Hematological and biochemical profiles of children with congenital heart diseases candidate for surgical repair

Mohammed H. Hassan[a], Ashraf Taye[b], Mohamed Abdelbary[c], Marwa Okasha[a*], Mohammed Farouk Abdel Hafez[d], Aml Abdel-Fattah Sayed Soliman[e], Ahmed Ghoneim[d], Amal Hofni [b], Ahmed Farouk[e]

[a] Medical Biochemistry and Molecular Biology Department, Faculty of Medicine, Qena University, Qena, Egypt.
[b] Pharmacology and Toxicology Department. Faculty of Pharmacy. Qena University, Qena, Egypt.
[c] Cardiothoracic Surgery Department, Faculty of Medicine, Qena University, Qena, Egypt.
[d] Cardiothoracic Surgery Department, Faculty of Medicine, Assiut University, Assiut, Egypt.
[e] B. Sc. in Pharmaceutical Science, Faculty of Pharmacy, Assiut University, Assiut, Egypt.

Abstract

Background: Congenital heart disease (CHD) is a leading cause of morbidity and mortality in children, often accompanied by hematological and biochemical abnormalities. While previous studies have explored these alterations, inconsistencies remain regarding their prevalence and clinical significance across CHD subtypes.

Objectives: To assess the prevalence and clinical significance of hematological and biochemical abnormalities across CHD subtypes

Patients and methods: This case-control study compared 60 CHD patients (15 each with VSD, ASD, TOF, and PDA) with 40 healthy controls. Venous blood samples were analyzed for complete blood count, liver/kidney function, and coagulation profiles.

Results: CHD patients exhibited significantly lower hemoglobin level with median of (10.45vs. 11 g/dL, p=0.011) and higher ALT levels with median of (33 vs. 25 IU/L, p<0.001) than controls. Subgroup analysis revealed elevated median of WBCs in PDA ($13.5\times10^3/mm^3$ compared to the median of other groups being ($10.6\times10^3/mm^3$ for VSD,$11\times10^3/mm^3$ for ASD,$10\times10^3/mm^3$ for TOF and $11\times10^3/mm^3$ for control, p<0.001) and increased AST for TOF patients (42 u/l, compared to median of other groups being 32 u/l for PDA,34 u/l for VSD,29 u/l for ASD and 38 u/l for control, p=0.008). INR variations were most pronounced in TOF with median of 1.1 and 1 for each PDA, VSD and ASD and 1.04 for control p=0.007).

Conclusion: CHD patients demonstrate distinct hematological and biochemical derangements, with subtype-specific patterns suggesting varied pathophysiological mechanisms. These findings underscore the need for tailored monitoring and early intervention to mitigate complications.

Keywords: Congenital heart disease; Hematological profile; Biochemical markers; Pediatric cardiology; Cyanotic heart disease

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***Correspondence**: marwa.okasha33@gmail.com

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Introduction

Congenital heart disease (CHD) is the most prevalent birth defect, affecting approximately 8–10 per 1,000 live births worldwide (Hoffman & Kaplan, 2002). It encompasses a spectrum of structural abnormalities in the heart and great vessels, ranging from simple defects (e.g., ventricular septal defects, VSDs) to complex cyanotic conditions (e.g., Tetralogy of Fallot, TOF). Despite advances in surgical and medical management, CHD remains a leading cause of infant mortality, accounting for nearly 40% of deaths from congenital anomalies **(Liu et al., 2019).**

CHD disrupts normal hemodynamics, leading to **chronic hypoxia,** pressure overload, and volume overload, which in turn contribute to multisystem complications **(Sachdeva et al., 2021).** These physiological stressors often manifest as: *Hematological abnormalities* (e.g., erythrocytosis, thrombocytopenia, coagulopathies) due to altered shear stress and hypoxia **(Zabala and Guzzetta, 2015).** *Liver dysfunction* is secondary to passive venous congestion, particularly in Fontan circulation patients **(Singh et al., 2018**). *Renal impairment* due to reduced cardiac output and neurohormonal activation **(Di Lullo et al., 2017).**

While cardiac outcomes in CHD have improved dramatically, non-cardiac complications (e.g., liver disease, anemia, coagulopathy) are increasingly recognized as major determinants of long-term morbidity and mortality (**Neidenbach et al., 2018**). For instance: *Anemia* worsens tissue oxygenation and is linked to poor surgical outcomes **(Felker et al., 2006**). *Thrombocytopenia and platelet* dysfunction increase bleeding and thrombotic risks (**Collins et al., 2008).** *Elevated liver enzymes* (ALT/AST) may indicate subclinical hepatic injury, which progresses silently in CHD patients **(Engelings et al., 2016).**

Our study aimed to compare hematological (Hb, WBCs, platelets) and biochemical (ALT, AST, creatinine, INR) profiles between CHD patients and healthy controls and identify subtype-specific variations (VSD, ASD, TOF, PDA) to guide targeted monitoring to correlate laboratory abnormalities with clinical outcomes to inform risk stratification. By addressing these gaps, our findings may contribute to **earlier detection and intervention** for non-cardiac complications in CHD, ultimately improving patient outcomes.

Patients and Methods:

Study Design and Setting: **Case-Control Study**

Rationale: This design was selected to efficiently compare hematological/biochemical profiles between CHD patients and healthy controls, minimizing cost and time compared to cohort studies.

Setting: Conducted at Qena University Hospitals' Cardiothoracic Surgery Department (November 2021–June 2024), a tertiary referral center serving a high-CHD-prevalence region.

Participant Selection

Inclusion Criteria:

1.**CHD Group (n=60):**

- Children aged 0–18 years with Echocardiographically confirmed VSD, ASD, TOF, or PDA.

Rationale: These subtypes represent common acyanotic (VSD, ASD, PDA) and cyanotic (TOF) CHDs, allowing comparison of pathophysiology.

Surgical candidates only, ensuring uniform disease severity.

2.**Control Group (n=40):**

Age-/sex-matched healthy children with normal cardiac exams.

Rationale: Matching reduces confounding by demographic variables.

Exclusion Criteria:

Comorbidities (renal/hepatic/neurological diseases) or familial dyslipidemia.

Rationale: Isolates CHD-specific effects by eliminating confounding conditions.
Metabolic disorders (e.g., glycogen storage diseases).
Rationale: These independently alter biochemical markers (e.g., ALT, AST).
Sample Size Calculation
G*Power 3.1.3 was used with:
Effect size = 0.5 (moderate, based on prior CHD studies).
α = 0.05, power (1-β) = 80%.
Output: Minimum 50 CHD patients (increased to 60 for subgroup analyses).
Rationale: Ensures adequate power to detect clinically meaningful differences.
Laboratory Protocols
Blood Collection: 7 ml venous blood:
Division:
2 mL in EDTA tubes: For CBC (analyzed within 2 hours to prevent platelet clumping).
3 mL in plain tubes: Clotted at 37°C for 30 min, centrifuged at 3500 rpm (4°C) to separate serum for:
Liver/kidney function tests (ALT, AST, creatinine, urea).
Rationale: 37°C incubation mimics physiological clotting conditions.
2 mL in sodium citrate tubes: Centrifuged similarly for PT/INR.
Rationale: Citrate chelates calcium to prevent *in vitro* clotting.
Analytical Methods:
CBC: Automated hematology analyzer (Sysmex XN-1000).
Liver/kidney tests: Spectrophotometry (Roche Cobas c501).
PT/INR: Coagulometry (STA Compact).
Rationale: Accredited methods ensure reproducibility.
Statistical analysis
Non-parametric tests (Mann-Whitney U, Kruskal-Wallis H):
Rationale: Data were non-normally distributed (Shapiro-Wilk $p<0.05$).
Spearman's correlation: Assessed relationships between Hb and ALT.
Logistic regression: Identified independent predictors of abnormal labs.
Software: SPSS v.27, significant p value considered when $p<0.05$.
Ethical approval code
Approved by South Valley University Ethics Committee **(No. SVU-MED-MBC004-4-25-3-23)**. Written parental consent obtained.
Rationale: Ensures compliance with Declaration of Helsinki.
Results
laboratory data between congenital heart disease patients and controls, in table 1 highlighting significant variances indicative of the physiological impact of congenital heart disease. In terms of hemoglobin levels, congenital heart disease patients exhibited a lower median of hemoglobin concentration (10.45g/dL) compared to controls (11g/dL), $P < 0.05$, **(Table 1, Fig.1)**.
Liver function tests further emphasize the impact of congenital heart disease alanine aminotransferase (ALT) which was significantly higher in cases with median of 33 IU/L compared to control median 25 IU/L ($p<0.05$) **(Table 1, Fig.2).**
While there was non-significant difference between cases and control regarding other parameters such as WBCs, platelet count, neutrophils, lymphocytes, aspartate aminotransferase (AST), urea, creatinine levels Prothrombin time and INR median, ($p>0.05$ for each) as shown in **Table 1**.

Table 1. Laboratory data of the study groups

Variables	Cases (n=60)	Control (n=40)	P-value
Hb (g/dl)			
Min.-Max.	7.3 - 16.9	9.8 - 12.7	

Median(Q1-Q3)	10.45(10-11)	11(10-11.93)	0.011* U
Wbcs (*10³/mm³)			
Min.-Max.	3.9 - 17	7.8 - 12.5	
Median(Q1-Q3)	10.2(7.85-13.38)	9.75(9.5-10)	0.120 U
Platlets (*10³/mm³)			
Min.-Max.	148 – 688	190 - 355	
Median(Q1-Q3)	243(230-316)	281.5(230-320)	0.893 U
Lymphocytes (%)			
Min.-Max.	33 - 71.6	30 - 55	
Median(Q1-Q3)	51(43.25-53)	44(38.25-53)	0.055
Neutrophils (%)			
Min.-Max.	19.4 – 57	32 - 55	
Median(Q1-Q3)	40.5(34-48)	41(36-43)	0.467 U
ALT(u/l)			
Min.-Max.	12 - 44.8	12 - 41	
Median(Q1-Q3)	33(29-38.25)	25(22-29)	<0.001** U
AST(u/l)			
Min.-Max.	14 - 64.5	24 - 44	
Median(Q1-Q3)	32(27-41)	38(34.25-40.5)	0.056 U
Creatinine (mg/dl)			
Min.-Max.	0.24 – 1	0.46 - 0.7	
Median(Q1-Q3)	0.5(0.5-0.6)	0.5(0.49-0.5)	0.072 U
Urea (mg/dl)			
Min.-Max.	15 – 35	17 - 23	
Median(Q1-Q3)	19(18-21)	19.5(18.1-21)	0.690 U
Prothrombin time (sec)			
Min.-Max.	12.3 - 16.5	12.5 - 14	
Median(Q1-Q3)	13.1(13-13.4)	13(12.63-14)	0.412 U
INR			
Min.-Max.	0.8 - 1.38	1 - 1.23	
Median(Q1-Q3)	1(1-1.1)	1.04(1-1.12)	0.123 U

The data were presented as the median and Interquartile range (Median (IQ)) for non-parametric data.

Abbreviations: P. value: Comparison between the two studied groups using **Mann-Whitney U** for nonparametric continuous data.

P. value > 0.05 considered statistically not significant, * p-value < 0.05 considered statistically significant, ** P < 0.01 considered highly statistically significant

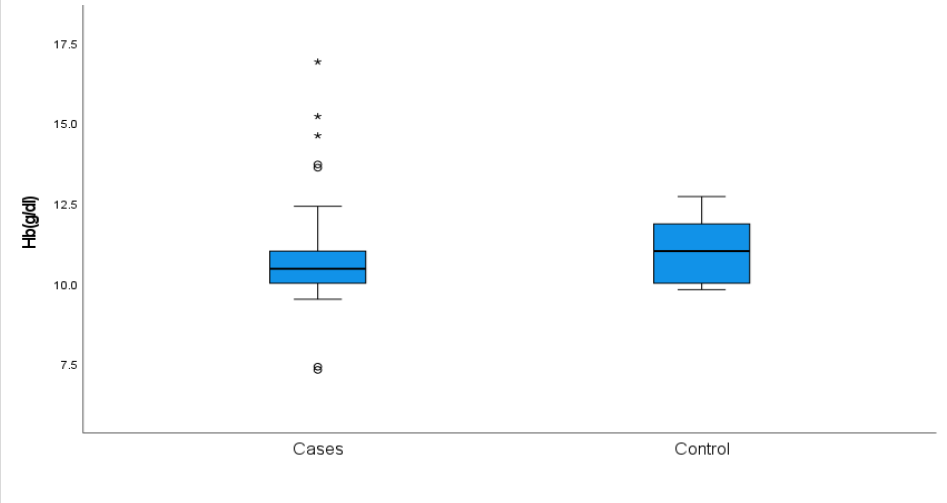

Fig 1. Boxplot chart showing median and interquartile range of Hb (g/dl) distribution between the two studied groups.

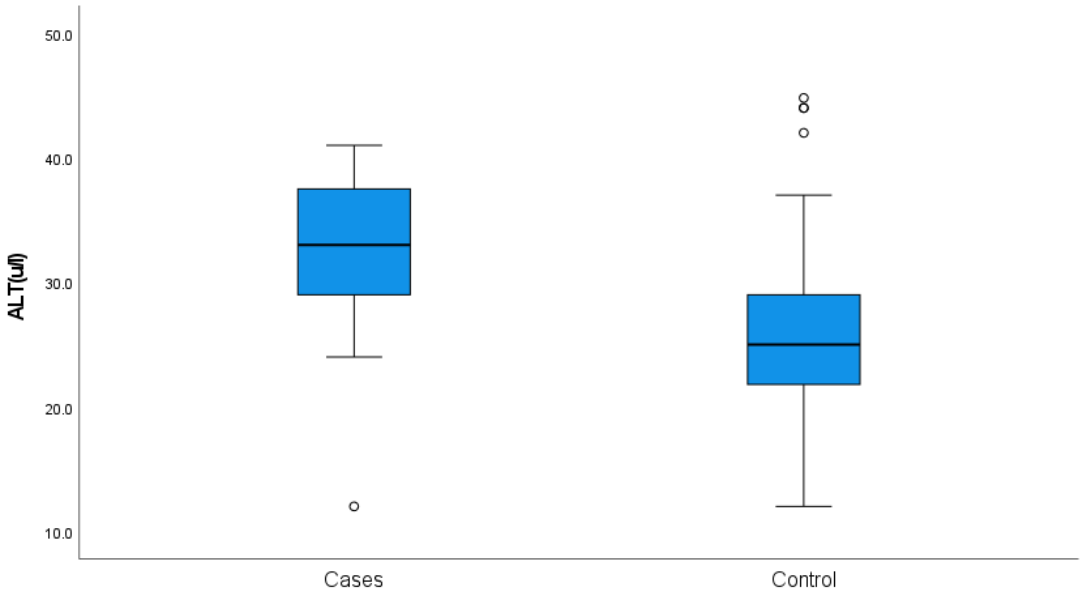

Fig 2. Boxplot chart showing median and interquartile range of ALT(u/l) distribution between the two studied groups.

Laboratory data of subgroups of congenital heart disease in table 2 revealed leucocytosis of PDA patients with median of 13.5 g/dl compared to other groups median (9.7 g/dl for each of ASD and TOF), 10.4g/dl for VSD and 9.75 g/dl for control, ($p<0.05$), **(Table 2, Fig.3).**

Also, lymphocytosis was observed in VSD patients with median of 51.5% followed by TOF median 51% compared to other groups

median 50% ,46% and 44% for ASD, PDA and control, ($p<0.05$)**.**

Similarly, there was significant decrease in AST levels in PDA and ASD patients with median of 29U/l and 32 U/l respectively compared to other groups median 34 U/l,42 U/l and 38 U/l for VSD, TOF and control respectively, ($p<0.05$)**, (Table 2, Fig 4).**

Also, significant decrease was observed considering INR in PDA, ASD and VSD with median of 1 for each group compared to 1.1 in TOF and 1.04 for control ($p<0.05$)**, (Table 2, Fig 5).**

Conversely there was non-significant difference among subgroups considering Hb level, platelets count, neutrophils, ALT, creatinine, urea and prothrombin time ($p>0.05$ for all).

Table 2. Laboratory data among included of the study groups

Variables	Type of congenital heart disease				Control	P-value
	PDA	VSD	ASD	TOF		
	n=15	n=15	n=15	n=15	n=40	
Hb(gldl)						
Min.-Max.	9.5 - 11	7.3 - 11.9	10 - 13.7	9.8 - 16.9	9.8 - 12.7	
Median(Q1-Q3)	10.5(9.5-10.7)	10.6(10-11)	11(10-11)	10(9.8-13.6)	11(10-11.93)	0.051 H
Wbcs (*10³/mm³)						
Min.-Max.	10.7 - 14.7	5.9 - 17	6 - 15	3.9 - 13	7.8 - 12.5	
Median(Q1-Q3)	13.5(12.3-14)	10.4(7.4-14.5)	9.7(7-9.8)	9.7(7.4-10.5)	9.75(9.5-10)	<0.001** H
Platelets(*10³/mm³)						
Min.-Max.	230 - 402	149 - 688	148 - 439	162 - 340	190 - 355	
Median(Q1-Q3)	240(230-302)	295(240-320)	240(230-294)	265(230-330)	281.5(230-320)	0.587 H
Lymphocytes (%)						
Min.-Max.	34 - 53	43 - 71.6	33 - 55	34 - 63	30 - 55	
Median(Q1-Q3)	46(42-53)	51.5(46-58)	50(36-51)	51(44-53)	44(38.25-53)	0.040* H
Neutrophiles (%)						
Min.-Max.	28 - 52	19.4 - 52	24 - 53	31 - 57	32 - 55	
Median(Q1-Q3)	36(33-42)	40(33-42)	42(36-50)	48(33-53)	41(36-43)	0.120 H
ALT(u/l)						
Min.-Max.	20 - 34	17 - 44.8	15 - 29	12 - 44	12 - 41	
Median(Q1-Q3)	24(22-25)	26(24-34)	28(24-29)	25(16-29)	25(22-29)	0.1 H
AST(u/l)						
Min.-Max.	14 - 45	14 – 61	24 - 41	16 - 64.5	24 - 44	
Median(Q1-Q3)	32(28-33)	34(27-45)	29(25-38)	42(27-44)	38(34.25-40.5)	0.008** H

Creatinine(mg/dl)						
Min.-Max.	0.48 - 0.7	0.24 - 1	0.3 - 0.7	0.42 - 0.7	0.46 - 0.7	
Median(Q1-Q3)	0.5(0.5-0.6)	0.5(0.4-0.6)	0.58(0.5-0.6)	0.5(0.5-0.6)	0.5(0.49-0.5)	0.342 H
Urea(mg/dl)						
Min.-Max.	15 - 24	16.1 - 29	15.4 - 22.5	18 - 35	17 - 23	
Median(Q1-Q3)	19(18-22)	20(19-21)	18(18-20)	21(19-22)	19.5(18.1-21)	0.069 H
Prothrombin time (sec)						
Min.-Max.	13 - 16.5	13 - 16.5	12.3 - 14	12.5 - 14.1	12.5 - 14	
Median(Q1-Q3)	13.2(13-14.2)	13(13-13.5)	13.2(13-13.4)	13(13-13.1)	13(12.63-14)	0.284 H
INR						
Min.-Max.	0.8 - 1.19	0.9 - 1.38	0.9 - 1.19	1 - 1.23	1 - 1.23	
Median(Q1-Q3)	1(0.8-1.1)	1(1-1.18)	1(1-1.03)	1.1(1-1.14)	1.04(1-1.12)	0.007** H

The data were presented as the median and Interquartile range (Median (IQ)) for non-parametric data.
Abbreviations: P. value: Comparison between all studied groups using **Kruskal–Wallis H** for nonparametric continuous data.
P. value > 0.05 considered statistically not significant, * p-value < 0.05 considered statistically significant, ** P < 0.01 considered highly statistically significant.

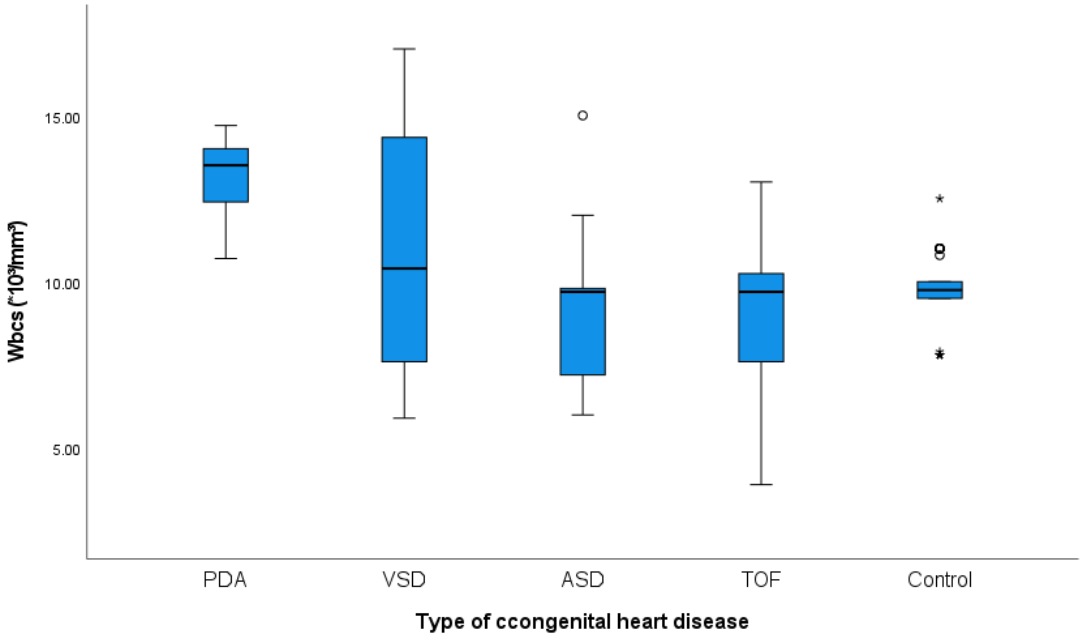

Fig 3. Boxplot chart showing median and interquartile range of Wbcs (*10³/mm³) among type of congenital heart disease subgroups.

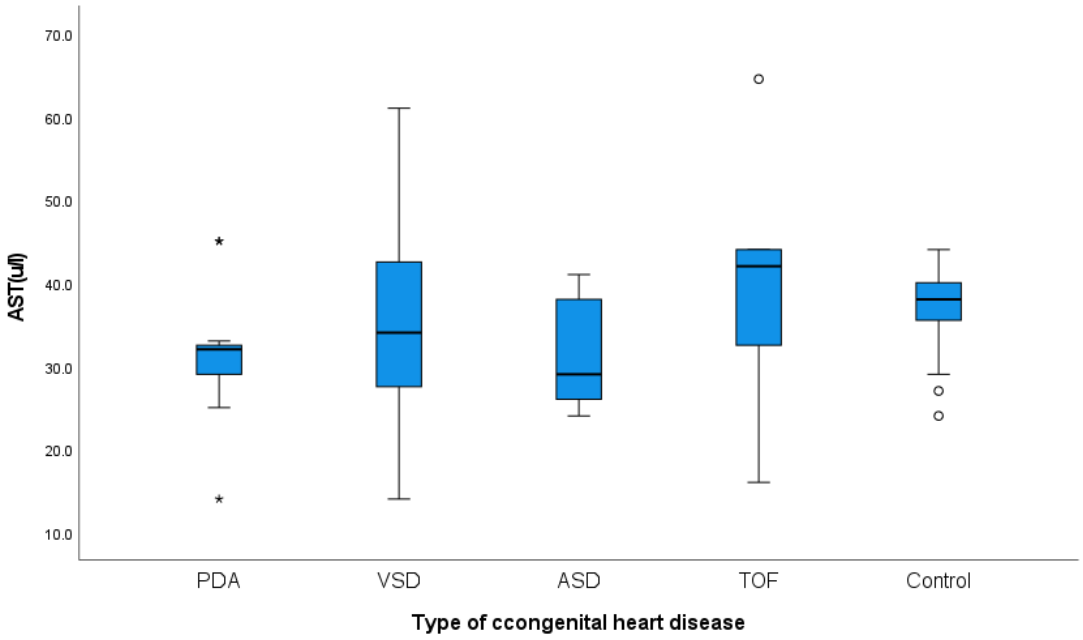

Fig 4: Boxplot chart showing median and interquartile range of AST (u/l) among type of congenital heart disease subgroups.

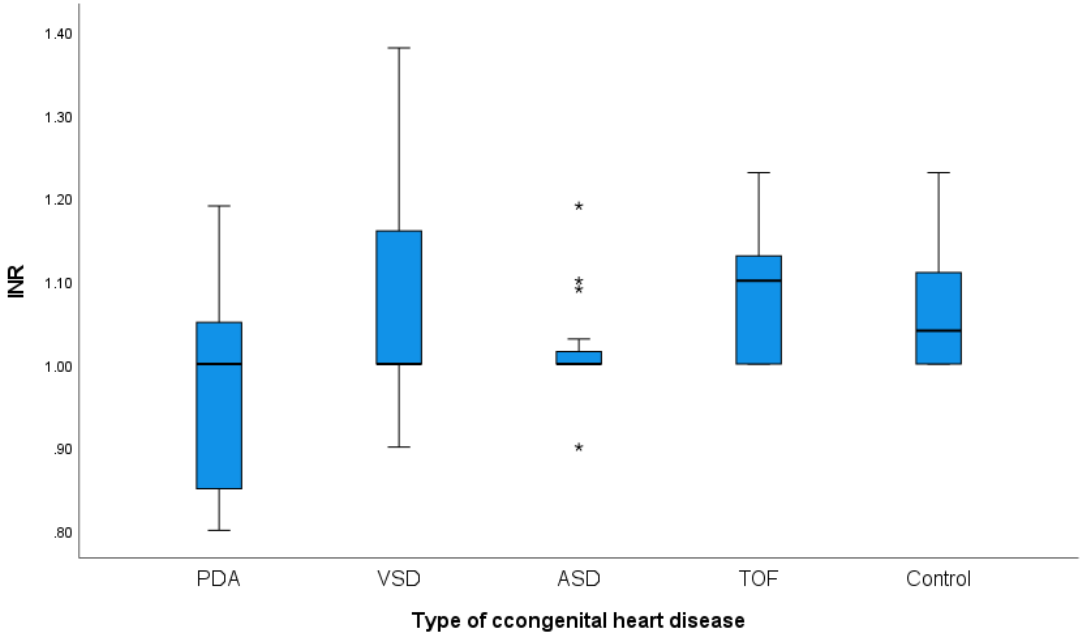

Fig 5: Boxplot chart showing median and interquartile range of INR among type of congenital heart disease subgroups.

Discussion

Congenital heart disease (CHD) remains the most common birth defect globally, affecting approximately 9 per 1,000 live births, with rising prevalence due to improved diagnostic methods **(Hoffman and Kaplan, 2002; Liu et al., 2019).** These structural cardiac abnormalities induce chronic hypoxia and

hemodynamic stress, leading to multi-system complications including erythrocytosis, coagulopathies, and hepatic dysfunction (**Zabala and Guzzetta, 2015; Singh et al., 2018).**

While surgical advances have improved survival, non-cardiac manifestations now account for 40% of late morbidity in CHD patients, particularly hematologic and hepatic abnormalities **(Neidenbach et al., 2018).** Recent studies report anemia in 30-50% of CHD cases, exacerbating cardiac workload and increasing mortality risk by 2-fold **(Felker et al., 2006 and Lui et al., 2017).** However, existing literature shows inconsistencies, with some studies documenting thrombocytopenia in cyanotic CHD **(Martínez et al., 2015)** while others report normal platelet counts **(Ootaki et al., 2007),** possibly due to variable study designs and CHD subtype distributions.

This lack of consensus underscores the need for standardized profiling of laboratory abnormalities across CHD subtypes to guide clinical monitoring. Our study, therefore, aimed to systematically compare hematological and biochemical parameters in children with major CHD types against healthy controls, with the goal of establishing subtype-specific risk profiles for early intervention.

Our present study highlights significant hematological and biochemical differences between children with congenital heart disease (CHD) and healthy controls, with notable variations among CHD subtypes. Our findings align with some previous studies but in contrast with others, reflecting the complex pathophysiology of CHD and its systemic effects.

Our Findings: CHD patients had significantly lower Hb levels (10.45 g/dL) compared to controls (11g/dL, p=0.011).

This is consistent with **Felker et al. (2006)**, who reported anemia as a common comorbidity in CHD, worsening heart failure and increasing mortality**. Lui et al. (2017)** also linked anemia to poor outcomes in cyanotic CHD due to chronic hypoxia and iron deficiency.

However, some studies, such as those by **Kajimoto et al. (2007)**, found erythrocytosis (high Hb) in cyanotic CHD due to compensatory polycythemia from chronic hypoxia. Our cohort included mixed CHD types (both cyanotic and acyanotic), which may explain the discrepancy.

Our Findings: WBC counts were higher in PDA patients (13.5 $\times 10^3/mm^3$, $p<0.001$), while platelet counts did not differ significantly between groups (p=0.893).

There are supporting studies with our finding**,** elevated WBCs in PDA may reflect chronic inflammation due to left-to-right shunting, as suggested by **Goel et al. (2000).**

In contrast, **Martínez et al. (2015)** reported thrombocytopenia in hypoxemic CHD due to platelet consumption and dysfunction. Our study did not find significant platelet differences, possibly because our cohort included both cyanotic and acyanotic CHD, diluting the effect.

Our Findings: ALT was significantly higher in CHD patients (33 u/l vs 25 u/l, $p<0.001$), with TOF patients showing the highest AST (42 u/l, p=0.008).

In agreement with our findings, **Singh et al. (2018)** found liver dysfunction in 6% of CHD patients, particularly post-Fontan surgery. Also, **Engelings et al. (2016)** reported cirrhosis in young CHD patients due to chronic venous congestion.

Some studies, such as **Asrani et al. (2013)**, argue that liver enzyme elevations in CHD are often mild and may not correlate with clinical severity. Our findings suggest subclinical liver injury, warranting long-term monitoring.

Our Findings: INR varied significantly among CHD subtypes (p=0.007), with TOF patients showing the highest values (1.1).

Aligned with our findings, **Arslan et al. (2011)** reported coagulation abnormalities in

cyanotic CHD due to platelet dysfunction and factor deficiencies.

Another study by **Paraskevi et al. (2024)** reported that the hemostatic profile is deranged early in the course of CHD**.**

Conclusion

Our study confirms that CHD patients exhibit distinct hematological and biochemical abnormalities, some of which align with prior research while others differ. These variations may stem from differences in CHD subtypes, disease severity, and patient selection. Future multicenter studies with larger cohorts and longitudinal follow-up are needed to refine risk stratification and optimize management strategies.

Limitations

Single-center design may limit generalizability.

Small subgroup sizes (n=15 per CHD type) reduce statistical power.

Lack of long-term follow-up prevents assessment of how these abnormalities impact surgical outcomes.

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