Original Research

Prevalence and Patterns of Neuro-developmental problems among children with Congenital Heart Diseases attending a tertiary institution in South East Nigeria

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Abstract

Background

Continued progress in early diagnosis and therapeutic options has contributed to the increased survival of infants with CHD with attendant NDD which is of profound personal and public health significance.

Aim

To determine the prevalence and patterns of neuro-developmental problems in children with CHD.

Methods

A cross-sectional study consisting of 40 children with CHD attending the Cardiology clinic of University of Nigeria Teaching Hospital (UNTH), as well as 40 age and gender-matched controls with no heart disease recruited from children's outpatient and well-baby clinics. A semi-structured pretested questionnaire was used in documenting socio-demographic data. General and systemic examinations including cardiovascular and central nervous system assessments were done. The echocardiography report from UNTH was reviewed and the type of CHD documented. Neurodevelopmental assessment using The Malawi Developmental Assessment Tool (MDAT) was carried out by the researchers. Data were analysed using IBM Statistical Package for Social Sciences (SPSS 20.0 version). Chi-Square were used to compare age and gender and other demographic variables with Yates correction where appropriate. Bivariate analysis was performed using the type of CHD to identify cardiac lesions associated with NDD. Significant statistical level was set as a p-value < 0.05.

Results

Forty subjects and 40 controls aged 6-60months with a male to female ratio of 3:2 were studied. Thirty-seven (92.5%) of the subjects had one or more symptoms of CHD. NDD was noted in 23 (57.50%) children with CHD compared to six (15.0%) of the controls. (χ = 15.63, p< 0.0008). The differences in the number of children with delay across all domains for both groups were (p= <0.001). While 17 (42.5%) patients with CHD had a delay in more than one domain (global delay), none of the control had a delay in more than one domain. The difference in the number of domains with NDD for patients and their controls was statistically significant (p<0.001). Though there is no significant correlation between age (χ2 =7.243; p = 0.203) and gender (χ2 =0.017; p = 0.896) of children with NDD, the younger age group were more affected. NDD was also commoner in children with Tetralogy of Fallot (TOF) 5 (62.5%).

Conclusion

NDD was common in children with CHD and a significant number had a global delay when compared with their controls.

Keywords: Prevalence, neurodevelopmental problems, CHD, Children, Enugu.

Introduction

Congenital heart disease is one of the most common birth defects accounting for nearly one-third of all major congenital anomalies[1,2]. It may occur as a complex cardiac anomaly with several associations with associated morbidity and mortality[2]. The prevalence of CHD varies from countries and races. For instance, in China, Xiaocheng[3] et al in their study among 1,817 children with CHD noted the overall prevalence of 16.4 per 1,000 live births. It is noted in Asia, the highest CHD birth prevalence, at 9.3 per 1,000 live births. Their findings in Europe was significantly higher than in North America with 8.2 per 1,000 live births and 6.9 per 1,000 live births, respectively[1,4,5]. In the United States, CHD affect almost 1% of births, which translates to about 40,000 children per year[6]. The prevalence of CHD was also noted in Enugu; the target area of the current study. For instance, Chinawa et al[7], in Enugu, South East Nigeria, among 31,795 children noted a prevalence of children with cardiac disease as 2.2% per 1,000 live births. The commonest CHD seen in their study was VSD and followed by TOF.

NDD are among the most common extra-cardiac complications affecting about 20 - 30% of newborn with CHD. Schmitt et al [10] documented a prevalence of NDD among newborn with CHD as 9.8% and noted that this was almost tripled in children with down syndrome. Furthermore, Feldmann et al[12] had noted various degrees of intellectual impairments in children with CHD. They noted impairment in cognitive and executive function to be worse in children with uni-ventricular heart defect compared with those with ventricular septal defect.

Studies on NDD in children with CHD are scanty in Nigeria and in Enugu, South east Nigeria. Features of NDD is often misdiagnosed or neglected. This missed diagnoses may lead to reduced intelligent quotient (IQ) scores in school[13-15]. If

https://dx.doi.org/10.4314/mmj.v37i2.6

the children with NDD are left without any intervention, at the stage of adolescent, they may develop worsening executive function, and challenges in independent living[15-22]. As a result of late interventions for children with NDD in the region, their optimal functioning is not achieved as depicted by many of them not having access to any form of education and impairment in expressive language ability[23].

Studies done on neuro-developmental outcome of children in the study locality has been on the general population, and none has been done on children with CHD.

This study explored the prevalence and patterns of neuro-developmental problems of children with CHD at the University of Nigeria Teaching Hospital (UNTH) Enugu and compared it with that of their age and sex-matched children without CHD. It will leverage the specialist cardiology clinic in UNTH Enugu, to institute early screening for identification and early interventions on NDD, to improve prognosis and enhance children's access to evidence-based care by trained health providers. It will also contribute to the literature in Nigeria and in Africa generally.

Methods

Study design

This was a cross-sectional study done at the Paediatric Cardiology and Out-patient Clinics of UNTH Ituku/Ozalla Enugu, Nigeria from February to April 2023. Patients and control were recruited consecutively until the sample size is reached.

Study population

Forty subjects and 40 controls with CHD with no form of heart disease as controls matched for age and gender. Children with CHD whose parents gave consent were included in the study. Those excluded from the study were: Children with clinically recognizable genetic syndromes such as Downs' syndrome, Turners syndrome, those with extra cardiac congenital anomalies such as hydrocephalus, cleft lip and palate, those with confirmed diagnoses of other chronic illnesses such as chronic kidney disease, chronic liver disease, Human Immunodeficiency Virus (HIV) infection and sickle cell anaemia.

Those with a history of either hypoxic-ischaemic encephalopathy at birth or severe hyperbilirubinemia in the neonatal period or prematurity (Children born before 37 completed weeks), children already diagnosed with neurologic and neuro-developmental disorders, such as cerebral palsy and seizure disorder, attending the Paediatric neurology clinic were also excluded.

Ethical consideration

Ethical approval was obtained from the Health Research Ethics Committee of the University of Nigeria, Ituku-Ozalla (UNTH), while informed consent was obtained from the parents or caregivers of all participants. The children found to have NDDs were referred to the Neurology Clinic of UNTH for follow-up. Parents and caregivers were counseled on ways to stimulate their children's development.

Data collection and subject handling

A structured validated questionnaire was used to obtain socio-demographic and perinatal data. This questionnaire had been used by other studies and validated by Gladstone[29] et al. The questionnaire was validated after preliminary and qualitative studies. The validation involved the use of a draft developmental assessment tool which comprised of 162 items in four domains. In the course of the content validity testing, they expanded the draft tool to 185 items. This was used in the assessment of 1,426 normal rural children less than six year of age from rural Malawi. Finally, 136 items were included the questionnaire after removing all cofounders. The tool was validated by comparing age-matched normal children with those with 120 children with malnutrition and 80 children with neurodisabilities. Validity was achieved for items within 94%-100% and with kappas scores of >0.4 for inter-observer immediate, delayed, and intra-observer testing.

This scale is locally developed in Africa and as such is culturally relevant tool designed as an African tool and created for African children. It shows good reliability, validity, and sensitivity for assessing children with neuro-disabilities[29-31].

General and systemic examinations, including cardiovascular and neurological assessment, were done by the researchers and findings were documented. For children with CHD, the echocardiography report from UNTH was reviewed, and the type of CHD was documented. The neurodevelopmental assessment was subsequently done by the Researchers using The Malawi Developmental Assessment Tool (MDAT). This was done in a quiet consulting room, with a parent present, and each lasted for about 30 ± 10 minutes. 34 items were tested in each domain. Some items needed only the parent's report, while some required passive observation and the rest items required direct administration to the child. The assessment started with the calculation of the child's age from the date of birth given by the mother. Test items were then administered, starting from the less specialized to advanced: social, fine motor, language, and then gross motor. The starting column was based on the child's chronological age, using the normal reference range. The child's age was located on the X-axis and a vertical line was drawn at that point. The child will be tested for items that intersect the line, then tested forward until the child failed 6 consecutive items, and thereafter the child was tested backwards from the chronological age until the child passed 6 consecutive items. An appropriate box for each item tested was checked. The right response is "Passed","failed" or "don't know" were scored for each item. 'Don't know" scoring was used when a pass or fail can't be given by the examiner. If the child failed two or more items below or to the left of the line (the vertical line that intersects the child's age on the X axis), the child failed the domain which means some delay in the domain. If the child passed all the items or failed only one item below the line for his age, the child passed the domain which signified normal development or no delay in the domain. The researchers collated each assessment and identified children with isolated neurodevelopmental domain delay, NDD in more than one domain (Global Developmental delay), and no NDD.

Social class estimation

This was calculated using mother's education and fathers' occupation as shown in appendix 1. The mean of four scores (two for the father and two for the mother) to the nearest whole number is the social class to be assigned to the child.

Definition of Terms

The Malawi Developmental Assessment Tool (MDAT) is a culturally acceptable and widely used tool for assessing Neuro-developement patterns in children. This is validated

and widely used in children.

No NDD - no delay is seen in any of the developmental domains.

NDD - a child failed to attain developmental milestones when compared to children of the same age range; when a child has a delay in any of the domains of development.

Global developmental delay- a significant delay is noted in two or more domains in children less than 5 years.

Social delay only - isolated delay in social domain.

Gross motor delay only - isolated developmental delay in gross motor domain.

Fine motor delay only - isolated developmental delay in fine motor domain.

Language delay only- isolated developmental delay in language domain.

Data Analysis

Data collected were recorded and analysed using IBM Statistical Package for Social Sciences (SPSS) version 20. Data was represented in tables, using figures where appropriate. Type of cardiac lesion were placed in frequency and percentage. Chi-Square were used to compare age and gender and other demographic variables with Yates correction where appropriate. Bivariate analysis was performed using the type of CHD to identify cardiac lesions associated with NDD. Significant statistical level was set as a p-value < 0.05. The Malawi Developmental Assessment Tool (MDAT) was used to assess domains of NDD in children with CHD

Results

The study was carried out on forty children with CHD aged 6 months to 5 years and 40 children with no form of heart disease matched for age and gender as controls. There were more males than females in both groups in a ratio of 3:2. There was no significant difference in the socioeconomic class of both subjects and controls; however, the majority of children were from low socioeconomic class. (Table I)

Table I: Socio-demographic characteristics of the study population

Variable	CHD (n=40)	Controls (n=40)	Total	χ^2	p-value
Age group (Months)				<0.01	1.000
<12	13(32.5)	13(32.5)	26(32.5)		
12-23	11(27.5)	11(27.5)	22(27.5)		
24-35	8(20.0)	8(20.0)	16(20.0)		
36-47	3 (7.5)	3 (7.5)	6 (7.5)		
48-59	1 (2.5)	1 (2.5)	2 (2.5)		
60 or >	4(10.0)	4(10.0)	8(10.0)		
Gender				<0.01	1.000
Male	24(60.0)	24(60.0)	48(60.0)		
Female	16(40.0)	16(40.0)	32(40.)		
Socioeconomic class				0.251	0.882
Upper	8(20.0)	8(20.0)	16(20.0)		
Middle	14(35.0)	16(40.0)	30(37.5)		
Lower	18(45.0)	16(40.0)	34(42.5)		

χ^2 = Chi-square

One or more symptoms or signs of CHD, such as chronic cough, progressive weight loss, easy fatigability, bluish discolouration, displaced apex beat and cardiac murmur, were documented in 37 (92.5%) patients.

Types of heart lesions in children with CHD

A total of 27 (67.5%) children with CHDs had acyanotic CHD and the most common lesions were ventricular septal defects (37.5%), followed by patent ductus arteriosus (12.5%). Of the cyanotic type, majority of patients had tetralogy of Fallot and constituted 20% of all cardiac lesions in the patients. (Table II) None of these patients have had any intervention for their heart defect.

https://dx.doi.org/10.4314/mmj.v37i2.6

Table II: Types of cardiac lesions in children with CHD

Type of CHD	Frequency (% of overall CHD)
Acyanotic CHD	27(67.5)
Cyanotic CHD	13 (32.5)
Types of Acyanotic CHD	
Ventricular septal defect (VSD)	15 (37.5)
Patent Ductus Arteriosus (PDA)	5 (12.5)
VSD + PDA	4 (10.0)
Atrial septal defect (ASD)	3 (7.5)
Types of Cyanotic CHD	
Tetralogy of Fallot	8 (20.0)
Total anomalous pulmonary venous drainage (TAPVD)	2 (5.0)
Tricuspid atresia	2 (5.0)
Double outlet right ventricle (DORV)	1 (2.5)
TOTAL	40 (100)

Table III: Different domains of NDD in children with CHD and controls

Domains	CHD (n=40)	Controls (n=40)	Fisher's Test
Gross motor delay			
Yes	18(45.0)	1 (2.5)	0.000
No	22(55.0)	39(97.5)	
Fine motor delay			
Yes	13(32.5)	1 (2.5)	<0.001
No	27(67.5)	39(97.5)	
Language delay			
Yes	13(32.5)	2(5.0)	0.003
No	27(67.5)	38(95.0)	
Social delay			
Yes	14(35.0)	2 (5.0)	<0.000
No	26(65.0)	38(95.0)	

Table IV: Number of domains with NDD in the study participants

Number of domains	CHD (n=40)	Controls (n=40)	Fisher's Test	p-value
None	19(47.5)	34(92.5)	58.420	<0.001*
One	4(10.0)	6 (7.5)		
Two	7(17.5)	0 (0.0)		
Three	3 (7.5)	0 (0.0)		
Four	7(17.5)	0 (0.0)		

*= Statistically significant, Percentage in parenthesis

https://dx.doi.org/10.4314/mmj.v37i2.6

Table V: Comparison of NDDin Acyanotic and Cyanotic Participants

Neuro-Developmental	Type of CHD				
Domain	Acyanotic	Cyanotic	Total	χ^2	p
Delay					
Yes	14 (51.9)	9 (69.2)	23(57.5)	1.08	0.30
No	13 (48.1)	4 (30.8)	17(42.5)		
Total	27 (100.0)	13 (100)	40(100)		
Gross motor					
Yes	11 (40.7)	7 (53.8)	18 (45.0)	0.61	0.44
No	16 (59.3)	6 (46.2)	22 (55.0)		
Total	27(100.0)	13(100.0)	40(100.0)		
Fine Motor					
Yes	10 (37.0)	3 (23.1)	13 (32.5) 27 (67.5)	0.78	0.38
No	17 (63.0)	10 (76.9)			
Total	27(100.0)	13(100.0)	40(100.0)		
Language					
Yes	8 (29.6)	5 (38.5)	13 (32.5)	0.31	0.58
No	19 (70.4)	8 (61.5)	27(67.5)		
Total	27(100.0)	13 (100.0)	40(100.0)		
Social					
Yes	7 (25.9)	7 (53.8)	14 (35.0)	0.01	0.08
No	20 (74.1)	6 (46.2)	26(65.0)		
Total	27(100.0)	13 (100.0)	40(100.0)		
Global delay					
Yes	9 (33.3)	8 (61.5)	17 (42.5)	2.86	0.09
No	18 (67.7)	5 (38.5)	23 (57.5)		
Total	27(100.0)	13(100.0)	40(100.0)		

Table VI: Distribution of NDD by age

Age group	Any delay				
In months	Yes	No	Total (%)	χ^2	P
<12	8 (34.7)	5 (29.4)	13 (32.5)	7.243	0.203
12-<24	9 (39.1)	2 (11.8)	11 (27.5)		
24-<36	3 (13.0)	5 (29.4)	8(20.0)		
36-<48	2 (8.7)	1 (5.9)	3 (7.5)		
48-<60	0 (0.0)	1 (5.9)	1 (2.5)		
60>	1 (4.3)	3 (17.6)	4(10.0)		

https://dx.doi.org/10.4314/mmj.v37i2.6

NDD was noted in 23 (57.50%) children with CHD compared to six (15.0%) of the controls. This was statistically significant ($\chi = 15.63$, $p< 0.0008$). The NDDs noted were 18 (45%), 13 (32.5%), 13 (32.5%) and 16 (40%) for motor, fine motor, language and social domains respectively.

For the controls, two children each had delay in the language and gross motor domain while one child each had delay in the social and fine motor domain as shown in Table III. The differences in the number of children with delay across all domains for both groups were statistically significant ($p= <0.001$).

While 17 (42.5%) patients with CHD had delay in more than one domain (global delay), none of the control had delay in more than one domain (Table IV). The difference in the number of domains involved in the NDD for patients and their controls was statistically significant ($p<0.001$).

Comparison of NDD in Acyanotic and Cyanotic Participants

Out of the 27 children with acyanotic heart lesion and 13 with cyanotic lesion, 14 (51.9%) and 9 (69.2%) respectively had delay in at least one domain (Table V). The difference in the number of children with acyanotic and cyanotic CHD with NDD was not statistically significant ($p=0.30$).

There was no statistically significant difference between children with acyanotic and cyanotic heart lesions for any of the NDD ($p\geq 0.05$). See Table V

Age group 12 to < 24 months had the highest number and proportion (9, 39.1%) of children with CHD that have any form of developmental delay. There was no association between age group and NDDin the patients ($\chi2 =7.243$; $p = 0.203$).

Also, 60.1% of those with delay were males (14 patients) while 39.1% were females (9 patients). There was no significant difference between the number with delay and sex of the patients ($\chi2 =0.017$; $p = 0.896$).

Discussion

Congenital heart disease is on in the increase due to advances in diagnosis[32-35]. This study had shown that children with CHD had NDD in several domains compared to control. The current study also revealed the prevalence of NDD in children with CHD as 57.50% compared to 15.0% seen in the controls[36]. Loblen et al noted a nearly similar higher prevalence of 44% In NDD in CHD when compared to the general population (44%). The finding in this study was higher than that obtained from Naef et al[37]. who noted a prevalence of 5.3%. Geographical and racial differences as well as a robust sample size of 233 used by Naef[37] et al could explain these differences in prevalence values[38-41]. This study noted a prevalence of 42.5% developmental delay in more than one domain. However, Donofrio et al[41] documented a higher prevalence of 75% in their series in children with CHD presenting with more than 1 domain of developmental delay. In their study, Bayley Scales of Infant Development was used to assess cognitive, language, and motor skills and this was done in 99 children in about 6 occasions in the first 3 years of their lives[39,40]. This present study did not follow up their subjects and the study methods were different.

NDD was noted mainly in 45% of children with gross motor delay compared with other domain of developmental delay. In certain literature, where motor development of 194 children with CHD were compared with that of controls, 58.7% of the children with CHD had major deficits in gross motor skills when compared with 21.9% seen in children with no CHD[42] Similarly the finding of major neurological defects seen among children with Tetralogy of Fallot documented in this study was akin to that noted by Stieh et al[43]where children with TOF showed a significant decrease in mean MQ than children with acyanotic heart disease[44] Birna et al[44] in their work, documented a significant delay in fine motor development in children with CHD compared with children without CHD. Persistent low cardiac output, metabolic acidosis and attendant hypoxia may explain this phenomenon[44-49].

Language and social NDD were also seen in 32.5% and 40% of children with CHD when compared with that seen in 5% and 2.5% of controls respectively. This finding was corroborated by Brandlistuen et al[50], who noted symptoms of communication and social impairment among Children aged 18 months[50]. A synopsis of genetic, environmental and brain alterations that occurs before and after birth could explain the impairment of language and social skills among children with CHD[51-53].

This study reveals no age or gender association in children with CHD. In a study among 194 subjects with CHD, though no difference was noted for gender, however, older children showed more severe deficits compared with younger children[54-56]. In addition, the study also showed that the proportion of children with neurodevelopmental among cyanotic patients were more than acyanotic patients. This may be due to effect of chronic hypoxia in the brain that is common among the patients with cyanotic heart defects. Similar findings were obtained by Uke et al[55] in India.

The high sample size and methods of recruitment of subjects could explain the age difference seen both studies. Besides, it is important to note that developmental delay in children with CHD is age dependent within the first year of life, it manifests as delayed motor milestones, in children. At adolescents, they have problems with executive function, leading to difficulties in academic performance and challenges in independent living[5,6,10].

Conclusion

NDD was common in children with CHD, and a significant number had a global delay when compared with their controls. Though there is no significant correlation between age and gender of children with NDD, the younger age group were more affected. NDD was also commoner in children with Tetralogy of Fallot (TOF).

Recommendation

Children with CHD should be screened early for NDD, and urgent steps taken to follow them up so as to avert any neurological sequel that may follow this disorder. Early and periodic neuro-developmental assessment in children with CHD may enhance early identification of significant neuro-developmental deficits. This allows for early intervention with appropriate therapies and special needs services for these children. Early intervention leads to enhanced academic, behavioral, and adaptive functioning, and a better quality of life.

Declaration

Ethical Consideration

The Ethical clearance was obtained by the research and ethic committee of the University Of Nigeria Teaching Hospital

https://dx.doi.org/10.4314/mmj.v37i2.6

Enugu.

Consent for publication:

Not applicable

Availability of data and materials

To protect the participants' anonymity, the data will not be shared.

Competing Interest

The authors declare that they have no competing interests.

Funding

This study was not funded by any organization. We bore all the expenses that accrued from the study.

Author contributions

NCO and JMC conceived and designed this study while IOA, KDA, FAU, VOO, AAE, NAU, and JMC helped in the critical revision of the article. All authors have read and approved the manuscript.

Acknowledgement

We acknowledge those that work in the records department for retrieving all necessary documents

References

1.Chinawa JM, Ujunwa FA. Medical and Social Outcomes in the Management of Cardiac Diseases in Children. In: Common Pediatric Diseases: Current Challenges. Nima Rezael, Noosha samieefar (eds). Bentham Book Publishers 2003; 2 ;DOI:10.2174/9789815124187123 0201

2. Chinawa JM, Obu HA, Eke CB, Eze JC. Pattern and clinical profile of children with complex cardiac anomaly at University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu State, Nigeria. Niger J Clin Pract. 2013 Oct-Dec;16(4):462-7. doi: 10.4103/1119-3077.116890. PMID: 23974740.

3.Xiaocheng Liu, Gongshu Liu, Ping Wang, Yunzhou Huang, Enqing Liu, Dongbei Li et al. Prevalence of congenital heart disease and its related risk indicators among 90 796 Chinese infants aged less than 6 months in Tianjin, International Journal of Epidemiology, 2015; 44: 884–893

4.Dolk H., Loane M., Garne E. European Surveillance of Congenital Anomalies (EUROCAT) Working Group (2011). Congenital heart defects in Europe: prevalence and perinatal mortality, 2000 to 2005. Circulation 2011;123:841–849.

5. Bernier P, Stefanescu A, Samoukovic G., Tchervenkov CI.The challenge of congenital heart disease worldwide: epidemiologic and demographic facts. Semin Thorac Cardiovasc Surg 2010; 13:26–34.

6.Hoffman JL, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol. 2002;39(12):1890-1900.

7.Chinawa JM, Eze JC, Obi I, Arodiwe I, Ujunwa F, Adiele KD, Obu HA. Synopsis of congenital cardiac disease among children attending University of Nigeria Teaching Hospital Ituku Ozalla, Enugu. BMC Res Notes 2013; 6: 475

8.Sizarov A, Boudjemline Y. Novel materials and devices in the transcatheter management of congenital heart diseases—the future comes slowly (part 1). Arch Cardiovasc Dis 2016; 109: 278–85.

9.Snookes SH, Gunn JK, Eldridge BJ, et al. A systematic review of motor and cognitive outcomes after early surgery for congenital heart disease. Pediatrics 2010;125: 818–82

10.Schmitt KRL, Sievers LK, Hütter A, Abdul-Khaliq H, Poryo M, Berger F, Bauer UMM, Helm PC, Pfitzer C. New Insights into the Education of Children with Congenital Heart Disease with and without Trisomy 21. Medicina (Kaunas). 2023 Nov 14;59(11):2001. doi: 10.3390/medicina59112001.

11.Rollins CK. A mixed bag: Differential influences of oxygenation and perfusion on brain development in congenital heart disease. J Thorac Cardiovasc Surg 2016;152:960–1.

12. Feldmann M, Bataillard C, Ehrler M, Ullrich C, Knirsch W, Gosteli-Peter MA, Held U, Latal B. Cognitive and Executive Function in Congenital Heart Disease: A Meta-analysis. Pediatrics. 2021 Oct;148(4):e2021050875. doi: 10.1542/peds.2021-050875.

13.Latal B. Neurodevelopmental outcomes of the child with congenital heart disease. Clin Perinatol 2016;43:173–85.

14.Ali SS. A brief review of risk – factors for growth and developmental delay among preschool children in low income countries countries. Advanced biomedical reeesssearch. 2013; 2.

15.Rollins CK, Newburger JW. Cardiology patient page. Neurodevelopmental outcomes in congenital heart disease. Circulation. 2014 Sep 30;130(14):e124-6. doi: 10.1161/CIRCULATIONAHA.114.008556. PMID: 25266864; PMCID: PMC6277140.

16.Wernovsky G. Current insights regarding neurological and developmental abnormalities in children and young adults with complex congenital cardiac disease. Cardiol Young. 2006;16(Suppl 1):92–104. [PubMed] [Google Scholar] [Ref list]

17.Wernovsky G, Licht DJ. Neurodevelopmental Outcomes in Children With Congenital Heart Disease-What Can We Impact? Pediatr Crit Care Med. 2016 Aug;17(8 Suppl 1):S232-42. doi: 10.1097/PCC.0000000000000800. PMID: 27490605; PMCID: PMC4975480.

18.Marino BS, Lipkin PH, Newburger JW, et al. Neurodevelopmental outcomes in children with congenital heart disease: evaluation and management. A Scientific Statement from the American Heart Association. Circulation. 2012;126:1143–1172. [PubMed] [Google Scholar] [Ref list]

19.Gaynor JW, Stopp C, Wypij D, et al. Neurodevelopmental Outcomes after Cardiac Surgery in Infancy: A multi-center retrospective analysis of patient factors associated with early outcomes in 1,770 subjects. Pediatrics. 2015;135:816–25.

20.Vignol, F.S.; Aikawa, P.; da Silveira, T.B.; Tavella, R.A.; Mahtani-Chugani, V.; Sanz, E.J.; da Silva Júnior, F.M.R. Neurodevelopmental Outcomes among Brazilian Children with Cyanotic Congenital Heart Disease and Its Associated Factors. Medicina 2022, 58, 1669. https://doi.org/ 10.3390/medicina58111669

21.Miller SP, McQuillen PS, Hamrick S, Xu D, Glidden DV, Charlton N, Karl T, Azakie A, Ferriero DM, Barkovich AJ, Vigneron DB. Abnormal brain development in newborns with congenital heart disease.N Engl J Med. 2007; 357:1928–1938.CrossrefMedlineGoogle Scholar

22.Marino BS, Lipkin PH, Newburger JW, Peacock G, Gerdes M, Gaynor JW, Mussatto KA, Uzark K, Goldberg CS, Johnson WH, Li J, Smith SE, Bellinger DC, Mahle WT; American Heart Association Congenital Heart Defects Committee, Council on Cardiovascular Disease in the Young, Council on Cardiovascular Nursing, and Stroke Council. Neurodevelopmental outcomes in children with congenital heart disease: evaluation and management: a scientific statement from the American Heart Association.Circulation. 2012; 126:1143–1172.

23.Sudfeld CR , McCoy DC, Danaei G , Fink G, Ezzati M, Andrews KG. Linear growth and child development in low- and middle-income countries: a meta-analysis. Pediatrics.

24.Fisher VJ, Morris J, Martines J. Developmental screening tools: feasibility of use at primary healthcare level in low and middle – income settings. Journal of health, population and nutrition. 2014; 32 (2): 314

25.Ford ND, Stein AD, Risk factors affecting child congnitive development: a summary of nutrition, environment. And maternal – child interaction indictors for Sub – Ssharan African. Journal of developmental origins of health and disease. 2016; 7(2): 197 -217.

26.Bakare MO, Munir KM, Bello – Mojeed MA. Public health and

research funding for childhood neurodevelopmental disorders in Sub Saharan Africa: a time to balance priorities. Health care in low resource settings. 2014;2 (1).

27.Lata K, Mishra D, Mehta V, Juneja M. Nuerodevelopmental status of children aged 6-30 months with congenital heart disease. Indian paediatrics. 2015; 52(11): 957 - 60

28.International Cardiac Collaborative on Neurodevelopment (ICCON) Investigators. Impact of operative and postoperative factors on neurodevelopmental outcomes after cardiac operations. Ann Thorac Surg 2016;102:843–9.

29.Gladstone M, Lancaster GA, Umar E, Nyirenda M, Kayira E, van den Broek NR, et al. (2010) The Malawi Developmental Assessment Tool (MDAT): The Creation, Validation, and Reliability of a Tool to Assess Child Development in Rural African Settings. PLoS Med 7(5): e1000273. https://doi.org/10.1371/journal.pmed.1000273

30. Chinawa AT, Chinawa JM. Compendium of cardiac diseases among children presenting in tertiary institutions in southern Nigeria: a rising trend. Libyan J Med. 2021 Dec;16(1):1966217. doi: 10.1080/19932820.2021.1966217.

31.Parpia T, Svensen E, Elwood S, Wanjuhi A, Blacy L, Bayo E et al. Cognitive Outcomes at 18 Months: Findings from the Early Life Interventions for Childhood Growth and Development in Tanzania (ELICIT) Trial. Am J Trop Med Hyg. 2021;106(2):441-445.

32.Engel M, Kochilas L. Pulse oximetry screening: a review of diagnosing critical congenital heart disease in newborns. Med Devices 2016; 9: 199–203.

33.Cardiol Young . 2022 Sep 12;1-8. doi: 10.1017/S1047951122001469. Online ahead of print. Prevalence of neurodevelopmental disorders in a clinically referred sample of children with CHD Hayley J Loblein 1 2 3, Patrick W Vukmirovich 1, Mary T Donofrio 2 4, Jacqueline H Sanz 1 2 3 Affiliations expand

34.Khairy P, Ionescu-Ittu R, Mackie AS, et al. Changing mortality in congenital heart disease. J Am Coll Cardiol 2010;56: 1149–57.

35.Billotte M, Deken V, Joriot S, Vaksmann G, Richard A, Bouzguenda I, Godart F, Baudelet JB, Rakza T, Nguyen The Tich S, Guillaume MP. Screening for neurodevelopmental disorders in children with congenital heart disease. Eur J Pediatr. 2021 Apr;180(4):1157-1167. doi: 10.1007/s00431-020-03850-x. Epub 2020 Oct 29. PMID: 33119792.

36.Loblein HJ, Vukmirovich PW, Donofrio MT, Sanz JH. Prevalence of neurodevelopmental disorders in a clinically referred sample of children with CHD. Cardiology in the Young. 2023;33(4):619-626. doi:10.1017/S1047951122001469

37.Naef N, Liamlahi R, Beck I, Bernet V, Dave H, Knirsch W, Latal B. Neurodevelopmental Profiles of Children with Congenital Heart Disease at School Age. J Pediatr. 2017 Sep;188:75-81. doi: 10.1016/j.jpeds.2017.05.073. Epub 2017 Jul 11. PMID: 28709631

38.Mussatto KA, Hoffmann RG, Hoffman GM, Tweddell JS, Bear L, Cao Y, Brosig C. Risk and prevalence of developmental delay in young children with congenital heart disease. Pediatrics. 2014 ;133:570-7

39.Gaynor JW, Stopp C, Wypij D, et al. Neurodevelopmental outcomes after cardiac surgery in infancy. Pediatrics 2015;135: 816–25.

40. Lata K, Mishra D, Mehta V, Juneja M. Neurodevelopmental Status of Children Aged 6-30 Months With Congenital Heart Disease. Indian Pediatr. 2015;52(11):957-60.

41.Donofrio MT, Massaro AN. Impact of congenital heart disease on brain development and neurodevelopmental outcome. Int J Pediatr. 2010;2010:359390. doi: 10.1155/2010/359390. Epub 2010 Aug 24. PMID: 20862365; PMCID: PMC2938447.

42.Barkovich MJ. Pediatric Brain Maturation and Migration Disorders. Diagnostics (Basel). 2022 Apr 30;12(5):1123. doi: 10.3390/diagnostics12051123. PMID: 35626279; PMCID: PMC9139849.

43.Stieh J, Kramer HH, Harding P, Fischer G. Gross and fine motor development is impaired in children with cyanotic congenital heart disease. Neuropediatrics. 1999 Apr;30(2):77-82. doi: 10.1055/s-2007-973464. PMID: 10401689.

44.Birna Bjarnason-Wehrens, Sandra Schmitz, Sigrid Dordel, Motor Development in Children with Congenital Cardiac Diseases, European Cardiology 2008;4(2):92–6

45.Christina S, Michael V, Walter K,Reto H,Giancarlo N,Jon C et al. Neurodevelopmental outcome, psychological adjustment, and quality of life in adolescents with congenital heart disease. Eur J Cardiovasc Prev Rehabil 2008;12:1143-1149

46.Morton PD, Ishibashi N, Jonas RA, Gallo V. Congenital cardiac anomalies and white matter injury. Trends Neurosci. 2015 Jun;38(6):353-63. doi: 10.1016/j.tins.2015.04.001. Epub 2015 May 1. PMID: 25939892; PMCID: PMC4461528.

47.Miller SP, McQuillen PS, Hamrick S, Xu D, Glidden DV, Charlton N, Karl T, Azakie A, Ferriero DM, Barkovich AJ, Vigneron DB. Abnormal brain development in newborns with congenital heart disease. N Engl J Med 2007;357:1928e38.

48.Guo T, Chau V, Peyvandi S, Latal B, McQuillen PS, Knirsch W et al. White matter injury in term neonates with congenital heart diseases: Topology & comparison with preterm newborns. Neuroimage. 2019 Jan 15;185:742-749. doi: 10.1016/j.neuroimage.2018.06.004. Epub 2018 Jun 15. PMID: 29890324; PMCID: PMC6289608

49.Licht DJ, Shera DM, Clancy RR, Wernovsky G, Montenegro LM, Nicolson SC, Zimmerman R a, Spray TL, Gaynor JW, Vossough A. Brain maturation is delayed in infants with complex congenital heart defects. J Thorac Cardiovasc Surg 2009;137(3):529e36. Discussion 536e7

50.Brandlistuen, R.E., Stene-Larsen, K., Holmstrøm, H., Landolt, M.A., Eskedal, L.T. and Vollrath, M.E. Symptoms of communication and social impairment in toddlers with congenital heart defects. Child: Care, Health and Development,2011; 37: 37-43

51.Limperopoulos C, Tworetzky W, McElhinney DB, Newburger JW, Brown DW, Robertson RL, Guizard N,McGrath E, Geva J, Annese D, Dunbar-Masterson C, Trainor B, Laussen PC, Du Plessis AJ. Brain volume and metabolism in fetuses with congenital heart disease: evaluation with quantitative magnetic resonance imaging and spectroscopy. Circulation 2010;121(1):26e33.

52.Brossard-Racine M, Du Plessis AJ, Vezina G, Robertson R, Bulas D, Evangelou IE, Donofrio M, Freeman D, Limperopoulos C. Prevalence and spectrum of in utero structural brain abnormalities in fetuses with complex congenital heart disease. Am J Neuroradiol 2014;35(8):1593e9

53.Solène F, Ariane St-Denis, Julien H, Ala B, Lionel C, Anne G, Natacha T. Language development in children with congenital heart disease aged 12–24 months, European Journal of Paediatric Neurology, Volume 23, Issue 3, 2019, Pages 491-499,

54.Oyedeji GA. Socio-economic and cultural background of hospitalized children in Ilesha. Nig J Paed. 1985; 12: 111-7

55.Uke P, Gaikwad SB, Swarnkar K ,Lamture V, Khartade P. Neurodevelopmental assement of children with congenital heart diseases using Trivandrum developmental screening chart. JNeurosci Rural Pract 2023; 14(4):692-697.

APPENDIX 1 [52]

SOCIAL CLASSIFICATION SCHEME

SOCIAL CLASS	PROFESSION	EDUCATIONAL ATTAINMENT
I	Professional, Senior public servants, Owners of large business concerns, Senior military officers, large scale contractors.	University graduates or equivalents
II	Non-academic professionals e.g. Nurses, Secondary school teachers, Secretaries, Owners of medium sized business. Intermediate grade public servants	School certificate holders and equivalent
III	Non manual skilled workers including clerks, typists, telephone operators. Junior school teachers. Drivers	Grade II teachers or equivalent
IV	Petty traders. Labourers. Messengers.	Primary certificate
V	Unemployed. Full time house wives. Students. Subsistence farmers.	No formal education

https://dx.doi.org/10.4314/mmj.v37i2.6