Developmental assessment of infants with congenital heart disease

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Research Article

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Abstract

Background: Recently, marked advances in surgical and medical care for infants with congenital heart disease led to a growing population with a high risk of developmental delay. We aimed to identify developmental delay in these infants and its risk factors.

Methods: A prospective cross-sectional study on 100 infants with congenital heart disease. Developmental assessment was done by using Vineland Adaptive Behavior Scale. We searched for risk factors for developmental delay in these infants. Correlations were conducted between the degree of developmental delay and the potential risk factors. To our knowledge, this study has not been conducted in developing countries before.

Results: The median age of the study group is 12.5 months, while by using Vineland Adaptive Behavior Scale; it is equivalent to 9.5 months. There was a statistically significant developmental affection in infant who had risk factors**.**

Conclusions: Developmental delay is a common complication in infants with congenital heart disease. It has many risk factors; some of them could be modifiable. Thus, early screening for developmental delay and its risk factors are of a great value. This could help in applying preventive measures and early interventional programs. Vineland Adaptive Behavior Scale is a reliable tool in determination of developmental delay.

Background

Congenital heart disease (CHD) is considered one of the most common congenital defects in neonates with a birth prevalence of 8-12/1000 per live births **(1, 2).** Surviving infant are at a great risk for developmental delay. Many risk factors are related to this developmental delay, including poor perfusion, shock, acid-base disturbances, hypoxia and failure to thrive. Also, there are biological risk factors as underlying syndromes or genetic/developmental disorders, the circulatory abnormalities specific to the heart defect, the medical and surgical therapies required **(2, 3).** Developmental impairment occurs due to events that happen during intrauterine life, at surgery, or during the growing years. Recently, increasing survival rates in children with CHD have been associated with concern for brain integrity, developmental and neurological outcomes instead of heart-related morbidity and death **(3).** They have a pattern of developmental and behavioral impairment characterized by mild cognitive impairment, affected social interaction and impaired communication skills**.** Also, they have affected intelligence, academic achievement, language (development, expressive and receptive), visual construction and perception, attention, fine motor skills, gross motor skills, and maladjustment**.** Developmental screening tools are used to confirm developmental delay requiring highly trained personnel **(2).** These tools must be sensitive, valid and reliable in order to determine the developmental delay and its management **(4).** Application of preventive measures and early interventional programs are needed to achieve positive effect of these infant's development and their future academic achievement **(5).** We aimed to identify developmental delay in these infants and its risk factors using Vineland Adaptive Behaviour Scale (VABS).

Methods

We conducted a prospective cross-sectional study aiming to identify developmental delay in infants with CHD and its risk factors using VABS. 100 patients were voluntary enrolled in this study during their regular follow up at the Pediatric Cardiology Unit of Cairo University Children's Hospital. Written informed consent was obtained. Enrolment of participants was after approval of the Ethical and Scientific Committee of Kasralainy faculty of medicine Cairo University according to relevant guidelines and regulations. Inclusion criteria: Non syndromic infant with CHD, age range from 6 months to 24 months, before surgical correction or cardiac catheter intervention. Exclusion criteria: infants with clinically recognizable genetic syndromes or neurological disorders or post cardiac surgery.

Methods:

Full medical history:

The following data were collected from the parent of each infant:

- History of neonatal intensive care unit (NICU) admission
- Permaturity
- Type of feeding
- Physical developmental milestone (head support, sitting and walking)
- Language development (monosyllables and few words).

General examination:

- Central cyanosis
- Pallor

Anthropometric measures (body weight and length or height measurements were plotted on Egyptian Growth Curves performed by **Ghalli et al., 2008 (6).** The infant was considered underweight if his body weight percentile was below 3rd percentile**.** The infant was considered stunted if his length percentile was below 3rd percentile **(7).**

All patients were investigated by 2-Dimentional echocardiography for diagnosis of CHD.

Psychometric assessment was done by using Arabic version of VABS **(8, 9).** Its primary purpose was to assess the social abilities of an infant and diagnosis various disabilities. It consists of four main domains; communication, daily living skills, socialization, and motor skills. Each domain consists of subdomain with age equivalent for each skill. We used assessment of skills till age of 2 years. The communication domain evaluates the receptive and expressive communication skills. The daily living skills domain measures behaviour as well as domestic and community interaction skills. The socialization domain covers play and leisure time, interpersonal relationships and various coping skills. The motor skills domain measures both gross and fine motor skills **(10).**

We assessed the developmental age of each infant in a trial to provide specific program for his skills according to his chronological age in a further study to follow the infants in the same chronological age.

Electroencephalographic (EEG) record was performed for each infant to detect any abnormal record.

Statistical analysis

The collected data were revised, coded, tabulated, and introduced to a PC using the Statistical Package for Social Science (SPSS) software program version 22. The Chi-square test was used for calculating differences and comparing data between categories..Comparisons between groups were done using analysis of variance (ANOVA) with multiple comparisons post hoc test in normally distributed quantitative variables while non-parametric Kruskal-Wallis test and Mann-Whitney test were used for non-normally distributed quantitative variables (Chan, 2003a). Exact test was used instead when the expected frequency is less than 5 (Chan, 2003b). P-value level of significance was considered non-significant; if $P > 0.05$, significant; if $P < 0.05$, and highly significant; if $P < 0.01$.

Results

This prospective cross-sectional study included 100 infants with CHD (62 males and 38 females)**.** 22% of the infants had cyanotic CHD and 78% had acyanotic CHD confirmed by 2-Dimentional echocardiography. The infants' median of age was 12.5 months with inter-quartile range (IQR) 8-17.

Anthropometric measures:

The length median was 72cm (IQR 66-77), with 8% of the infants were stunted. The body weight median was 8.5 kg (IQR 7-10) and 14% of the infants were underweight.

According to VABS results, the median of their equivalent age was 9.5 months (IQR 6-13), which was lower than the median of chronological age of infants included in the study (12.5 months). The median of equivalent age of study group according to each developmental skill according to results of VABS is shown in **Table 1.**

VABS results comparing infants with different risk factors as shown in Tables 2, 3, 4:

1. Prematurity:

The study included 19 preterm infants;all of them (100%) were statistically delayed in both total motor skills and average equivalent age (**p value 0.035)**. 89.5%of them were statistically delayed in receptive behavior **(p value 0.021) (Table 2).**

2. History of NICU admission:

Thirty eight infants had history of NICU admission;allof them (100%) were statistically delayed in average equivalent age **(p value 0.001).**

97.4% of them were statistically delayed in total motor skills **(p value 0.036).** 86.8% of them were statistically delayed in receptive behavior **(p value 0.001)** and total communication skills **(p value 0.010).** 84.2% of them were statistically delayed in both personal behavior **(p value 0.001)** and total socialization field **(p value 0.033).** 78.9% of them were statistically delayed in play and leisure time **p value 0.047) (Table 2)**.

3. Nutritional risk factors:

Twenty two infants were fed with artificial milk formula; 86.4% of them were statistically delayed in personal behavior (**p value 0.008) (Table 2)**.

Also, twenty three infants had anemia; 87% of them were statistically delayed in play and leisure time (**p value 0.02) (Table 3).**

4. Growth parameters:

Eight infants were stunted in growth and showed statistically delayed in interpersonal relationship and total socialization field with **p value 0.36, 0.019** respectively **(Table 3).**

While 14 infants were underweight and showed statistically delayed in expressive behavior and gross motor skills with **p value 0.021, 0.04** respectively **(Table 3)**.

5. Type of congenital heart disease:

Twenty two infants had congenital cyanotic heart disease. All of them (100%) were statistically delayed in both total motor skills and average equivalent age (**p value 0.022).** 95.5% of them were statistically delayed in interpersonal relationship **(p value 0.02)** and fine motor skills **(p value 0.021**).90.9% of them were statistically delayed in both personal behavior and **(p value 0.002)** and total socialization field **(p value 0.025).** 86.4% of them were statistically delayed in receptive behavior **(p value 0.029) (Table 4)**.

6**. Abnormal EEG record:**

Twenty three infants had abnormal EEG record; all of them (100%) were statistically delayed in average equivalent age (**p value 0.018).**

91.4% of them were statistically delayed in receptive behavior (**p value 0.005**). 73.9% of them were statistically delayed in total daily life skills (**p value 0.002) (Table 4)**.

Classification of the infants according to the degree of developmental delay:

In the current study, 69% of the infants were classified as having severe developmental delay; as they had ≥ 3 affected developmental domain. While 30 infants were classified as having moderate developmental delay; as they had 1or 2 affected developmental domain. Relation between the potential risk factors and the severity of developmental delay was shown in **figure 1.**

Risk analysis for occurrence of developmental delay was conducted to detect the correlations between the degree of developmental delay and the potential risk factors as shown in **table 5 and figure 2** and revealed no statistical difference between the presence of one of these risk factor over the other as regard the degree of developmental delay**.**

Discussion

The aim of the current study was developmental assessment of infants with CHD using VABS focusing on four main domains; communication, daily life skills, socialization and motor skills.

We compared the results of VABS and the different risk factors that may affect their developmental status such as; prematurity, history of NICU admission, formula feeding, anemia, underweight, stunted growth, cyanotic heart disease and abnormal EEG.

Previous studies conducted by **Khalil et al** demonstrated that there is high risk of neurodevelopmental delay in form of seizures, hypotonia, hypertonia, motor asymmetry, absent suckling, feeding difficulties, cranial nerve abnormalities, lethargy, restlessness, agitation and autistic features in infants with CHD **(11).**

As regard results of VABS, almost all infants (99%) included in the current study demonstrated developmental delay in its multiple domains; communication, daily life, socialization and motor skills **(Table 1).**

This is in agreement with **Mebius et al.,** who demonstrated that there is a risk of neurodevelopmental delay in infants with CHD due to many factors as injury to multiple cerebral regions and alternation of cerebral blood flow that leads to impairment of oxygen and nutrient supply to brain **(12).** Also, **Marino et al.,** found a different pattern of neurodevelopmental and behavioural impairment with CHD characterized by mild cognitive impairment, impaired social interaction and impairments in core communication skills, as a result of multiple risk factors including the circulatory abnormalities specific to the heart defect, and the medical and surgical therapies required **(2).**

The current study goes in concordance with **Butler et al.,** who demonstrated that infants with CHD interact less with their environment because of their abnormalities in attention and difficulty with state regulation **(13).**

VABS results comparing infants with different risk factors

1. Prematurity:

Prematurity revealed to be a significant risk factor for developmental delay in infants with CHD especially in receptive behavior (p value **0.021)**, total motor skills (p value **0.035)** and average equivalent age with p value **0.035**. This is in line with **Woythaler et al.,** who followed 950 late preterm infants compared to 4900 infants and detected that preterm infants had significant developmental delay in different fields such as expressive language at 24 months and may increase to be severe at school age. It is due to many reasons as the brain is still developing and may have a risk to injury compared with full term infants because the brain growth is occurring under conditions differing from prenatal period and events occurring at this time involve the development of neurons and glia with organizational events at the cellular and molecular level **(14).**

It is concordant with **Mebius et al.,** who demonstrated that preterm infants are at risk for developing brain injury because of the complex mechanisms of destructive events and developmental issues. The preterm brain is associated with vulnerable

white matter, immature vasculature, and impaired auto-regulation and this brain injury is associated with developmental delay **(12).**

Also, **Jarjour** found that there are adverse developmental outcomes that are highly prevalent in the majority of very preterm infants. These was including cognitive, language, visual-perceptual, sensory, attention, and learning deficits. In addition to early recognition of the nature, degree and scope of neurological and developmental disability, as well as the high risk for adverse outcomes in premature infants, helps with counselling families concerning the child's prognosis and for referring them to appropriate early childhood intervention programs and special medical care **(15).**

Thus we attributed our results due to not only prematurity but also due to circulatory changes in infants with CHD.

2. History of NICU admission:

History of NICU admission among our infants (38%) showed a significant risk factor of developmental delay regarding receptive behavior (**p value 0.001),** total communication (**p value 0.010),** personal behavior (**p value 0.001)**, play and leisure time (**p value 0.047),** total socialization field (**p value 0.033)**, total motor skills (**p value 0.039)** and average equivalent age (**p value 0.001**).

This corresponds to **Philpott-Robinson et al.,** who noted that exposure to bright lighting in the NICU may have a detrimental effect on some aspects of later motor development, exposure to alarm sounds may disrupt the functional use of the tactile system and exposure to painful procedures has a negative effect on cognitive and motor development **(16).**

Also, **Fallah et al.,** found that infants admitted to the NICU showed degrees of developmental delay at the ages of 6 and 12 months, especially in the gross motor and personal-social developmental domains **(17).**

3. Nutritional risk factors:

Infants with artificial milk formula feeding (22%) demonstrated statistically significance delay in personal behavior (**p value 0.008)** when compared with breast fed infants.

In concordance with **Horta et al.,** who found that breastfeeding had long term consequences on performance in intelligence tests. This positive association between breast feeding and development may be attributed to the long-chain polyunsaturated fatty acids present in breast milk, which are important for brain development **(18).**

Iron deficiency anaemia was detected in 23% of the infants and it showed a significant risk factor for developmental delay in play and leisure time subdomain **(p value 0.02).**

Similarly **Ozmen et al.** detected significant relation between anaemia and developmental delay **(19).**

4. Growth parameters:

Stunted infants (8%) showed significant risk factor of developmental delay in interpersonal relationship and total socialization field with **p value 0.036, 0.019** respectively.

Ravishankar et al. detected that stunting in 37% of their patients correlated with reduction in brain size due to changes in structural proteins, growth factor concentrations, and neurotransmitter production, so these infants have poorer cognition, school achievement and psychosocial function **(20).**

Also, in current study, underweight infants (14%) showed a statistically significant risk factor of developmental delay in expressive behavior and gross motor skills with **p value 0.021, 0.04** respectively.

This is in agreement with **Lata et al.,** study revealed 57% of infants with CHD were underweight attributing that to malnutrition and in adequate caloric intake **(3).** In addition, **Luo et al.** detected that 1.2% were underweight, 1.6% were wasted. 20% of the

infants were significantly delayed in their cognitive development, while 32.3% were significantly delayed in their psychomotor development. Thus highlighted the important link between infant nutrition and early child development. There are multiple factors play a role such as micronutrient deficiency **(21).**

5. Type of congenital heart disease:

Infants with cyanotic CHD (22%) in the current study revealed statically significant developmental delayed than infants with acyanotic heart disease regarding receptive behavior **(p value 0.029)**, personal behavior **(p value 0.002)**, interpersonal relationship **(p value 0.02)**, total of socialization field **(p value 0.025)**, fine motor skills **(p value 0.021)**, total motor skills **(p value 0.022)** and average equivalent age with **p value 0.022)**.

In agreement with **Lata et al.,** who noted that children who had cyanotic CHD were at a higher risk of developmental delay due to chronic hypoxia caused by underlying CHD **(3).**

6**. Abnormal EEG record:**

Infants with abnormal EEG (23%) had significance developmental delay compared with infants with normal EEG in receptive behavior (**p value 0.005)**, total daily life skills (**p value 0.002)** and in average equivalent age (**p value 0.018)**.

Mulkey et al. study detected 60% of infants with CHD had abnormal EEG background patterns. It may provide relevant information about the infants' neurological status that may correlate with developmental outcome **(22).**

Also, **Limperopoulos et al.** conducted a study on infants with CHD, 18.5% of them had epileptiform activity and 33% of them had disturbances in background activity suggesting that EEG abnormalities may increase the likelihood of persistent neurologic deficits **(23).**

There was no any statistically difference between the presence of one risk factor over the other as regard the degree of developmental delay. This could be explained as 99 out of 100 infants had some degree of developmental delay, so, we could not reach which risk factor was the most significant. Yet, these risk factors should be considered during the assessment of infants with CHD.

Conclusion

Infants with CHD are at a higher risk for developmental delay mainly in communication, daily life skills, socialization and/or motor skills. It is mulifactorial including anaemia, malnutrition, formula fed, prematurity, cyanosis and NICU admission. VABS is an easy and reliable tool for screening of developmental delay. Early screening of infants with CHD for developmental delay and its risk factors are of a great value leading to apply preventive measures and early interventional programs to achieve positive effect on these infants development and for their academic achievement. Some of these risk factors could be modifiable as malnutrition, anemia and formula feeding. So, nutritional management and proper nutritional supplementation for these infants are very important and crucial for improving their developmental.

Declarations

Ethics approval and consent to participate:

The study had been approval by the ethical committee of Kasralainy faculty of medicine Cairo University according to relevant guidelines and regulations. A written informed consent was obtained from the parents or legal guardians of the infants.

Consent for publication:

Not applicable

Availability of data and materials:

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

S.Sh. revised and critically reviewed the manuscript. O.R.A. designed the study and reviewed the manuscript. A.E. collected the data. N.E. revised the manuscript. Sh.S. designed the study, drafted the initial manuscript, revised the manuscript and critically reviewed the manuscript.

All authors read and approved the final manuscript.

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Tables

Table 1: The median of equivalent age of study group according to each developmental skill as regard the results of VABS:

Field of developmental delay	Median (IQR)	Delayed (%)
Receptive behavior	10(7:15)	67
Expressive behavior	10(6:12)	84
Total communication	9.5(7:14)	72
Personal behavior	16(16:16)	62
Community	5(5:17)	85
Total daily life skills	11(9:15)	46
Interpersonal relationships	5 (4-16)	77
Play and leisure time	5(2.5:15)	67
Coping skills	11 (10-11)	58
Total of Socialization field	7(4:15)	72
Gross motor skills	8(4:12)	87
Fine motor skills	8(8:12)	80
Total motor skills	8(6:11.5)	90
Average equivalent age	9.5(6:13)	90

VABS: Vineland Adaptive Behavior Scale, IQR: interquartile range

Table 2: Comparison between the presence of prematurity, history of NICU or formula feeding as regard results of VABS:

Field of developmental delay	Full term (n=81)	Preterm (n=19)	P value	No History of NICU (n=62)	History of NICU (n=38)	P value	Breast feeding (n=78)	Artificial formula (n=22)	P value
	Number (%)	Number (%)		Number (%)	Number (%)		Number (%)	Number (%)	
Receptive behavior	50(61.7)	17 (89.5)	**0.021***	34 (54.8)	33 (86.8)	**0.001***	50 (64.1)	17 (77.3)	0.246
Expressive behavior	66 (81.5)	18 (94.7)	0.116	49 (79)	35 (92.1)	0.071	65 (83.3)	19 (86.4)	0.728
Total communication	55 (67.9)	17 (89.5)	0.059	39 (62.9)	33 (86.8)	**0.010***	53 (67.9)	19 (86.4)	0.179
Personal behavior	48 (59.3)	14 (73.7)	0.244	30 (48.4)	32 (84.2)	**0.001***	43 (55.1)	19 (86.4)	**0.008***
Community	68 (84)	17 (89.5)	0.529	50 (80.6)	35 (92.1)	0.105	66 (84.6)	19 (86.4)	0.838
Total daily life skills	34 (42)	12 (63.2)	0.095	24 (38.7)	22 (57.9)	0.062	32 (41)	14 (63.6)	0.060
Interpersonal relationships	63 (77.8)	14 (73.7)	0.706	44 (71)	33 (86.8)	0.067	59 (75.6)	18 (81.8)	0.543
Play and leisure time	53 (65.4)	14 (73.7)	0.491	37 (59.7)	30 (78.9)	**0.047***	51 (65.4)	16 (72.7)	0.513
Coping skills	49 (60.5)	9 (47.4)	0.297	40 (64.5)	18 (47.4)	0.092	47 (60.3)	11 (50)	0.389
Total of Socialization field	58 (71.6)	14 (73.7)	0.856	40 (64.5)	32 (84.2)	**0.033***	55 (70.5)	17 (77.3)	0.533
Gross motor skills	69 (85.2)	18 (94.7)	0.223	52 (83.9)	35 (92.1)	0.220	66 (84.6)	21 (95.5)	0.141
Fine motor skills	64 (79)	16 (84.2)	0.602	46 (74.2)	34 (89.5)	0.064	60 (76.9)	20 (90.9)	0.121
Total motor skills	71 (87.7)	19 (100)	**0.035***	53 (85.5)	37 (97.4)	**0.036***	68 (87.2)	22 (100)	0.673
Average equivalent age	71 (87.7)	19 (100)	**0.035***	52 (83.9)	38 (100)	**0.001***	69 (88.5)	21 (95.5)	0.296

VABS: Vineland Adaptive Behavior Scale**, NICU:** neonatal intensive care unit

Table 3: Comparison between the presence of anemia, stunted growth or underweight as regard results of VABS:

Field of developmental delay	No Anemia (n=77)	Anemia (n=23)	P value	Normal (n=92)	Stunted growth (n=8)	P value	Normal body weight (n=86)	Underweight (n=14)	P value
	Number (%)	Number (%)		Number (%)	Number (%)		Number (%)	Number (%)	
Receptive behavior	50 (64.9)	17 (73.9)	0.422	63 (68.5)	4 (50)	0.300	58 (67.4)	9 (64.3)	0.817
Expressive behavior	64 (83.1)	20 (87)	0.653	77 (83.7)	7 (87.5)	0.772	70 (81.4)	14 (100)	**0.021***
Total communication	54 (70.1)	18 (78.3)	0.446	68 (73.9)	4 (50)	0.169	62 (72.1)	10 (71.4)	0.959
Personal behavior	46 (59.7)	16 (69.6)	0.394	56 (60.9)	6 (75)	0.417	52 (60.5)	10 (71.4)	0.433
Community	65 (84.4)	20 (87)	0.762	77 (83.7)	8 (100)	0.099	72 (83.7)	13 (92.9)	0.337
Total daily life skills	34 (44.2)	12 (52.2)	0.498	41 (44.6)	5 (62.5)	0.329	38 (44.2)	8 (57.1)	0.368
Interpersonal relationships	57 (749)	20 (87)	0.196	69 (75)	8(100)	**0.036***	66 (76.7)	11 (78.6)	0.879
Play and leisure time	47 (61)	20 (87)	**0.020***	60 (65.2)	7 (87.5)	0.165	56 (65.1)	11 (78.6)	0.305
Coping skills	44 (57.1)	14 (60.9)	0.751	53 (57.6)	5 (62.5)	0.787	51 (59.3)	7 (50)	0.513
Total of Socialization field	52 (67.5)	20 (87)	0.069	64 (69.6)	8 (100)	**0.019***	61 (70.9)	11 (78.6)	0.546
Gross motor skills	66 (85.7)	21 (91.3)	0.467	80 (87)	7 (87.5)	0.965	73 (84.9)	14 (100)	**0.040***
Fine motor skills	60 (77.9)	20 (87)	0.324	72 (78.3)	8 (100)	0.053	68 (79.1)	12 (85.7)	0.551
Total motor skills	68 (88.3)	22 (95.7)	0.264	82 (89.1)	8 (100)	0.184	76 (88.4)	14 (100)	0.074
Average equivalent age	68 (88.3)	22 (95.7)	0.264	82 (89.1)	8 (100)	0.184	76 (88.4)	14 (100)	0.074

VABS: Vineland Adaptive Behavior Scale

Table 4: Comparison between the type of CHD or abnormal EEG as regard results of VABS:

Field of developmental delay	Acyanotic CHD (n=78)	Cyanotic CHD (n=22)	P value	Normal EEG (n=77)	Abnormal EEG (n=23)	P value
	Number (%)	Number (%)		Number (%)	Number (%)	
Receptive behavior	48 (61.5)	19 (86.4)	0.508	46 (59.7)	21 (91.3)	**0.005***
Expressive behavior	64 (82.1)	20 (90.9)	0.181	63 (81.8)	21 (91.3)	0.249
Total communication	53 (67.9)	19 (86.4)	0.673	52 (67.5)	20 (87)	0.069
Personal behavior	42 (53.8)	20 (90.9)	0.374	45 (58.4)	17 (73.9)	0.180
Community	64 (82.1)	21 (95.5)	0.757	64 (83.1)	21 (91.3)	0.310
Total daily life skills	34 (43.6)	12 (54.5)	0.520	29 (37.7)	17 (73.9)	**0.002***
Interpersonal relationships	56 (71.8)	21 (95.5)	0.868	61 (79.2)	16 (69.6)	0.334
Play and leisure time	49 (62.8)	18 (81.8)	0.508	53 (68.8)	14 (60.9)	0.476
Coping skills	49 (62.8)	9 (40.9)	0.926	42 (54.5)	16 (69.6)	0.200
Total of Socialization field	52 (66.7)	20 (90.9)	0.673	57 (74)	15 (65.2)	0.409
Gross motor skills	66 (84.6)	21 (95.5)	0.232	66 (85.7)	21 (91.3)	0.467
Fine motor skills	59 (75.6)	21 (95.5)	0.130	60 (77.9)	20 (87)	0.324
Total motor skills	68 (87.2)	22 (100)	0.298	69 (89.6)	21 (91.3)	0.809
Average equivalent age	68 (87.2)	22 (100)	0.298	67 (87)	23 (100)	**0.018***

VABS: Vineland Adaptive Behavior Scale, **CHD:** congenital heart disease, **EEG:** Electroencephalographic

Table 5: Risk analysis for occurrence of severe developmental delay

	Moderate developmental delay		Severe developmental delay		Odds ratio			
Risk factor	N	Row %	N	Row %	P value	OR	Lower 95% CI	Upper 95% CI
History of prematurity	5	26.3%	14	73.7%	0.674	1.27	0.41	3.92
History of NICU admission	12	32.4%	25	67.6%	0.722	0.85	0.35	2.05
History of artificial formula feeding	6	27.3%	16	72.7%	0.726	1.21	0.42	3.47
Cyanotic heart disease	9	40.9%	13	59.1%	0.220	0.54	0.20	1.45
Anemia	7	30.4%	16	69.6%	0.987	0.99	0.36	2.73
Abnormal EEG	7	31.8%	15	68.2%	0.861	0.91	0.33	2.53

N: number, **OR:** odds ratio, **NICU:** neonatal intensive care unit, **EEG:** Electroencephalographic

Figures

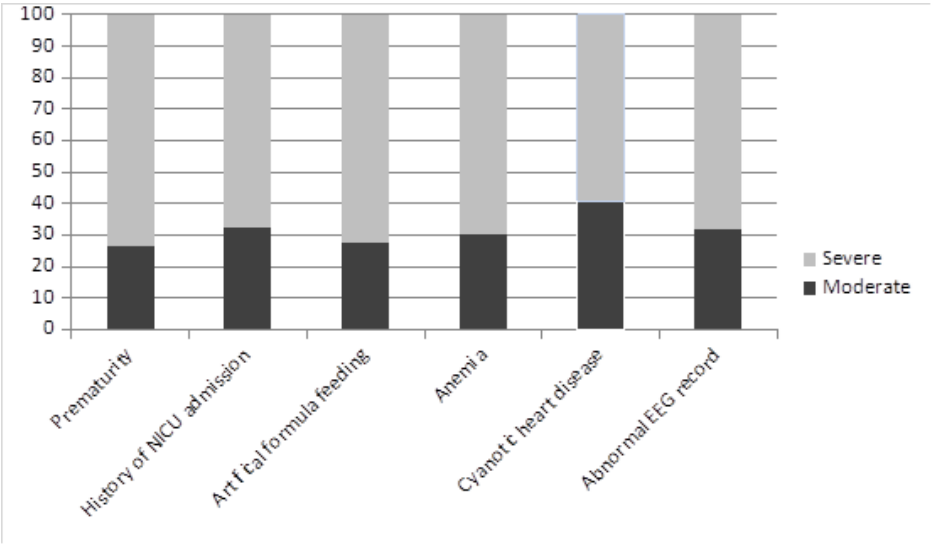

Figure 1

Relation between potential risk factors and severity of developmental delay

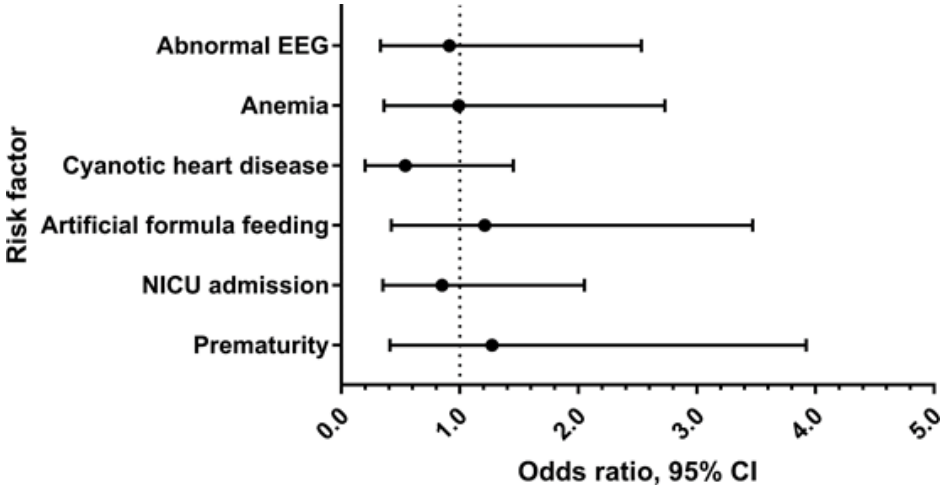

Figure 2

Odds ratio for various risk factors. Rounded markers represent estimates. Error bars represent 95% confidence limits. Dotted vertical line represents line of equality (odds ratio of 1.0). 95% confidence limits including the value 1.0 are not statistically significant.