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ORIGINAL ARTICLE

Risk Factors for Neurological Complications and Short-term Outcomes After Pediatric Heart Surgery: A Retrospective Analysis

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Abstract

Objective: **To assess the risk factors associated with neurological complications and poor short-term outcomes following pediatric heart surgery.**

Methodology: **A cross-sectional study was conducted in a cardiac intensive care unit between June 2019 and June 2022. The data of all children less than 15 years old who underwent open-heart surgery and had CT brain were extracted from hospital records. The primary outcome was the incidence of CNS insult, and secondary outcomes included death after surgery, length of stay in ICU and hospital. Data analysis was performed using SPSS version 23, and a p-value less than or equal to 0.05 was considered statistically significant.**

Results: **Total 1850 surgeries were performed in the specified period of time. The study included 208 children who had CT Brain, with a median age of 5 months. 2.81 % children had neurological complications, with 25 % of patients who had CT brain. The most common neurological complication was seizure (7.2 %). There were no significant differences observed between CNS insult and age, gender, syndrome, or prematurity ($p > 0.05$), except for a significant association between previous CNS insult and CNS insult after surgery ($p = 0.001$). Children with CNS insult had significantly higher ICU and hospital length of stay, mortality after surgery, and mortality within 2 weeks of surgery ($p \le 0.05$).**

Conclusion: **Seizure was most common neurological manifestation after cardiac surgeries in children. CNS insult after surgery was associated with worse outcomes, including longer hospital stays and increased mortality.**

Keywords: CNS insult, Complications, Cardiac surgery, Children, Neurological complications, Poor outcomes, Pediatric population

1. Introduction

Millions of children worldwide have congenital heart defects (CHD), which are characterized as anomalies in the heart's anatomy or/and great vessels at birth [1,2]. In a recent systematic review and meta-analysis, the global prevalence of CHD is reported as 9.4 per 1000 births during 1970–2017 [1]. Furthermore, it has been estimated that the age-standardized mortality rate for CHD is 4.9 per 100,000 in low-income countries and 1.2 per 100,000 in high-income countries [3]. In another recent study conducted at Saudi Arabia, the incidence of CHD is reported as 14.8 per 1000 births [4]. Over 20 % of the occurrence of CHD may be attributed to teratogen exposure, genetic abnormalities, or maternal diabetes, while 80 % of CHD patients had unidentified risk factors [1].

The mortality rate in children following cardiac surgery has decreased over the course of the past decade due to improvements in prenatal diagnosis, perioperative treatment, and advanced bypass

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procedures. Despite this, it has led to an increase in the morbidities like neurological complications [5,6]. Complications occurred in 43 % of pediatric cardiac surgeries performed both with and without cardiopulmonary bypass [3]. Seizures, which account for 70 % of cases from neurological sequelae, are the most common neurological complication [7]. Additional neurological complications consist hemiparesis, gaze palsies, peripheral nerve injury as phrenic nerve or brachial plexus, dyskinesia, and changes in personality [7]. It has been ascertained that neurological impairment can lead to neurodevelopmental delays and cognition impairments affecting the quality of life markedly [13].

To the best of our knowledge, there is a paucity of data pertaining to the occurrence of neurological problems following heart surgery in children in Saudi Arabia, as well as the risk factors associated with those complications. Therefore, the purpose of this study was to evaluate the occurrence of central nervous system complications in children who had recently undergone cardiac surgery, as well as the risk factors associated with developing these issues and the short-term outcomes of these patients.

Abbreviations

CHD	congenital heart defects
CNS	Central nervous system
CPR	Cardiopulmonary Arrest
ECMO	Extracorporeal membrane oxygenation
EEG	Electroencephalography
ICU	Intensive care unit
IQR	Interquartile Range
RACHS-1	Risk Adjustment for Congenital Heart Surgery
SPSS	Statistical package for social sciences

2. Methodology

It was a cross-sectional study conducted in cardiac intensive care unit between June 2019 and June 2022. Sample size of 200 was calculated using Open epi sample size calculator by taking statistics of neurological complications as 15.2 % [7], margin of error as 4.5 % and 95 % confidence level. The data of all children less than 15 years old of either gender who underwent open-heart surgery for congenital heart defects, admitted in cardiac intensive care unit and had CT brain secondary to CNS insult were extracted from hospital record. Children who had bleeding disorder and normal Glasgow coma scale 15/15 were excluded. EEG is done for the patients who had clinical seizures, and its nor routinely done for all patients. The samples were included in the study using non-random purposive sampling.

This study was initiated after taking approval from research ethics committee (RAC # 2211310) and informed consent was waived by RAC. Risk stratification system for congenital heart surgery was done according to the “Risk Adjustment for Congenital Heart Surgery (RACHS-1)”. The data regarding demographics, the appropriate perioperative and operative data including use of heparin dose, pre and post coagulation profile, the clamp time, pump time, pre and post-operated labs, extubation failure and days on ventilator were extracted. Primary outcome was incidence of CNS insult in form of clinical or subclinical symptoms evident radiologically. Secondary outcomes were death after surgery or before hospital discharge for the index hospitalization, length of stay in ICU and hospital. Data was collected using a pre-designed form that indicated the patients' identification number only. The database and all computer files relevant to this research were password protected and known only to the investigators and research coordinator. All files were kept in a secured office at the Heart Centre and available to the RAC for inspection as per KFSH&RC guidelines.

Statistical package for social sciences (SPSS) version 23 was used to analyze data. Missing and incomplete data were pretermitted from analyses. Qualitative variables were presented as count and percentage. Normality of quantitative variables were checked using Shapiro–Wilks test. All quantitative variables were non-parametric, therefore, presented as median and interquartile range (IQR). Mann–Whitney U test was used to compare quantitative outcomes, whereas, Chi-square/Fisher exact test was applied to compare qualitative outcomes. A p-value less than and equal to 0.05 was considered as statistically significant.

3. Results

Total 1850 surgeries were performed in the specified period of time. Total 208 children were included in the final analysis who had done CT brain for suspected brain injury after cardiac surgery. The median age of the children was 5 months ranging from 0 to 46 months. Most of the children were males (58.2 %), 10.09 % had syndrome of 208, 2.9 % were premature, and 9.1 % had previous CNS insult. Almost 41.8 % of the children who underwent definitive cardiac surgery had RACHS-1 category 2, followed by category 3 (34.6 %), respectively. About 6.7 % of the children underwent cardiopulmonary arrest (CPR) and 9.6 % underwent ECMO. The median duration of ventilation was 3 days (see Table 1). Other appropriate pre-operative and post-operative data are displayed in Table 2.

Table 1. Descriptive analysis of quantitative and qualitative variables (n = 208).

Variables	Statistics
Age (months)	5 (1–12)
Weight (kg)	7.37 (4.96–16.25)
Gender	
Male	121 (58.2)
Female	87 (41.8)
Syndrome	
Yes	21 (10.09)
No	187 (89.90)
Premature	
Yes	6 (2.9)
No	202 (97.1)
Previous CNS insult	
Yes	19 (9.1)
No	189 (90.9)
RACHS-1	
1	30 (14.4)
2	87 (41.8)
3	72 (34.6)
4	9 (4.3)
5	1 (0.5)
6	9 (4.3)
Clamp time (min)	53 (35–89)
Pump time (min)	88 (65–134)
Came open chest	
Yes	14 (6.7)
No	194 (93.3)
Re-explore	
Yes	27 (13)
No	181 (87)
Days on ventilation	3 (1–8)
ECMO	
Yes	20 (9.6)
No	188 (90.4)
CPR	
Yes	14 (6.7)
No	194 (93.3)
Extubation failure	
Yes	16 (7.7)
No	192 (92.3)

Median (IQR) or n(%).

Among the 1850 total surgeries, there was 2.81 % incidence of Neurological complications. Of 208 patients, who had CT brain, 52 of the patients had CNS insult (25 %), while, 156 (75 %) of the patients had no CNS insult. The most common neurological complication was seizure (7.2 %), followed by abnormal movements (mainly athetoid movements, myoclonic jerks) (4.3 %), respectively. The median ICU stay was 6 days and median hospital stay was 11 days. About 3.4 % of the children had mortality after surgery and 3.8 % of the children had mortality within 2 weeks of surgery (Table 3).

Table 2. Pre and post operative Coagulation Values.

Pre-operative platelets	327 (263–410)
Pre-operative INR	1.1 (1.0–1.2)
Pre-operative PT	14.7 (14.0–16.1)
Pre-operative lactate	1.7 (1.2–2.5)
Pre-operative APTT	37.7 (34.5–40.9)
Post-operative platelets	167 (116–220)
Post-operative INR	1.6 (1.4–1.8)
Post-operative PT	19.3 (18.1–21.3)
Post-operative lactate	2.0 (1.3–3.0)
Post-operative APTT	43.3 (37.5–49.9)

Median (IQR) or n(%).

Table 3. Descriptive analysis of study outcomes (n = 208).

Outcomes	Statistics
CNS symptoms (n = 52)	
Late consciousness	6 (2.9)
Absent brainstem reflexes	4 (1.9)
Agitation	8 (3.8)
Abnormal movement	9 (4.3)
Seizure	15 (7.2)
Twitching	2 (1)
Apnea	2 (1)
Epilepsy	2 (1)
Left hand weakness	2 (1)
Behavioral changes	2 (1)
ICU length of stay (days)	6 (3–11)
Hospital length of stay (days)	11 (6–21)
Mortality after surgery	
Yes	7 (3.4)
No	201 (96.6)
Mortality in 2 weeks	
Yes	8 (3.8)
No	200 (96.2)

Median (IQR) or n (%).

The proportion of CNS insult was almost same in all age groups and both genders. Whereas, in children without syndrome and prematurity had slightly higher proportion of CNS insult. However, there were insignificant differences observed between CNS insult and age groups (p = 0.626), gender (p = 0.808), syndrome (p = 0.615), prematurity (p = 0.632), respectively. The previous CNS insult had significant association with CNS insult after cardiac surgery with p-value = 0.018 (Table 4).

Table 4. Comparative analysis of CNS insult and risk factors (n = 208).

	CNS insult		p-value
	Yes	No	
Age groups			
≤1 months	26 (23.4 %)	85 (76.6 %)	0.626
1 month-1 year	21 (26.9 %)	57 (73.1 %)	
>1 year	5 (26.3 %)	14 (73.7 %)	
Gender			
Male	31 (25.6 %)	90 (74.4 %)	0.808
Female	21 (24.1 %)	66 (75.9 %)	
Syndrome			
Yes	9 (22 %)	32 (78 %)	0.615
No	43 (25.7 %)	124 (74.3 %)	
Premature			
Yes	1 (16.7 %)	5 (83.3 %)	0.632
No	51 (25.2 %)	151 (74.8 %)	
Previous CNS insult			
Yes	9 (47.4 %)	10 (52.6 %)	0.018*
No	43 (22.8 %)	146 (77.2 %)	

*Significant at 5 % level of significance.

Table 5. Comparison of CNS insult with ICU and hospital length of stay and mortality (n = 208).

	CNS insult		p-value
	Yes	No	
ICU length of stay (days)	17 (9–28)	4 (2–8)	0.001*
Hospital length of stay (days)	27 (19–65.7)	7 (6–13)	0.001*
Mortality after surgery			
Yes	5 (71.4 %)	2 (28.6 %)	0.004*
No	47 (23.4 %)	154 (76.6 %)	
Mortality within 2 weeks			
Yes	6 (75 %)	2 (25 %)	0.001*
No	46 (23 %)	154 (77 %)	

*Significant at 5 % level of significance.

The children with CNS insult after surgery had significantly longer ICU stay ($p = 0.001$), hospital stay ($p = 0.001$), mortality after surgery ($p = 0.004$) and mortality within 2 weeks of surgery ($p = 0.001$), respectively (Table 5).

4. Discussion

Pediatric cardiac surgery is a complex and high-risk procedure that aims to correct congenital heart defects in children [5,6]. While the surgery has a high success rate, there is a risk of neurological complications in some patients [8]. These complications can range from mild cognitive deficits to severe brain damage and can have a significant impact on the child's quality of life [9,10]. Saudia Arabia has made significant progress in the field of cardiac surgery over the past decades, with several state-of-the-art cardiac centers that give advanced surgical interventions to patients. But, still incidence of neurological complications after pediatric cardiac surgery in Saudi Arabia is relatively high as compared to other countries [11]. Hence, it is essential to understand the risk factors associated with neurological complications after pediatric cardiac surgery to identify high-risk patients and take necessary measures to prevent or minimize complications.

One of the significant risk factors for neurological complications after pediatric cardiac surgery is the age of the child. Younger children are more vulnerable to complications due to their developing brain. The immaturity of their neurological system and the vulnerability of their brain tissues to ischemia, hypoxia and other stresses associated with cardiac surgery [12]. Studies have shown that infants and young children are more likely to experience postoperative brain injury than older children [13]. In the current study, the median age was 5 Month and most of them were of age less than and equal to 1 year. However, we insignificant association between CNS insult and age ($p > 0.05$). While, in a study by Abdshah et al. conducted at Tehran found age was significantly associated with neurological complications [6]. Another study by Andropoulos et al. reported that infants under three months of age had greater risk of neurological complications [14]. A study from Saudi Arab by Radi et al. also revealed that incidence of neurological complications of 29.5 % in neonates, 9.6 % in infants, and 5.5 % in children age>1 year [15]. The inconsistencies in our findings and previous study findings might be due to differences in surgical techniques, patient populations, and criteria for diagnosing neurological complications.

In our study, 41.8 % were in RACHS-1 category 2. While, 6.7 % of the children underwent CPR post operatively. Total of 9.6 % had ECMO insertion, including 2.5 % ECPR. In our policy, sedation is kept off till child is appropriately awake, and CT brain is performed after 24 h. Additionally, 93.3 % of the children came without open chest and the median days on ventilation was 3 days. The complexity of the cardiac defect and the surgical procedure required to correct it are the predictors for neurological complications [13,16]. More complex procedures require longer operating times, increased use of cardiopulmonary bypass, and higher rates of intraoperative hypotension, all of which increase the risk of neurological complications [16]. Additionally, children with preexisting neurological conditions, such as epilepsy, are at a higher risk of post-operative brain injury. Moreover, postoperative factors such as hypotension, seizures, and infections can also contribute to the development of neurological complications [13]. We found 9.1 % of the patients with previous CNS insult. Furthermore, we found significant association between previous CNS insult and development of neurological complications. A recent study by Bojan et al. included 416 children who underwent cardiac surgery and found that children with abnormal preoperative neurological status are more at risk of post-operative CNS insult including focal deficits, seizures and altered mental status [17]. These results suggest that close attention should be paid to preoperative neurological assessment in children undergoing cardiac surgery, and early intervention may be necessary to minimize the impact of pre-existing neurological abnormalities on postoperative outcomes.

In the current study, we found that the most common neurological complication was seizure (7.2 %), followed by abnormal movement (myoclonic jerks, and athetoid movements) (4.3 %), respectively. Several studies have also reported the high frequency of neurological complications after pediatric cardiac surgery. A retrospective study by

Elnaggar et al. found that 15.2 % of children who underwent cardiac surgery had neurological complications, including seizures (n = 11), disturbed conscious level and stroke (n = 3) [7]. Chrysostomou et al. reported that 12 % of the ECMO runs had neurological complications, but it does not provide specific information about seizures or strokes [18]. In a review by Walsh et al. suggested that cardiopulmonary bypass, deep hypothermia, and circulatory arrest during congenital heart disease surgery can lead to neurological complications, including stroke, seizures, and cognitive deficits [19]. In another study by Avila-Alvarez et al. found that acute neurological complications was developed in 38 children out of 900, of which 44.7 % were in central nervous system and 55.3 % were in the peripheral nervous system. The most complications were seizures (n = 8), hypoxic-ischemic encephalopathy events (n = 4), cerebrovascular accidents (n = 4), and reversible neurological deficit (n = 1), respectively [20]. Hence, the high frequency of neurological complications emphasizes the need for careful monitoring and early intervention in this high-risk population.

The mechanisms underlying the association between CNS insults and poor outcomes after pediatric cardiac surgery are not fully understood. It has been hypothesized that the systemic inflammatory response that occurs after surgery may contribute to CNS insults by causing endothelial dysfunction and blood–brain barrier disruption [14]. Additionally, the use of cardiopulmonary bypass during surgery can lead to micro-emboli and hypoxia, which can also contribute to CNS insults. [14] In the current study, we found higher ICU stay, hospital stay, mortality after surgery and mortality within 2 weeks of surgery in children with CNS insult. Mortality was related with multi-organ failure, not solely related to CNS complications. Arslanoğlu et al. found that 33.3 % of the children who developed neurological complications expired and 66.7 % were discharged [5]. They found that presence of CNS insult soon after surgery was significantly associated with mortality among children after cardiac surgery ($p = 0.001$). In another study by Elnagger et al. 86 % of the children with congenital heart defects who underwent cardiac surgery discharged from ICU and 14 % of the children died during the ICU stay having mean duration of hospital stay as 15 days [7]. Thus, prevention of CNS insults is an important goal in the management of pediatric cardiac surgery patients. Strategies that have been shown to reduce the incidence of CNS insults include optimizing perioperative oxygenation, maintaining blood pressure within a narrow range, and minimizing the cardiopulmonary bypass time. Further research is needed to better understand the mechanisms underlying this association and to develop effective prevention and management strategies.

The strengths of the study include the focus on a vulnerable population, comprehensive data, appropriate statistical analysis, important findings with clinical implications, and the potential for further research. Our study had few limitations. The study is retrospective in nature, which may limit the ability to draw causal conclusions or control for potential confounding factors. The study was conducted at a single center, which may limit the generalizability of the findings to other settings. The sample size of 208 children is relatively small, which may limit the statistical power of the study and increase the risk of Type II error. The exclusion of 37 children due to missing or incomplete data may introduce bias and limit the generalizability of the results. The study lacks detailed information on some important factors that could affect the outcomes of interest, such as the type of cardiac surgery performed, the severity of the cardiac condition, and the specific interventions used.

5. Conclusion

The study provides important insights into the outcomes of children who undergo cardiac surgery, particularly in relation to CNS insult. The high proportion of patients with previous CNS insult underscores the importance of careful evaluation and management in this population. The finding that CNS insult after surgery is associated with significantly worse outcomes, including longer ICU and hospital stays and increased mortality, highlights the need for targeted interventions to reduce the risk of this complication. Overall, these results suggest that careful monitoring and management of patients with a history of CNS insult and those undergoing cardiac surgery is critical to improving outcomes in this vulnerable population.

Author contribution

Conception and design of Study: MS, YAA, BA, LAA, SK, RG, ZYA. Literature review: MS, YAA, BA, LAA, SK, RG, ZYA. Acquisition of data: MS, YAA, BA, LAA, SK, RG, ZYA. Analysis and interpretation of data: MS, SK, ZYA. Research investigation and analysis: MS, SK, RG. Data collection: LAA, SK. Drafting of manuscript: MS, YAA, BA, RG, ZYA. Revising and editing the manuscript critically for important intellectual contents: YAA, BA, RG. Data preparation and presentation: MS, YAA, SK, RG. Supervision of the research: MS, YAA, RG, ZYA. Research coordination and management: MS, YAA, BA.

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Conflicts of interest

There is no conflict of interest.

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