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Variables affecting neurodevelopmental outcomes in infants with critical congenital heart disease

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Variables Affecting Neurodevelopmental Outcome in Infants with Critical Congenital Heart Disease

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Background

- The mortality of cardiac conditions in infancy is improving with advances in surgical planning and medical management.
- Neurologic morbidity remains significant, and clinically correlating an infant with their neurologic exam, MRI/EEG, and subsequent developmental testing remains a challenge.

Objective

- To Identify factors associated with poor neurodevelopmental outcomes in infants with critical congenital heart defects (CCHD) as assessed by the Bayley Scales of Infant and Toddler Development Edition IV (Bayley).

Methods

- Retrospective, single site study
- Neonates were inborn or admitted to the neonatal or cardiac intensive care units after diagnosis of CCHD requiring cardiac surgery
- 2015-2020, n=383, Bayleys done at 12 mo (36.3%) and 24 mo (25.8%)
- Primary outcomes: neurologic exam, MRI, and EEG at discharge as well as 12- and 24-month Bayleys
- Statistical analysis= univariable logistic regression, Fisher exact test, chi square analysis, Wilcoxon-Mann-Whitney test

Results

Table 1. Patient characteristics

Bayley at 12-month		Normal N = 81	Abnormal N = 58	p-value[c]	SMD[d]
Maternal age[a]		28 (25, 31)	29 (24, 32)	0.77	0.04
Maternal race	Minority	16 (20%)	13 (22%)	0.87	0.07
Marital status	Single	22 (27%)	21 (36%)	0.34	0.20
Prenatal counseling	Yes	51 (63%)	39 (67%)	0.73	0.09
Delivered at FHC	Yes	43 (53%)	35 (60%)	0.50	0.15
Deliver mode	C-section	23 (28%)	25 (43%)	0.11	0.31
Sex	Female	34 (42%)	24 (41%)	>0.99	0.01
Gestation age (weeks)[a]		39 (37, 39)	39 (38, 39)	0.71	0.06
Birth weight (kg)[a]		3.2 (2.7, 3.6)	3.2 (2.7, 3.5)	0.55	0.09
Norman	A	33 (41%)	29 (50%)	0.34	0.26
	B	32 (40%)	16)28%)		
	C	16 (20%)	13 (22%)		
Respiratory complication.	No	63 (78%)	43 (74%)	0.62	0.17
	Distress	7 (9%)	8 (14%)		
	Failure	11 (14%)	7 (12%)		
Genetic diagnosis		**36 (44%)**	**21 (36%)**	**0.045**	**0.43**
No					
	VUS	35 (43%)	20 (35%)		
	Yes	10 (12%)	17 (29%)		
CHD repair		**43 (53%)**	**12 (21%)**	**<0.001**	**0.71**
Biventricular					
Length of stay (days)[a]		**37 (24, 60)**	**62 (41, 119)**	**<0.001**	**0.62**
Enteral feeding at D/C		**36 (44%)**	**47 (81%)**	**<0.001**	**0.82**
Abnormal neurologic exam		3 (4%)	8 (14%)	0.052	0.36
Abnormal EEG		4/38[b] (11%)	8/33[b] (24%)	0.20	0.37
Abnormal MRI		**16/42[b] (38%)**	**23/35[b] (66%)**	**0.03**	**0.58**
Failure To Thrive		**39 (48%)**	**46 (79%)**	**<0.001**	**0.69**

Bayley at 24-month		Normal N = 61	Abnormal N = 38	p-value[c]	SMD[d]
Maternal age[a]		28 (25, 32)	28 (23, 31)	0.28	0.19
Maternal race	Minority	9 (15%)	11 (29%)	0.15	0.35
Marital status	Single	14 (23%)	17 (45%)	0.04	0.47
Prenatal counseling	Yes	39 (64%)	22 (58%)	0.70	0.12
Delivered at FHC	Yes	35 (57%)	20 (53%)	0.80	0.10
Deliver mode	C-section	21 (34%)	18 (47%)	0.29	0.27
Sex	Female	28 (46%)	16 (42%)	0.87	0.08
Gestation age (weeks)[a]		39 (37, 39)	38 (36, 39)	0.052	0.35
Birth weight (kg)[a]		**3.2 (2.8, 3.6)**	**2.8 (2.4, 3.3)**	**0.006**	**0.50**
Norman	A	26 (43%)	18 (47%)	0.89	0.10
	B	25 (41%)	14 (37%)		
	C	10 (16%)	6 (16%)		
Respiratory complication	No	45 (74%)	23 (61%)	0.38	0.29
	Distress	6 (10%)	6 (16%)		
	Failure	10 (16%)	9 (24%)		
Genetic diagnosis	No	27 (44%)	19 (50%)	0.15	0.41
	VUS	25 (41%)	9 (24%)		
	Yes	9 (15%)	10 (26%)		
CHD repair	Biventricular	31 (51%)	16 (42%)	0.52	0.18
Length of stay (days)[a]		**41 (25, 82)**	**77 (41, 169)**	**0.004**	**0.53**
Enteral feeding at D/C		**29 (48%)**	**30 (79%)**	**0.004**	**0.69**
Abnormal neurologic exam		**1 (2%)**	**7 (18%)**	**0.005**	**0.58**
Abnormal EEG		3/27[b] (11%)	7/19[b] (37%)	0.07	0.63
Abnormal MRI		**16/42[b] (38%)**	**23/35[b] (66%)**	**0.03**	**0.58**
FTT		**30 (49%)**	**30 (79%)**	**0.006**	**0.65**
Yes					

[a] median (1st quartile, 3rd quartile); [b] Among patients who had EEG or MRI scans; [c] Wilcoxon Mann-Whitney test for maternal age, gestational age, birth weight, and length of stay, Fisher's exact test for abnormal neurologic exam, and Chi-squared test for all the other variables; [d] standardized mean difference

Figure 1. Abnormal Bayley exams and associated patient characteristics

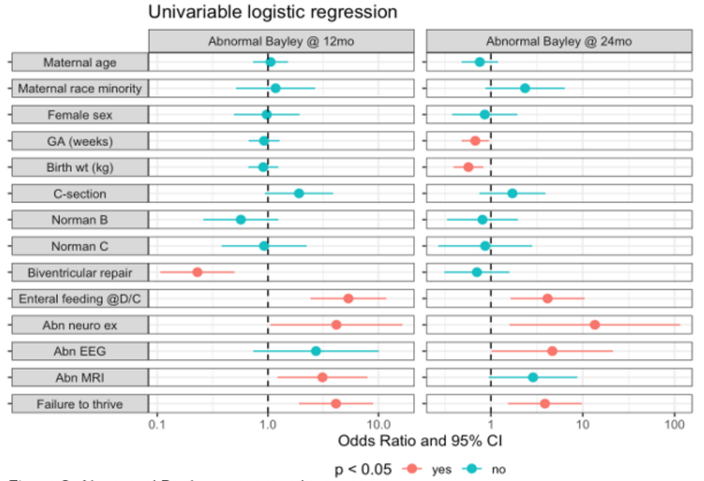
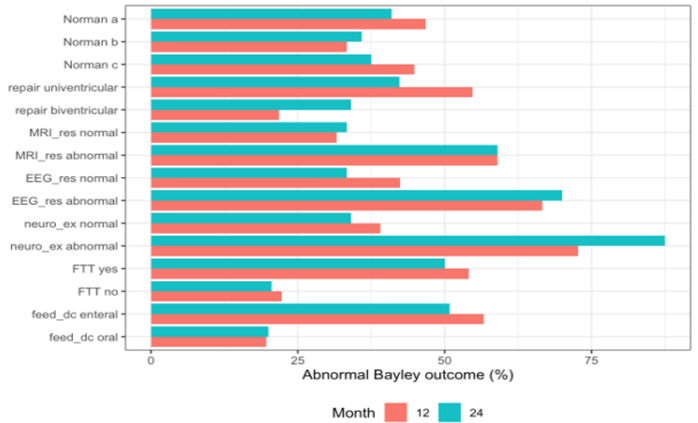


Figure 2. Abnormal Bayley outcomes by category



Results

40% of Bayleys were abnormal (gross motor, expressive language)

145 infants with EEGs, 17% showed seizures or focal slowing.

Of these abnormal EEGs, 45% had an abnormal Bayley.

146 MRIs, 58% showed ischemia, infarct, atrophy, stroke, or hemorrhage.

Abnormal Bayley at 12 mo 3.11x higher with abnormal MRI (95% CI 1.22-7.94, d= 0.63)

73% and 87.5% of abnormal neuro exams had abnormal Bayleys (12 and 24 mo)

Conclusion

- Delineating risk factors in infants with congenital heart defects could aid in predicting long-term neurodevelopmental outcomes.
- Statistically significant predictors of abnormal Bayleys include:
  - Enteral feeding at discharge
  - Single ventricle repair
  - Failure to thrive
  - Abnormal neuro exam
  - Abnormal MRIs
  - Increased length of stay
  - Genetic diagnosis
  - Lower BW
- Abnormal neurologic exams, MRI, and EEG at discharge can be associated with abnormal Bayleys in childhood.