"NEURODEVELOPMENTAL STATUS BEFORE AND AFTER CORRECTIVE CARDIAC SURGERY IN CHILDREN AGED 6 MONTHS TO 3 YEARS, A ONE YEAR HOSPITAL BASED LONGITUDINAL STUDY".

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ABSTRACT

"NEURODEVELOPMENTAL STATUS BEFORE AND AFTER CORRECTIVE CARDIAC SURGERY IN CHILDREN AGED 6 MONTHS TO 3 YEARS, A ONE YEAR HOSPITAL BASED LONGITUDINAL STUDY".

INTRODUCTION: It is estimated that more than 2,00,000 Indian children are born with congenital heart diseases. At least 20 percent of these are critical heart disease which require early intervention with corrective surgery. The surgical procedures usually involve the use of cardiopulmonary bypass (CPB), cardioplegia and total circulatory arrest (TCA). These modalities have been speculated to cause noxious insult to the developing brain and result in neurodevelopmental sequelae. As critical is the survival of a child with cardiac disease, intact survival and its importance cannot be overlooked. The objective of this study is to find the association of neurological sequelae with the intervention modalities.

OBJECTIVES:

- Primary objective: To assess and compare the preoperative and postoperative neurodevelopmental status of children aged 6 months to 3 years with congenital heart disease undergoing corrective cardiac surgery with cardiopulmonary bypass.
- Secondary objective: To determine the effects of intra operative events on neurodevelopmental outcomes in the children undergoing corrective surgery with cardiopulmonary bypass.

METHODS: Observational study conducted between January 2020 to December 2020 in 38 children aged 6 months to 3 years undergoing corrective cardiac surgery at KLE's Dr Prabhakar Kore Hospital. The pre-operative and post-operative neurodevelopmental assessment were done using DASII scoring system. The intra-operative parameters were collected from hospital records.

RESULTS: Amongst the 38 children assessed, 9 had cyanotic CHD. The mean pre-operative mental and motor quotients were 96.05 and 94.06 respectively with the post-operative assessment showing a reduction in both mental and motor domains at 87.77 and 87.54 respectively. The children with Cyanotic congenital heart disease showed a steeper decline in post-operative neurodevelopmental scores. There were 3 children in whom severe neurodevelopmental delay was observed but they showed recovery and caught up to normal status within a span of 3 to 4 months. The hemodilution that occurs as a part of the procedure involving Cardiopulmonary bypass is significantly correlated to the decline in both mental and motor domains Pearson co-efficient of 0.285 and 0.218 respectively and a p value of 0.006 and 0.014 respectively. The decline in mental quotient was correlated with lowest value of pH (p value-0.039) and the same was observed in the Acyanotic group but not in the cyanotic group. The Acyanotic group showed similar correlation between the duration of aortic cross clamp and the decline in both domains of DASII score. The duration of cardiopulmonary bypass influenced the minimum value of hematocrit and hence indirectly influenced the change in DASII scores.

CONCLUSION:

Neurodevelopmental delay in children with congenital heart disease can be as a result of the disease process in itself or can also be due to the interventions. The children showed delay in both mental and motor domains of DASII neurodevelopmental assessment scores post operatively though it was not statistically significant. The hemodilution that occurs as a part of the procedure involving Cardiopulmonary bypass is significantly correlated to the decline in both mental and motor domains of the neurodevelopmental scores in children. Acidosis during the Cardiopulmonary bypass also significantly impacts the reduction in mental domain of the neurodevelopmental scores in children. Close intra operative monitoring for parameters such as pH, hematocrit can help in prevention of adverse neurological outcomes and help in intact survival of children with congenital heart disease.

Keywords:

Congenital heart disease, Cardio-Pulmonary Bypass, Neurodevelopmental Assessment.

LIST OF ABBREVIATIONS USED

IQ	Intellectual Quotient
CHD	Congenital Heart Disease
CPB	Cardio-Pulmonary Bypass
TCA	Total Circulatory Arrest
DASII	Developmental Assessment Scale for Indian Infants
VSD	Ventricular Septal Defect
ASD	Atrial Septal Defect
TOF	Tetralogy of Fallot
PDA	Patent Ductus Arteriosus
BT Shunt	Blalock Taussig Shunt
SIRS	Systemic Inflammatory Response Syndrome
MUF	Modified Ultra-Filtration
ATPase	Adenosine Tri Phosphatase
PA	Pulmonary Artery
EEG	Electro Encephalo-Gram
GAC	General Adaptive Composite
BSID	Baroda Scale for Infant Development
CNS	Central Nervous System
CoA	Coarctation of aorta

TAPVC	Total Anomalous Pulmonary Venous Return
HCT	Hematocrit
ECMO	Extra Corporeal Membrane Oxygenator
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
CPK	Creatine Phospo Kinase
PRES	Posterior Reversible Encephalopathy Syndrome

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INTRODUCTION

Neurodevelopment - How a child’s brain grows and matures, is an important aspect which determines many factors in its life. The importance of neurodevelopment in a child can be known by the words of Dr Ronald S Illingworth- “A thorough knowledge of normal development of a child is just as fundamental to a pediatrician as is anatomy to a surgeon”. It is a continuous and complex process which starts in utero and becomes more intense in the first few years of the child’s life. The level of neuro development and the child’s abilities are so much more relevant in the fast paced, intellectually based present scenario of the human society. Its survival is indirectly dependent on the level of maturation and the abilities as in, it determines the vocation, economy and prosperity in adulthood.

The process of neurodevelopment is at its most crucial during the first few years of childhood in which the child’s brain matures both structurally and in function. This process is influenced by genetic, biological and environmental factors. Many pioneers in the field have seen that a child who is affected by any insult to the brain or even to the normal life through malnutrition or lack of stimulation will have a profound reduction in the intellectual quotient (IQ). The critical period of development and learning is so vital in that any stimuli later in life after that initial period will not result in adequate learning responses in the child. This is termed as sensitive period and is defined as a period at which learning as a response to appropriate stimuli is easier than in later life. This concept has been of keen interest to educationalists and Maria Montessori was one of the first to recognize this sensitive period of learning.

It was found that children are more sensitive to learning colors, shapes and texture in this critical period rather than later in life if not stimulated to learn at that critical phase. Thus, the concept of kindergarten and nurseries have evolved as places for adequate learning stimulation for the child. The developing child in its first three years is in a very critical period of development. This concept of sensitive period is however opposed and sometimes proven inadequate because of a neuroplasticity. But the importance of the critical period cannot be overlooked.

Sick children during this age period are particularly at risk for picking up such an insult to the developing brain. Along with the disease process in itself, any interventions carried out during the sensitive period in a child's life can have an impact in their normal development.

It is estimated that more than 2,00,000 children are born with congenital heart diseases in India[1]. Amongst these children, at least 20 percent are born with critical heart disease which require early intervention with corrective surgery for their survival. As a result of improving levels of healthcare in the country, easier access to healthcare, improved levels of education and literacy amongst parents and many other factors, the number of children with such heart diseases being treated though low has increased significantly. The mainstay of treatment for these children is corrective cardiac surgery at an early age. The surgical procedures usually involve the use of cardiopulmonary bypass (CPB) along with cooling of blood for cardio-protection and sometimes even an arrest of circulation termed as total circulatory arrest (TCA). These modalities have been speculated to cause noxious insult to the developing brain and result in neurodevelopmental sequelae.

The objective of this study is to find the association of such sequelae with the interventions and also to ascertain whether any delay is caused as a result of the heart disease in itself. As important is survival of a child with cardiac disease, intact and a healthy survival and its importance cannot be overlooked.

OBJECTIVES OF THE STUDY

PRIMARY OBJECTIVE:

- To assess and compare the preoperative and postoperative neurodevelopmental status of children aged 6 months to 3 years with congenital heart disease undergoing corrective cardiac surgery with cardiopulmonary bypass.

SECONDARY OBJECTIVE:

- To determine the effects of intra operative events on neurodevelopmental outcomes in the children undergoing corrective surgery with cardiopulmonary bypass

REVIEW OF LITERATURE

Congenital Heart Disease in India, a perspective

Congenital heart disease is amongst some of the most common birth defects. They are defined as “structural or functional defects of the heart which are present at birth”. India sees about 1,50,000 to 2,00,000 children born with congenital heart disease every year [1]. This high burden of congenital heart disease is in part, due to the high birth rate that the nation has. (table 1). One child amongst a hundred live births is expected to have a congenital heart disease considering the global incidence rates[2]. The incidence rates based on hospital-based studies are not much different. A study conducted at a community hospital in central concluded that the prevalence at birth was around 8 in 100 live births[3]. The actual numbers may be still higher than the predicted values because of the high rates of yet prevailing non-institutional deliveries and other factors such as maternal infections during pregnancy.

Amongst these staggering number of children born with congenital heart disease; studies estimate at least a third to a half of these children are born with “critical congenital heart disease”[1]. For such children, the first year of life is the critical time in which intervention is required and only then will they survive to see adulthood.

Table 1 – Demographics of CHD in India.

Population of India	**1,210,193,422**
Crude birth rate	**21.8**
Incidence of congenital heart disease	**8/1000 live births**
Estimated number of children with CHD	**≈2,00,000**
Number of children with critical CHD	**≈66,000 – 1,00,000 (1/3 to ½ of CHD)**

Such children, if diagnosed early, get access to proper facilities, surgical and medical care, it is estimated that 95% of these children will have a good prognosis and survivability[4]. It is at this phase where proper clinical examination at birth, pulse oximetry screening for critical congenital heart disease and a good neonatal care becomes that much more relevant and makes a difference to these children.

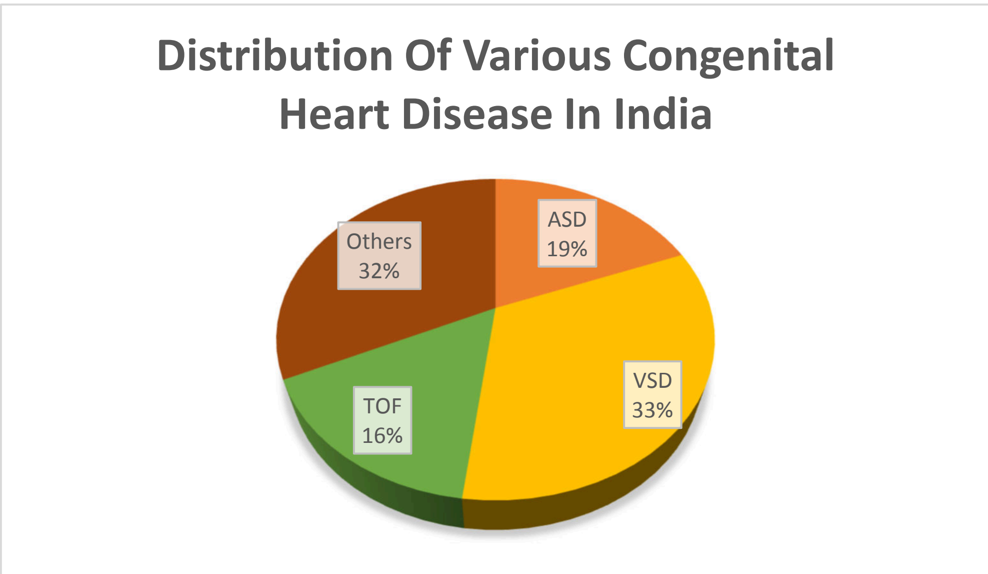

Fig 1. Data from a study published by Ritu Dixit et al representing the prevalence of types of congenital heart diseases.

The number of pregnant women undergoing antenatal ultrasonography has increased in the past few years due to an improvement in access to healthcare and better education. However, there hasn't been a good number of children with congenital heart disease who are prenatally diagnosed. A study conducted in the USA concluded that only about 63% of congenital heart disease was prenatally diagnosed [5]. The numbers in the Indian scenario can be estimated to be much more dismal based on the same considering lack of infrastructure in the sub urban or rural healthcare facilities for ultrasonography, lack of trained experts in sonography in these areas and reduced number of antenatal visits by the pregnant women.

Very few such children are diagnosed at birth and many of them go undiagnosed. The delay in diagnosis can be attributed to a large number of births in unsupervised settings such as home-deliveries though there has been an increased number of hospital-based deliveries due to government initiatives to promote the same. The rural and semi urban health facilities have various drawbacks such as lack of trained personnel and lack of equipment for them to be able to diagnose or screen the children for congenital heart disease. Pre-discharge screening by pulse oximetry for critical congenital heart disease is rarely practiced even in many of the urban health care facilities.

Because of many of the above-mentioned factors, there is a significant delay after which the child usually reaches a centre which treats CHD. It is also due to the lack of knowledge of many primary care providers in diagnosing a congenital heart disease, regarding the modalities available for management of a child with CHD and the technological advances that have occurred which help in managing such children and providing a favourable outcome. Many parents are not encouraged to proceed with treatment or rather discouraged to proceed with management because of lack of awareness and fears of poor long-term outcome and high costs.

According to the data as per a study published in 2005, only a meagre 5% of the children diagnosed with congenital heart disease underwent some sort of surgical correction in India. This number is quite low and shows a huge difference between the demand and supply of accessible healthcare in children with congenital heart disease in India. But since 2005, there are a large number of institutes which have come up which cater to these children with congenital heart ailments. Though the number of centres has increased, many of these centres are inaccessible to a major chunk of the population and diseased children due to various reasons such as delay in diagnosis, economic constraints, geographic location and accessibility etc.

The scenario in the southern Indian states is much better compared to their central, north and the north eastern counterparts. The southern states have a higher number of centres which cater to such children. Along with a higher per capita income and a better literacy rate, an average parent in a south Indian state is better endowed to get his child treated when compared to the northern part of India. Because of a higher population, higher birth rates, low socio- economic status and reduced number of centres which are available at the geographical location, these children in such states are at a much higher risk of not being able to access treatment.

Since many of these institutes are in the private sector, affordability of these treatment modalities is arguable. India, which has a lot of its population below the poverty line, and many children with congenital heart disease who belong to such families, cannot afford for the treatment. There are not many government institutes which cater for these children and there hasn't been an increase in such institutes in the recent years to match the demand. This results in over dependence of the poor population on these government institutes ultimately leading to over-burdened departments, long waiting lists and hence delays in treatment. Many such children succumb to the complications and co morbidities as a result of the delay in definitive treatment. These children will be suffering from severe malnutrition, cardiac failure, pulmonary arterial disease by the time they get treatment and such children even though undergo surgical treatment, may have unfavourable outcomes or long-term sequelae.

A child, when diagnosed with a congenital heart disease, if its parents decide to go ahead with management will have to travel with the family to a distant location leaving behind the job or business which is many times the sole source of income. The parent not only has to arrange for the expenses of the hospital but also for additional expenses of transport, stay, food and etc which is not easy for an average Indian parent. The cost of treatment for CHD is high and the family should provide for it from their own money. Very few people in India have other means such as insurance and government aid for health and even if they do have, the various costs are not fully covered. The costs not only include surgery but also neonatal care, prolonged pre op and post-operative hospital stay, various investigations and imaging modalities etc.

Though there are various government aided schemes, NGOs philanthropic societies which help in covering these costs, there is a very poor knowledge about the same in the minds of the common man. Rashtriya Bal Swasthya Karyakram (RBSK) is a government scheme which is helpful in this regard. It caters to children under the age of 18 with birth defects and other diseases. Though this scheme is helpful, social awareness is still less and it needs a lot more time for the benefits to be seen in the statistical scenario of congenital heart disease burden.

In general, it can be concluded that congenital heart disease is a huge burden in child healthcare. Rapid population growth, lack of healthcare funding, competing priorities, inefficient and inadequately equipped infrastructure and shortage of trained staff are some of the major roadblocks to cardiac care of children with CHD. Though there are improvements in the standards of living and due to the increased number of centres which cater cardiac surgical care, we are seeing cardiac surgeries be accessible to a larger number of children.

CARDIOPULMONARY BYPASS

Cardiac surgery has evolved from being restricted to simple external cardiac procedures during the early years, to the complicated intra cardiac repairs which correct almost any type of cardiac defects during the present time. During the 1940s, the cardiac procedures were restricted to the exterior of the heart, such as ligation of PDA, repair of coarctation of aorta and creation of Blalock-Taussig shunt. There was a need for a procedure which maintained the oxygenation and pumping functions of the lungs and the heart respectively in order to maintain life while the heart was being operated upon. This was necessary for the correction of intra cardiac defects.

A breakthrough in this quest was the use of an oxygenator. The initial rotating disc oxygenator was used by Gibbon in 1953 during a procedure to close endocardial cushion defect [7]. Further he completed the closure of an atrial septal defect by using a film oxygenator in the same year which became the first instance of successful human intracardiac repair. There was another instance when Lillehei and others performed a closure of a ventricular septal defect in a one-year old child using cross circulation with his father who functioned as an oxygenator in the year 1955. The devices for oxygenation improved further by the year 1960 due to the invention of the bubble oxygenators and membrane oxygenators. After the advent of better oxygenation in cardiopulmonary bypass, more complicated intra-cardiac repairs were possible and have thus evolved to the current levels. An attempt has been made to describe the components of cardiopulmonary bypass in the next sections.

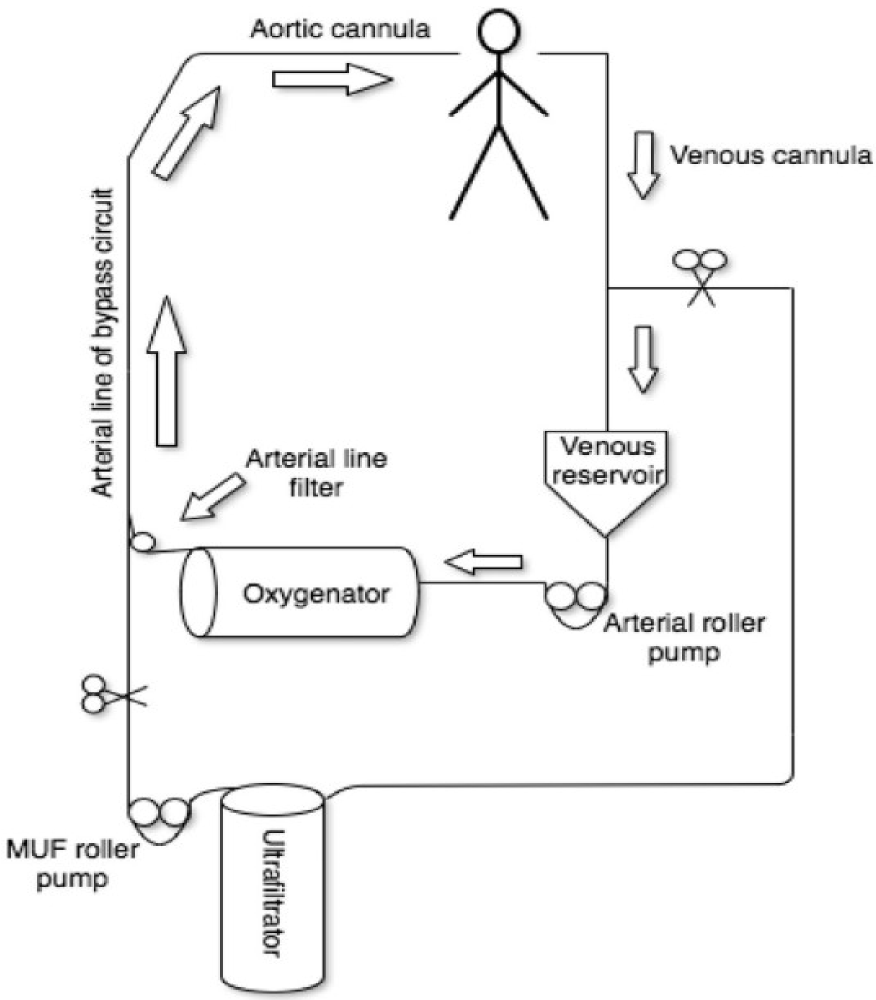

Fig 2. A schematic representation of cardiopulmonary bypass circuit.

COMPONENTS OF CARDIOPULMONARY BYPASS

Cardiopulmonary bypass is an extra-corporeal circuit which allows for maintenance of physiological support of heart-lung function during cardiac surgery in which the venous blood is drained, oxygenated and pumped back into the arterial circulation of the patient. The name, Heart-Lung machine is an apt description of the function of the device. The cardiopulmonary bypass machines include pumps, cannulae, tubing, reservoir, oxygenator, heat exchanger, and arterial line filters. Other than these, modern CPB machines also consist of pressure, temperature, oxygen saturation, haemoglobin blood gas and electrolyte monitoring systems along with safety features such as bubble detector, reservoir low level safety alarm.

PUMP:

They are the driving force of the CPB circuit. There are two types of pumps. Roller pumps have two rollers on a rotating arm which compresses a length of tubing to push blood forward. Whereas the centrifugal pump has cones stacked within a housing which when rotated rapidly, create negative pressure at one inlet and a positive pressure at the other and hence causing blood flow.

Roller pumps are known to cause haemolysis and hence not encouraged to be used in longer procedures. The centrifugal pumps do not have this drawback. They are however dependent on afterload. If the systemic vascular resistance at the patient’s end increases, the generated cardiac output decreases unless flow is increased. Centrifugal pumps hence can be a better option to improve platelet preservation and neurological outcomes in longer procedures.

CANNULAE:

They connect the patient to the cardiopulmonary bypass circuit. The arterial cannula is inserted into the ascending aorta and the venous cannula is inserted into the right atrium. The cannulae are reinforced to prevent kinking and are made up of polyvinylchloride material.

RESERVOIR:

It is a space to collect the blood drained from the heart. They can allow for a passive drainage of blood from the heart or suction can be applied to assist drainage. They have a defoaming facility and also maintain a suitable blood in order to avoid air entry into the arterial circuit.

OXYGENATOR

It is an interface which allows for oxygenation of blood within the cardiopulmonary bypass circuit. There were many types such as bubble oxygenators and film oxygenators which are from the past. Currently membrane oxygenators are in use which have hollow microporous polypropylene fibres. Blood flows around the fibres and gas flows through the fibre. These systems reduce the chances of air embolism and newer oxygenators have integrated filters to remove such emboli. The heat exchanger is usually placed proximal to the oxygenator to avoid the gaseous emboli which get released as a result of temperature changes of oxygen saturated blood.

CARDIOPLEGIA SYSTEM:

During any cardiac surgery, the aorta is cross clamped. This causes myocardial ischemia. Here the value of cardioplegia is ascertained. It is a technique used to induce an electromechanical arrest of the heart to create a reduced myocardial oxygen demand and thus resulting in myocardial protection during cardiac surgery.

While the arterial cannula is inserted distal to the cross clamp, the cardioplegia cannula is inserted proximally. It can be delivered antegrade into the aortic root or even retrograde into the coronary sinus.

Cardioplegia can be based in a crystalloid solution or even blood based. Potassium based solutions are usually used.

The application of cardiopulmonary bypass in paediatric population is a greater challenge when compared to its use in adults. This is due to various factors such as lesser size, immaturity of the cardia, anatomical complexities and physiological differences in children[8]. In the following section, the major differences in paediatric cardiopulmonary bypass system is discussed.

PERFUSION PRESSURES AND BLOOD FLOW

Children have a wide range of acceptable blood pressures. It is not a fixed value as in adults and widely varies with the age and weight of the child. A neonate may require much lower pressures whereas a 14-year-old child might require pressures as high as an adult.

Pulse pressure is known as the mean driving force for perfusion. When the aorta is clamped, the pulse pressure drops significantly and thus it may lead to the release of various vasoactive factors. This causes many physiological changes in the systemic resistance and other parameters [9]. adults in contrast to children, have stenotic lesions and other abnormalities which necessitate a higher flow velocity and hence a higher driving pressure. But children do not need such higher pressures.

Table 2 – Typical blood pressure ranges during CPB [10].

Age	Mean blood pressure range (mmhg)
<1 month	30-45
1-12 months	40-50
1-10 years	45-60
10-16 years	50-70
>16 years	60-90

PRIMING:

Priming is a process in which the circuits of cardiopulmonary bypass is de-aired. It is done using priming solutions which have a mixture of crystalloids and colloids. Based on the haemoglobin levels of the child, an amount of blood can be added since the priming process causes hemodilution. This hemodilution along with a decreased colloid osmotic pressure results in a phenomenon in which fluid leaks from blood vessel. This causes tissue edema. The optimum level of haematocrit during CPB is debated upon.

Further, due to the rapid decrease in viscosity, blood pressure also tends to fall during the initiation of cardiopulmonary bypass.

Various factors such as body mass, effective organ perfusion and temperature, decide the optimal systemic blood flow levels in children. The data for the optimal flow is not clearly defined as such for the pediatric population. Further, the calculations for optimal flow can be rendered inadequate by the presence of shunt lesions, complex intracardiac connections in children [11].

LEFTWARD SHIFT OF OXYHEMOGLOBIN DISSOCIATION

The curve of dissociation of oxygenated haemoglobin shows a leftward shift as the temperature of blood decreases. The temperature of blood decreases due to the induction of hypothermia. It is initiated because it has an organ protective effect by reduction of metabolic demands due to a reduced temperature. Hypothermia also causes an increase in the blood viscosity and counters the hemodilution that effects as a result of the cardiopulmonary bypass priming. Hypothermia also causes a reversible inhibition of clotting factors and platelets.

A shift of the dissociation curve to the left means that it is more difficult for the oxygen to dissociate from the haemoglobin molecule and reach tissues. Hence leading to tissue hypoxia. This results in a steep rise in venous oxygen concentrations with the onset of cardiopulmonary bypass, suggesting that the decrease in oxygen transport falls more rapidly than the decrease in metabolism. However as soon as the warming is initiated, the venous oxygen saturation falls rapidly [12].

The pH of blood becomes more alkaline as hypothermia is initiated [13]. This is mainly due to the increased dissolution of carbon dioxide in blood. The blood oxyhemoglobin dissociation curve shifts to the left with acidosis and hypothermia. During cardiopulmonary bypass, the alkalinity balances the shift to left due to decreased temperature and hence improves tissue perfusion.

INFLAMMATION:

The cardiopulmonary bypass is considered a foreign substance by the blood and it results in initiation of inflammatory reaction. The most serious amongst those is SIRS, Systemic Inflammatory Response Syndrome. The syndrome results in increased permeability of vessel walls, fever, leucocytosis or leukocytopenia and coagulation defects. In order to suppress the inflammation, steroid administration during cardiopulmonary bypass has been tried, especially in neonates and has been shown to be of some benefit [14].

MODIFIED ULTRAFILTRATION:

Ultrafiltration is usually done after the end of cardiopulmonary bypass to remove the excess free water and hence increase hematocrit. It is done until a satisfactory rise in hematocrit is achieved. The advantages of MUF include reduced myocardial edema, reduced inotrope dependence, reduced inflammatory mediators, improved hematocrit and blood pressure, better coagulation profile and hence reduced risk of bleeding [15].

CARDIOPLEGIA:

Cardioplegia is used to protect the heart from ischaemic injury. Though the immature heart of children is resistant to ischaemic injury, it can be more prone to reperfusion injury due to calcium overload. This occurs as a result of immaturity of calcium ATPase in children [16]. To address these concerns, Del Nido cardioplegia was introduced. Del Nido cardioplegia has the following characteristics;

Blood is added to the cardioplegia solution which results in promotes aerobic metabolism and also acts as a buffer. Lidocaine has been added to provide sodium channel blockade and hence counteracts the adverse effects of high potassium level induced depolarization arrest [17]. Magnesium has been added which acts as a blocker of calcium channels.it helps in post cardioplegia recovery. The composition of Del Nido cardioplegia has been described in the tables below [18].

Table 3. contents of plasma-Lyte A

Plasma – Lyte A	mEq/L
Na	140
K	5
Mg	3
Cl	98
Acetate	27
Gluconate	23

Table 4. Additives to plasma-Lyte A

Additives (per 1L of Plasma- Lyte)	
Mannitol 20%	16.3 mL
Magnesium sulfate 50%	4 mL
Potassium chloride (2 mEq/ml)	13 mL
Sodium bicarbonate (2 mEq/ml)	13 mL
Lidocaine 1%	13 mL
Dilution (blood: cardioplegia)	1:4

NEUROLOGICAL IMPLICATIONS OF CONGENITAL HEART DISEASE AND ITS MANAGEMENT.

Congenital heart diseases have a wide array of neurological implications as a result of the primary disease process. The effects maybe be cerebrovascular pathology, cognitive impairment or due to the associated anomalies of the central nervous system.

CEREBROVASCULAR COMPLICATIONS OF CONGENITAL HEART DISEASE:

Congenital heart diseases constitute one of the most common etiologies for cerebral emboli in children. They account for about 20%of the ischemic brain infarctions in children[19]. Structural heart defects such as Tetralogy of Fallot, transposition of great arteries and hypoplastic left heart have a high probability of causing stroke. Septal defects and valvular heart disease contribute little. Paradoxical embolism and cardiac arrythmia are responsible for stroke in a few children.

Polycythemia in cyanotic CHD can cause an increase of thrombosis. Children with CHD and anemia, have an increased risk of arterial stroke [20]. now it seems that the occurrence of congenital heart disease with iron deficiency anemia has a risk for both arterial and venous strokes.

Venous emboli are usually filtered out by the pulmonary capillary plexus and are not allowed to enter the arterial side of circulation. But it can occur in defects which allow for the venous clot to bypass the pulmonary circulation. Unless for any cardiac defect such as septal defect or other lesions with a high intrinsic stroke risk, the venous emboli do not cross over to the arterial circulation. These shunts may produce only left to right shunts. But there may be a small amount of right to left shunt during Valsalva manoeuvre or due to raised pressures in the pulmonary artery. The gold standard for diagnosis of a patent foramen ovale is the technique of contrast Echo in which agitated saline is injected intravenously and echo is done for patent foramen ovale and right to left shunt during Valsalva manoeuvre. Other causes of vascular complications are atrial septal aneurysms and atrial fibrillation.

CONGENITAL HEART DISEASE AND INFECTIVE EMBOLI:

There is a higher risk of secondary embolism due to infective endocarditis in children with congenital heart disease. Most of the emboli contained streptococcal bacteria and a few of them contained staphylococci[21]. The cerebral complications occurred more commonly associated with staphylococcal infective endocarditis and emboli than any other organism [22].

There are various other causes of neurological problems in congenital heart disease, such as associated brain anomalies, associated syndromes, and also some of the treatment modalities used to treat congenital heart disease.

NEUROLOGICAL COMPLICATIONS OF MANAGEMENT OF CONGENITAL HEART DISEASE:

Various complications arise from the treatment modalities used for congenital heart disease. Strokes can occur routinely as a result of cardiac catheterization in congenital heart disease. However, it is not absolute that the procedure or the condition is differentiated to be the cause. Low flow cardiopulmonary bypass is known to cause mild injuries whereas deep hypothermic circulatory arrest is known to cause reduced intelligence quotient, acute clinical seizures and abnormal EEG in children [23].

Many movement disorders have been described post cardiac surgery. Choreo-athetoid movement after cardiac surgery is a known entity which is also called post pump chorea. The abnormal movements affect the muscles of the face, tongue muscles and limbs. Most often are transient but can persist in a few children [24].

Hence congenital heart disease or its management options cause varied neurological sequelae and neurodevelopmental anomalies. In the next section, we discuss about the various methods of neurodevelopmental assessment in children.

NEURODEVELOPMENTAL ASSESSMENT METHODS

Developmental screening observes how a child grows and changes over time and whether a child meets the typical developmental milestones in playing, learning, speaking, behaving, and moving. Whereas a developmental assessment observes a child and assigns particular scores in gross motor, fine motor, language and verbal, social and emotional domains.

Various screening tools and scales have been developed for the same purpose.

BAYLEY III

The Bayley's scale for infant and toddler development is the gold standard in neurodevelopmental assessment of children. It is based on a broad cross-section of infant and child research. It follows a time-tested method of using standardized assessment procedures to provide toddlers and infants with tasks and situations that capture their interest and provide an observable set of behavioral responses. The structure of the Bayley-III Scales allows clinicians to administer each of the five scales independent of others. This feature makes the tool better in identifying the specific area of delay. Each scale and subtest then may be administered and scored correctly and efficiently. Performance measured by the Bayley-III is summarized through the use of various scores for each subtest, and composite scores for each scale, together with percentile ranks, developmental age equivalents, and growth scores. A total score is not provided, because a total score that aggregates a child's performance on all five scales is not informative.

There are five components of Bayley's scoring system:

COGNITIVE SCALE

There are 91 items in the assessment of cognitive scale. Its items assess children's sensorimotor development, exploration and manipulation of objects, object relations, concept formation, and memory. It takes into consideration that from birth till 2 years of age, the child is more interested to explore new objects and find a way to play with a new object and further after 2 years, the regular play such as mouthing of toys is replaced by advanced levels of play. It involves playing with a pretence such as holding the toy near the ear in the pretence of having a phone conversation and other activities[25].

LANGUAGE SCALE:

The Language Scale measures two major aspects of language: receptive and expressive communication skills. These skills are displayed differently, and may or may not develop independently. The 49-item Receptive Communication subtest assesses preverbal behaviours, including a child's ability to recognize sounds. The 48-

item Expressive Communication subtest assesses preverbal communication and vocabulary use.

MOTOR SCALE:

The Motor Scale assesses fine motor and gross motor skills separately. The 66-item Fine Motor subtest assesses how well children use their hands to engage their environment, eyes and fingers. How well children control and move their body is assessed by the 72-item Gross Motor subtest.

SOCIAL-EMOTIONAL SCALE:

The 35-item Social-Emotional Scale identifies normal social and emotional developmental milestones of infants and toddlers. This information is gathered through a questionnaire completed by the child's caregiver. The scale is derived from the Greenspan Social-Emotional Growth Chart [26]. The Social-Emotional Scale measures children's functional emotional skills. It includes self-regulation and interest in the world.

ADAPTIVE BEHAVIOR SCALE:

The 241-item Adaptive Behaviour Scale assesses the child's independent display of skills needed in normal daily living. A General Adaptive Composite (GAC) provides an overall measure of adaptive development based on the following 10 skill areas: Communication (e.g., the child's speech, language, and non-verbal skills), Community Use (e.g., the child's interest in activities outside the home and ability to recognize various community locations), Health and Safety (e.g., how readily a child shows caution and an ability to avoid physical danger), Leisure (e.g., forms of play and the ability to follow rules), Selfcare (e.g., the child's eating, toileting, and bathing behaviours), Self-direction (e.g., how readily the child shows self-control, follows directions, and makes choices), Functional Pre-academics (e.g., the child's skills at letter recognition, counting, and drawing simple shapes), Home Living (e.g., the degree to which a child helps adults with household tasks and cares for his or her personal possessions), Social (e.g., how well the child gets along with other people, uses manners, assists others, and recognizes emotions), and Motor (e.g., the child's locomotion skills and manipulation of the environment).

DASII – DEVELOPMENTAL ASSESSMENT SCALE FOR INDIAN INFANTS

DASII is a version of developmental screening which is derived from Bayley scale for infant development. It is modified to suit the Indian scenario. The whole screening tool consists of two scales. A scale to assess motor development which consists of 67 items. The scale to assess mental development consists of 163 items.

The motor development scales assess the child's development in terms of its motor abilities such as supine to erect posture, locomotion and basic locomotive skills such as climbing, jumping and skipping. It also records the ability to do manipulatory behaviours such as reaching for an object, picking up and handling things, putting or throwing an object in a directed manner.

The mental developmental scales identify the child's cognizance of the objects in its surroundings, perception and pursuit of moving objects, ability to explore them and trying to do meaningful manipulation with the objects.it also includes spatial relations, manual dexterity. The scale for mental development also includes assessment of the child's development in terms of language, comprehension, communication, imitative behaviour and social interaction. In total 230 items in both the scales assess both the domains of development.

METHODOLOGY

The study was conducted in KLES DR Prabhakar Kore Hospital between January 2020 till December 2020

STUDY DESIGN:

Hospital Based Longitudinal study

STUDY DURATION AND STUDY PERIOD:

One year duration from January 2020 to December 2020

PLACE:

KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi, a teaching hospital affiliated to Jawaharlal Nehru Medical College, Belagavi.

SOURCE OF DATA:

All children between ages 6 months to 3 years undergoing open heart surgery for correction of congenital heart disease in KLE's Dr Prabhakar Kore Hospital.

INCLUSION CRITERIA:

All children between ages 6 months to 3 years undergoing open heart surgery for correction of congenital heart disease in KLE's Dr Prabhakar Kore Hospital between January 2020 till December 2020

EXCLUSION CRITERIA:

- Children with clinically recognisable genetic syndromes.
- Children undergoing palliative surgeries.
- Children with visual impairment
- Children with auditory impairment
- Children with prior cardiac surgery
- Children with CNS malformations
- Children or parents not willing to participate in the study.

SAMPLE SIZE :

Sample size was calculated by the formula –

$$\frac{z^2 p(1-P) \,/\, \varepsilon^2}{1+\left[\frac{z^2 \times p * (1-p)}{E^2 N}\right]}$$

Where ε^2 is margin of error taken as 0.5

P = proportion of interest= 75 percent prevalence

N= population size – 60

Z= critical value – 1.96 for 95 % confidence level

Using this equation, a sample size of 48 was obtained.

ETHICAL CLEARANCE:

Prior to the commencement, study was approved by the institutional ethical committee, Jawaharlal Nehru Medical College, Belagavi.

INFORMED CONSENT:

Parents of the children with congenital heart disease who fulfilled the eligibility criteria were briefed about the nature of the study and a written informed consent was obtained in the language known to them.

METHODOLOGY:

Any child between the age of 6 months to 3 years with congenital heart disease and preemptively being evaluated for surgery were considered. If the child fulfilled the eligibility criteria, he/she was enrolled into the study.

After taking the consent, relevant data was obtained from the parents and recorded in a structured proforma.

The demographic details, presenting complaints, details of diagnosis, age at diagnosis, relevant details of medications were recorded in the proforma.

Once the tentative date of surgery was known, the child was subjected to DASII evaluation by a certified clinical psychologist at the child development centre, KLES Dr Prabhakar Kore hospital. The performance of each child was recorded in the proforma in the domains – mental scales, motor scales and developmental scale.

After the children underwent corrective cardiac surgery under cardiopulmonary bypass, the child was followed up after a period of 3 months and again was subjected to DASII evaluation and the scores were noted.

The intra operative parameters such as duration of cardiopulmonary bypass, duration of aortic cross clamp, minimum values of pH and hematocrit during the procedure etc. were collected from hospital records.

OUTCOME VARIABLES:

The outcome variable was DASII score prior to and after corrective cardiac surgery.

DATA ANALYSIS:

The data which was obtained was coded and entered into Microsoft excel worksheets and analyzed using SPSS version 20 and OpenEpi version 3.1.0

Continuous variables were expressed as Mean ± Standard Deviation. The DASII scores were calculated before and after interventions and compared using mean and standard deviations and Wilcoxon signed-rank test. Shapiro-Wilk's test is used to check the normality of variables. A non-parametric test (Wilcoxon signed-rank test) was used as the study outcome values did not have normal distribution. The intra operative parameters are compared with using Multiple linear regression analysis to check the potential predictors of change in DASII scores. An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it has been considered as significant.

RESULTS

RESULTS OF THE STUDY – NEURODEVELOPMENTAL STATUS BEFORE AND AFTER CORRECTIVE CARDIAC SURGERY IN CHILDREN AGED 6 MONTHS TO 3 YEARS, A ONE YEAR HOSPITAL BASED LONGITUDINAL STUDY.

A one year, hospital based observational study was conducted at KLES Dr Prabhakar kore hospital. All children between ages 6 months to 3 years undergoing open heart surgery for correction of congenital heart disease were subjected to DASII evaluation before and after surgery. The intra operative parameters were collected from hospital records.

The study included 38 children who underwent corrective cardiac surgery over a span of one year.

DEMOGRAPHIC DATA

1. **AGE DISTRIBUTION**

All 38 children were between the ages of 6 months to 36 months with a mean age of 12.14 months.

Table 5 – Age Distribution of Children Enrolled In The Study

	N	%
0-6 MONTHS	9	23.6%
7-12 MONTHS	14	36.8%
1-2 YEAR	9	23.6%
ABOVE 2 YEARS	6	16%
TOTAL	38	100%

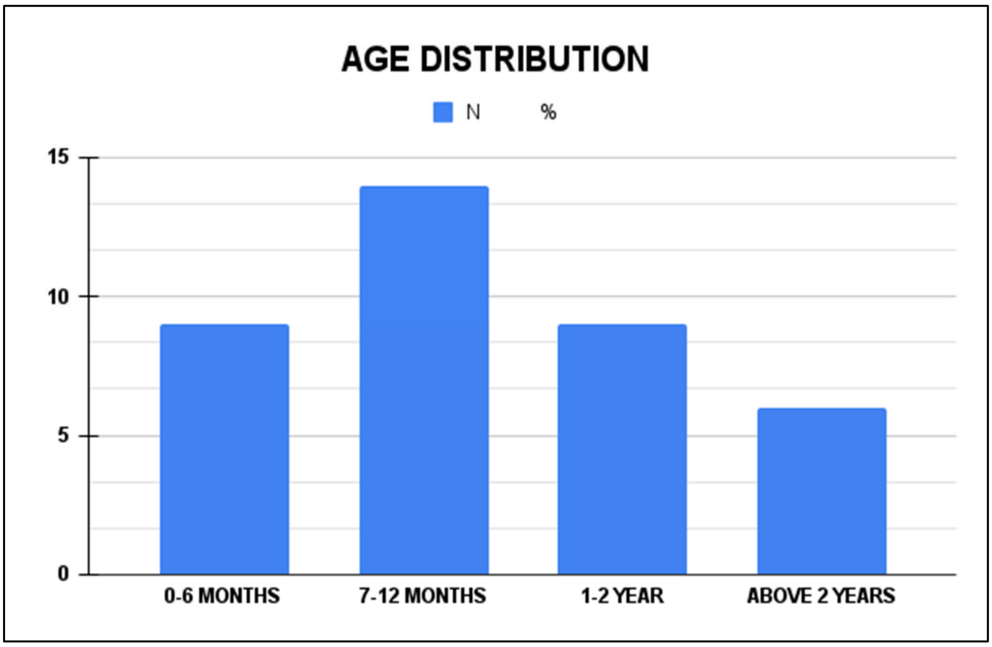

Figure 3 – Age distribution Histogram.

2. GENDER DISTRIBUTION

Out of the 38 children enrolled in the study, 24 were male and 14 were female.

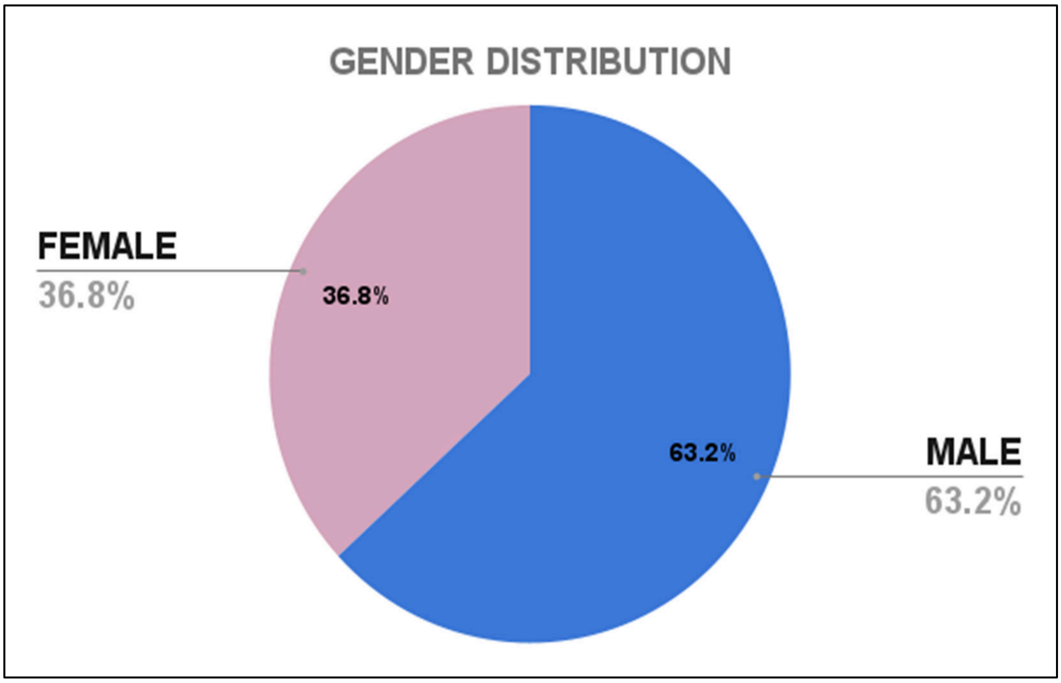

Figure 4- Pie chart showing Male:Female ratio in study participants

The male to female ratio was 1.71:1 which could be due to the reason that a male child is more likely to be brought to the hospital for early treatment rather than a female child.

3. TYPE OF HEART DISEASE

The children included in the study belonged to both cyanotic and Acyanotic heart disease groups. The distribution of can be depicted as follows.

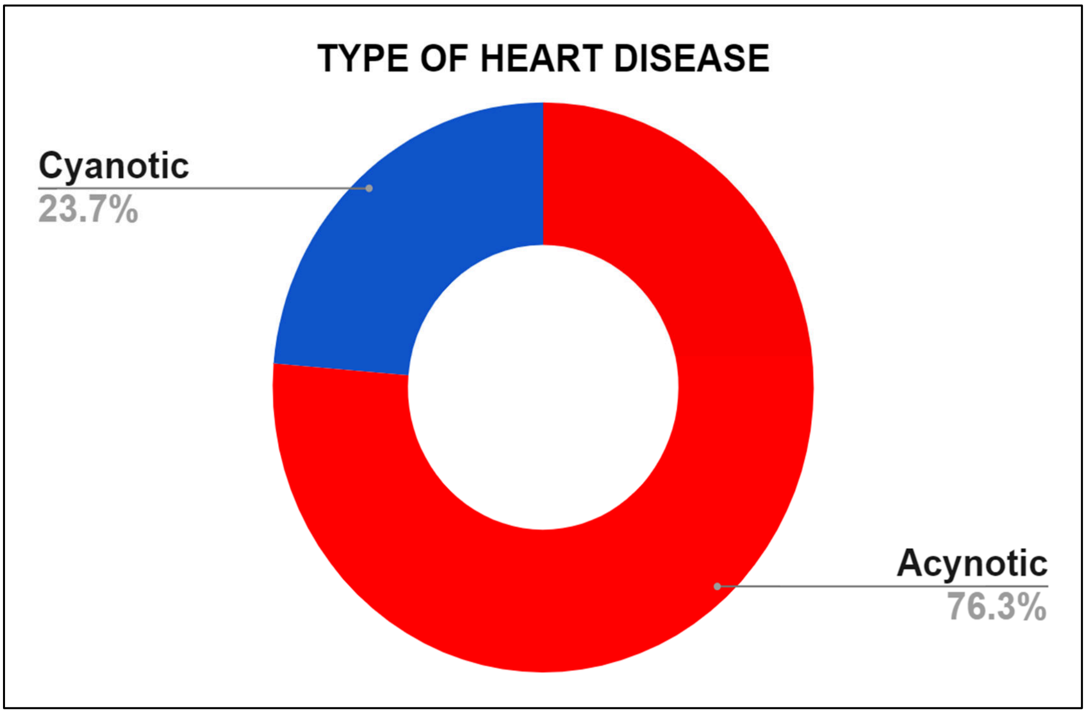

Figure 5- Type of Heart Disease (Cyanotic/ Acyanotic)

4. CONGENITAL HEART DISEASE – DIAGNOSIS

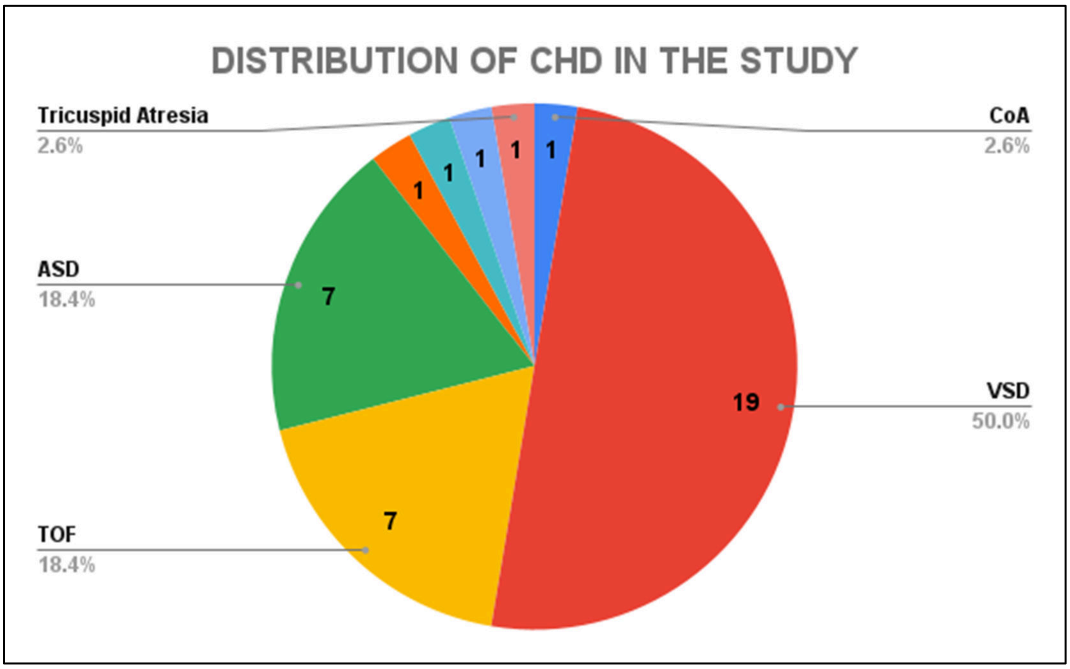

Figure 6- Pie chart showing the distribution of various congenital heart disease

5. **AGE AT DIAGNOSIS**

The children in the study were assessed to when the diagnosis of Congenital Heart Disease was made. None of them had been detected in utero and a very few of them were diagnosed at birth. The children were diagnosed to have heart disease at an average age of 3.32 months. This happened probably once the cardiac failure started to set in and the child showed symptoms which led to the diagnosis.

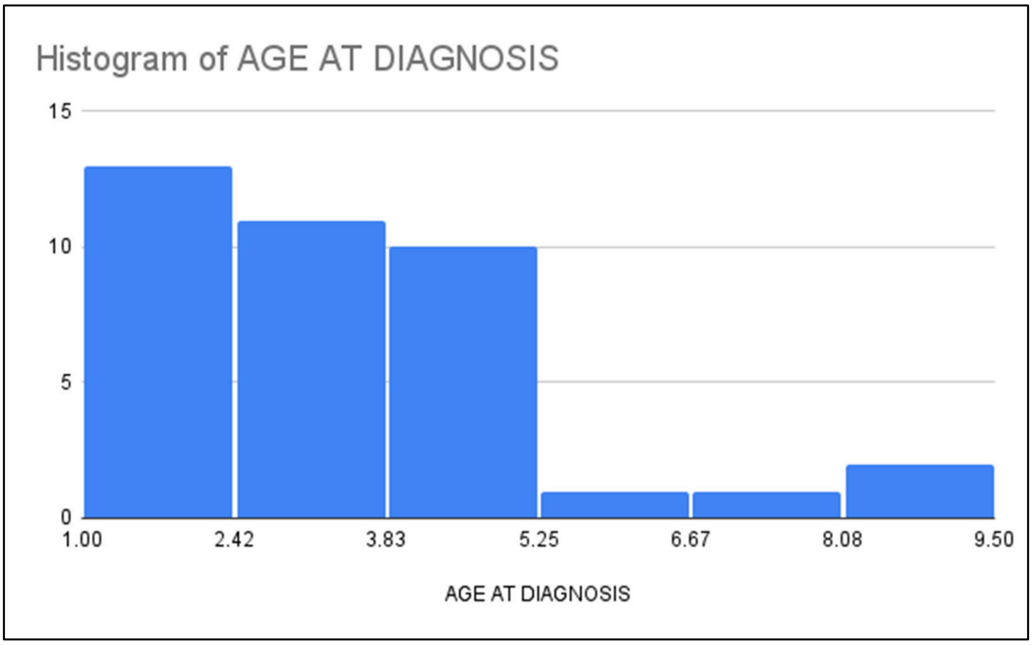

Figure 7 – Age at diagnosis of CHD

INTRA OPERATIVE PARAMETERS

1. **Duration of Cardio-Pulmonary Bypass (CPB)**

The children undergoing corrective cardiac surgery are subjected to a Cardio Pulmonary Bypass which takes the function of the heart. On an average, each child spent about 57+/-25.72 minutes on the cardiopulmonary bypass. The duration of CPB is suggested to have various implications on the neurological outcomes as discussed in the later sections.

2. **Duration of Aortic Cross Clamp**

Once the cardiopulmonary bypass is initiated, the aorta is clamped and the output into aorta is taken over entirely by the cardiopulmonary bypass machine. The duration for which the clamp is placed across the aorta is taken as cross clamp time. On an average, the cross clamp time was 33.48+/-19.03 minutes.

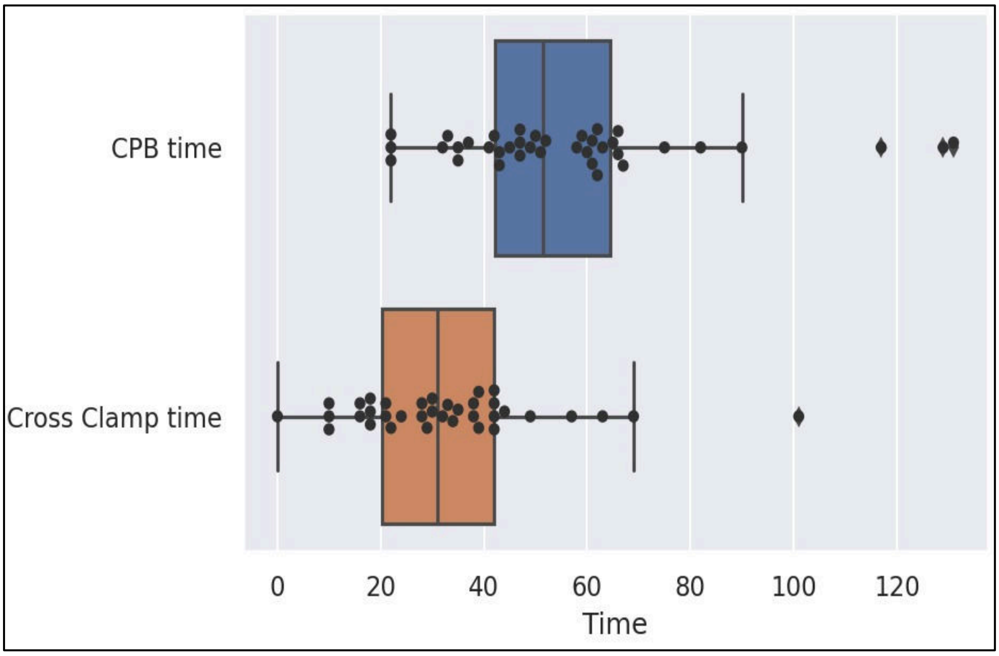

Figure 8- Box plot showing the median, 25th and 75th centiles of CPB time and Cross Clamp Time

3. MINIMUM VALUE OF HEMATOCRIT

Once the child is to be initiated on the Cardiopulmonary Bypass, the cardiopulmonary bypass circuit takes up an amount of blood volume. Therefore, it is primed with an amount of cross matched blood. The total blood volume and other values are altered because of the same and hence the hematocrit changes. There may be a risk of hemodilution. Hence, we measured the minimum value of hematocrit during the course of each procedure. The mean least hematocrit was 27.47±3.90.

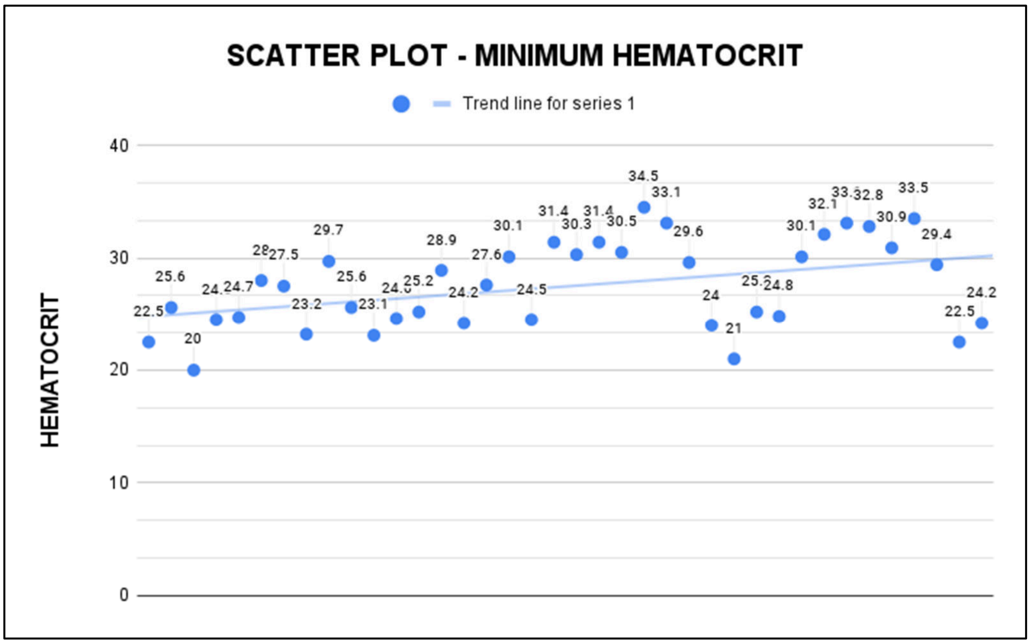

Figure 9- Graph depicting the minimum hematocrit during CPB.

4. MINIMUM VALUE OF pH

The perfusion of tissues during Cardiopulmonary Bypass is an important factor which was monitored during the surgery. Acidosis indicates reduced tissue perfusion and hence the minimum value of pH was measured in all the subjects during the procedure. The mean least value of pH was 7.33±0.06.

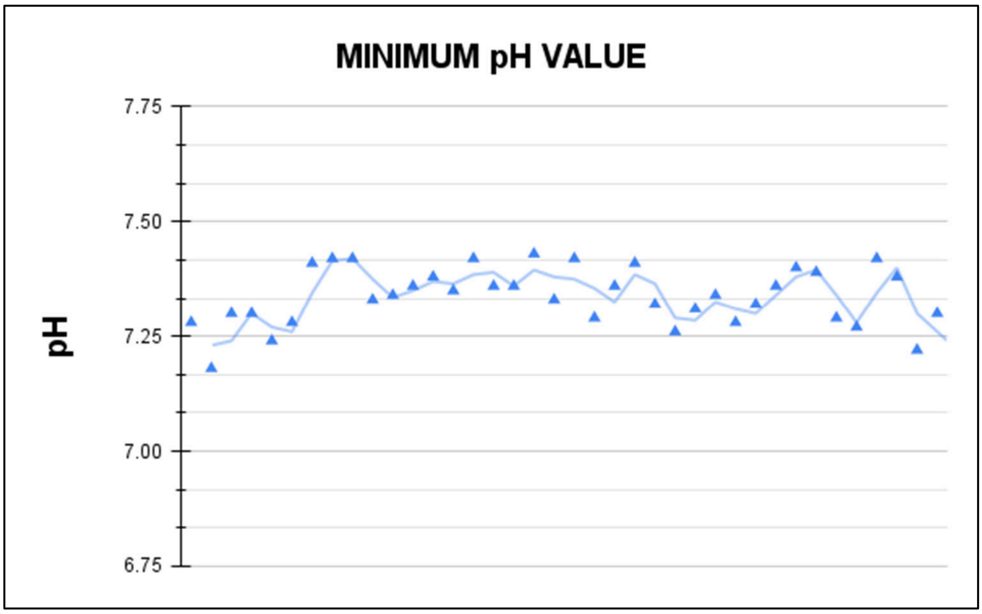

Figure 10- Minimum value of pH depicted as a plot with trending average line.

NEUROLOGICAL ASSESSMENT PARAMETERS

The primary objective of the study was to ascertain the changes in neurodevelopmental status after corrective cardiac surgery with cardiopulmonary bypass. The neurological status was assessed by using DASII neurological assessment tool, before and after cardiac surgery. Children with conditions that might affect neurological status, such as blindness, deafness, visually identifiable genetic syndromes etc.

The scores were represented in two major domains – mental quotient and motor quotient and the final developmental quotient is an average of the two domains.

The mean preoperative developmental score was 93.62+/-12.9. when the same was measured three months after surgery, the mean developmental scores had a significant decline with a mean value of 87.54+/-23.45.

Table 6 – Pre-operative and post-operative DASII scores.

Parameters	Pre-operative	Post-operative	p-value
Mental Quotient	96.35+/-7.93	87.77+/-23.33	0.05
Motor Quotient	94.06+/-9.86	87.5+/-23.45	0.354
Developmental Quotient	93.62+/-12.9	87.54+/-23.45	0.852

The two values were subjected to paired t test to test the strength of association which revealed a T value of 1.31 with a non-significant p value of 0.852.

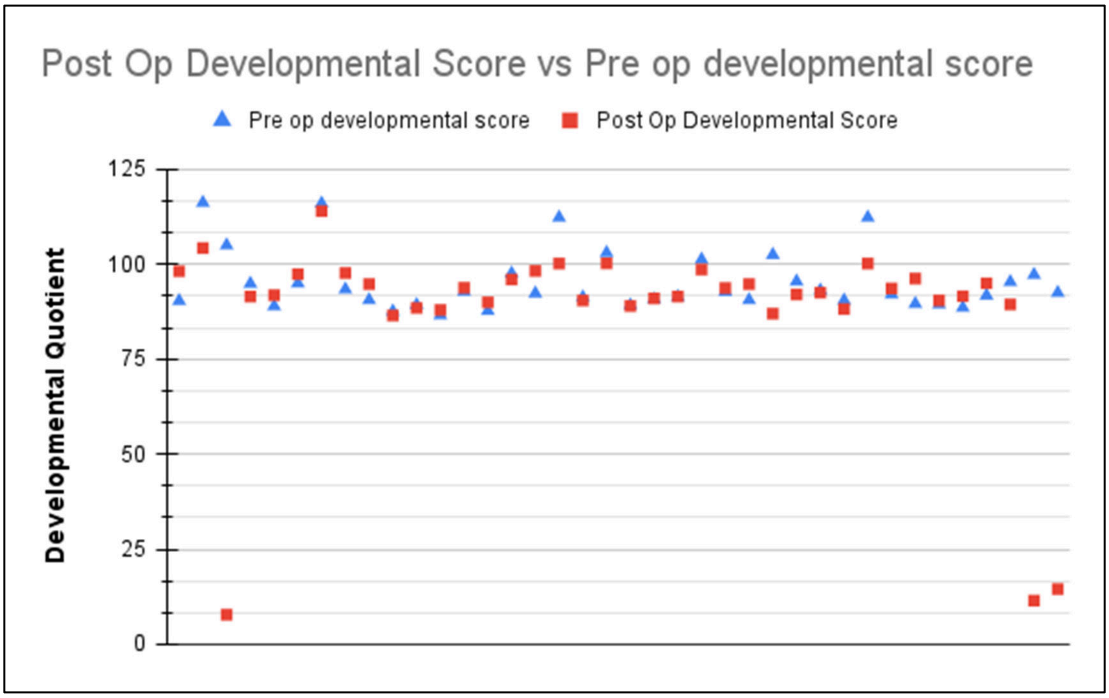

Figure 11- Chart depicting trends in developmental score

When the two different domains were specifically observed, the mean pre-operative mental quotient was 96.35+/-7.93 and the post-operative scores were considerably lesser with a mean score of 87.77+/-23.33, t test showed that the values are different with a p value of 0.05 which was approaching statistical significance. The motor quotient however had a mean pre-operative score of 94.06+/-9.86 and a reduced post-operative mean of 87.5+/-23.45 with a p value of 0.11 which made it statistically non-significant.

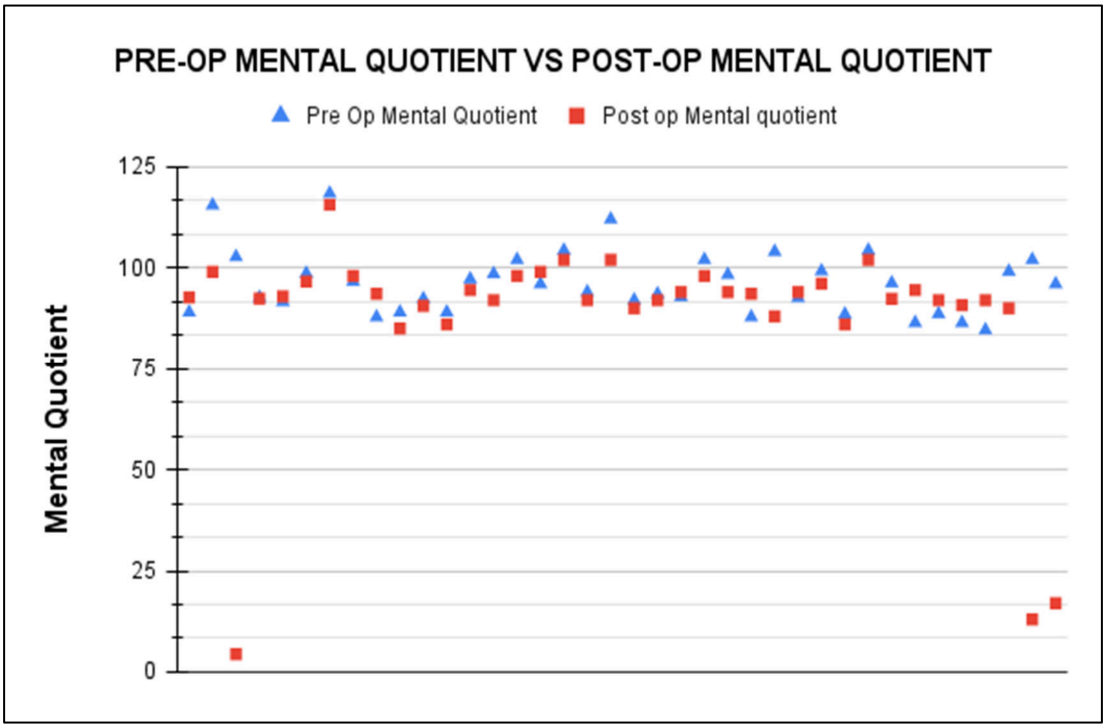

Figure 12- Chart depicting trends in mental quotient.

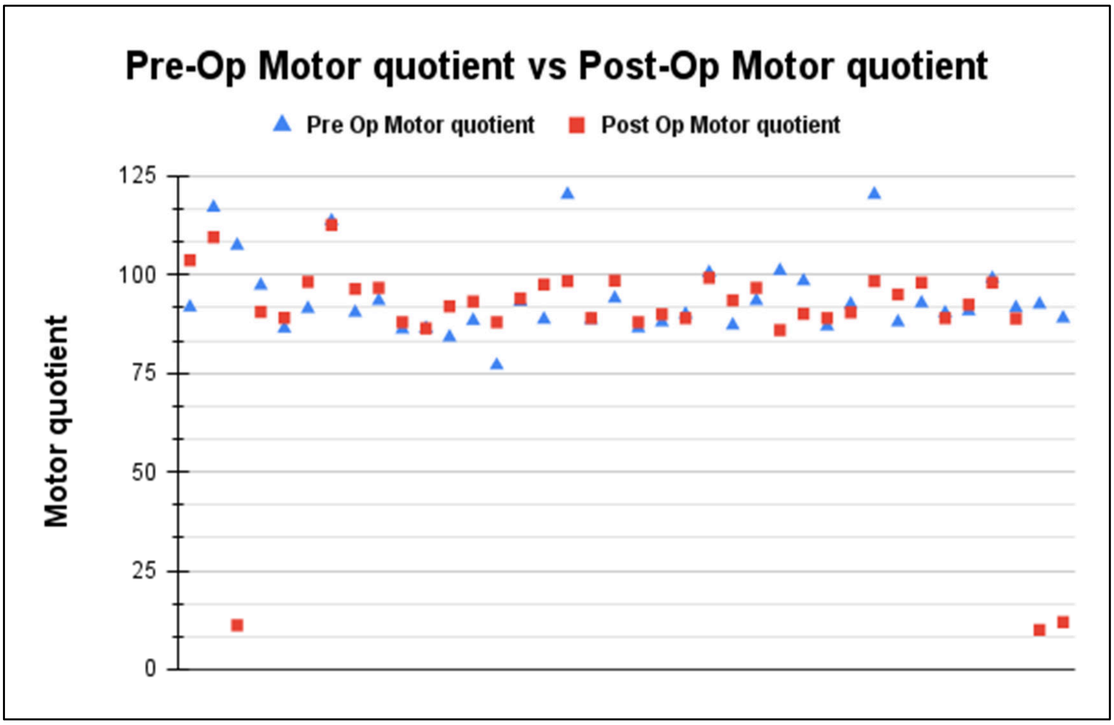

Figure 13- Chart depicting trends in motor quotient.

CORRELATION BETWEEN INTRA OPERATIVE PARAMETERS AND THE NEURODEVELOPMENTAL CHANGES

To know which intra operative parameters were significant in their association with change in neurodevelopmental status, we compared each intra operative parameter against the change in neurodevelopmental scores using linear regression analysis.

1. DURATION OF CARDIOPULMONARY BYPASS

When the Duration of Cardiopulmonary Bypass was compared to change in DASII scores, we obtained the following results. The change in mental scores were correlated negatively to the duration of cardiopulmonary bypass with a Pearson's correlation coefficient of -0.125 but it was statistically non-significant with a p value of 0.456.

The change in motor scores were correlated negatively with the duration of Cardiopulmonary bypass with a Pearson's correlation co-efficient of -0.59 with a p value of 0.724 which was non-significant.

The change in overall Developmental scores were correlated negatively with the duration of cardiopulmonary bypass with a Pearson's correlation coefficient of -0.195 and a non-significant p value of 0.240.

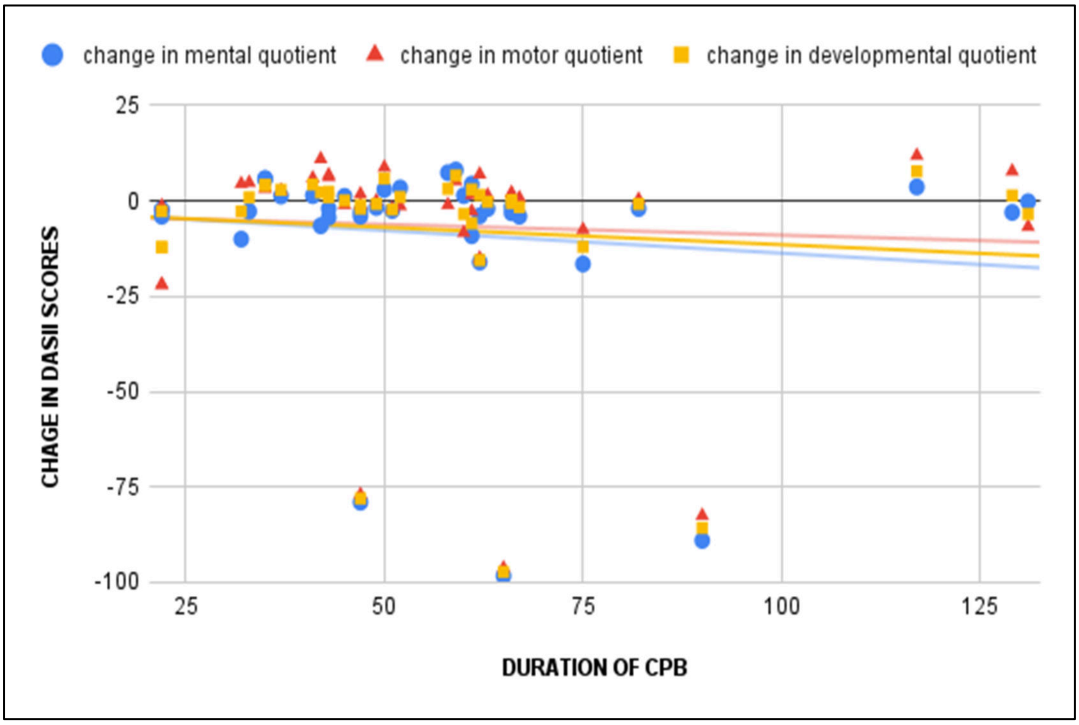

Figure 14- Scatter plot showing correlation between changes in DASII scores with duration of CPB with trend lines.

2. MINIMUM VALUE OF HEMATOCRIT

We tried to assess the correlation between the change in DASII scores with the minimum value of hematocrit during the cardiopulmonary bypass.

The minimum value of hematocrit was correlated with the change in mental scores with a Pearson's coefficient of 0.225 and a p value which was significant at 0.006. Whereas the motor score change was also correlated with the minimum value of hematocrit. The Pearson's coefficient was 0.218 with a statistically significant p value of 0.014. The change in overall developmental quotient was correlated to the minimum value of hematocrit with a Pearson's coefficient of 0.188 with a p value of 0.042 which was significant.

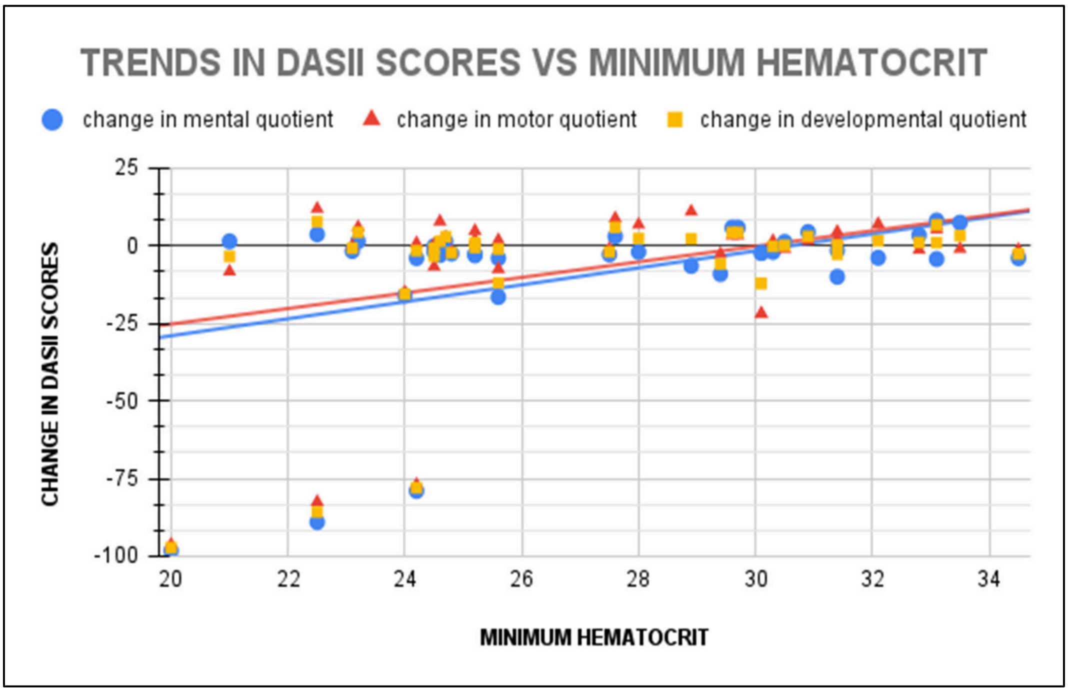

Figure 15- Scatter plot showing changes in DASII scores correlated with minimum value of hematocrit.

3. MINIMUM VALUE OF pH

The acidosis during surgery is represented by the minimum value of pH during the cardiopulmonary bypass. We tried to find the association of neurodevelopmental changes with acidosis by correlation between minimum value of pH and change in hematocrit.

The minimum value of pH was correlated to the change in developmental quotient by a Pearson's correlation coefficient of 0.304 with a p value of 0.838.

When the individual domains were observed, the change in mental quotient was correlated with the minimum hematocrit with a Pearson's co efficient of 0.337 and with a significant p value of 0.039. However, the change in motor quotient did not have a significant correlation with the minimum hematocrit with a Pearson's coefficient of 0.300 and a p value of 0.067.

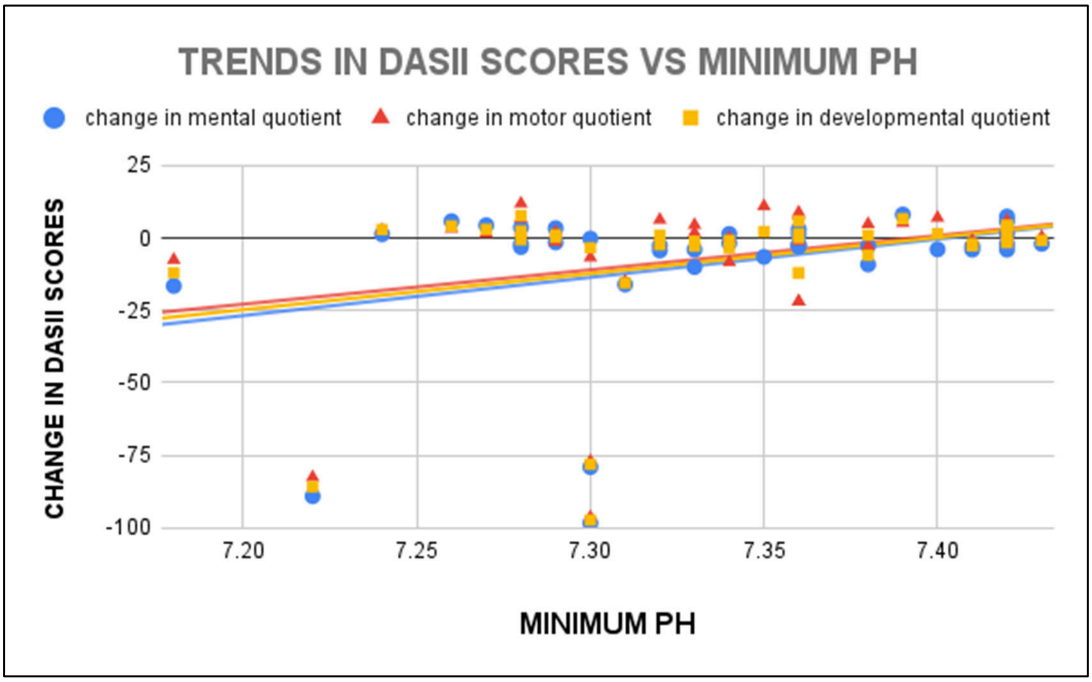

Figure 16- Scatter plot showing trends in DASII scores with minimum pH.

ACYANOTIC VS CYANOTIC HEART DISEASE

The difference in behaviour between Cyanotic and Acyanotic heart diseases in terms of the neurodevelopmental changes and correlation with various intra operative parameters were ascertained.

THE CYANOTIC GROUP

We analysed the data from 9 cyanotic congenital heart diseases amongst 38 subjects.

Neurodevelopmental status

The mean pre-operative developmental score was 94.31+/-5.88 whereas the mean post-operative developmental score was 72.84+/-35.11. There was a significant reduction in the mean scores of about 22 percent.

Table 7 – Mean and Standard deviation of pre-operative and post-operative DASII scores (cyanotic group).

PARTICULARS	PRE-OPERATIVE MEAN ±STD DEV	POST-OPERATIVE MEAN ±STD DEV
Mental quotient	94.51+/-6.61	72.83+/-35.53
Motor quotient	94.12+/-7.69	73.08+/-35.01
Developmental quotient	94.3+/-5.88	72.84+/-35.11

The normality of data distribution was tested using Shapiro Wilk test and was found that the data distribution was not normal and had a skew. Hence, a non-parametric test- Wilcoxon signed rank test was used to find the association between the pre op and post op values. The same was used to test the changes in pre-operative and post-operative values in the mental and motor domains.

Table 8 – Comparison of Pre-Operative and Post-operative median scores using Wilcoxon signed rank test.

Parameters	Pre-operative	Post-operative	p-value
Mental Quotient	94 (84.6, 104)	88 (4.4, 96.1)	0.07422
Motor Quotient	92.5 (84.2, 107.4)	89 (11.16, 98)	0.1383
Developmental Quotient	92.5 (86.6, 105)	93.8 (7.78, 95)	0.09766

Though there was a drastic reduction in mean scores across all the three parameters in the post-operative period, the non-parametric test did not reveal a statistically significant difference between the median scores across the pre-operative and post-operative scores amongst the three quotients.

INTRA-OPERATIVE PARAMETERS AND CORRELATION WITH NEURODEVELOPMENTAL STATUS.

The intra-operative parameters were assessed for their correlation using linear regression analysis and it was found that none of the intra-operative parameters had a significant association with the change in neurodevelopmental scores.

Table 9 – Correlation between intra operative parameters and change in DASII scores (Cyanotic group).

Particulars		Duration of Cardiopulmonary Bypass	Duration of Aortic Cross Clamp	Minimum value of hematocrit	Minimum value of pH
Delta Mental Quotient	Pearson Correlation	-0.293	-0.223	0.389	0.434
	p value	0.444	0.563	0.301	0.243
Delta Motor Quotient	Pearson Correlation	-0.252	-0.186	0.463	0.464
	p value	0.513	0.631	0.209	0.208
Delta Developmental Quotient	Pearson Correlation	-0.298	-0.229	0.423	0.447
	p value	0.436	0.554	0.256	0.227

THE ACYANOTIC GROUP

We analysed the data of 29 Acyanotic Congenital Heart Disease subjects amongst the 38.

Neurodevelopmental scores

The pre-operative and post-operative DASII scores were compared using Paired T test. There was a small reduction in the mean scores in all the three domains. But, the change in scores were not statistically significant.

Table 10 – Mean and standard deviation of pre-operative and post-operative DASII scores in the Acyanotic group.

PARTICULARS	PRE-OPERATIVE MEAN ±STD DEV	POST OPERATIVE MEAN ±STD DEV	T value	P value
Mental quotient	96.92+/-8.31	92.41+/-16.2	1.31	0.132
Motor quotient	94.04+/-10.56	92.02+/-16.98	1.76	0.535
Developmental quotient	93.40+/-14.48	92.24+/-16.49	0.275	0.0783

INTRA-OPERATIVE PARAMETERS AND CORRELATION WITH NEURODEVELOPMENTAL STATUS

The intra operative parameters in the Acyanotic group were assessed for their correlation with the change in DASII scores using linear regression analysis. It was found that Duration of Aortic cross clamp was significantly correlated with the change in DASII scores in all the three domains.

Table 11- Correlation between intra operative parameters and the change in neurodevelopmental scores (acyanotic group).

		Duration of cardiopulmonary bypass	Duration of Aortic cross clamp	Minimum hematocrit	Minimum pH
Delta Mental Quotient	Pearson Correlation	0.274	0.597	0.279	0.387
	p value	0.151	0.001	0.143	0.038
Delta Motor Quotient	Pearson Correlation	0.226	0.375	0.297	0.336
	p value	0.238	0.045	0.117	0.075
Delta Developmental Quotient	Pearson Correlation	0.207	0.443	0.29	0.268
	p value	0.281	0.016	0.127	0.16

The duration of Aortic cross clamp was correlated significantly with change in DASII scores in all three domains.

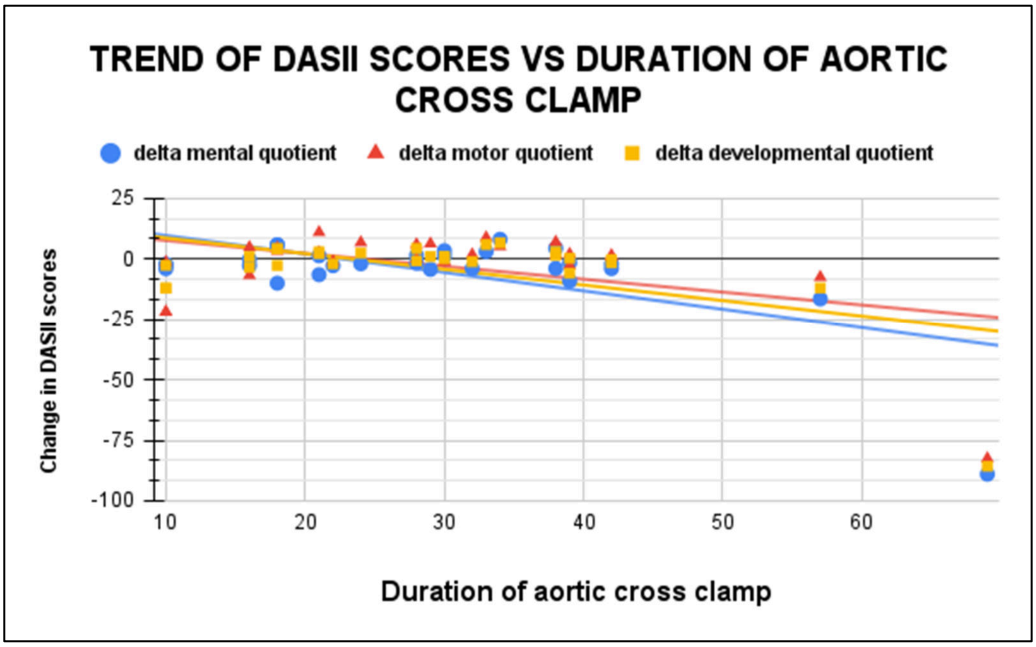

Figure 17- Correlation between change in DASII scores with duration of aortic cross clamp (Acyanotic CHD)

The minimum value of pH which is an indicator of acidosis during the cardiopulmonary bypass was correlated significantly with change in mental quotient of DASII scores.

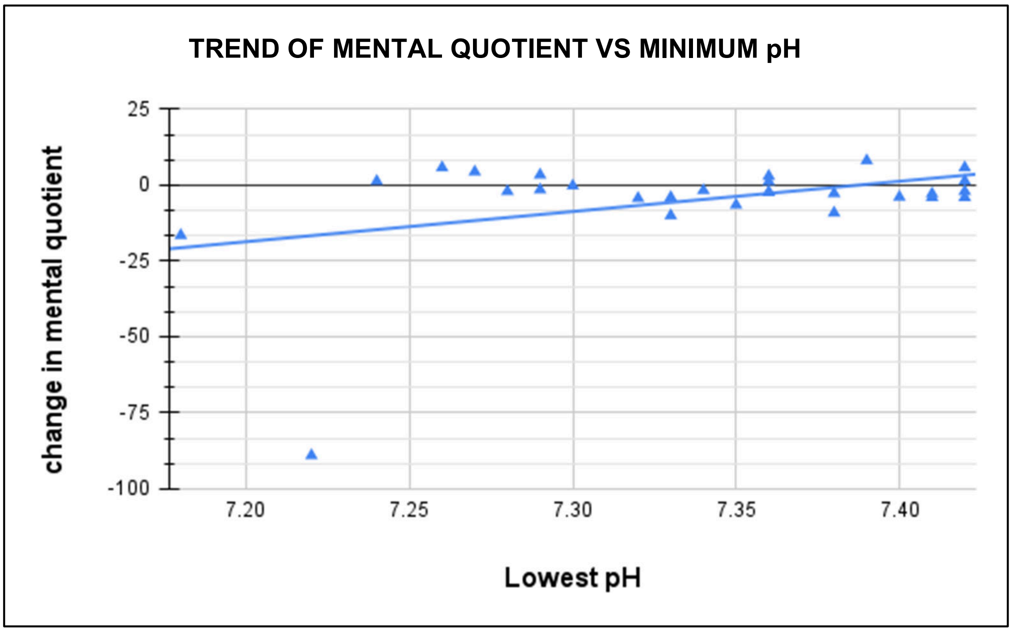

Figure 18 - Correlation between change in mental quotient and minimum value of pH.

DISCUSSION

Congenital Heart Disease is an important health issue in India. The disease burden of children with congenital heart disease is very high. As the healthcare infrastructure continues to improve in the country, the number of children who can access cardiac surgical correction is increasing. The corrective cardiac surgery is a boon to children with congenital heart disease but can also lead to neurodevelopmental sequelae because of the cardiopulmonary bypass involved. The technique of cardiopulmonary bypass, though refined and updated since years, still holds a risk for neurodevelopmental delay in children. There are very few studies which assess for the neurodevelopmental sequelae and further no studies which use the neurological assessment which is specifically created for Indian infants. The aim of our study is to find the reduction in neurodevelopmental scores after surgery and to identify the intra-operative factors which influence the neurodevelopmental sequelae.

The study was conducted over a period of 1 year between January 2020 and December 2020 at KLES Dr Prabhakar Kore Hospital. All children between 6 months to 3 years who underwent corrective cardiac surgery were included in the study after taking informed consent. The children were subjected to DASII neurological assessment before the surgery and 3 months after surgery. The intra-operative data were collected from hospital records. DASII scoring system assesses the child's neurodevelopmental status in two domains, mental quotient and motor quotient. The average of the two will be given as the developmental quotient of the child. All the three values are age adjusted percentage values and are sensitive to neurodevelopmental delays occurring in the post-operative period.

The data obtained was tabulated into Microsoft Excel sheets and processed using OpenEpi software version 2.3.0 and SPSS version 20.

The age of children included was between 6 months to 3 years which is the age that DASII scoring system can assess and is the most common age for correction of cardiac defects. The mean age of the children included was 12.14±6.7 months. The study conducted by Ergin Arslanoğlu et al[27], screened for neurological outcomes in 3849 children with a mean age of 60.59 ± 46.44 months. The age of children varies as per the demographics of the population, age at diagnosis. We can infer that as the education improves, the children with symptoms are identified earlier and are brought to the hospital for early medical or surgical care. Better antenatal monitoring also has a role in determining the age of diagnosis and hence mean age at surgery. The mean age at diagnosis in our study was 3.32±2.08 months. Though most of the children were diagnosed after congestive cardiac failure had set in, few of them were antenatally diagnosed and many others were found out incidentally on regular visits to the primary care provider.

Majority of the children in our study belonged to the age group between the age of 7 months to 1 year- 36.8%. The second most prevalent age group was of the age between 1 to 2 years-23.6%. This may be due to the fact that surgical interventions are postponed for a period of time till the child gains adequate weight to be fit for a safe surgery. Though the children may be diagnosed earlier, they will be started on decongestant therapy and treated conservatively along with regular follow-ups till they attain a particular weight.

The gender distribution of our study was a male predominant one. 24 (63.2%) of the 38 children assessed were male and 14 (36.8%) were female. The male: female ratio was 1.71:1. Other studies such as the one conducted by Ergin Arslanoğlu et al[aa] 49.4% were female and 50.6% male. The gender discrepancy in our study can be due to the various social practices in the region where male child is given a preferential treatment and has a higher chance of making it early to the hospital for treatment or obtaining treatment at all. As a result of various government schemes such as “Beti Bachao- Beti Padhao” to promote the wellbeing of a female child and improving standards of education, the female children are probably at a better position to receive same standard of care. As the habits, practices, mindset and beliefs of people especially in the rural communities improve, an improvement in the health of the girl child can be expected.

The type of heart disease and its influence on neurodevelopmental outcomes is well debated. We collected data from 29 (76.3%) children with Acyanotic congenital heart disease and 9 (23.7%) children with cyanotic heart disease. The lower numbers of cyanotic CHD could be because of the fact that cyanotic heart diseases with the exception of TOF are relatively much severe and the neonate with a cyanotic CHD will be sicker than its Acyanotic counterpart and hence has a higher chance of mortality. It has been proposed that neonates with lower cerebral oxygenation index tend to have a smaller brain mass in a study by Varsha Jain et al[28]. The study measured brain volumes by MRI in term children with congenital heart disease and also measured cerebral perfusion. They concluded that reduced brain oxygen concentration can lead to increased risk of neurodevelopmental sequelae similar in profile to periventricular leukomalacia in preterm neonates. By this, we can assume that congenital cyanotic CHDs may hold a higher risk of having neurodevelopmental sequelae.

The intraoperative parameters were collected from hospital records. The mean duration of Cardiopulmonary Bypass in our study was 57+/-25.72 minutes. This duration is of importance as the child will be on an artificial support of the CPB machine which involves various changes in the homeostasis. As described by Whitaker et al[29] There has been improvement in neurological outcomes after changes in components of the CPB machine such as use of membrane oxygenators instead of bubble oxygenators, use of arterial line filters etc. The use of leucocyte depleting filters, as per Allen S et al[30], helps in reducing end organ damage by reducing the inflammatory mediators during CPB. The use of centrifugal pumps over rolling pumps also have been proposed to reduce the cellular damage during CPB as proposed by Moen O, Fosse E et al[31]. The source of tissue injury is mainly due to the Systemic Immune Response Syndrome (SIRS) which occurs from the contact of blood to the exterior foreign material in CPB tubing. This can be largely prevented by the use of Heparin coated tubing of the newer CPB machines which reduces contact activation- inflammation and also reduces reperfusion injury as suggested by Aldea GS et al[32].

A study conducted by Martin Bendszuz et al[33] which had a mean CPB time of 129 ± 37 minutes compared to 57+/-25.72 minutes. Though almost all the latest advances have been implemented in terms of CPB technology and methods, there seems to be a high incidence of neurodevelopmental sequelae in children undergoing corrective cardiac surgery. In our study, we found that longer the duration of CPB, higher are the chances of neurodevelopmental sequelae though it was not a direct relationship or a statistically significant one. The CPB time influences the minimum value of hematocrit which, by our study can be attributed to have a significant correlation with the decline in neurodevelopmental scores in both the mental and motor domains. When the data was analysed with respect to the type of heart disease, we found that the cardiopulmonary bypass duration did not significantly affect children with either cyanotic heart disease or Acyanotic heart disease in the change in DASII scores.

The minimum value of hematocrit during cardiopulmonary bypass was another intra-operative factor that our study investigated. In the past, it was believed that more the hemodilution, better for the CPB due to better microcirculation as a result of the lower viscosity. Though it had a drawback of decreasing the carrying capacity of blood for oxygen as described by Kirklin et al[34]. Though in adults, a study conducted by Gordon et al[35], concluded that lower the hematocrit, higher the chances of morbidity, mortality and chances of failure to wean from CPB. One study conducted by Mathew et al[36] had to be stopped by the safety monitoring committee because of the adverse outcomes in the lower hematocrit patients. In the pediatric age group, a study conducted by Jonas RA et al[37], a randomised control trial which compared the neurological outcomes in children undergoing cardiac surgery with a high and a low hematocrit group. It considered 21.8% hematocrit as a lower level and 27.8% as the higher level of hematocrit. They observed that there was a significantly higher serum lactate levels indicating hypoxia, lower cardiac index- suggesting shock and the lower hematocrit group performed wore on psychomotor developmental scores with a reduction of about 9 percent on average. This is comparable to our study in which we found out that the minimum value of hematocrit correlates with the decline in DASII scores in all the three domains with a p values of 0.006, 0.014 and 0.042 for mental, motor and developmental quotients respectively. Though when analysed for cyanotic heart disease group and Acyanotic heart disease groups, the minimum value of hematocrit did not significantly affect the change in neurodevelopmental scores. We can assume that dilution is required for cardiopulmonary bypass but considerably lower levels of dilution again lead to reduced oxygen carrying capacity of blood and hence may cause hypoxic injury to the brain and hence cause the neurodevelopmental sequelae.

The pH maintenance during CPB is an important factor which can decide the neurodevelopmental sequelae. The alpha stat strategy used in the procedure involves maintenance of a static level of arterial PCo2 at 40 mmhg at a temperature of 30 degree C whereas a pH stat strategy is used in children which is supposedly a better method to maintain homeostasis where in the pH is maintained at 7.4 with arterial pco2 at 40mmhg at temperature of 37 degree C. a study conducted by Jonas RA et al[38] concluded that the alpha stat strategy along with circulatory arrest gave better psychometric intelligence scores in infants operated for transposition of great arteries. But another study conducted by Wong et al[39] suggested that there was in increase in incidence of choreoathetosis as a part of post pump chorea after the use of alpha stat strategy in infants. A further larger study conducted by Bellinger et al[40] to find the differences in neurological outcomes with respect to the two pH management strategies did not find a significant difference in the Bayley's developmental scoring system in the infants operated with either the alpha stat or the pH stat strategies. In our study we tried to analyse the effects of acidosis on poor neurodevelopmental outcomes and it was found that the minimum value of pH did correlate with an increased decline of mental quotient amongst the domains of DASII scores with a p value of 0.039 which was statistically significant. When the subjects were divided into Cyanotic and Acyanotic groups, the minimum value of pH again significantly affected only the Acyanotic CHD group in terms of reduction of neurodevelopmental scores.

Thus, we can ascertain that severe acidosis during cardiopulmonary bypass is a factor which causes adverse neurodevelopmental sequelae.

Children with congenital heart disease can have some amount of neurodevelopmental delay by the virtue of the pre exiting disease process itself. A study conducted by Lata, K., Mishra, D et al[41] used DASII scoring system as used in our study to ascertain the neurodevelopmental status in children with congenital heart disease. They assessed 75 children and found that 25% of them had a significant delay accounting to <70% in motor quotient and 12% of them in the mental quotient. They concluded that there was a significant delay in motor scores than mental scores (p=0.048). whereas in our study, we did not find any children with significant neurodevelopmental delay in the preoperative period. The mean pre-operative mental scores- 96.35+/-7.93 were higher than motor scores-94.06+/-9.86 but there was no statistically significant difference in the scores.

The neurodevelopmental outcomes after cardiac surgery have been well studied. The “Boston circulatory arrest trial” was one of the landmark studies in the field of cardiothoracic surgery which laid the foundation of many other studies on neurodevelopmental outcomes. In this study, Wypij D, Newburger JW et al[23] studied the neurodevelopmental outcomes in children with d transposition who underwent arterial switch surgery under total circulatory arrest. The children were assessed not with a single scoring system for neurodevelopment but by various methods such as IQ, mathematical performance, reading, time to solve grooved pegboard and to test apraxia- mayo test was used. They concluded that there were no significant neurodevelopmental adverse sequelae unless the duration of TCA crossed 41 minutes.

Though there have been various studies conducted on the same, there are no studies which have used DASII scoring system which is tailormade for the Indian infants and there hasn't been an analysis of the correlation between the neurodevelopmental scores and the intra-operative parameters.

A study conducted by Gaynor et al[42] studied the neurodevelopmental outcomes in infants after surgery. Bayley's scoring system 2 was used and it revealed that there was a significant reduction of both psychomotor development and the motor development indices compared to the standard mean. They also followed the children over a long term and concluded that many of the children do improve the scores but some of them need societal adjustments for normal life. The factors that were significant for neurodevelopmental adverse outcomes as per the study was the education of mother, socio-economic status and presence of genetic syndromes.

Another study conducted by the international cardiac collaborative on neurodevelopment[43] which analysed 1770 children undergoing cardiac surgeries, stated that the preoperative and intra-operative factors are much less important than the patient characteristics, post-op hospital stay, duration of ventilation need for ECMO which are correlated more significantly to the reduction in psychomotor and motor developmental scores in the post-operative period.

Though our study found a reduction in the post-operative scores after 3 months of surgery, the reduction was not drastic enough to be called developmental decline in either the cyanotic or Acyanotic group. Though the cyanotic group (N=9) showed a steep decline in the post-operative neurodevelopmental scores, the statistical tests did not deem the values to be significant to represent the general population.

There were 3 children who had a profound neurodevelopmental decline after surgery. The details have been described below.

Child A, 1 year 7 months old male with TOF with normal neurodevelopmental scores pre operatively, underwent open cardiac repair. Post operatively he required a higher inotrope support and had a longer wean off time from the ventilator. The child developed seizures on post op day 3 and was treated with anti-epileptics. The child was seizure free and was extubated but was found to have profound neuroregression post operatively. The DASII scores had reduced significantly in the first follow-up. CT scan revealed that he had developed a subacute infarct in the left frontal region. The child had a recovery within a matter of 6 months and a near normal neurodevelopmental score on the second follow-up.

Child B, a 6-month-old female child with VSD was operated on cardiopulmonary bypass for VSD patch closure. The child needed increased inotrope support and could not be weaned off ventilator due to poor neurological response. The CT brain showed features of global hypoxic ischemic injury. And EEG showed encephalopathic changes. The child was later found to have elevated CPK levels for which the child was suspected to have uremic encephalopathy. The child had a decline in the neurodevelopmental scores on first follow-up but improved to near normal levels after 6 months.

Child C, 8-month-old female child with tricuspid atresia was operated for the same. The child had pleural effusion in the post-operative period for which a drain was inserted. The child later developed seizures for which she was treated with antiepileptics. Since the CPK levels were high, a diagnosis of Rhabdomyolysis related Posterior Reversible Encephalopathy Syndrome was made. The child had a severe decline in neurodevelopmental score on follow-up but now has recovered back to normal neurodevelopmental status.

The study has its limitations in the three children with significant delay affecting the mean scores. We also had a reduced number of patients undergoing cardiac surgery as a result of the pandemic situation and hence the reduced sample size and resulting difficulty in obtaining a reproducible and reliable result. The follow-up was also made at 3 months post operatively but we may need another follow-up at about one year post operatively to assess whether the improved hemodynamics post-surgery have an impact on the neurodevelopmental outcomes and improve the neurodevelopmental scores.

CONCLUSION

- Children undergoing corrective cardiac surgery associated with use of cardiopulmonary bypass are at a significant risk of having adverse neurodevelopmental sequelae.
- The children showed delay in both mental and motor domains of DASII neurodevelopmental assessment scores post operatively though it was not statistically significant.
- The children with Cyanotic congenital heart disease showed a steeper decline in post-operative neurodevelopmental scores compared to children with Acyanotic congenital heart disease.
- The duration of Cardiopulmonary bypass affects the decline in neurodevelopmental scores in these children.
- The hemodilution that occurs as a part of the procedure involving Cardiopulmonary bypass is significantly correlated to the decline in both mental and motor domains of the neurodevelopmental scores in children.
- Acidosis during the Cardiopulmonary bypass also significantly impacts the reduction in mental domain of the neurodevelopmental scores in children.
- In the children with Acyanotic congenital heart disease, the duration of aortic cross clamp has an impact in reduction of neurodevelopmental scores in both mental and motor domains and is an important factor in adverse neurological sequelae following cardiac surgery in children.

SUMMARY

The study was conducted over a period of 1 year between January 2020 and December 2020 at KLES Dr Prabhakar Kore Hospital. All children between 6 months to 3 years who underwent corrective cardiac surgery were included in the study after taking informed consent. The children were subjected to DASII neurological assessment before the surgery and 3 months after surgery. The intra-operative data were collected from hospital records. DASII scoring system assesses the child's neurodevelopmental status in two domains, mental quotient and motor quotient. The average of the two will be given as the developmental quotient of the child. All the three values are age adjusted percentage values and are sensitive to neuro developmental delays occurring in the post-operative period.

The data obtained was tabulated into Microsoft Excel sheets and processed using OpenEpi software version 2.3.0 and SPSS version 20.

- The study included 38 children who underwent corrective cardiac surgery over a span of one year.
- All 38 children were between the ages of 6 months to 36 months with a mean age of 12.14±6.7 months.
- The gender distribution of our study was a male predominant one. 24 (63.2%) of the 38 children assessed were male and 14 (36.8%) were female. The male: female ratio was 1.71:1
- Majority of the children in our study belonged to the age group between the age of 7 months to 1 year- 36.8%. The second most prevalent age group was of the age between 1 to 2 years-23.6%.

- The type of heart disease – amongst 38- 29 (76.3%) children with Acyanotic congenital heart disease and 9 (23.7%) children with cyanotic heart disease were assessed.
- The mean duration of Cardiopulmonary Bypass in our study was 57+/-25.72 minutes.
- The mean duration of aortic cross clamp was 33.48+/- 19.03 minutes
- The mean Minimum value of hematocrit was 27.47+/-3.90.
- The mean least value of pH was 7.33+/-0.06
- The mean pre op DASII scores were; developmental quotient was 93.62+/-12.9, the mental quotient was 96.35+/-7.93 and the motor quotient was 94.06+/-9.86.
- The mean post-operative scores were 87.77+/-23.33 in the mental domain, 87.5+/-23.45 in the motor domain and the developmental quotient was 87.54+/-23.45
- The post-operative mental score was different to the pre-operative score with a p value of 0.05.
- In the cyanotic group (n=9), the pre-operative median was 94 in the mental domain, 92.5 in the motor domain and 92.5 in the developmental quotient.
- The post-operative scores in the cyanotic group were (median) 88 in the mental score, 89 in the motor scale and 93.8 in the developmental scores.
- The pre and post-operative values were compared using Wilcoxon signed rank test and the difference was deemed statistically insignificant.
- In the Acyanotic group, the preoperative and the post-operative DASII scores did not differ significantly on the paired t test.

- Amongst the intra operative parameters, the parameters such as cardiopulmonary bypass time, duration of aortic cross clamp did not have a significant correlation with the decline in DASII scores.
- The minimum value of hematocrit had a significant correlation with the decline in DASII scores. It correlated with the change in mental scores by a Pearson's coefficient of 0.285 with a p value of 0.006, with change in motor scores by a Pearson's coefficient of 0.218 and a p value of 0.014 and developmental score change with a Pearson's coefficient of 0.251 and a p value of 0.042 all of which were statistically significant.
- The minimum value of hematocrit also influenced the change in mental scores with a Pearson's coefficient of 0.337 and a p value of 0.039
- There was no significant correlation between the intra operative factors and the decline in neurodevelopmental scores in the cyanotic group.
- In the Acyanotic group however, the duration of aortic cross clamp significantly affected decline in mental scores by a Pearson's coefficient of 0.597 and a p value of 0.001, decline in motor scores by a Pearson's coefficient of 0.375 with a p value of 0.045 and change in developmental scores with a pearson's coefficient of 0.443 and a p value of 0.016.

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ANNEXURE - I

INFORMED CONSENT FORM

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH

'Neurodevelopmental status before and after corrective cardiac surgery in children aged 6 months to 3 years' - a one-year hospital based longitudinal study.

Principal Investigator:

Co – investigator:

Introduction: You are being invited to participate in this study to find out **Neurodevelopmental status before and after corrective cardiac surgery in children aged 6 months to 3 years**. Participation of your child will help us to know the factors determining developmental delay in children with congenital heart disease. There is a very high burden of children suffering from congenital heart disease in India. The above-mentioned study will therefore answer various questions regarding the occurrence of developmental delay as a morbidity associated with congenita heart disease. It will help improve the quality of life of all such children suffering from congenital heart disease. Hence the present study is undertaken. Participation in this study is completely voluntary.

Explanation of procedures: In this study, you will have to answer a few prepared questions regarding the condition of your child. If you agree to participate, then only questions will be asked to you. At any moment, you can withdraw from the study. Information will be collected using pre-tested-designed questionnaire. The child will be evaluated for neurodevelopmental status using an assessment tool called DASII, which will be conducted by a certified clinical psychologist. The assessment will be done twice, once before and once after the surgery.

Possible Benefits: The investigator does not promise that you will receive direct benefit in this study. It will benefit the whole community.

Possible Risks: There is no risk involved in this study.

Benefits from the study: Reduction in morbidity and mortality and plan for timely intervention in case of diagnosis of developmental delay as a part of assessment for the study.

Confidentiality; All the data collected will remain confidential and only aggregated data will be published. Your personal identity will not be revealed.

Withdrawal: Your participation in this study is purely voluntary. You may decide to participate or not. Even though you decide not to participate, you will not be deprived of the benefits of this study.

Costs of Participation: The cost of the study will be borne by the subjects if they can afford. If not, it will be borne by the researcher. It involves the cost of neurodevelopmental assessment in two settings. There will be no additional cost to you for participating in this study.

Payment of Participation: There will be no incentives to you for participating in this study.

<u>Questions</u>:

If you have any questions regarding the study, you should contact Principal Investigator Department of Paediatrics. J. N. Medical College, Belagavi, 590010,

If you have any questions about your rights as a study participant, you may contact Chairman, Institutional Ethics Committee on Human Subjects' Research, J.N. Medical College, Belagavi -590010,

<u>Legal Rights</u>: By signing this consent form; you are not waiving any of your Legal rights.

Consent statement:

"I volunteer and consent to participate in the study. I have read (or it has been read to me in the language known to me) the information sheet thoroughly. Full opportunity was given to me to ask questions. I am fully satisfied with the answers to the questions I wanted to ask. I hereby voluntarily agree to participate in this research project".

____________________________ _________________________

Name of the Participant — Signature of the parent or Left-Hand Thumb impression

____________________________ _________________________

Name of Investigator — Signature of investigator

Date: ________________________ Place: ________________________

ANNEXURE-II

PROFORMA

Neurodevelopmental status before and after corrective cardiac surgery in children aged 6 months to 3 years' - a one-year hospital based longitudinal study.

Sl. No: _______ Date of registration: ___________________

- NAME:
- MOTHER'S NAME:
- FATHER'S NAME
- AGE
- DIAGNOSIS:
- DATE OF BIRTH :
- TYPE OF DELIVERY:
- GESTATIONAL AGE – TERM / PRETERM
- CORRECTED GESTATIONAL AGE:
- ANY H/O BIRTH ASPHYXIA- Y/N
- H/O CNS INFECTIONS- Y/N
- H/O SEIZURES – Y/N
- AGE AT DIAGNOSIS OF HEART DISEASE :
- ANY MEDICATIONS BEING GIVEN FOR THE CONDITION- Y/N (IF YES SPECIFY)
- ANY PROCEDURES DONE- Y/N (IF YES SPECIFY)
- ANY IMPAIRMENT OF VISION/HEARING- Y/N

BRIEF HISTORY OF SYMPTOMATOLOGY OF THE CONDITION:

ECHO REPORT PRIOR TO SURGERY:

DASII SCORE BEFORE SURGERY-

MENTAL QUOTIENT

MOTOR QUOTIENT

DEVELOPMENTAL QUOTIENT

DETAILS REGARDING SURGERY:

- DATE OF SURGERY:
- TIME DURATION OF SURGERY
- DURATION OF CARDIOPULMONARY BYPASS:
- MINIMUM VALUE OF HEMATOCRIT
- DURATION OF AORTIC CROSS CLAMP
- DURATION OF TOTAL CIRCULATORY ARREST:
- OTHER DETAILS

DASII SCORE AT 3 MONTHS POST SURGERY-

MENTAL QUOTIENT

MOTOR QUOTIENT

DEVELOPMENTAL QUOTIENT

ANY OTHER SIGNIFICANT INFORMATION:

ANNEXURE III - ETHICAL C LEARANCE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)

JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)

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Ref: MDC/DOME/ 225 **Date: 24/12/2019**

To,
BM01190011
PG student in Paediatrics,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"NEURODEVELOPMENTAL STATUS BEFORE AND AFTER CORRECTIVE CARDIAC SURGERY IN CHILDREN AGED 6 MONTHS TO 3 YEARS, A ONE YEAR HOSPITAL BASED LONGITUDINAL STUDY"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Anita Dalal)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

ANNEXURE IV – KEY TO MASTERCHART6

CPB TIME	–	Cardio-Pulmonary Bypass time
TCA TIME	–	Total Circulatory Arrest time
VSD	–	Ventricular Septal Defect
ASD	–	Atrial Septal Defect
TAPVC	–	Total Anomalous Pulmonary Venous Return
PDA	–	Patent Ductus Arteriosus
PAH	–	Pulmonary Artery Hypertension
TOF	-	Tetralogy of Fallot

ANNEXURE V –MASTERCHART

S.no	I.P. number	Age	Diagnosis	Type of Heart Disease	Age at diagnosis(months)	CPB time (minutes)	cross clamp time	Minimum value of Hematocrit	Temperature of solution for cardioprotection	TCA time	Lowest pH	Pre Op Mental Quotient	Pre Op Motor quotient	Pre op developmental score	Post op Mental quotient	Post Op Motor quotient	Post Op Developmental Score	delta mental	delta motor	delta developmental
1	998074	7 m	CoA	acyanotic	6	117	0	22.5	3	25	7.3	89	91.78	90.39	92.66	103.7	98.16	3.66	11.88	7.77
2	999046	1y 1m	Multiple VSD	acyanotic	4	75	57	25.6	3	0	7.2	115.5	117	116.2	99	109.5	104.25	-16.5	-7.5	-12
3	1000081	1 y 7 m	TOF	cyanotic	3	65	51	20	3	0	7.3	102.7	107.4	105	4.4	11.16	7.78	-98.3	-96.2	-97.2
4	999547	1 y	SVC ASD	acyanotic	8	131	16	24.5	32	0	7.3	92.6	97.3	94.9	92.4	90.6	91.5	-0.2	-6.7	-3.4
5	1000834	8 m	Inlet VSD	acyanotic	5	37	21	24.7	4	0	7.2	91.6	86.42	89	92.9	89.1	91.9	1.3	2.68	2.9
6	1000726	8m	PM VSD, Severe PAH	acyanotic	3.5	43	24	28	4	0	7.3	98.6	91.4	95	96.6	98.2	97.4	-2	6.8	2.4
7	1006361	7 m	VSD	acyanotic	3	47	22	27.5	3	0	7.4	118.4	113.6	116	115.6	112.6	114	-2.8	-1	-2
8	1010845	11 m	VSD, Sev. PAH	acyanotic	4	41	28	23.2	3	0	7.4	96.6	90.42	93.4	98	96.4	97.72	1.4	5.98	4.32
9	1011495	7 m	ASD	acyanotic	1	35	18	29.7	3	0	7.4	87.8	93.4	90.6	93.6	96.7	94.8	5.8	3.3	4.2
10	1013412	14 m	PM VSD	acyanotic	4	47	32	25.6	3	0	7.3	89	86.2	87.6	85	88	86.5	-4	1.8	-1.1
11	1013163	1 y	VSD, Tricuspid septal aneurysm	acyanotic	2	49	28	23.1	3	0	7.3	92.3	86.4	89.3	90.6	86.4	88.5	-1.7	0	-0.8
12	1012730	8 m	VSD	cyanotic	2	129	101	24.6	3	0	7.4	89	84.2	86.6	86	92	88	-3	7.8	1.4
13	1012581	1 y 6 m	VSD	acyanotic	1	33	16	25.2	3	0	7.4	97.2	88.4	92.8	94.5	93.2	93.8	-2.7	4.8	1
14	1015659	6 m	TAPVC	acyanotic	1	42	21	28.9	3	0	7.4	98.5	77	87.75	92	88	90	-6.5	11	2.25
15	1015902	6 m	VSD,	acyanotic	4	67	42	24.2	3	0	7.4	102	93.2	97.6	98	94	96	-4	0.8	-1.6
16	1016585	6 m	Large VSD, PML, Small PDA	acyanotic	2	50	33	27.6	3	0	7.4	96	88.7	32.35	99	97.5	98.25	3	8.8	65.9
17	1017408	1 y 3 m	ASD	acyanotic	9	22	10	30.1	3	0	7.4	104.3	120.3	112.3	102	98.4	100.2	-2.3	-21.9	-12.1
18	1016588	1 y 6 m	TOF	cyanotic	1	82	63	24.5	3	0	7.4	94	88.6	91.3	92	89	90.5	-2	0.4	-0.8
19	1019709	2 y 6 m	VSD	acyanotic	5	32	18	31.4	3	0	7.3	112	94	103	102	98.5	100.25	-10	4.5	-2.75
20	1022240	6 m	VSD	acyanotic	3	63	42	30.3	3	0	7.4	92	86.5	89.2	90	88	89	-2	1.5	-0.2

S.no	I.P. number	Age	Diagnosis	Type of Heart Disease	Age at diagnosis(months)	CPB time (minutes)	cross clamp time	Minimum value of Hematocrit	Temperature of solution for cardioprotection	TCA time	Lowest pH	Pre Op Mental Quotient	Pre Op Motor quotient	Pre op developmental score	Post op Mental quotient	Post Op Motor quotient	Post Op Developmental Score	approx delta mental	approx delta motor	approx delta developmental
21	1023524	6 m	VSD	acyanotic	2.5	66	39	31.4	3	0	7.3	93.5	88	90.75	92	90	91	-1.5	2	0.25
22	1024719	1 y 3 m	VSD + PDA	acyanotic	3	45	30	30.5	3	0	7.4	92.8	90	91.4	94	89	91.5	1.2	-1	0.1
23	1025523	6 m	PDA	acyanotic	2.5	22	10	34.5	3	0	7.4	102	100.5	101.25	98	99.2	98.6	-4	-1.3	-2.65
24	1026431	9 m	ASD, VSD	acyanotic	1	43	29	33.1	3	0	7.3	98.3	87.2	92.75	94	93.5	93.75	-4.3	6.3	1
25	1028620	7 m	ASD	acyanotic	1	35	18	29.6	3	0	7.3	87.8	93.4	90.6	93.6	96.7	94.8	5.8	3.3	4.2
26	1031414	2 y	TOF	cyanotic	4	62	49	24	3	0	7.3	104	101	102.5	88	86	87	-16	-15	-15.5
27	1032701	2 y	TOF	cyanotic	5	60	42	21	3	0	7.3	92.6	98.4	95.5	94	90.1	92.05	1.4	-8.3	-3.45
28	1034416	2 y	TOF, ASD	cyanotic	4.5	66	42	25.2	3	0	7.3	99.2	87	93.1	96.1	89	92.55	-3.1	2	-0.55
29	1034427	9 m	TOF	cyanotic	2	51	35	24.8	3	0	7.3	88.5	92.5	90.5	86	90.5	88.25	-2.5	-2	-2.25
30	1035840	11 m	ASD	acyanotic	9	22	10	30.1	3	0	7.4	104.3	120.3	112.3	102	98.4	100.2	-2.3	-21.9	-12.1
31	1036540	2 y	VSD	acyanotic	3	62	38	32.1	3	0	7.4	96.2	88	92.1	92.3	95	93.65	-3.9	7	1.55
32	1036838	10 m	VSD	acyanotic	3.5	59	34	33.1	3	0	7.4	86.4	92.8	89.6	94.5	98	96.25	8.1	5.2	6.65
33	1039350	10 m	VSD	acyanotic	4	52	30	32.8	3	0	7.3	88.6	90.3	89.45	92	89	90.5	3.4	-1.3	1.05
34	1039355	6 m	VSD, ASD	acyanotic	2	61	38	30.9	3	0	7.3	86.4	90.8	88.6	90.8	92.4	91.6	4.4	1.6	3
35	1041977	2 y	TOF	cyanotic	1	58	44	33.5	3	0	7.4	84.6	99	91.8	92	98	95	7.4	-1	3.2
36	1042690	6 m	VSD	acyanotic	3	61	39	29.4	3	0	7.4	99.1	91.6	95.35	90	88.9	89.45	-9.1	-2.7	-5.9
37	1056246	5m	VSD	acyanotic	3	90	69	22.5	3	0	7.2	102	92.5	97.25	13	10	11.5	-89	-82.5	-85.8
38	1056399	8m	Tricuspid atresia	cyanotic	3	47	34	24.2	3	0	7.3	96	89	92.5	17	12	14.5	-79	-77	-78