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Effect of Cardio-Pulmonary Bypass Machine on Thyroid Function Tests in Children with Congenital Heart Diseases Undergoing Open Heart Surgeries

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Abstract:

Background: Congenital cardiovascular defects, or congenital heart defects, are structural abnormalities that result from improper development of the heart or major blood vessels. **Aim**: To detect thyroid dysfunction in children with CHD undergoing open heart surgeries on cardiopulmonary bypass and effect of thyroid dysfunction on postoperative ICU stay, period of mechanical ventilation, morbidity and mortality. **Patients and methods**: This was a Cross-sectional analytic study performed on fifty patients with congenital heart defects, 25 of them suffering from Cyanotic heart defects and 25 of them suffering from Acyanotic heart defects. This study was performed in a tertiary cardiac center throughout the interval from May 2022 to April 2023 in cases undergoing cardiac surgery to repair congenital heart defects. **Results**: There was significant statistical difference found between cyanotic and acyanotic groups regarding (post operative) TSH (p-value 0.020). There was significant statistical negative correlation between (post operative) TSH with bypass time, Cross Clamp, duration of MV, ICU stay and inotropic score and a high significant statistical positive correlation between (post operative) TSH with So2 and shows significant statistical negative correlation between post operative fT3 with duration of MV, ICU stay and inotropic score. **Conclusion**: Monitoring thyroid function in children with congenital heart disease is crucial, as CPB affects Thyroid function tests and other body systems, with a strong relationship with ICU stay, duration of MV, and morbidity and mortality post open heart surgeries.

Keywords: Cardio-pulmonary bypass machine, Thyroid function tests, Congenital heart diseases

1. Introduction

Congenital cardiovascular defects, or congenital heart defects, are structural anomalies that result from improper development of the heart or major blood vessels. Defects vary in their severity, ranging from tiny pinholes between chambers that may resolve spontaneously to significant abnormalities that may requires surgical intervention before school age. In some cases, these defects can lead to fetal mortality, death during infancy, or death during childhood (1). Cases with cyanotic congenital cardiovascular disorders had a higher incidence of subclinical hypothyroidism compared to cases with acyanotic cardiovascular disorders. Subclinical hypothyroidism has been related to multiple negative cardiovascular consequences and a higher risk of developing overt hypothyroidism (2).

The major purpose of the cardio-pulmonary bypass machine is to ensure continuous blood flow throughout the body while the heart undergoes manipulation. A blood pump facilitates the movement of blood volume in a forward direction through a membrane oxygenator, enabling the rapid transfusion of oxygenated blood back into the systemic circulation (3). The presence of thyroid hormone is crucial for the proper neurocognitive brain growth in infants, and even temporary hypothyroidism can lead to negative neurodevelopmental consequences. For infants with congenital heart disease who are already at a high risk of long-term developmental delay, it is important to detect hypothyroidism, even if it is temporary. Regular monitoring of thyroid function may be necessary to lower the chances of neurodevelopmental disabilities (4).

This study aimed to detect thyroid dysfunction in children with CHD undergoing open heart surgeries on cardiopulmonary bypass and effect of thyroid dysfunction on postoperative ICU stay, length of mechanical ventilation, morbidity and mortality.

Patients and methods

This was a Cross-sectional analytic study performed on fifty cases with congenital heart defects, 25 of them suffering from Cyanotic heart defects and 25 of them suffering from Acyanotic heart defects. This study was performed in a tertiary cardiac center during the period from May 2022 to April 2023 in patient undergoing cardiac surgery to repair congenital heart defects.

Inclusion criteria: Infants / Children with congenital heart disorder undergoing surgical intervention on cardiopulmonary bypass.

Exclusion criteria: Infants / Children with non-operable congenital heart disease, Children with conditions associated with chronic systemic diseases e.g. Liver diseases, renal diseases, Thyroid dysfunction and Patients with genetic syndromes ex: Down syndrome.

Ethical consideration

The approval of local authority from research ethics committee Cairo University Code: MD-139-2022.

Methods

All cases have been exposed to the following:

History with special attention to Age, Sex, diagnosis, Family history, Symptoms suggestive of increase or decrease in thyroid hormones, Symptoms of heart failure, Medication history**, patients were reviewed, and the following were documented:** Total bypass time, ischemic cross clamp time, complications in operation room, ICU stay, duration of mechanical ventilation, thyroid dysfunction, inotropic score, **examination** Body weight, height, body surface area, o2 saturation**, intervention, studied patients underwent the following investigations**: **Routine Laboratory investigations** Complete blood Count HB, HCT, Platelets Samples were done on Beckman coulter DxH 500, **Routine biochemistry investigations** SGPT, SGOT, Urea, Creatinine, Na, K, Albumin, Bilirubin total and direct. Samples were done on Beckman coulter AU480 (chemistry analyzer). **Specific laboratory investigations**: Thyroid function tests TSH, freeT3, freeT4, Samples withdrawn day before and 24hr after open heart surgery, Samples withdrawn using EDTA tubes and plain vacutainer tubes, under complete aseptic precautions 3 ml of venous blood withdrawn in specific tubes and sent immediately to the laboratory for analysis. We used Access2 immunoassay system of Beckman coulter to run thyroid function tests.

Sample size

Fifty patients, twenty-five of them were cyanotic and the other twenty-five were acyanotic.

Statistical analysis

The data that was collected underwent revision to ensure that it was complete and logically consistent. Data that was pre-coded has been inputted into the computer utilizing the Microsoft Office Excel Software Program 2019. The data that had been pre-coded was subsequently transferred and put into the Statistical Package of Social Science Software program, version 26 (SPSS), for statistical analysis. The information has been summarized as mean, standard deviation, median, and IQR for quantitative variables. The Mann Whitney U test has been utilized to compare independent variables, while the Wilcoxon Signed Ranks Test was utilized to compare dependent variables. If the p-value was less than 0.05, it was considered significant. For qualitative variables, the data was summarized as a percentage and incidence. The Chi-square test has been utilized to compare the groups. If the p-value was less than 0.05, it was considered significant.

Results

Table (1): Comparison between cyanotic and acyanotic patients regarding age, sex, BW, high and BSA

		Cyanotic	Acyanotic	p value	
Sex n (%)	**Male**	11 (44)	12 (48)	0.555	NS
	Female	14 (56)	13 (52)		
Age/ month	**mean ±**	21.9 ±	40.6 ±	0.002	HS
	sd	32.8	26.1		
	median (IQR)	7.5 (0.3, 20.0)	48.0 (12.0, 120.0)		
Weight / KG	**mean ±**	9.4 ±	13.8 ±	0.01	S
	sd	6.9	6.5		
	median (IQR)	8.0 (2.5, 12.3)	15.5 (7.6, 28.0)		
Height / CM	**mean ±**	77 ±	92 ±	0.016	S
	sd	26	23		
	median (IQR)	70 (56, 89)	97 (72, 105)		
BSA / m2	**mean ±**	0.5 ±	0.6 ±	0.034	S
	sd	0.2	0.2		
	median (IQR)	0.4 (0.2, 0.6)	0.6 (0.4, 0.7)		

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
BSA, Body Surface Area

The current study included 27 (54%) females and 23 (46%) males. Their age ranged between 0.3 and 120 months. Their weight ranged between 2.50 and 28Kg.

Table shows that there is no significant statistical difference found between cyanotic and acyanotic groups regarding sex while shows that there is a high significant statistical difference between them regarding Age (p-value 0.002) and shows significant statistical difference between them regarding Body Weigh (p-value 0.010) , Height (p-value 0.016) and BSA (p-value 0.034). (Table 1)

Table (2): Comparison between cyanotic and acyanotic patients regarding postoperative Thyroid function tests:

		Cyanotic	Acyanotic	p value	
TSH (postop)	**mean ±**	0.7 ±	1.1 ±	0.02	S
	Sd	0.3	0.6		
	median (IQR)	0.6 (0.4, 0.9)	0.87 (0.55, 1.45)		
fT3 (postop)	**mean ±**	2.5 ±	2.8 ±	0.177	NS
	Sd	0.9	0.7		
	median (IQR)	2.4 (1.7, 3.1)	2.74 (2.48, 3.21)		
fT4 (postop)	**mean ±**	1.1 ±	1.1 ±	0.472	NS
	Sd	0.2	0.2		
	median (IQR)	1.1 (1.0, 1.2)	1.12 (1, 1.23)		

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

There was significant statistical difference found between cyanotic and acyanotic groups regarding post-operative TSH (p-value 0.020), while there is insignificant statistical difference found between them regarding post-operative fT4 and post-operative fT3. (Table 2)

Table (3): Correlation between bypass time, duration of Cross Clamp, duration of MV, ICU stay, inotropic score and Thyroid functions

		TSH (postop)	fT3(postop)	fT4 (postop)
So2%	**R**	0.409	0.140	-0.036
	P	0.003	0.336	0.808
BYPASS Time	**R**	-0.308	-0.265	-0.077
	P	0.030	0.063	0.596
Cross Clamp	**R**	-0.314	-0.204	-0.031
	P	0.026	0.155	0.833
Duration of MV / day	**R**	-0.309	-0.278	0.018
	P	0.029	0.051	0.900
ICU stay / day	**R**	-0.325	-0.277	-0.108
	P	0.021	0.052	0.454
inotropic score	**R**	-0.306	-0.323	0.005
	P	0.030	0.022	0.973

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

There was significant statistical negative correlation between post-operative TSH with bypass time, Cross Clamp, duration of MV, ICU stay and inotropic score and a high significant statistical positive correlation between post-operative TSH with So2 and shows significant statistical negative correlation between post-operative fT3 with duration of MV, ICU stay and inotropic score. (Table 3)

Table (4): Correlation between changes in Thyroid functions and mortality:

	Mortality											
	Yes					**No**					**p value**	**sig**
	Mean	**Standard Deviation**	**Median**	**Percentile 25**	**Percentile 75**	**Mean**	**Standard Deviation**	**Median**	**Percentile 25**	**Percentile 75**		
TSH (preop)	**3.409**	**3.357**	**1.990**	**1.230**	**4.730**	**2.939**	**1.296**	**2.610**	**1.860**	**3.730**	**0.706**	**NS**
Pre-operative fT3	**3.03**	**0.91**	**2.53**	**2.48**	**3.80**	**3.97**	**0.73**	**3.81**	**3.51**	**4.35**	**0.046**	**S**
Pre-operative fT4	**1.25**	**0.23**	**1.32**	**1.04**	**1.43**	**1.13**	**0.24**	**1.02**	**0.97**	**1.24**	**0.227**	**NS**
Post-operative TSH	**0.600**	**0.258**	**0.480**	**0.460**	**0.770**	**0.917**	**0.564**	**0.690**	**0.490**	**1.140**	**0.214**	**NS**
Post-operative fT3	**2.30**	**1.08**	**2.04**	**1.56**	**2.71**	**2.73**	**0.80**	**2.63**	**2.21**	**3.21**	**0.311**	**NS**
fT4 (postop)	**1.15**	**0.09**	**1.20**	**1.12**	**1.21**	**1.11**	**0.21**	**1.10**	**0.99**	**1.21**	**0.359**	**NS**

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

There was a significant statistical Correlation between pre-operative fT3 and mortality (p-value 0.046) while it shows no significant statistical correlation between other variables. (Table 4)

Table (5): Comparison between pre and post-operative Thyroid function after CPB regarding all patients as one group

	Mean	Standard Deviation	Median	Percentile 25	Percentile 75	p value	
TSH (preop)	2.986	1.565	2.595	1.810	3.960	<0.001	HS
TSH (postop)	0.885	0.548	0.690	0.480	1.120		
fT3 (preop)	3.87	0.79	3.80	3.48	4.35	<0.001	HS
fT3(postop)	2.69	0.83	2.63	2.09	3.21		
fT4 (preop)	1.14	0.24	1.03	0.97	1.32	0.783	NS
fT4 (postop)	1.12	0.20	1.12	0.99	1.21		

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

There is a high significant statistical difference found between TSH (preop) and TSH (postop) and between fT3 (preop) and fT3 (postop) p<0.001 and insignificant statistical difference found between fT4 (preop) and fT4 (postop) p>0.05. (Table 5)

Table (6): Comparison between cyanotic and acyanotic patients regarding BYPASS Time, Cross Clamp, OR Complications, ICU stay, Duration of MV and Mortality:

		Cyanotic	Acyanotic	p value	
BYPASS Time	**mean ±**	111 ±	72 ±	<0.001	HS
	sd	31	34		
	median (IQR)	108 (93, 121)	62 (45, 86)		
Cross Clamp	**mean ±**	73 ±	47 ±	<0.001	HS
	sd	29	28		
	median (IQR)	68 (55, 85)	39 (30, 58)		
ICU stay (days)	**mean ±**	7 ±	3 ±	<0.001	HS
	sd	5	4		
	median (IQR)	5 (4, 9)	2 (2, 3)		
Duration of MV (days)	**mean ±**	4 ±	2 ±	0.001	HS
	sd	5	4		
	median (IQR)	2 (1, 4)	1 (1, 1)		
OR Complications n (%)	**No**	24 (100.0)	22 (84.6)	0.405	NS
	Yes	0 (0.0)	4 (15.4)		
Mortality n (%)	**No**	20 (83.3)	25 (96.2)	0.131	NS
	Yes	4 (16.7)	1 (3.8)		

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

There was insignificant statistical difference found between cyanotic and acyanotic groups regarding OR complications, BYPASS Time and Mortality p>0.05. (Table 6)

Discussion

Our study showed that there is a high significant statistical difference between cyanotic and acyanotic groups regarding bypass time (p-value < 0.001) as median bypass time is 108 min for cyanotic group and 62 min for acyanotic group, X-Clamp (p-value < 0.001) as median Cross Clamp time is 68 min for cyanotic group and 39 min for acyanotic group, ICU stay / day (p-value < 0.001) as median ICU stay / (days) is 5 days for cyanotic group and 2 days for acyanotic group and Duration of MV / day (p-value 0.001) as median Duration of MV / (days) is 2 days for cyanotic group and 1 days for acyanotic group.

Like our results a prospective observational study by **Altin et al., (5)** that include sixty cases who underwent open-heart surgeries

The study was conducted at a tertiary cardiac center between September 2014 and March 2015 to investigate congenital heart abnormalities treated with cardiopulmonary bypass. Two study groups have been established for the research. One group comprised thirty patients with acyanotic congenital heart disorder, while the other group had thirty cases with cyanotic congenital heart illness. Demonstrate a strong and statistically significant difference between the cyanotic and acyanotic groups in terms of bypass time (p-value less than 0.008), Cross Clamp (p-value less than 0.01), as well as ICU stay / day (p-value less than 0.005). However, the study indicates that there is statistically insignificant difference between both groups in terms of the period of mechanical ventilation (MV) (p-value 0.097).

Altin et al., (6) conducted another prospective trial with sixty-four cases with congenital heart defects.The study was conducted utilizing the database of a specialized cardiac center from June 2014 to January 2015. Every case had open-heart operation to treat congenital heart defects while being supported by cardiopulmonary bypass. Two study groups were established. One group included thirty cases with acyanotic congenital cardiovascular disease, whereas the other group comprised thirty-four cases with cyanotic congenital cardiovascular disease. Show that there is a high significant statistical difference between cyanotic and acyanotic groups regarding bypass time (p-value less than 0.0001), Cross Clamp (p-value < 0.0001) and ICU stay / day (p-value less than 0.029) but the same study shows that there is non-significant statistical difference between them regarding Duration of MV (p-value 0.253).

Our study demonstrations that there is significant statistical difference found between cyanotic and acyanotic groups regarding postoperative TSH (p-value 0.020) while it illustrations that there is no significant statistical difference found between them regarding postoperative fT4 and postoperative fT3 (post op).

Tehrani et al. conducted a cross-sectional study involving 120 cases with congenital cardiac disorders at Shahid Beheshti University of Medical Sciences in Tehran from April 2018 to February 2019. The study consisted of two groups. One group included ninety-four cases with acyanotic congenital cardiovascular disease, whereas the second group included twenty-six cases with cyanotic congenital heart illness. Indicates that there is statistically insignificant difference between them in terms of pre-operative fT3 (p-value less than 0.24), pre-operative fT4 (p-value 0.25), and pre-operative TSH (p-value 0.47).

A previous cross-sectional study conducted by **Holland et al. (8)** examined fourteen cases with congenital heart disorder at the Surgery Branch of the National Heart, Lung, and Blood Institute,

National Institutes of Health from November 1990 to November 1990. The study found statistically insignificant difference between the cases in terms of pre-operative fT3 (p-value above 0.05), pre-operative fT4 (p-value over 0.05), and pre-operative TSH (p-value above 0.05).

The results of our study indicate a highly significant statistical difference between pre-operative and post-operative TSH (p-value less than 0.001) and between pre-operative and post-operative fT3 (p-value less than 0.001). However, no statistically significant difference has been discovered between pre-operative and post-operative fT4.

A separate study conducted by **Wang et al., (9)** examined 165 cases with congenital cardiac illness at Children's Hospital of Nanjing Medical University from June 2017 to May 2020. The study revealed a notable statistical difference between pre-operative and post-operative fT3 levels, with a p-value of 0.05.

Our study exhibited that there was significant statistical positive correlation between pre-operative fT3 with So2 (p-value 0.043) and it showed that there is high significant statistical negative correlation between pre-operative fT3 with bypass time (p-value 0.001), cross clamp (p-value 0.001), duration of mechanical ventilation (MV) (p-value 0.004), ICU stay (p-value 0.006) and inotropic score (p-value 0.003).

Similar to our study a Prospective observational study by **Plumpton and Haas, (10)** that included 36 patients with congenital heart illness at a tertiary referral center for congenital heart surgery from June 2003 to May 2004 Show that there was high significant statistical negative association between fT3 (preop) with bypass time (p-value less than 0.001).

Our study showed a high significant statistical Negative correlation between fT4 (preop) with So2 (p-value < 0.001) and a high significant statistical positive correlation between fT4 (preop) with bypass time (p-value < 0.001), cross clamp (p-value 0.001), duration of MV (p-value 0.004), ICU stay (p-value 0.000) & inotropic score (p-value 0.000).

Another retrospective cohort study by **Shen et al., (11)** that included 118 patients with congenital heart disease at Cardiovascular Intensive Care Unit (CVICU) of Nanjing First Hospital, an urban, tertiary care, teaching Medical College Hospital in China from March 2019 to December 2020 Shows that there is non-significant statistical correlation between pre-operative fT4 with duration of MV (p-value 0.098).

Our study showed non-significant statistical correlation between pre-operative TSH with duration of MV (p-value 0.750).

Similar to our study **Shen et al., (11)** stated that there was non-significant statistical correlation between pre-operative TSH with duration of MV (p-value 0.601).

Our study showed significant statistical negative correlation between TSH (postop) with bypass time (p-value 0.030), cross-clamp (p-value 0.026), duration of MV (p-value 0.029), ICU stay (p-value 0.021) & inotropic score (p-value 0.030).

Marks et al reported in their study that there was non-significant statistical correlation between Pre-operative TSH with bypass time (p-value 0.070) **(12)**.

Our study showed a high significant statistical positive correlation between post-operative TSH with So2 (p-value 0.003).

Our study showed significant statistical negative correlation between post-operative fT3 with duration of MV (p-value 0.051), ICU stay (p-value 0.052) and inotropic score (p-value 0.022).

A study by **Marks et al., (12)** Showed that there is a significant statistical negative correlation between fT3 (postop) with inotropic score (p-value < 0.045).

Our study showed a non-significant statistical negative correlation between post-operative fT4 with duration of MV (p-value 0.900).

Like our study by **Shen et al., (11)** Showed that there is a non-significant statistical correlation between post-operative fT4 with duration of MV (p-value 0.141).

Our study shows that there is significant statistical correlation between pre-operative fT3 (preop) with Mortality (p-value 0.046).

Limitaions

The study was done on a limited number of patients; larger sample size is needed to have more statistically significant results & Short term follow up.

Recommendations

Long term follow-up of thyroid functions is required for those patients, a large multicenter study is indicated to involve a higher number of cases with different diagnosis.

Conclusion

It's very important to monitor Thyroid function in children with congenital heart disorder before and following CPB. CPB has effects on Thyroid function tests and other body systems. Effect of CPB on Thyroid function Tests have strong correlation with ICU stay and duration of MV, morbidity and mortality post open heart surgeries.

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