Original Research Article

"Assessment of intelligence quotient (IQ) and behavior in children post cardiac surgery in early childhood- a prospective observational study".

ABSTRACT

INTRODUCTION: Congenital heart disease (CHD) is defined as a gross structural abnormality of the heart or intrathoracic great vessels that is actually or potentially of functional significance.The major deformities and motor delays can be easily identified. But the changes in neurodevelopmentcan be easily missed in outpatient follow-ups, which leads to affection on their academic performance and executive functioning at a later age.The goal of this study is to assess the impact of early childhood cardiac surgery on intelligence and behavior at a later age and to assess the factors responsible for the negative impact on intelligence and behavior.

METHODS: The study was conducted in a tertiary care hospital from June 2021 to September 2022 in 6–17-year age group children who underwent open heart surgery at any time in their first 5 years of life. On follow-up, the children were assessed clinically, and then intelligence and behavior wereassessed using Raven's standard progressive matrix and Childhood Behaviour Checklist,respectively.Previous data were collected from medical records.

RESULTS:75 patients were included in the study. None of them had behavioral abnormalities. Socio-economic class[p-value 0.02], weight at first surgery[p-value 0.003], preoperative saturation[p-value 0.03], aortic cross-clamp time[p-value 0.007], and postoperative inhaled Nitric Oxide requirement[p-value 0.02] were observed to have a negative impact on intelligence.

CONCLUSION: The level of intelligence and behavior in children after surgery has improved dramatically with a more negative impact on intellectual capacityobserved with cyanotic congenital heart disease.

KEYWORDS: Behavior,Cardiopulmonary bypass,Cyanotic congenital heart disease, Intelligence Quotient,Oxygen saturation, Socioeconomic status.

1. INTRODUCTION

Congenital heart disease (CHD) is defined as a gross structural abnormality of the heart or intrathoracic great vessels that is actually or potentially of functional significance [1]. The birth prevalence of CHD is estimated to be 9 per 1,000 live births [2]. The estimated number of children born with CHD every year in India approximates 240,000, considering the birth prevalence of CHD [3]. The incidence of severe CHD requiring catheter-based or surgical intervention is 3 per 1000 live births [4].

Because of recent advances in pediatric cardiovascular therapy, mortality rates for children with congenital heart disease have dropped dramatically, while survival rates have increased. An estimated 85% of children diagnosed with CHD survive into adulthood [5]. Despite these advances, survivors are suffering from long-term sequelae like neurocognitive defects. The etiology of intelligence and behavior-related affection in CHD is multifactorial, involving disease-specific, treatment-related, patient-specific, and socioeconomic factors [6]. The major deformities and motor delays can be easily identified. But the changes in neurodevelopment, like intelligence and behavior, can be easily missed in outpatient follow-ups. In clinical practice, these problems are underestimated and not recognized properly. Hence, there is more chance for impairment in intelligence and behavior in these children at a later age which may affect the child's academic performance and executive functioning.

The goal of this study is to assess the impact of cardiac surgery in early childhood on intelligence and behavior at a later age. The prevalence of morbidities such as the impact on development, intelligence, behavior, and social interactions are still unknown. In this study, we have attempted to assess the effect of cardiac surgeries on these neurodevelopmental parameters and also tried to identify the causative factors so that preventive measures can be instituted.

2. METHODOLOGY

The study was conducted in a tertiary care hospital over a period of 15 months from June 2021 to September 2022. Children in the age group of 6-17 years, who underwent open heart surgery any time in their first 5 years of life were included in the study. Children up to 5 years of age, who underwent only percutaneous cardiac intervention, children who were preterm born or with a history of birth asphyxia, children with genetic and chromosomal syndromes or anomalies, children with developmental delay preoperatively and children whose parents not giving consent for the study were excluded from the study.The minimum sample size required was calculated as 70, using the formula N = Z α2 pq/d2 considering the prevalence of 10% and clinical allowable error of 7%. No confounders as they were excluded from the study.The patients who came to out-patient were randomly chosen for the study and asked to do the test by themselves to reduce the bias.

2.1.Data Collection:

Following approval from the institutional ethical committee and written or informed consent from the parents, all children who came to cardiology outpatient for follow-up after a minimum of one-year post-cardiac surgery and met the inclusion criteria were enrolled in the study. The preoperative, intraoperative, and postoperative data were collected from the patient's medical records and they were assessed for intelligence and behavioral changes.

2.2.Assessment of Intelligence and Behavior:

During follow-up, the patients included were assessed clinically and further assessed for intelligence and behavior. Raven's standard progressive matrix, a nonverbal test was used for IQ assessment. It comprises 60 items in 5 sets; each set contains 12 items. It is a diagrammatic puzzle. Each puzzle has a part missing that is placed in increasing order of difficulty and the person taking the test has to find among the options provided. The score obtained for each patient was converted into a percentile according to the reference chart and then classified into different grades of intelligence. The Childhood Behaviour Checklist (CBCL) is used to obtain standardized parent reports of behavioral and emotional problems in children. The grades of intelligence were described as percentages and compared with all the variables and appropriate tests were used for statistical significance.

2.3.Statistical Analysis:

Based on the distribution of data, descriptive statistics were explained by frequencies with percentages for qualitative data and median with range for numerical data. The Chi-square test or Fisher's exact test was used to analyze qualitative data, and the Kruskal-Wallis test or Mann-Whitney-Wilcoxon test was used to analyze numericaldata, as appropriate. All statistical analyses were carried out at a 5% level of significance with a p-value less than 0.05 was considered statistically significant. Data wereanalyzed using SPSS version 28.0 and results were presented using appropriate graphs and charts, wherever applicable, using Microsoft Excel.

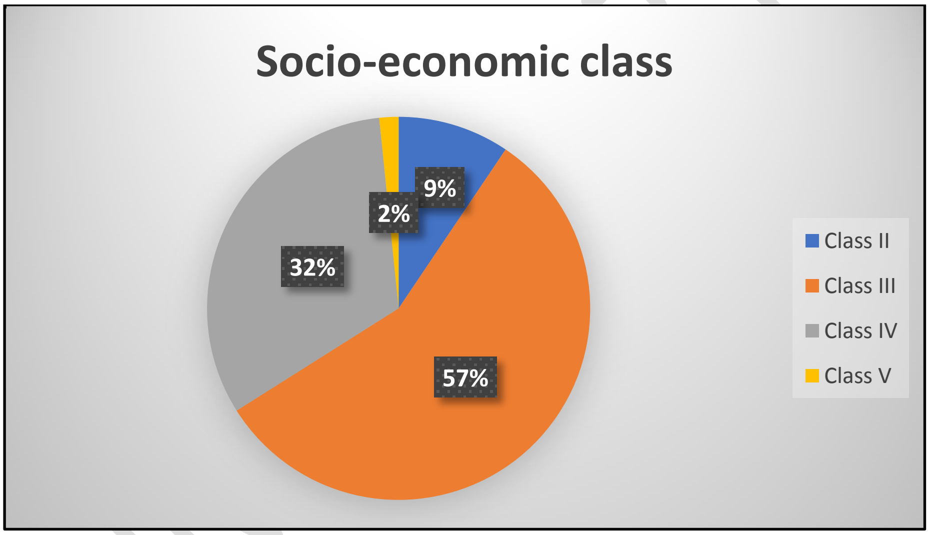
2.4.Ethical Clearance: Institutional Ethical committee approval was obtained [IEC Application Number: ACH-DNB-057/06-21]

3. RESULTS

3.1.Demographiccharacteristics:

75 patients were included in the study.The age of the children in the study cohort was 6 to 17 years, with a median age of 9 years. The median weight of the children included was 24 kg [a range of 11 kg - 82 kg]. The median height of the children included was 132 cm [a range of 102cm - 166cm]. The socio-economic class was determined using the Kuppuswamy classification. Among the 75 children, 7 [9%] were noted to be in Class II [upper middle class], 42 [57%] children in Class III [Lower middle class], 24 [32%] children in Class IV [upper lower class] and 2 [2%] children in Class V [lower class].[Fig 1]showsthe distribution of socio-economic class in the study cohort.

Fig 1 Pie diagram showing the distribution of socio-economic class



3.2.Preoperative characteristics:

The number of children with cyanotic CHD in the study cohort was 48 [64%] and those with acyanotic CHD was 27 [36%].The majority were single ventricle cases [30.6%], followed by Ventricular Septal Defect (VSD) [24%] and Tetralogy of Fallot (TOF) [22.7%]. VSD was most common in the acyanotic CHD group. Preoperative symptoms were present in 71 [94.6%] patients. The majority of the symptoms were cyanosis in cyanotic CHD, and recurrent respiratory tract infection, poor weight gain in acyanotic CHD group. Preoperatively, cyanotic spells were present in 12 [16%] children. The median pre-operative saturation of the study cohort was 85% [range of 50%-100%]. [Fig 2] shows the distribution of pre-operative saturation[SpO2] in the study cohort. Pre-operative characteristics of the study cohort are described in Table 1.

Fig 2 Pie diagram showing the distribution of pre-operative SpO2

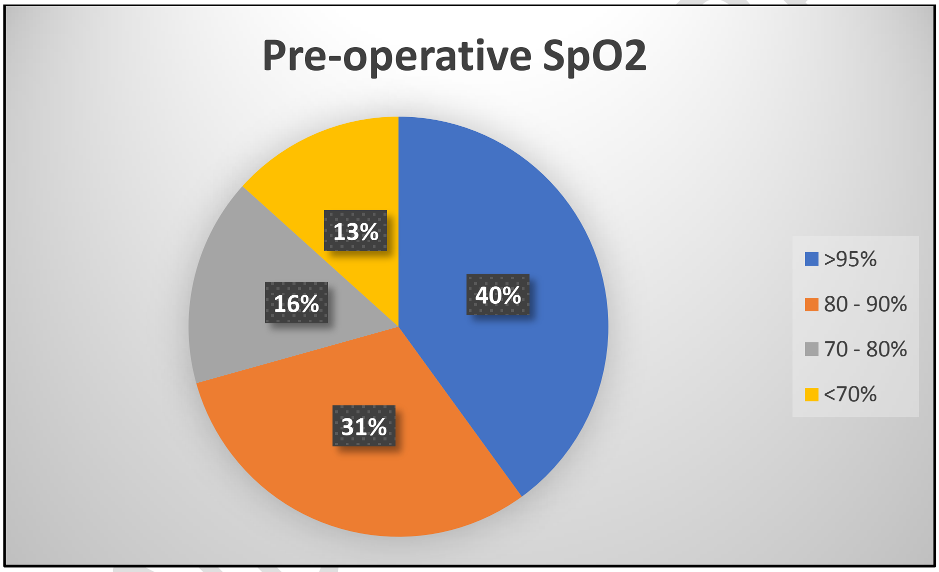


Table 1 Preoperative characteristics of the study cohort

Preoperative characteristics		**Frequency**	**Percentage**
Gender	Male	50	66.7%
	Female	25	33.3%

Age of diagnosis	First month	39	52%
	1month to 1 year	26	34.7%
	>1 year	10	13.3%
Age of first surgery	First month	3	4%
	1 month to 6 months	10	13.3%
	6 months to 1 year	20	26.6%
	1 year to 2 years	13	17.3%
	>2 years	29	38.7%
Weight at first surgery	Upto 3Kg	8	10.7%
	3 to 5Kg	5	6.7%
	5 to 10Kg	36	48%
	>10Kg	26	34.6%
Number of surgeries	1	60	80%
	2	12	16%
	3	3	4%

Frequency and percentage of individual variables

Surgeries undergone by cyanotic CHD constitute 16% with Glenn followed by Fontan. Three [4 %] patients required three surgeries: one Double Inlet Left Ventricle [DILV] patient who required a Pulmonary Artery [PA] band followed by Glenn and Fontan; one TOF with pulmonary atresia patient who required twice Blalock-Taussig [BT] shunt followed by conduit; and 1 Ebstein anomaly patient who underwent tricuspid valve repair initially followed by conversion to univentricular repair. 12 [16%] patients are waiting for Fontan completion; one child with TOF underwent a BT shunt and is waiting for Intra-cardiac Repair [ICR]. The table showing intra-operative and post-operative characteristics of the study cohort is described in Table 2.

Table 2 Intraoperative and postoperative characteristics of the study cohort

Intraoperative characteristics		**Frequency**	**Percentage**
CPB time (0 -282 minutes)	< 120 minutes	45	60%
	>120 minutes	27	36%
Hypothermia (0-34 C)	Mild	17	22.7%
	Moderate	30	40%
	Deep	22	29.3%
	Profound	3	4%
Aortic cross-clamp time (0 -186minutes)	< 60 minutes	37	49.3%
	>60 minutes	30	40%
Postoperative characteristics		**Frequency**	**Percentage**
Duration of ventilation	< 21 days	51	68%
	>21 days	3	4%
	Nil	21	28%
ICU Stay	< 14 days	66	88%
	>14 days	9	12%
Chest open		3	4%
iNO		2	2.7%
Hypotension		5	6.7%
PFO		22	29.3%
Sepsis		7	9.3%

Arrhythmia	5	6.7%

Frequency and percentage of individualvariables; *iNO-Inhaled Nitric Oxide

3.3.Follow-up characteristics:

19 [25.3%] patients were symptomatic on the present follow-up visit to the OP, and 56 [74.7%] were asymptomatic on the present follow-up. Patients in the univentricular group who are yet to complete their final repair like those who had Glenn, Pulmonary Artery [PA] band, and Blalock-Taussig [BT] shunt surgeries, had symptoms on follow-up. The comorbidities present on follow-up were: 12 [16%] patients came for Fontan completion, 2 [2.7%] had free Pulmonary Regurgitation [PR], 8 [10.7%] had branch pulmonary artery stenosis, and 53 [70.7%] patients were normal on follow-up

3.4.Comparison between cyanotic and acyanotic CHD groups:

Cyanotic CHD patients required surgery at an earlier age and lower weights, as they required a greater number of surgeries including staged palliations. They required prolonged Cardiopulmonary Bypass (CPB) time [p value 0.008] as well as prolonged Intensive Care Unit [ICU] stay [p value 0.016]. The majority of acyanotic CHD cases were VSD [24%]and Atrial Septal Defect [ASD][8%]which require surgery at later ages with good weight and also less duration of CPB and ICU stay with the absence of symptoms on follow-up.

3.5.Comparison between univentricular and biventricular repair:

Among the 48 cyanotic CHD patients, 24 [50%] underwent univentricular repair, and 24 [50%] underwent biventricular repair. As the number of TOF cases in our study cohort was more[22.7%], cyanotic spells [25%] were found to be more in the biventricular repair group with a p-value of 0.04. Median CPB time and aortic cross-clamp time in the study cohort was 100 minute and 54 minutes respectively. The univentricular repair group required less CPB duration and aortic cross-clamp time with less degree of hypothermia than that of the biventricular group. On follow-up symptoms and comorbidities were present in the cyanotic CHD group and univentricular repair group with a p-value of 0.000 and 0.008 respectively. Median saturation on follow-up after univentricular repair was 84.5% and after biventricular repair was 100%, with a p-value of 0.000. The saturation in the univentricular group is lower on follow-up because some of the patients underwent only one palliation and the final palliation is yet to be done. Table 3 summarizes the various characteristics and their statistical significance.

Table 3 Significance of various characteristics with cyanotic vsacyanotic CHD group and Univentricular vs biventricular repair group

Characteristics	**CyanoticvsAcyanotic CHD p Value**	**Univentricular vs Biventricular repair p Value**
Age at first surgery	0.001	0.2
Weight at first surgery	0.004	0.8
Socio economic class	0.6	0.4
Number of surgeries	0.005	0.017
Cyanotic spell	0.005	0.04
Pre-operative SpO2	0.000	0.08
CPB time	0.008	0.002
Hypothermia	0.1	0.03

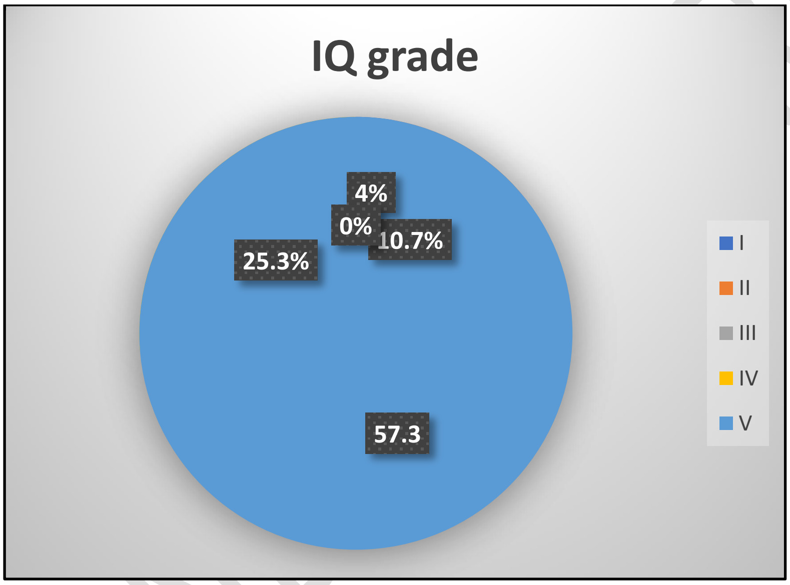
Aortic cross-clamp	0.4	0.000
ICU stay	0.016	0.7
iNO	0.2	1

Mann Whitney test for pre-operative SpO2 and Chi-Square test for other variables; *iNO-Inhaled Nitric Oxide

3.6.Association with IQ grade:

All patients had their IQs graded, and 2 [2.7%] were in grade I, 8 [10.7%] were in grade II, 43 [57.3%] were in grade III, 19 [25.3%] were in grade IV, 3 [4%] were in grade V.[Fig 3] shows the distribution of IQ grade in the study cohort.

Fig 3 Pie diagram showing the distribution of IQ grades



Age at diagnosis, age of first surgery, number of surgeries, pre-operative symptoms, cyanotic spell, type of heart disease [cyanotic and acyanotic CHD], and type of surgery [univentricular repair and biventricular repair] showed no association with the level of intelligence. Poor socio-economic class, lower weight at first surgery, lower pre-operative saturation, prolonged aortic cross-clamp duration, and postoperative iNO requirement were observed to have a statistical significance with poor IQ grades. [Fig4] shows a box and whisker plot showing the significance of preoperative saturation and IQ grade. The significance of these characteristics with IQ grades is summarized in Table 4.

Fig 4 Box and whisker plot showing the distribution of preoperative saturation with IQ grade

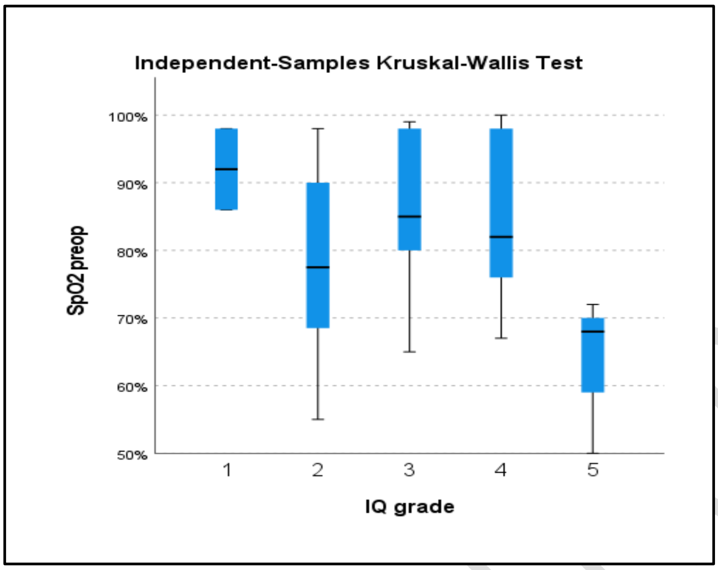


Table 4 Significance of various characteristics with IQ grade

Association with IQ grade	P Value
Socio-economic class	0.02
Weight at first surgery	0.003
Pre-operative SpO2	0.03
Aortic cross-clamp time	0.007
Post-operative iNO requirement	0.02

Kruskal Wallis test for Pre-operative SpO2 and Chi-Square test for other variables; *iNO-Inhaled Nitric Oxide

4. DISCUSSION

Single ventricle physiology [47.9%] constitutes the majority of our patients, who requires staged palliation followed by TOF [35.4%] cases who require intracardiac repair within 1 year of age with a weight of 5-10 kg. 66.6% of the acyanotic cases were VSD who required surgery after 2 years of age with > 10Kg weight. Cyanotic CHDs such as Transposition of Great Arteries[TGA], Double Inlet Left Ventricle [DILV],and Tricuspid Atresia required surgery at a lower weight of <5 kg. Hence, age at first surgery and weight at first surgery was significantly lower in the cyanotic CHD group than in the acyanotic CHD group.The majority of the children in the study [80%] required only one open-heart surgery which includes shunt closure in acyanotic CHDs and biventricular repair in TOF cases with conduits or patches. Staged palliation is required for univentricular physiology patients; hence the number of surgeries is also more. A study done by Gaynor et al [7] showed comparable results in both univentricular and biventricular repair groups.

Longer CPB duration was noted in the cyanotic CHD group and also in the biventricular repair group, which is due to complex cyanotic congenital heart diseases and the complexity of the surgery. Biventricular repairs like arterial switch operations, placement of conduits, patches, etc. were required more in our study. These surgeries are more complex and necessitate technical expertise, extending the duration of CPB, duration of aortic cross-clamp, and deepness of cooling. More cooling was required to protect the myocardium. The study done by Shakya et al [8] also observed that aortic cross-clamp duration was longer in the biventricular repair group than in the univentricular group, with a p-value of 0.000 which is comparable to our present study. Cyanotic CHD patientsrequired >2 weeks ICU stay for various reasons like a stormy ICU course, ventricle adaptation failure, lung collapse, sepsis, pleural effusions, etc. which was the same as the previous studies. Whereas, acyanotic CHD patients required lesser ICU stay as they are technically successful with less CPB duration and without postoperative complications.

In the present study, low socioeconomic class, lower weight at first surgery, lower pre-operative saturation, prolonged aortic cross-clamp, and requirement of iNO were found to have significant associations with poor intelligence grades. The majority of children were of the lower middle class [Class III] and they had good IQ grades. No children from the upper class [Class I] and only 2 children from the lower class [Class V], had IQ grades of III and IV. This showed low IQ in lower socioeconomic classes. Previous studies by Vukojevic et al[9] and Largo et al[10]showed that low socio-economic status affects children's mental health and academic achievements.A study done by Schaefer et al [11] noted high IQ in children from high socio-economic status. Severe intellectual impairment [IQ grade V] was observed in 3 children and all of them underwent surgery with less weight. 2 children with weight of <5kg and one with 5-10kg weight. The majority of patients in the study cohort were intellectually average (IQ grade III), and they underwent their first surgery at larger weights. Lower weight during surgery is a known cause of significant morbidities. The lower the preoperative saturation, the greater the intellectual impairment. Lower saturation causes chronic hypoxia of the brain, which eventually leads to intellectual abnormalities. According to the study done by Shakya et al [8], there was no association noted between development quotient and pre-operative saturation, which is different from our study.

There wereseveral studies showed a negative association between CPB duration and IQ level. Forbess et al [12] and Mussatto et al [13] showed a significant association between CPB and IQ, with the longer the duration of CPB, the lower the IQ. The study done by Shakya et al [8] had a median CPB duration of 163 minutes which doesn't show any association between neurodevelopmental outcome and CPB duration. The International Cardiac Collaborative on Neurodevelopment (ICCON) Investigators [14] compared neurodevelopmental outcomes in the diagnostic subgroups TGA and TOF. The median CPB duration in TGA was 132, and in TOF was 80, which showed an association between a longer duration of CPB and lower neurodevelopment.However, the present study didn’t show an association between CPB duration and IQ because the median CPB duration was 100, which signifies the improvement in cardiac surgeries over time.

Below average intellectual capacity [IQ grade IV] was observed more in patients who required prolonged aortic cross-clamp time. Above-average [IQ grade II] and intellectually average [IQ grade III] intellectual capacity was observed more in patients who required a shorter duration of the aortic cross-clamp. Hence, prolonged aortic cross-clamp time is associated significantly with lower IQ grades. Sarrechia et al.[15] showed a significant association between aortic cross-clamp time and IQ level, which is comparable to our study.

Postoperative iNO was required by only 2 patients in our study cohort. One of these two patients had severe intellectual impairment of grade V, while the other had intelligence of grade III. Statistical analysis revealed a significant negative relationship between the requirement for iNO and intelligence level with a p-value of 0.02. Severe pulmonary artery hypertension [PAH] postoperatively necessitates the need for iNO. Severe PAH leading to increased susceptibility to brain injury may be the reason for the affection in intelligence. There were no studies that observed an association between iNO and IQ.

The majority of the children had issues like arguing back and fighting with their parents. Some children are dependent on their parents, and some fail to finish the work. However, all of the children in our study group scored in the 93rd percentile on the Likert scale. Hence, it was concluded that congenital cardiac surgeries don’t have any effect on behavioral abnormalities. Various studies[15-17]showed that preoperative hypoxia and cardiocirculatory insufficiencies during surgery can adversely cause long-term behavioral problems. Our study doesn’t support this, as the children will eventually grow over the abnormalities because of timely interventions and surgeries, and also because brain plasticity during the critical phase of development helps in preserving cognitive functions. Different studies[18-19]showed that intelligence and neurocognition were affected even after successful surgeries. A study done by Sterken et al[20] between the age group of 4 -7 years, doesn't show any neurocognitive abnormality post-cardiac surgery. The majority of patients in our present study fall in average IQ grade which shows improvement in intelligence and behavior after cardiac surgery in childhood due to the advances in diagnosis and treatment.

4.1.Limitations of the study:

The study's major drawback is the small sample size and short study period.More number of neonates operated on for critical CHD would have shown an increase in the incidence of Grade V IQ and also a negative impact of CPB time on intelligence.We intended to use Wechsler Intelligence Scale IV in children found to have below-average intellectual capacity because it is a higher standard test for intelligence. However, the test could not be done due to financial constraints.

4.2.Recommendations:

A larger sample size is needed for the study. A multicentre prospective randomized study with a larger number of patients may help to validate the results of the study.Further studies with a more uniform study population, e.g., post-ICR for TOF are recommended.

5. CONCLUSION

Due to the improvement in hypoxia following early diagnosis, timely surgeries, and improvement in surgical methods, the level of intelligence and behavior in children after surgery has improved. Factors like weight at first surgery, pre-operative saturation, aortic cross-clamp time, and iNO requirement were more in the cyanotic group revealing the fact that cyanotic heart disease will have a more negative impact on intellectual capacity as compared to acyanotic CHD. The assessment of intelligence can be done in OP with ease using this simple scale which helps to keep a low threshold for early identification of these abnormalities.

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