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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	16 (20%)	13 (22%)	0.87	0.07
Marital status	22 (27%)	21 (36%)	0.34	0.20
Prenatal counseling	51 (63%)	39 (67%)	0.73	0.09
Delivered at FHC	43 (53%)	35 (60%)	0.50	0.15
Deliver mode	23 (28%)	25 (43%)	0.11	0.31
Sex	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	33 (41%)	29 (50%)	0.34	0.26
	B	32 (40%)	16 (28%)	
	C	16 (20%)	13 (22%)	
Respiratory complication	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	37 (24, 60)	62 (41, 119)	<0.001	0.62
Length of stay (days) ^a	36 (44%)	47 (81%)	<0.001	0.82
Enteral feeding at D/C	3 (4%)	8 (14%)	0.052	0.36
Abnormal neurologic exam	4/38 ^b (11%)	8/33 ^b (24%)	0.20	0.37
Abnormal EEG	16/42 ^b (38%)	23/35 ^b (66%)	0.03	0.58
Abnormal MRI	39 (48%)	46 (79%)	<0.001	0.69
Failure To Thrive				

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	9 (15%)	11 (29%)	0.15	0.35
Marital status	14 (23%)	17 (45%)	0.04	0.47
Prenatal counseling	39 (64%)	22 (58%)	0.70	0.12
Delivered at FHC	35 (57%)	20 (53%)	0.80	0.10
Deliver mode	21 (34%)	18 (47%)	0.29	0.27
Sex	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	26 (43%)	18 (47%)	0.89	0.10
	B	25 (41%)	14 (37%)	
	C	10 (16%)	6 (16%)	
Respiratory complication	45 (74%)	23 (61%)	0.38	0.29
	Distress	6 (10%)	6 (16%)	
	Failure	10 (16%)	9 (24%)	
Genetic diagnosis	27 (44%)	19 (50%)	0.15	0.41
No	VUS	25 (41%)	9 (24%)	
	Yes	9 (15%)	10 (26%)	
CHD repair	31 (51%)	16 (42%)	0.52	0.18
Biventricular	41 (25, 82)	77 (41, 169)	0.004	0.53
Length of stay (days) ^a	29 (48%)	30 (79%)	0.004	0.69
Enteral feeding at D/C	1 (2%)	7 (18%)	0.005	0.58
Abnormal neurologic exam	3/27 ^b (11%)	7/19 ^b (37%)	0.07	0.63
Abnormal EEG	16/42 ^b (38%)	23/35 ^b (66%)	0.03	0.58
Abnormal MRI	30 (49%)	30 (79%)	0.006	0.65
FTT				
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

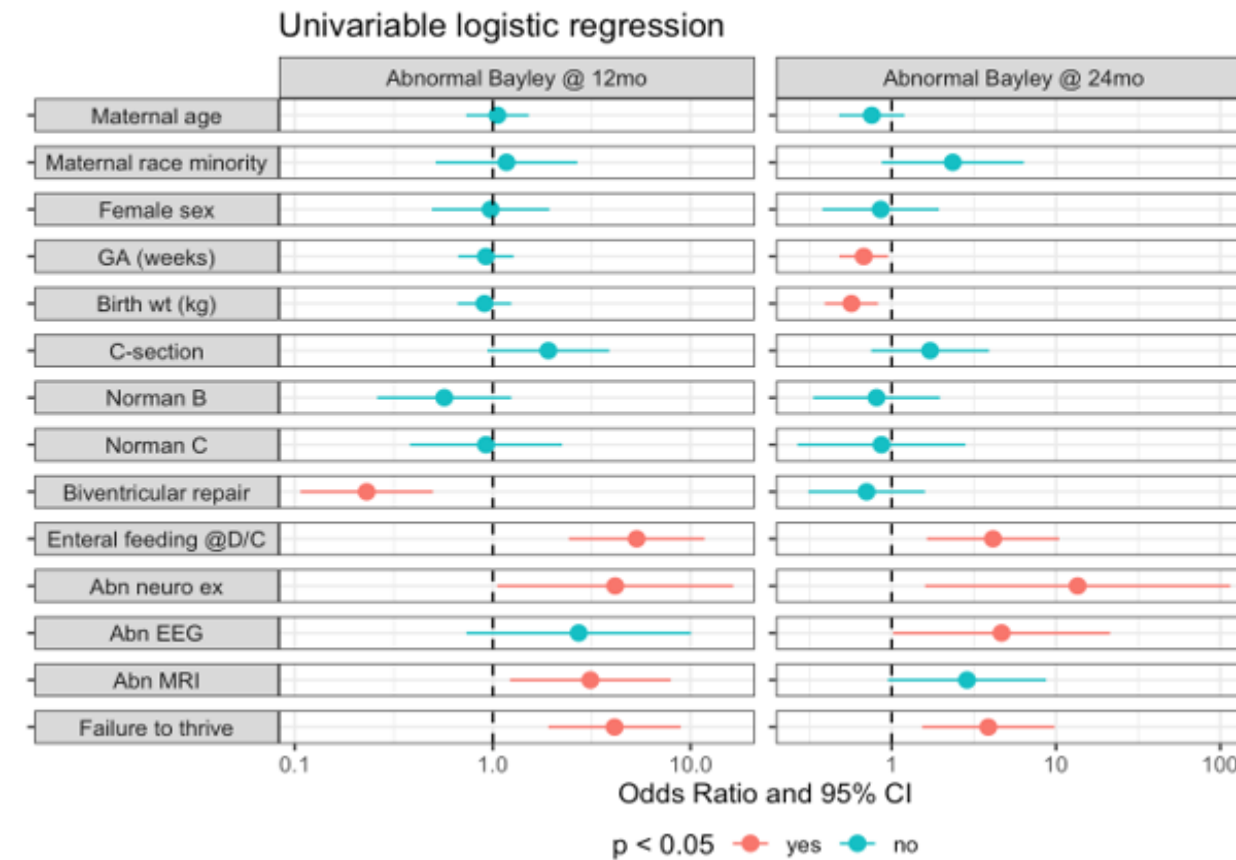
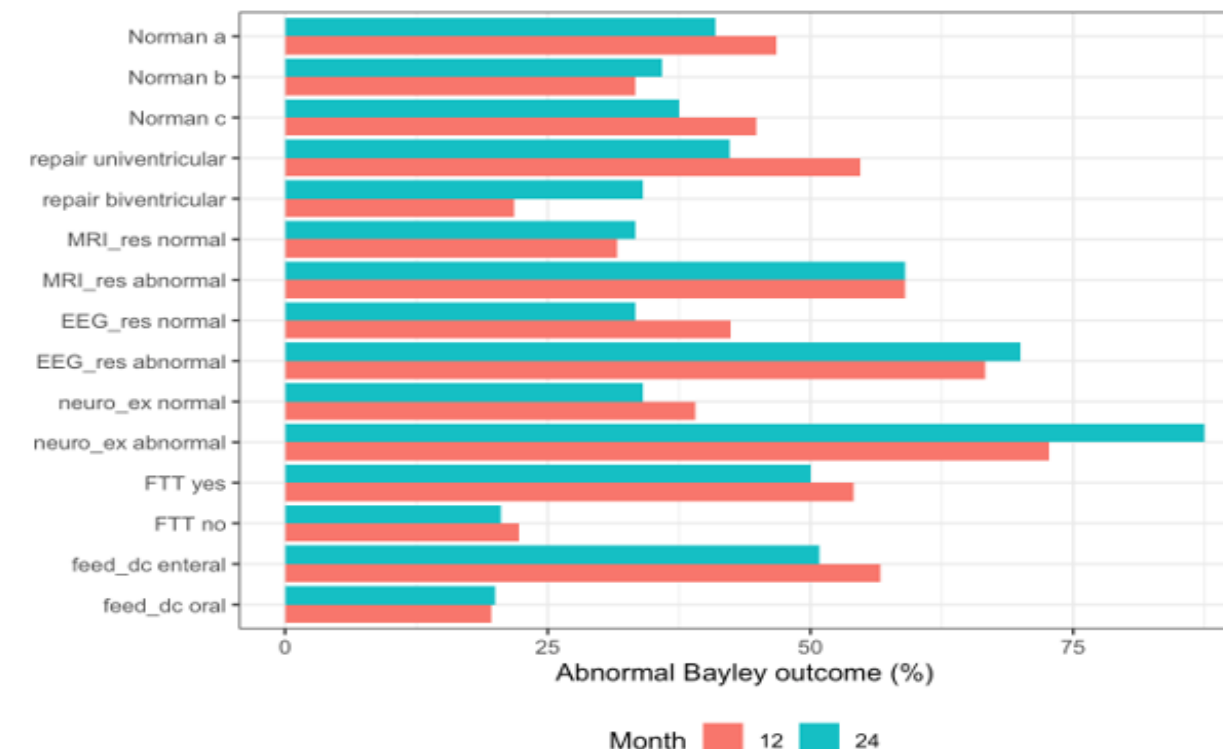


Figure 2. Abnormal Bayley outcomes by category



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.