective screening and treatment strategies, both to improve parental quality of life (QOL) and to help promote optimal development for high-risk infants.

Therefore, the objective of this study was to characterize key dimensions of parent and family well-being at hospital discharge in parents of neonates with acute symptomatic seizures. We hypothesized that both parent and infant characteristics would be associated with higher reported levels of anxiety and depression, lower reported levels of parental QOL, and greater impact on family well-being.

Methods

Data for these analyses were obtained from the *Neonatal Seizure Registry-II*, which is a prospective, multi-center observational cohort study of children with acute symptomatic neonatal seizures (NCT02789176). Infant-parent dyads were enrolled during the neonatal admission at nine participating children's hospitals in the United States and are being followed until 24 months corrected age. Each site has a level IV NICU and follows the American Clinical Neurophysiology Society guideline for continuous electroencephalographic monitoring in neonates (16). A parent and stakeholder advisory panel composed of parents of children who experienced seizures in infancy assisted with study design, survey selection, and data interpretation. Study personnel coding clinical variables were blinded to the results of parent well being assessments.

Study inclusion criteria were: infants <44 weeks postmenstrual age at seizure onset; seizures due to an acute symptomatic cause (including, but not limited to HIE, ischemic stroke, or ICH); and parent(s) who were English or Spanish literate (with assistance of interpreter). Infants were excluded from the study if they: were at risk for adverse outcome independent of seizures and underlying brain injury (including but not limited to inborn errors of metabolism, fetal infection, brain malformation, or genetic syndrome); had transient cause for seizures (e.g., hypocalcemia, hyponatremia, or hypoglycemia without brain injury); had neonatal-onset epilepsy syndromes; or did not survive the initial hospital admission. The study was approved by the institutional review boards of all study sites, and a parent of every enrolled infant provided written informed consent.

Parent Measures

One parent per family completed a suite of validated survey instruments near the time of discharge from the NICU via paper forms, online, by telephone, or in-person with a trained research assistant, depending on their preference. The NICU discharge surveys included 63 items that comprised three clinically important measures of parent and family well-being: (1) Hospital Anxiety and Depression Scale (HADS) (17); (2) World Health Organization Quality of Life (WHOQOL-BREF) scale (18); and (3) Revised Impact On Family (IOF) scale (19).

The HADS is a well-validated, 14-total item measure including subscale measures of symptoms of anxiety (7-items) and depression (7-items) with each item rated on a 4-point, 0 to 3 scale (20,21). Total subscale scores 0–7 on each subscale are considered normal. Scores 8–10 suggest borderline anxiety (HADS anxiety sub-scale) or depressive (HADS depression sub-scale) symptoms, and scores >10 are considered ‘abnormal (cases)’. Scores in the borderline and abnormal range represent clinically important symptoms of anxiety or depression (17). The HADS has been used extensively in research to characterize the impact of NICU hospitalization (22–24) and childhood illness (25,26) on parent psychological well-being, including parents of children with established epilepsy (27–29).

The WHOQOL-BREF measures four domains of health-related QOL. It includes 24 items (rated 1 to 5) as follows: physical health (7-items), psychological health (6 items), social relationships (3 items), and environment (8 items). It also includes two general questions on self-perceived QOL and general health (18). The scores are transformed into a scale ranging from 0 to 100, with 0 indicating worst and 100 indicating best QOL. The WHOQOL-BREF has been used to assess QOL in parents of preterm infants (30, 31), parents of infants with congenital anomalies (32), and children with epilepsy (33).

The revised IOF is a 15-item measure of parental perception (each rated on a 1 to 4 scale) of the ill child’s impact on the family (19,34). The overall score represents a single construct of personal, family and social impact (15 items), with higher scores indicating a greater impact on the family. Additionally, two subscales, financial strain (4 items; higher scores indicate more financial strain) and coping (6-items; higher scores indicate worse coping) are measured separately, but not included in the overall score. The IOF has been used extensively to measure the impact of infant and child illness, as well as disability across a range of neonatal and childhood conditions (35–38), including childhood epilepsy (39).

Infant Measures

Infant characteristics, seizure etiology, treatment, and co-morbidities were determined by chart review. Infants were considered to have a complex medical condition if they were born preterm (<37 weeks completed gestation), had surgical congenital heart disease, or required extracorporeal membrane oxygenation.

Data analysis

All analyses were conducted with SAS™ Software version 9.4 (Cary, NC). Univariate statistics described the sample. Bivariate analyses were completed as a first step towards

understanding the role of potential predictors. Missing data were minimal, with complete or near complete data (missing for ≤2 participants) for all independent variables with the exception of maternal education, which was missing for n = 20. Because of the small amount of missing data on all other variables and to avoid the analysis burden of multiple imputation, we included a category of unknown maternal education so as to not lose those participants from our analytical sample. As a sensitivity analysis, we reran our primary analysis with only complete cases (n = 122). Initial models included all parent and infant variables that may be associated with the overall scores for each of the parent and family well-being measures (Figure 1, online), We then adopted a hierarchical regression approach in which we grouped predictors into logical sets. *Baseline* measures included demographic characteristics (parent sex, highest maternal education level, race/ethnicity, private or public insurance) and clinical characteristics (infant sex, mode of delivery, inborn [study center] vs outborn [home or referral]). *Seizure characteristics* included seizure etiology, EEG seizure burden (defined as: none, few [<7], many [≥7], frequent recurrent but not fulfilling the definition of status epilepticus, and status epilepticus [seizures ≥50% of a 1-hour EEG epoch], number of anti-seizure medications at discharge), anti-seizure medications. *Clinical course* descriptors included complex medical condition (including preterm birth, congenital heart malformation, need for extracorporeal membrane oxygenation), feeding tube or respiratory support at discharge (including home oxygen or ventilator support including continuous positive airway pressure), and chronological age at discharge. We tested for the significance of the seizure and clinical course variables beyond baseline variables as groups using partial F-tests. This approach reduced the impact of multiple testing because: a) we only pursued statistical significance of the individual variables in a group if the group of variables led to a statistically significant improvement (a gateway testing procedure) in the model, and b) we determined the order of testing (baseline then other groups of variables) *a priori*. Thus, our final model included only variables that contributed as part of a statistically significant group. We reported p-values for group testing as well as the individual variable coefficients and p-values when the group of variables was statistically significant. We also reported the Akaike Information Criterion (AIC) as a measure of overall model fit. We then repeated the modeling procedures for the measures of well-being with subscales (WHOQOL-BREF and IOF). Effect sizes (Cohen's *d*) were calculated to demonstrate the magnitude of effect for significant associations by dividing the coefficient by the standard deviation of the outcome, derived from the root mean square residual of the regression model.

Results

Sample characteristics

Of the 150 parents approached, 6 declined (4%) to participate. No reasons were given. The final sample consisted of 144 parents (111 mothers (77%), 32 fathers (22%), 1 parent did not specify). Fifty-nine percent of the infants were male and the median gestational age at birth was 39.3 weeks (IQR 37.5–40.4 weeks) and median chronological age at discharge was 17.0 days (IQR 9.0 – 36.5 days). Twenty-five (17%) of the infants were preterm (<37 weeks gestation), with a median gestational age of 33.0 weeks (IQR 31.9–36.3, range 23.6–36.9 weeks). There was no difference in chronological age at discharge between preterm and full-

term infants with complex medical conditions. Most (69%; n=100) of the infants were outborn (e.g. delivered at hospital other than study center and transferred after delivery to study center for subsequent care) and median Apgar scores at 1 and 5 minutes after birth were 4 (2–8) and 8 (5–9), respectively. The primary seizure etiologies were HIE (38%), ischemic stroke (29%), and ICH (19%). Most (90%) of the infants had EEG documented seizures after admission to the study site, and 93 (65%) were discharged on one or more anti-seizure medication (range 1–3 medications), with 19 (13%) receiving more than one anti-seizure medication at hospital discharge. Table 1 provides a full sample description.

The distributions of overall and subscale scores for the outcome measures were normal without any notable skewness. There were no statistically significant differences on the overall or subscale scores between mothers and fathers on any of the outcome measures. Table 2 provides the mean levels of parent anxiety, depression, quality of life (QOL), and family impact scores. At discharge, 54% of parents had anxiety scores in the borderline (24%) or clinical (30%) range and 32% of parents had depression scores in the borderline (19%) or clinical (13%) range (Figure 2). Mean QOL and subscale scores were in the upper third of the scale range (better QOL), and mean family impact scores were in the lower third of the scale range (less impact).

Multi-level modeling of variables associated with parent well-being.

Table 3 (online) reports the bivariate zero order correlation matrix and Table 4 (online) reports the results of the hierarchical regression modeling. For the outcomes of depression and QOL, the models that included seizure characteristics and clinical course variables were both statistically significant. For anxiety, neither group of variables contributed. For family impact, clinical course, but not seizure characteristics, contributed.

Table 5 lists the results for individual predictors within the groups for the significant outcomes of depression, QOL, and family impact. Further model reduction for the depression outcome and the clinical course predictors showed that infant age at discharge was statistically significant (p=0.007) with an estimated increase in HADS depression score of 0.3 (95% CI 0.1 – 0.5) for each additional week of hospitalization, after dropping discharge with a feeding tube or respiratory support, but complex medical condition was not (p=0.62).

For both depression and QOL, seizure etiology was statistically significant, with parents of infants with an etiology of HIE reporting more depression (mean depression score difference 2.8 (95% CI 0.8 – 4.7); effect size Cohen's d =0.73) and lower QOL (mean QOL score difference 10.5 (95% CI 0.5 – 20.5); effect size Cohen's d = 0.52) compared to parents of infants with ICH. The same pattern was seen when comparing HIE to other seizure etiologies, with a mean increase for depression score of 2.7 (95% CI 0.4 – 5.0) (effect size Cohen's d = 0.71) and mean decrease in QOL score of 15.6 (95% CI 3.2 – 27.9) (effect size Coehn's d = 0.78). The rates of abnormal depression scores (cases) were 15% for parents of infants with HIE, 7% for those with infants with ICH, and 5% for other seizure etiologies. The rates of abnormal anxiety scores (cases) were 33% for parents of infants with HIE, 15% for those with infants with ICH, and 29% for other seizure etiologies. Parental QOL was also lower with greater infant age at discharge, with each additional week of hospitalizion

decreasing QOL score by 1.3 (95% CI 0.01 – 2.6). Only maternal education of college or more (compared to less than a college graduate) was associated with greater impact on the IOF scale in the final model (mean difference 5.4 (95% CI 1.4 – 9.4); effect size Cohen's d = 0.60).

Results of the sensitivity analysis using complete cases (n = 122) were similar, with the regression coefficient for age at discharge now significant in the full model for depression without further model reduction. The regression coeffieicent for age at discharge was close to statistically significant in the full model for QOL, although further model reduction and dropping discharge with a feeding tube or respiratory support brought the p-value to the level of significance.

Tables 6–8 (online) provide further results for the parent and family well-being measures with subscales (WHOQOL-BREF and IOF). For the social dimension of the parental QOL and the financial dimension of the impact on family, clinical course, but not seizure characteristics, contributed to the statistical models. For the physical, psychological, and environmental dimensions of QOL, as well as the coping dimension of the impact on family, neither the seizure characteristics, nor the clinical course contributed to the models significantly. Parents of infants who were older age at discharge had poorer QOL in the social dimension compared with parents of infants who were younger at discharge, with a score decrease of 1.4 (95% CI 0.3 – 2.6) for every additional week of hospitalization. Parents of unknown race reported worse coping than parents of other races (mean difference 5.4 (95% CI 0.01 – 10.8); effect size Cohen's d = 2.13) and parents of infants who were outborn reported worse coping than parents of inborn infants (mean difference 1.3 (95% CI 0.3 – 2.3); effect size Cohen's d = 0.53).

Discussion

This study characterizes the association between acute symptomatic neonatal seizures and parent and family well-being. At the time of their child's discharge from the neonatal admission, more than half of parents of infants with neonatal seizures experienced clinically important symptoms of anxiety and almost one-third experienced clinically important symptoms of depression. We found relevant associations between demographic and clinical characteristics, infant's seizure characteristics and markers of parent and family well-being including depression, QOL, and family impact with medium to large effect sizes ranging from 0.52 to 0.78. Although parental anxiety was very prevalent, it was not associated with any of the characteristics measured in this study. This may suggest that all parents of infants with neonatal seizures would benefit from preventative anxiety reduction interventions, and that those with risk factors should be screened and offered services to prevent depression.

Parents in this sample experienced more symptoms of depression than mothers of preterm infants at discharge (23) or than either mothers or fathers of children with epilepsy (27). However, the frequency of anxiety symptoms was similar to that reported for mothers of preterm infants at discharge (23) and is also similar to that reported for mothers of children (0–18 years of age) with epilepsy (27). Parental QOL and and family impact scores were comparable to those reported by parents of children with other serious neonatal or childhood

medical conditions (31,33). These findings are worrying because symptoms of anxiety and depression and poor QOL and family coping at discharge from the NICU are likely to persist and have been shown to interfere with family function and child development (3,4,10,11,13). These findings further underscore the need for universal mental health screening and treatment services for NICU families.

Parental QOL was lower with greater infant chronological age at discharge. This association is consistent with findings from other studies about the difficulties faced by families of children with long intensive care hospital stays (40) and complex care at home after NICU discharge (41). Of the demographic characteristics, more advanced maternal education was associated with greater family impact. This has not been previously reported, and may indicate greater concerns among more educated parents about the ability for their child to achieve academically, or how the infant's condition has or will affect the family. Overall impact on the family was correlated only with maternal education level, with mothers with higher education levels reported higher impact on the family. Others have shown that socioeconomic status (but not maternal education) was a significant predictor of maternal QOL in mothers of children with epilepsy, along with self-rated health status, sleep, sense of mastery, and optimism (42). Further research will be needed to confirm and explain these findings.

This study is the first to report seizure etiology significantly correlating with parent well-being. We can only speculate as to why parents of infants whose seizures were caused by HIE would report more symptoms of depression, and lower overall QOL than parents of infants with seizures related to other acute etiologies. HIE occurs in 1–2/1,000 live births and is, by far, the most common cause for seizures in the neonatal period (43). As such, information about the risk of neurodevelopmental disability after HIE is widely available through the medical literature, medical and parent group resources, as well as medicolegal websites that target this condition, particularly when compared to other causes of early life seizures. For many parents of infants with HIE, an unexpected perinatal crisis occurred after a relatively normal pregnancy taken to term. Infants are often transferred to facilities away from the mother, who may be dealing with her own health complications (44). Existing data suggest that communication challenges, including fragmented communication, difficulty processing complex medical information, and prognostic uncertainty, may be amplified for parents with HIE (45, 46). Together, these factors may account for the more severe mental health symptoms in these parents. Interestingly, seizure burden and anti-seizure medication treatment were not significantly associated with dimensions of parent or family well-being, as has been found in other studies (42,47). These findings require further investigation.

Several limitations should be noted when considering these findings. First, although this was a multi-site sample, the participants were recruited from large tertiary urban medical centers and may not be representative of all regions and centers where acute neonatal seizures are treated. Moreover, although there was some racial/ethnic diversity and similar proportions of public and private insurance in the sample, maternal education was higher than average and the proportion of fathers in the study was relatively small (20%); therefore further studies with larger and more diverse samples are needed to confirm these findings. Second, this study includes a limited number of predictors; there may be additional prenatal and postnatal

factors such as neurological prognosis and physician communication that could be associated with parent and family well-being. Our findings indicate that a significant proportion of parents and families may experience difficulties in coping, which warrants further study and targeted clinical interventions within the family support structure.

Based on the strength of these findings and the large literature on mental health problems experienced by parents of infants and children requiring intensive care (6,40), NICU providers should consider implementing mental health screening for all parents prior to discharge, as well as referral and preventative services (5,48,49) for parents of infants with seizures in the neonatal period.

In summary, symptoms of anxiety and depression at the time of NICU discharge are common among parents of newborns with acute symptomatic seizures. Factors that are associated with poorer parent and family well-being (with medium to large effect sizes) include higher level of maternal education, HIE seizure etiology, and higher chronological age at discharge. These findings are a call to action to improve mental health screening and services for parents of infants with neonatal seizures, and can help providers to target and support the highest risk families. Future studies are needed to understand how parent and family well-being changes over time, and to determine the effectiveness of screening, prevention and treatment for parents during their infant's neonatal admission.

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Abbreviations:

EEG	Electroencephalography
HADS	Hospital Anxiety and Depression Scale
HIE	Hypoxic ischemic encephalopathy
IOF	Impact On Family
ICH	Intracranial hemorrhage
NICU	Neonatal intensive care unit
QOL	Quality of life
WHOQOL-BREF	World Health Organization Quality of Life

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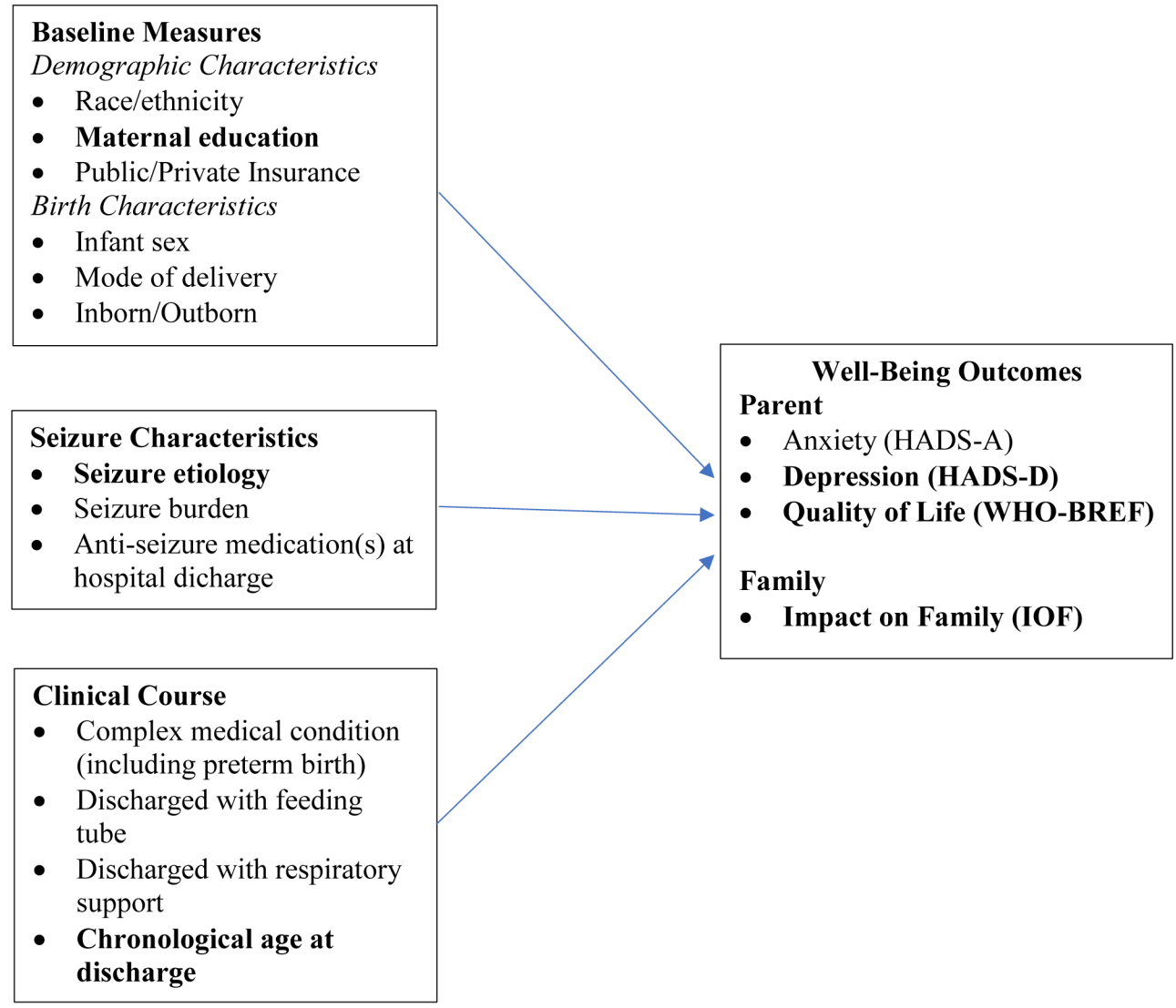

Bold = significant associations ($p<0.05$) in final model

Figure 1.

Hypothesized and actual relationships between parent and infant characteristics and family well-being at discharge for 144 parents of newborns with acute symptomatic seizures.

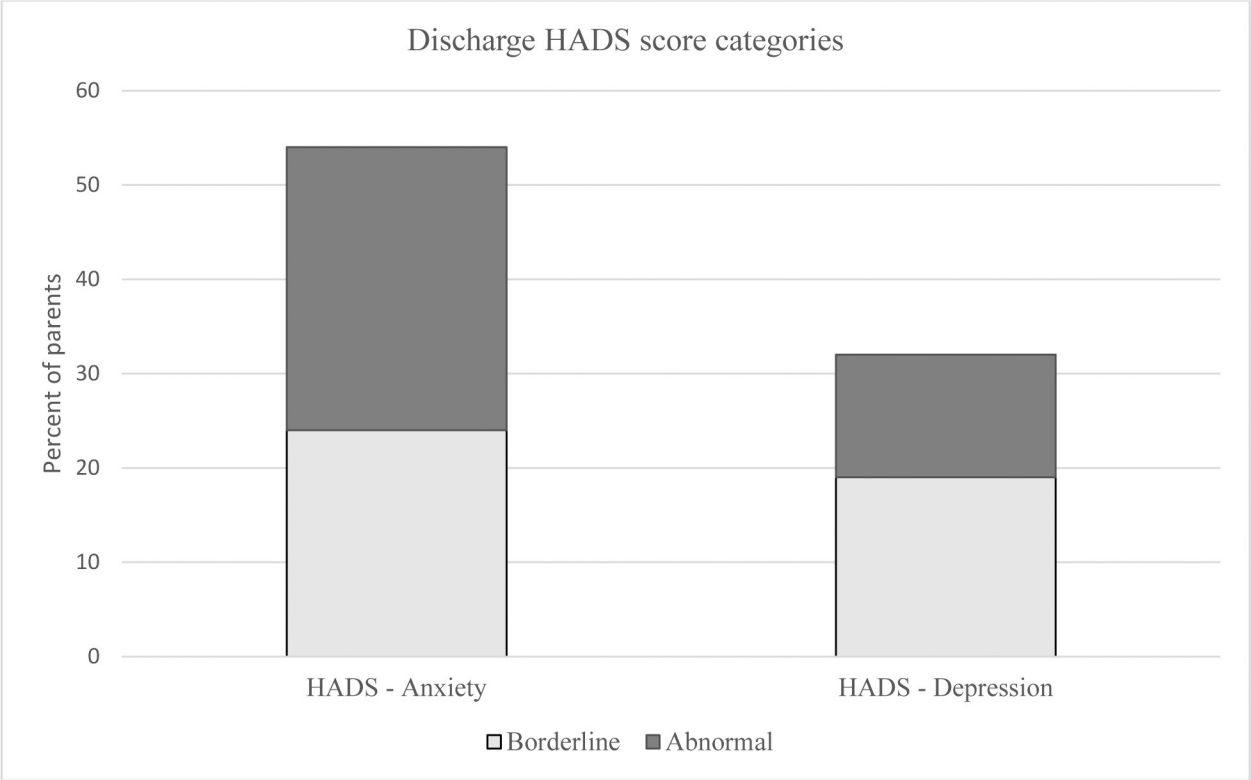

Figure 2.
Depression and anxiety at discharge for 144 parents of neonates with acute symptomatic seizures

Table 1.

Clinical and demographic characteristics of 144 infant/parent dyads of children with acute symptomatic neonatal seizures.

	N=144
Baseline Measures: Demographic Characteristics	
Race	
White	85 (59%)
Black/African American	13 (9%)
Asian	11 (8%)
American Indian/Alaskan Native	2 (1%)
Native Hawaiian / Other Pacific Islander	2 (1%)
Mixed Race (combine with more than 1 race)	5 (4%)
Other	19 (13%)
Unknown/Not reported/Declined to answer	7 (5%)
Ethnicity	
Hispanic or Latino	27 (19%)
Not Hispanic or Latino	112 (78%)
Unknown / Not reported/ Declined to answer	5 (3%)
Maternal education (highest achieved)	
Some education/high school not completed	8 (6%)
High school graduate	25 (17%)
Some college	26 (18%)
College graduate	39 (27%)
Graduate study	26 (18%)
Unknown/unavailable/declined to answer	20 (14%)
Insurance type	
Private	79 (55%)
Public	65 (45%)
Baseline Measures: Clinical Characteristics	
Male sex	85 (59%)
Preterm	25 (17%)
Outborn	100 (69%)
Mode of Delivery	
Vaginal	66 (46%)
Operative vaginal	5 (3%)
Scheduled cesarean section	10 (7%)
Emergent cesarean section	62 (43%)
Unknown	1 (1%)
1 minute Apgar score	4 (2 – 8)
5 minute Apgar score	8 (5 – 9)

	N=144
Seizure Characteristics	
Primary seizure etiology	
Hypoxic ischemic encephalopathy	55 (38%)
Perinatal Ischemic stroke	41 (28%)
Intracranial hemorrhage	27 (19%)
Other	21 (15%)
Hypothermia treatment	41 (28%)
EEG Seizures (at study center)	
None	15 (10%)
Rare EEG seizures (< 7)	45 (31%)
Many isolated EEG seizures (>=7)	29 (20%)
Frequent recurrent EEG seizures	30 (21%)
Status epilepticus	25 (17%)
Anti-seizure medication prescribed at hospital discharge	
None	52 (36%)
Phenobarbital	78 (54%)
Levetiracetam	25 (17%)
Other	11 (8%)
More than one anti-seizure prescribed at hospital discharge	19 (13%)
Clinical Course Characteristics	
Complex medical condition	43 (30%)
Discharged with feeding device	41 (28%)
Respiratory support at discharge	12 (8%)
Chronological age at hospital discharge, *days*	17 (9–36)

Data are reported as n (%) or median (interquartile range)

Table 2.

Well-being at discharge for 144 parents of neonates with acute symptomatic seizures.

Outcome	N	Mean ± SD
HADS – Depression (0 to 3 scale; higher scores indicate more depression)	144	5.7 ± 4.1
HADS – Anxiety (0 to 3 scale; higher scores indicate more anxiety)	144	8.4 ± 4.3
WHOQOL-BREF (0 to 100 transformed scale; higher scores indicate better functioning)[1]		
Overall	142	73.3 ± 20.5
Physical	140	70.2 ± 16.6
Psychological	141	71.6 ± 18.3
Social	141	75.4 ± 19.1
Environment	142	73.1 ± 16.2
Self-perceived quality of life	142	4.0 ± 1.0
General health	141	3.9 ± 0.9
IOF (1 to 4 scale)		
Overall (higher score indicates more impact)	142	34.8 ± 9.7
Financial (higher score indicates more financial problems)	143	10.6 ± 3.0
Coping (higher score indicates worse coping)	142	8.3 ± 2.5

HADS=Hospital Anxiety and Depression; WHOQOL-BREF=World Health Organization Quality of Life Brief Assessment; IOF=Impact on Family

[1]WHO-QOL BREF: Transformed scores

Table 3:

Zero-order correlation matrix.

	HADS - Depression	HADS - Anxiety	WHOQOL BREF Overall	WHOQOL BREF Physical	WHOQOL BREF Psychological	WHOQOL BREF Social	WHOQOL BREF Environment	IOF Overall	IOF Financial	IOF Coping
Parent sex	−0.02	0.03	−0.07	0.12	−0.07	0.04	−0.01	−0.05	−0.10	−0.05
Race	−0.11	−0.02	−0.03	0.03	0.01	0.09	0.28	−0.04	−0.13	0.00
Maternal education	0.05	0.05	−0.05	−0.06	−0.11	−0.05	0.01	0.23	0.07	−0.04
Private insurance (vs. public)	0.05	0.14	−0.10	0.01	−0.07	0.07	0.30	0.04	−0.10	0.04
Emergency C-section (vs. all other modes of delivery)	0.06	0.12	0.00	−0.08	−0.01	0.10	−0.04	0.07	−0.01	0.00
Preterm birth (vs. term birth)	0.08	0.14	−0.08	−0.11	−0.11	−0.12	−0.07	0.10	0.09	−0.03
Outborn (vs. inborn)	0.16	0.16	−0.10	0.03	0.02	−0.01	0.09	0.21	0.11	−0.18
Seizure etiology	−0.08	−0.03	0.09	0.06	0.06	0.03	0.02	−0.07	−0.01	−0.05

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Table 4.

Hierarchical model fitting for parent and family well-being overall scores for 144 parents of neonates with acute symptomatic seizures.

				Outcome	HADS-Depression			HADS-Anxiety			WHOQOL-BREF Overall			IOF Overall	
					AIC	p		AIC	p		AIC	p		AIC	p
1. Base model (demographics, birth characteristics)					782	n/a		794	n/a		1193	n/a		984	n/a
2. Base model + Seizure characteristics (compared to model 1)					764	0.05		782	0.51		1160	0.09		964	0.49
3. Base model + Clinical course (compared to model 1)					775	0.14		790	0.65		1175	0.07		964	0.004
4. Base model + Seizure characteristics + Clinical course					754			778			1139			942	
(compared to model 2)						0.03			0.53			0.02			0.002
(compared to model 3)						0.01			0.44			0.03			0.25

HADS=Hospital Anxiety and Depression; WHOQOL-BREF=World Health Organization Quality of Life Brief Assessment; IOF=Impact on Family, AIC=Akaike Information Criterion (smaller values are better fitting models). P-value tests against indicated model.

Table 5.

Multi-level models accounting for clustering within institution predicting parent and family well-being for 144 parents of neonates with acute symptomatic seizures, accounting for identity of responder.

Regression Coefficients				
		Estimate (SE)		
Effect		**HADS - Depression**	**WHOQOL BREF Overall**	**IOF Overall**
Baseline (Demographic and clinical) Characteristics				
Race	**Non-White**	1.4 (0.8)	0.1 (4.2)	2.5 (1.8)
	Unknown race	1.0 (4.4)	0.4 (22.2)	−6.5 (9.7)
	White, non-Hispanic	-	-	-
Maternal education	**College graduate or more**	0.5 (0.9)	1.6 (4.6)	5.4 (2.0) **
	Missing	0.3 (1.2)	−1.0 (5.8)	5.8 (2.6) *
	Not a college graduate	-	-	-
Private insurance (vs. public)		1.0 (0.9)	−5.1 (4.5)	0.2 (2.0)
Emergency c-section (vs. all other modes of delivery)		−0.2 (0.8)	2.4 (3.7)	1.7 (1.6)
Preterm birth (vs. term birth)		0.5 (1.4)	−2.5 (7.2)	−4.6 (3.1)
Outborn (vs inborn)		−0.3 (0.8)	0.2 (4.2)	−2.6 (1.8)
Seizure Characteristics				
Seizure etiology	**ICH**	−2.8 (1.0) **	10.5 (5.0) *	
	Ischemic stroke	0.3 (0.8)	−1.5 (4.5)	
	Other	−2.7 (1.2) *	15.6 (6.2) *	
	HIE	-	-	
Many or frequent EEG seizures (compared to none or few)		0.0 (0.8)	−4.7 (3.9)	
Total seizure medications at discharge		−0.1 (0.6)	0.2 (2.7)	
Clinical Course				
Age at discharge (weeks)		0.2 (0.1)	−1.3 (0.7) *	0.2 (0.3)
Discharge with feeding tube or ventilatory support (vs. not)		1.0 (1.0)	−5.5 (5.2)	2.9 (2.2)
Complex medical condition (vs. none)		−1.0 (1.2)	4.7 (6.6)	5.4 (2.8)

HADS=Hospital Anxiety and Depression; WHOQOL-BREF=World Health Organization Quality of Life Brief Assessment; IOF=Impact on Family; EEG=electroencephalogram; HIE=Hypoxic ischemic encephalopathy; ICH=Intracranial hemorrhage.

* p <0.05;

** P<0.01

Table 6.

Hierarchical model fitting for parent QOL subscale scores.

Outcome	WHOQOL-BREF Physical		WHO QOL-BREFpsychological		WHOQOL-BREF social		WHOQOL-BREF environment	
	AIC	p	AIC	p	AIC	p	AIC	p
1. Base model (demographics, birth characteristics)	1117	n/a	1151	n/a	1159	n/a	1118	n/a
2. Base model + Seizure characteristics (compared to model 1)	1089	0.26	1121	0.18	1134	0.66	1091	0.33
3. Base model + Clinical course (compared to model 1)	1103	0.37	1138	0.48	1113	0.08	1104	0.23
4. Base model + Seizure characteristics + Clinical course	1073		1106				1075	
(compared to model 2)		0.13		0.20		0.02		0.08
(compared to model 3)		0.10		0.09		0.24		0.13

WHOQOL-BREF=World Health Organization Quality of Life Brief Assessment

Table 7.

Hierarchical model fitting for impact on family well-being overall scores.

	IOF financial		IOF coping	
Outcome	**AIC**	**p**	**AIC**	**p**
1. Base model (demographics, birth characteristics)	695	n/a	643	n/a
2. Base model + Seizure characteristics (compared to model 1)	688	0.84	638	0.82
3. Base model + Clinical course (compared to model 1)	682	0.004	640	0.23
4. Base model + Seizure characteristics + Clinical course	674		635	
(compared to model 2)		0.002		0.02
(compared to model 3)		0.62		0.74

IOF=Impact on Family

Table 8.

Multi-level models accounting for clustering within institution predicting parent and family well-being subscale scores (n = 144) and accounting for identity of responder.

Solution for Fixed Effects							
		Estimate (SE)					
Effect		**WHOQOL-BREF Physical**	**WHOQOL-BREF psychological**	**WHOQOL-BREF social**	**WHOQOL-BREF environment**	**IOF financial**	**IOF coping**
Baseline (Demographic and clinical) Characteristics							
Race	**Non-White**	−1.2 (3.3)	−2.3 (3.7)	−1.7 (3.8)	−5.8 (3.1)	0.9 (0.6)	0.1 (0.5)
	Unknown race	−19.6 (18.0)	−17.0 (19.8)	−18.0 (20.3)	−14.1 (16.8)	−1.8 (3.1)	5.4 (2.7) *
	White, non-Hispanic	-	-	-	-	-	-
Maternal education	**College graduate or more**	−4.0 (3.7)	−1.2 (4.1)	2.8 (4.3)	0.3 (3.5)	0.9 (0.6)	0.1 (0.6)
	Missing	−0.4 (4.8)	−4.5 (5.2)	−4.8 (5.4)	−2.2 (4.4)	0.7 (0.8)	−0.9 (0.7)
	Not a college graduate	-	-	-	-	-	-
Private insurance (vs. public)		0.9 (3.7)	−4.0 (4.1)	−1.8 (4.2)	6.3 (3.5)	−0.4 (0.6)	0.1 (0.6)
Emergency cesarean-section (vs. all other modes of delivery)		−2.8 (2.9)	−0.5 (3.2)	4.3 (3.4)	−0.3 (2.7)	0.0 (0.5)	0.0 (0.4)
Preterm birth (vs. term birth)		−5.3 (4.2)	−5.4 (4.6)	1.8 (6.5)	−2.8 (3.9)	−1.4 (1.0)	0.3 (0.6)
Outborn (vs inborn)		−3.0 (3.3)	−3.2 (3.7)	−1.9 (3.9)	−3.2 (3.1)	−0.2 (0.6)	1.3 (0.5) *
Seizure Characteristics							
Seizure etiology	**ICH**						
	Ischemic stroke						
	Other						
	HIE						
Many or frequent EEG seizures (compared to none or few)							
Total seizure medications at discharge							
Clinical Course							

Solution for Fixed Effects							
		Estimate (SE)					
Effect		**WHOQOL-BREF Physical**	**WHOQOL-BREF psychological**	**WHOQOL-BREF social**	**WHOQOL-BREF environment**	**IOF financial**	**IOF coping**
Age at discharge (weeks)				−1.4 (0.6)*		0.1 (0.1)	
Discharge with feeding tube or ventilatory support (vs. not)				3.2 (4.7)		0.9 (0.7)	
Complex medical condition (vs. none)				0.3 95.9)		1.4 (0.9)	

WHOQOL-BREF=World Health Organization Quality of Life Brief Assessment; IOF=Impact on Family; EEG=electroencephalogram; HIE=Hypoxic ischemic encephalopathy; ICH=Intracranial hemorrhage.

* p <0.05