"TO ESTABLISH THE CORRELATION BETWEEN THE LEVEL OF SERUM NT-PRO BRAIN NATRIURETIC PEPTIDE AND THE SEVERITY OF LEFT TO RIGHT SHUNT (QP/QS) RATIO IN CHILDREN WITH ACYANOTIC CONGENITAL HEART DISEASE – A CROSS-SECTIONAL STUDY"

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Dr. DNYANESH D K M.D., L.L.B
Professor & Head
Department of Paediatrics
J N Medical College
KAHER
Belagavi, Karnataka

Dr. Dnyanesh D.K
PROFESSOR & HEAD
DEPARTMENT OF PEDIATRICS
J. N. Medical College, Belagavi

Date: 28/03/2025
Place: JNMC, Belagavi

Dr. N S MAHANTASHETTI M.D.
Principal
J N Medical College
KAHER
Belagavi, Karnataka

PRINCIPAL
Jawaharlal Nehru Medical College
BELAGAVI

Date: 28/03/2025
Place: JNMC, Belagavi

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(Recognized by National Medical Commission, New Delhi)

Accredited 'A+' Grade by NAAC (3rd Cycle) **Placed in Category 'A' by MoE (GoI)**

Nehru Nagar, Belagavi- 590 010, Karnataka, INDIA

0831 - 2471350 0831 - 2470759 www.jnmc.edu rincipal@jnmc.edu

Ref No: MDC/PG/ Date: 25-03-2025

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Chairperson-Antiplagiarism Committee &
Principal,
J. N. Medical College, Belagavi.

To,
Reg. No. BM0122003
Postgraduate Student,
2022-23 Batch,
Department of Paediatrics
J. N. Medical College, Belagavi.

ETHICAL CLERANCE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A+' Grade by NAAC in (3rd Cycle) Placed in Category 'A' by MHRD (GoI)
JNMC INSTITUTIONAL ETHICS COMMITTEE
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref No.MDC/JNMCIEC/ 92 **Date: 26/03/2023**

To.
BM0122003
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 **"TO ESTABLISH THE CORRELATION BETWEEN THE LEVEL OF SERUM NT-PRO BRAIN NATRIURETIC PEPTIDE AND THE SEVERITY OF LEFT TO RIGHT SHUNT (QP/QS) RATIO IN CHILDREN WITH ACYANOTIC CONGENITAL HEART DISEASE – A CROSS SECTIONAL STUDY",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee.

(Dr. Smita Sonoli)
Member Secretary
JNMC Institutional Ethics Committee
J.N.Medical College, Belagavi.

(Dr. Harsha Hegde)
Chairman,
JNMC Institutional Ethics Committee
J.N.Medical College, Belagav

LIST OF ABBREVIATIONS

- **NT-ProBNP**: Serum NT-Pro Brain Natriuretic Peptide
- **Qp/Qs**: Left-to-right shunt ratio
- **CHD**: Congenital Heart Disease
- **Acyanotic**: Refers to the type of congenital heart disease
- **Children**: The study population
- **Cross-Sectional Study**: The study design.
- **ASD**: Atrial Septal Defect
- **VSD**: Ventricular Septal Defect
- **PDA**: Patent Ductus Arteriosus
- **Acyanotic CHD**: Acyanotic Congenital Heart Disease
- **Echo**: Echocardiographic evaluation
- **Hemodynamics**: Hemodynamic evaluation
- **Pediatric/Children**: Study population

ABSTRACT

Background: Congenital heart disease (CHD) is a leading cause of morbidity and mortality in children, with left-to-right shunts (e.g., ASD, VSD, PDA) being common acyanotic defects. Accurate assessment of shunt severity, quantified by the Qp/Qs ratio, is critical for clinical management. Echocardiography remains the gold standard but is resource-intensive. Serum N-terminal pro-Brain Natriuretic Peptide (NT-proBNP) has emerged as a potential biomarker for shunt severity, particularly in resource-limited settings.

Objective: This study aimed to establish a correlation between serum NT-proBNP levels and the Qp/Qs ratio in children with acyanotic CHD and determine a cut-off value for predicting significant shunting.

Methods: A cross-sectional study was conducted on 60 children diagnosed with ASD, VSD, or PDA at KLEH Dr. Prabhakar Kore Charitable Hospital. Shunt severity was classified as mild (Qp/Qs <1.5), moderate (1.5–2.0), or severe (≥2.0) using Doppler echocardiography. Serum NT-proBNP levels were measured and correlated with shunt severity. Statistical analysis included ROC curve analysis to determine diagnostic accuracy.

Results: NT-proBNP levels increased significantly with shunt severity: mild (62.55 ± 22.78 pg/ml), moderate (143.40 ± 37.39 pg/ml), and severe (365.38 ± 138.98 pg/ml) ($p < 0.001$). A strong positive correlation was observed between NT-proBNP levels and Qp/Qs ratio ($p < 0.001$). ROC analysis revealed an optimal NT-proBNP cut-off of 112 pg/dl for predicting significant shunting (Qp/Qs >1.5), with 94% sensitivity and 88.89% specificity (AUC = 0.991). Severe shunting was most prevalent in ASD (68.2%), followed by VSD (50.0%) and PDA (33.3%).

Conclusion: Serum NT-proBNP levels correlate strongly with the severity of left-to-right shunting in acyanotic CHD. A cut-off of 112 pg/ml can reliably identify significant shunting, offering a cost-effective screening tool, especially in resource-limited settings.

Keywords: NT-proBNP, Qp/Qs ratio, Acyanotic congenital heart disease, Left-to-right shunt, Echocardiography, Biomarker, Pediatrics.

CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Congenital heart defects (CHD) are defined as abnormal cardiocirculatory structure or function present at birth, although they are often not detected until later in life. In the last half-century, the outlook for children with heart disease has changed dramatically with improved imaging methods, such as echocardiography, computed tomography, and magnetic resonance imaging [1, 2]. Congenital heart disease (CHD) affects six to eight per 1000 live births [1, 2]. However, only 20% of babies with CHD would be identified if the examination of the fetal heart were confined to traditional high-risk groups, such as increased nuchal translucency, family history of CHD, and teratogen exposure [1]. Additionally, the ability to pharmacologically manipulate the duct has revolutionized the management of the sick neonate with major heart disease. Lesions that were previously considered lethal are now routinely treated. Consequently, the great majority of children with major heart disease now reach adulthood in good health [3, 4].

The birth prevalence of severe CHD has been consistently reported as 1.5–1.7 per 1000 live births [5-7]. Echocardiography is associated with higher birth prevalence as many milder cases are also detected [6-8]. Similarly, hospital-based data is unlikely to be representative of community prevalence in low- and middle-income countries (LMIC), where a substantial proportion of births occur at home. Critical CHD, especially those dependent on the patency of the ductus arteriosus, may go undiagnosed in these settings [9, 10].

Most studies reported from India are on prevalence at a given point in time, and not on prevalence at birth. Many reported studies are based on data from pediatric patients reporting to hospitals, leading to a possible sampling bias [11-14]. The profile of

patients with CHD that present to healthcare facilities in LMIC is largely determined by the natural history of individual conditions [15, 16].

Incidence or Birth Prevalence

Incidence or birth prevalence has been reported only in a few studies from India, which also include only babies born in the hospital [15, 16]. In two of these studies, echocardiography was performed for all newborns. The birth prevalence of CHD in these studies was higher in comparison to data available from other countries [15, 16]. Several other studies have reported the prevalence of CHD during childhood, and it varies from 1.3 to 9.2 per 1000 population [15, 16]. Gross disparity exists between high-income countries and low- and middle-income countries (LMIC) as far as the care of children with CHD is concerned. Whereas one cardiac center caters to a population of 120,000 in North America, 16 million people are served by one center in Asia [15, 16].

Indian Settings

In the latest report from AIIMS India, congenital heart disease (CHD) is the most frequently occurring congenital disorder, responsible for 28% of all congenital birth defects. Considering a birth prevalence of 9 per 1000, the estimated number of children born with CHD every year in India approximates 240,000, posing a tremendous challenge for families, society, and the healthcare system [15, 16]. Of the 240,000 children born with CHD each year in India, about one-fifth would need early intervention to survive the first year of life. A large pool of older infants and children who may have survived despite no intervention adds to the burden of CHD [15, 16].

There are marked regional variations in the population and crude birth rates in various parts of India. The total number of births is much higher in Northern and Eastern parts of India (Delhi, Jammu and Kashmir, Punjab, Haryana, Himachal Pradesh, Rajasthan, Uttar Pradesh, Uttarakhand, Bihar, Jharkhand, Orissa, and West Bengal) compared to the rest of the four regions (Southern, Western, Central, and North-East) [15, 16].

Based on the information provided by 47 centers in India, there is a clear paradox as many centers are located in regions with a lower burden of CHD. When considering critical CHD (requiring intervention in the first year of life), the Southern and Western states of India have fared much better than other regions [15, 16]. On the contrary, states such as Uttar Pradesh, Bihar, Jharkhand, and Madhya Pradesh, which presumably have a much higher CHD burden compared to the rest of the states, have fared much worse [15, 16]. The data suggest that children born with serious CHD in Southern India have a 70% chance of receiving good cardiac care, even if we consider that some of the children operated on in these centers are from other parts of India. In contrast, babies born in Eastern and Central parts of India have a much lower chance of receiving intervention [15, 16].

Environmental and Genetic Risk Factors

CHD is a multifactorial condition influenced by both environmental and genetic factors. Maternal exposure to air pollution, toxic chemicals, parental smoking, maternal obesity, and maternal health conditions (e.g., diabetes) all increase the risk of congenital anomalies, including CHD [15, 16]. In addition to environmental influences, genetics plays a central role in the pathogenesis of CHD. Earlier studies using karyotyping techniques revealed that ~12% of CHD patients have aneuploidies, such as Trisomy 13, 18, or 21 (Down syndrome), or monosomy X (Turner syndrome)

[15, 16]. Advances in genome sequencing have enabled researchers to identify rare de novo variants associated with CHD, providing valuable insights into the molecular pathways involved in cardiogenesis [15, 16].

TABLE I BIRTH PREVALENCE OF CONGENITAL HEART DISEASE IN INDIA

Author [Ref.]	*No. screened*	*Screening method*	*No. with CHD*	*Prevalence/ 1000 live births*
Khalil, *et al.* [15]	10964	Clinical examination only	43	3.9
Vaidyanathan, *et al.* [16]	5487	Clinical, Pulse oximetry, Echocardiography in all cases	Minor*: 408 at birth 119 at 6 weeksMajor**:17	Minor CHD*:74.4 at birth 21.7 at 6 weeks Major CHD**:3.1
Sawant, *et al.* [17]	2636	Clinical; echocardiography in suspected cases only	35	13.3
Saxena, *et al.* [18]	20307	Clinical, Pulse oximetry, Echocardiography in all cases	Significant#: 164 Major##: 71 Major##: 4.5/1000	Significant#: 8.1 (95% CI 6.94; 9.40)

*CHD: congenital heart disease; *Those which are likely to normalize by 6 weeks and include; atrial septal defect >5mm, patent ductus Arteriosus >2 mm with left ventricular volume overload, ventricular septal defect with gradient of >30 mmHg, aortic stenosis/pulmonic stenosis with gradients of <25 mmHg and pulmonary artery branch stenosis with gradients of <20 mmHg; **CHD that is likely to require early intervention; #atrial septal defect >5 mm, patent ductus arteriosus >2 mm with left ventricle volume overload, restrictive VSD, and valvular aortic/pulmonary stenosis with gradients <25 mmHg (in addition to Major CHD); ##any CHD that is likely to require intervention within the first year, including newborns with critical CHD that require intervention within the first 4 weeks of life.*

TABLE II PREVALENCE OF CONGENITAL HEART DISEASE IN CHILDREN BEYOND NEONATAL AGE

Author [Ref]	*Age group (y)*	*Setting*	*Place of study*	*Total No.*	*Screening method*	*No. with CHD*	*Prevalence per 1000*
Gupta, *et al.* 1992 [19]	6-16	Community	Jammu	10263	Clinical	8	0.8
Vashishtha, *et al.* 1993 [20]	5-15	School	Agra	8449	Clinical	44	5.2
Thakur, *et al.* 1995 [21]	5-16	School	Shimla	15080	Clinical	30	2.25
Chadha, *et al.* 2001 [22]	<15	Community	Delhi	11833	Clinical	50	4.2
Misra, *et al.* 2009 [23]	4-18	School	Eastern Uttar Pradesh	118212	Clinical Echo for suspected cases only	42	1.3
Kumari, *et al.* 2013 [24]	5-16	School	Dist. Prakasam, Andhra Pradesh	4213	Clinical and Echo in all	39	9.2
Saxena, *et al.* 2013 [25]	5-15	School	Ballabgarh, Haryana	14716	Clinical Clinical and echo	3577	2.37 5.23
Bhardwaj, *et al.* 2016 [26]	All age groups 19.5 y	Community	Himachal Pradesh	1882 (<18 y: 660)	Clinical Echo for suspected cases only	12	6.312.95 (in <18 y)
Nisale, *et al.* 2016 [27]	1st to 10th class	School	Latur, Maharashtra	3,53,761	Clinical Echo for suspected cases only	143	0.4

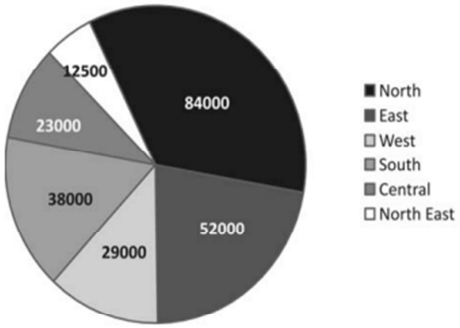


FIG. 1 *Regional distribution of infants born with CHD in India every year. (See color figure at website)*

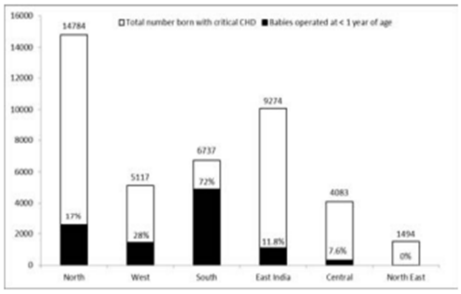


FIG. 2 *Regional distribution of infants with critical heart disease accessing surgery as compared to total number born with critical heart disease.*

Fetal Echocardiography and CHD Diagnosis

In the **fetal circulation**, the right and left ventricles operate in a **parallel circuit**, unlike the series circuit seen in newborns or adults. The placenta serves as the primary organ for gas and metabolite exchange, while the lungs, which are non-functional in utero, receive minimal blood flow due to pulmonary vasoconstriction. Three key fetal structures—the **ductus venosus**, **foramen ovale**, and **ductus arteriosus**—facilitate this unique circulation. Oxygenated blood from the placenta (umbilical venous blood, with a partial pressure of oxygen [Po2] of 30-35 mm Hg) bypasses the liver via the ductus venosus and mixes with deoxygenated blood from the lower body in the inferior vena cava (IVC). This mixed blood enters the right atrium and is preferentially directed across the **foramen ovale** into the left atrium, supplying the left ventricle and, subsequently, the ascending aorta, which perfuses the brain and upper body. In contrast, deoxygenated blood from the superior vena cava (SVC) flows into the right ventricle and is ejected into the pulmonary artery. Due to high pulmonary vascular resistance, most of this blood bypasses the lungs via the **ductus arteriosus**, entering the descending aorta to perfuse the lower body and return to the placenta [1, 2].

At birth, the transition to postnatal circulation involves the closure of these fetal shunts. The **foramen ovale** closes as left atrial pressure increases, and the **ductus arteriosus** constricts due to rising oxygen levels. However, in some infants, these shunts fail to close, leading to congenital heart defects (CHDs) such as **atrial septal defect (ASD)**, **ventricular septal defect (VSD)**, and **patent ductus arteriosus (PDA)**. These defects result in **left-to-right shunts**, causing volume overload and potential complications such as congestive heart failure, failure to thrive, and pulmonary hypertension if left untreated [3, 4].

The severity of these shunts is quantified by the **Qp/Qs ratio**, which measures the ratio of pulmonary to systemic blood flow. Echocardiography is the primary diagnostic tool for assessing shunt severity, but it has limitations, particularly in resource-limited settings where access to skilled cardiologists and advanced imaging facilities is scarce [5, 6]. In such scenarios, biomarkers like **N-terminal pro-B-type natriuretic peptide (NT-proBNP)** offer a promising alternative. NT-proBNP is released by ventricular cardiomyocytes in response to volume overload and myocardial stretching, making it a sensitive marker for cardiac stress and shunt severity [7, 8].

Despite its potential, **no Indian reference ranges or cut-off points** have been established for NT-proBNP levels in relation to shunt severity in children with acyanotic CHD. This study aims to address this gap by establishing a correlation between serum NT-proBNP levels and the Qp/Qs ratio, providing a cost-effective and accessible tool for early diagnosis and intervention in resource-limited settings [9, 10].

As fetal echocardiogram became widely available, prenatal diagnosis of critical CHD became possible [3]. This resulted in the ability to individualize care and improve outcomes. Despite these advances, not all CHDs are diagnosed before birth. In a recent study, the prevalence of CHD determined by echocardiography screening at birth was higher and more accurate than that obtained from birth defect registries [4].

Natriuretic Peptides (NPs) and Their Role

Natriuretic peptides (NPs) are key proteins that improve and regulate circulation. They are essential proteins that act on blood vessels, causing them to widen or dilate [1]. These peptides are expressed predominantly by cardiomyocytes of the mixed secretory-contractile phenotype in atrial and ventricular walls. In addition to regulating blood pressure, NPs inhibit cardiac hypertrophy and remodeling [2].

Discovery and Role of B-Type Natriuretic Peptide (BNP)

The B-type natriuretic peptide (BNP) was initially identified in porcine brain tissue in 1988 and was previously referred to as the "brain natriuretic peptide." Later, researchers determined that the primary site of its release is cardiac ventricular cells, particularly in response to ventricular distention [5]. Following this discovery, abundant literature emerged regarding the utilization of BNP as a potential biomarker to measure the presence and severity of heart failure [6].

Physiological Actions of Natriuretic Peptides

The natriuretic peptides, including BNP, ANP, and proBNP, are secreted primarily by atrial and ventricular cardiomyocytes in response to stretching. They have vasodilatory and natriuretic actions, along with inhibition of the renin-angiotensin-aldosterone system (RAAS) and cardiac sympathetic activity. They are established as

the most powerful markers for heart failure diagnosis and prognosis across a spectrum of cardiovascular diseases [17, 18].

Need of the Study:

The aim is to establish a reference range of NT-proBNP with the severity of shunt in acyanotic congenital heart diseases. No Indian reference ranges or cut-off points have been established yet for the classification of shunt severity (mild, moderate, severe) in CHDs. Since the quantity of shunt is not always perfectly determined by echocardiography and there is an immense shortage of cardiologists in the country, especially in rural areas, we aimed to evaluate whether the serum level of BNP can be used as a screening marker for determining the amount and severity of left-to-right shunt in patients with VSD, ASD, PDA, and other acyanotic conditions, thus establishing a cut-off point for surgical intervention as well [19, 20]. It would also serve as a good way to triage patients for echocardiography. Determining the severity of the shunt can help prevent morbidities and also reduce the overall burden of infant CHDs progressing into adulthood without treatment [21].

Congenital heart disease (CHD) is one of the most common congenital anomalies, with a birth prevalence of approximately **9 per 1000 live births** in India. This translates to an estimated **240,000 children born with CHD annually**, of whom about **20% require early intervention** to survive the first year of life [15, 16]. Despite advances in diagnostic and therapeutic techniques, a significant proportion of children with CHD, especially in rural and resource-limited settings, remain undiagnosed or untreated. This leads to preventable complications such as **congestive heart failure**, **failure to thrive**, and **Eisenmenger syndrome**, which significantly impact the quality of life and survival of affected children [15, 16].

The severity of left-to-right shunts in acyanotic CHD, quantified by the **Qp/Qs ratio**, is a critical determinant of disease progression and the need for surgical intervention. However, accurate assessment of shunt severity using **echocardiography** can be challenging, particularly in resource-limited settings where there is a **shortage of skilled cardiologists and diagnostic facilities** [5, 6]. This often results in delayed diagnosis and intervention, leading to poorer outcomes for children with CHD. In such settings, a simple and accessible biomarker for shunt severity could play a crucial role in improving early diagnosis and timely management.

Natriuretic peptides, particularly **N-terminal pro-BNP (NT-proBNP)**, have emerged as powerful biomarkers for assessing cardiac volume overload and heart failure. However, **no Indian reference ranges or cut-off points** have been established for NT-proBNP levels in relation to shunt severity in children with acyanotic CHD [17, 18]. This gap in knowledge limits the utility of NT-proBNP as a screening tool in Indian populations, where the burden of CHD is particularly high. Establishing such reference ranges would enable the use of NT-proBNP as a reliable biomarker for shunt severity, particularly in resource-limited settings.

In India, there is a stark disparity in access to specialized cardiac care, with **one cardiac center serving 16 million people** in Asia compared to **one center serving 120,000 people** in North America [15, 16]. Additionally, there is a severe shortage of pediatric cardiologists, with **one cardiac surgeon per 25 million population** in Asia compared to **one per 3.5 million** in North America [3]. In such settings, NT-proBNP could serve as a **cost-effective and accessible biomarker** for triaging patients and determining the need for further diagnostic evaluation or surgical intervention. This would help prioritize high-risk patients for echocardiography and surgical intervention, ensuring optimal utilization of limited resources.

Early identification of children with severe left-to-right shunts and timely surgical intervention can prevent complications such as **congestive heart failure**, **failure to thrive**, pulmonary hypertension and **Eisenmenger syndrome** [19, 20]. By establishing a correlation between NT-proBNP levels and shunt severity, this study aims to provide a reliable tool for early diagnosis and intervention, thereby improving outcomes for children with acyanotic CHD. This is particularly important in regions with limited access to specialized cardiac care, where delayed diagnosis and intervention are common.

A significant proportion of children with CHD in India, particularly in rural and underserved areas, go untreated due to delayed diagnosis and lack of access to specialized care. By providing a **simple and accessible biomarker** for shunt severity, this study could help reduce the burden of untreated CHD and improve the overall quality of life for affected children [15, 16]. Furthermore, NT-proBNP has the potential to serve as a **screening tool** for triaging patients for echocardiography, particularly in settings where access to advanced diagnostic facilities is limited. This would ensure that high-risk patients receive timely evaluation and intervention, ultimately reducing the burden of CHD in India.

The need for this study arises from the **high prevalence of CHD in India**, the **challenges in diagnosing shunt severity**, the **lack of Indian reference ranges for NT-proBNP**, and the **resource limitations in rural and underserved areas**. By establishing a correlation between NT-proBNP levels and shunt severity, this study aims to provide a **cost-effective and accessible tool** for early diagnosis and intervention, ultimately improving outcomes for children with acyanotic CHD and reducing the burden of untreated disease.

Significance of study

Outline of dissertation:

To establish the correlation between serum NT-PRO Brain Natriuretic Peptide levels and left-to-right shunt severity (Qp/Qs ratio) in children with acyanotic congenital heart disease – A cross-sectional study. Dr. _____, PG Resident, KLE Academy of Higher Education and Research, Belagavi. **Guide**: Dr. _____, Professor, Department of Paediatrics, KLE Academy of Higher Education and Research, Jawaharlal Nehru Medical College, Belagavi. **Institution**: KLE Academy of Higher Education and Research, Jawaharlal Nehru Medical College, Belagavi. This study aims to correlate NT-PRO BNP levels with the severity of left-to-right shunts (Qp/Qs ratio) in children with acyanotic congenital heart disease. By exploring this relationship, the study seeks to validate NT-PRO BNP as a potential biomarker for assessing disease severity and guiding clinical management in pediatric cardiology. The study will include children with acyanotic CHD, measuring NT-PRO BNP levels and the Qp/Qs ratio to evaluate the correlation between these two parameters.

AIMS AND OBJECTIVES

Aim of the Study:

The aim of this study is to **establish a correlation between serum NT-proBNP levels and the severity of left-to-right shunt (Qp/Qs ratio)** in children with acyanotic congenital heart disease (ASD, VSD, PDA, and other acyanotic conditions). Additionally, the study aims to **determine a cut-off point for surgical intervention** based on NT-proBNP levels, which could serve as a screening tool in resource-limited settings.

Objectives of the Study:

1. **Primary Objective:**

To establish a correlation between serum NT-proBNP levels and the severity of left-to-right shunt (Qp/Qs ratio) in children with acyanotic congenital heart disease (ASD, VSD, PDA, and other acyanotic conditions) based on echocardiographic and hemodynamic evaluations.

2. **Secondary Objective:**

To determine a cut-off point for surgical intervention in children with acyanotic congenital heart disease based on serum NT-proBNP levels.

REVIEW OF LITERATURE

Fetal Circulation

The transition from fetal to postnatal circulation is one of the most dramatic physiological adaptations in human life. In the fetal circulation, the **right and left ventricles** operate in a **parallel circuit**, unlike the **series circuit** seen in newborns or adults. This parallel arrangement is maintained by three key fetal structures: the **ductus venosus**, **foramen ovale**, and **ductus arteriosus**. The **placenta** serves as the primary organ for gas and metabolite exchange, while the **lungs**, which are non-functional in utero, receive minimal blood flow due to high **pulmonary vascular resistance (PVR)**. Blood is diverted away from the pulmonary circulation, ensuring efficient oxygen delivery to the developing fetus [1, 2].

Oxygenated blood from the placenta enters the fetus via the **umbilical vein**, with a partial pressure of oxygen (Po2) of **30-35 mm Hg**. Approximately 50% of this blood flows into the **hepatic circulation**, while the remainder bypasses the liver through the **ductus venosus**, mixing with deoxygenated blood from the lower body in the **inferior vena cava (IVC)**. This combined blood flow (Po2 of **26-28 mm Hg**) enters the **right atrium** and is preferentially directed across the **foramen ovale** into the **left atrium** by the **eustachian valve**. This pathway ensures that the most oxygenated blood reaches the **left ventricle (LV)**, which supplies the **ascending aorta** and perfuses the **brain** and **upper body** [3, 4].

In contrast, deoxygenated blood from the **superior vena cava (SVC)** (Po2 of **12-14 mm Hg**) enters the **right atrium** and flows across the **tricuspid valve** into the **right ventricle (RV)**. From the RV, blood is ejected into the **pulmonary artery**, but due to

high PVR, only about **5%** enters the lungs. The majority bypasses the lungs via the **ductus arteriosus**, flowing into the **descending aorta** to perfuse the **lower body** and return to the placenta via the **umbilical arteries**. This arrangement ensures that the **upper body** receives blood with a higher Po2 than the **lower body**, which is primarily supplied by the RV [5, 6].

Changes in Circulation After Birth

The transition from fetal to postnatal circulation involves a shift of gas exchange from the **placenta** to the **lungs**. This transition is marked by several key changes:

1. **Closure of the Placental Circulation**:
    - The removal of the placenta leads to an **increase in systemic vascular resistance (SVR)**, as the placenta, which had the lowest vascular resistance in the fetus, is no longer part of the circulation.
    - The cessation of umbilical venous flow results in the **closure of the ductus venosus** [9, 10].
2. **Establishment of Pulmonary Circulation**:
    - Lung expansion at birth causes a **rapid fall in pulmonary vascular resistance (PVR)** due to the vasodilating effect of oxygen on the pulmonary vasculature. This leads to an **increase in pulmonary blood flow** and a **fall in pulmonary artery (PA) pressure**.
    - The **foramen ovale** closes functionally as **left atrial (LA) pressure** exceeds **right atrial (RA) pressure**, which falls due to the closure of the ductus venosus.

- The **ductus arteriosus** closes in response to increased arterial oxygen saturation, completing the transition to postnatal circulation [11, 12].

3. **Pulmonary Vascular Resistance (PVR)**:

   - At birth, PVR is as high as SVR due to the thick smooth muscle layer in the pulmonary arterioles and alveolar hypoxia from collapsed lungs.
   - With lung expansion and increased oxygen tension, PVR falls rapidly, followed by a slower decline over the first **6-8 weeks** as the medial layer of pulmonary arterioles thins.
   - A further decline in PVR occurs after the first **two years**, associated with the growth of alveolar units and their associated vessels [13, 14].

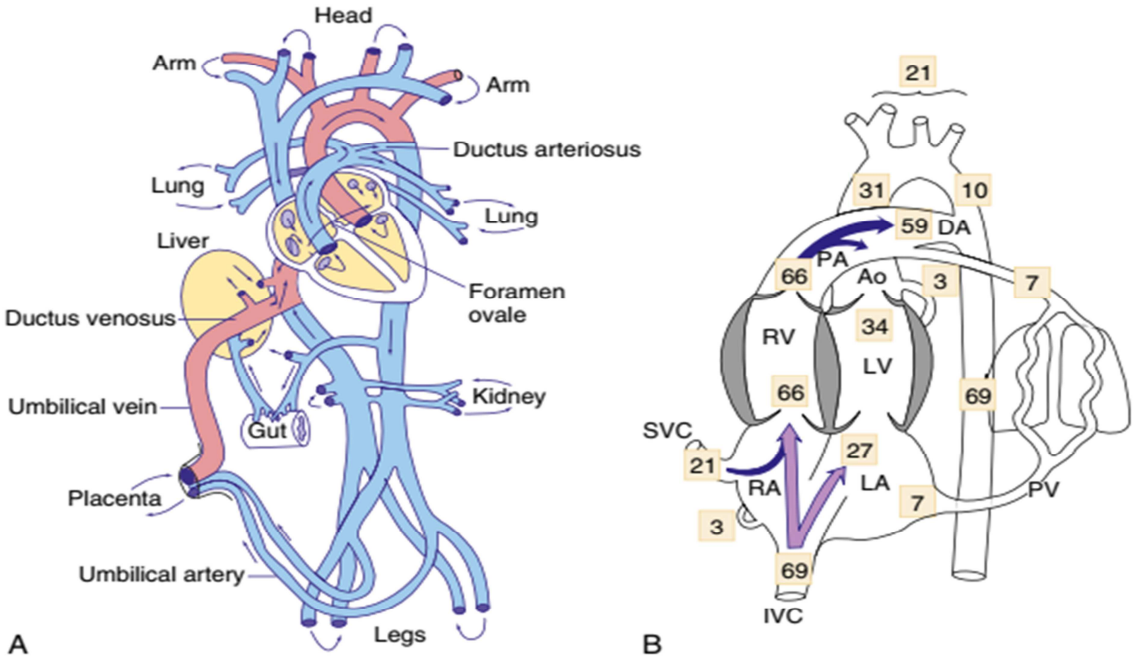


Fig: A The human circulation before birth. Red indicates more highly oxygenated blood, and arrows indicate the direction of flow. More highly oxygenated blood from the placenta passes through the foramen ovale from the right to the left atrium, thus bypassing the lungs. B, Percentages of combined ventricular output that return to the fetal heart, that are ejected by each ventricle, and that flow through the main vascular channels. Ao, Aorta; DA, ductus arteriosus; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; PA, pulmonary artery; PV, pulmonary veins; RA, right atrium; RV, right ventricle; SVC, superior vena cava. (From Rudolph AM. Congenital Diseases of the Heart. Chicago.)

CLASSIFICATION of CONGENITAL HEART DISEASES:

Acyanotic Congenital Heart Defect

Acyanotic CHD can be further subdivided into obstructive lesions (e.g., pulmonic stenosis, aortic stenosis, coarctation of the aorta) and lesions characterized by left-to-right shunting with an associated increase in pulmonary blood flow (e.g., VSDs, ASDs, patent ductus arteriosus, endocardial cushion defects).

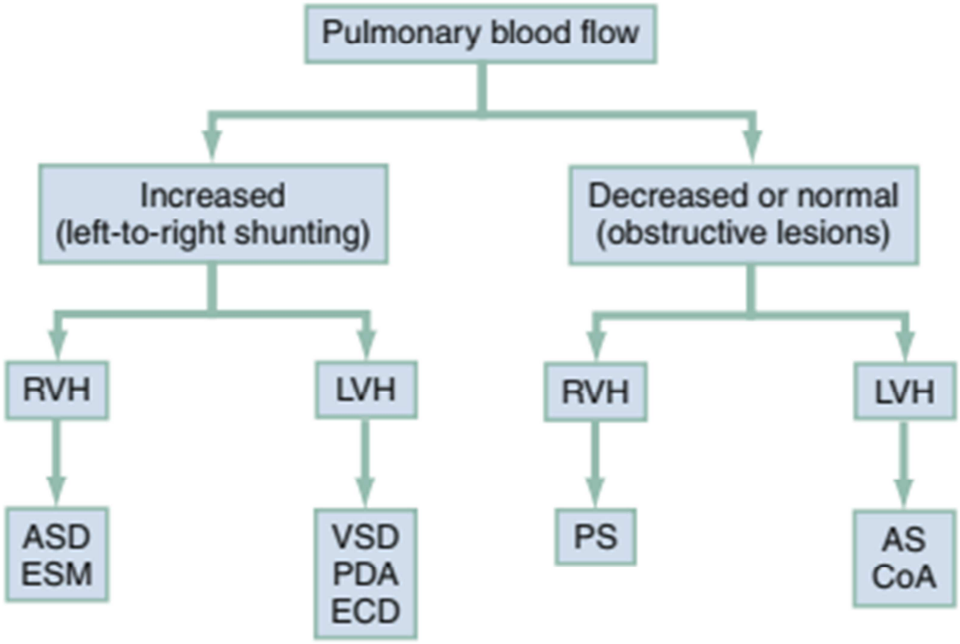


Fig. Clinical clues to diagnosis of acyanotic congenital heart defects. AS, Aortic stenosis; ASD, atrial septal defect; CoA, coarctation of the aorta; ECD, endocardial cushion defect; ESM, Eisenmenger syndrome; LVH, left ventricular hypertrophy; PDA, patent ductus arteriosus; PS, pulmonic stenosis; RVH, right ventricular hypertrophy; VSD, ventricular septal defect.

Cyanotic Congenital Heart Diseases

Cyanotic CHDs are a result of either decreased pulmonary blood flow to the lungs or right-to-left shunting of desaturated blood directly into the systemic circulation.The classic cyanotic CHDs can be remembered by the five Ts: truncus arteriosus, transposition of the great arteries, tricuspid atresia, Tetralogy of Fallot, and total anomalous pulmonary venous return. Other forms of cyanotic CHD include Ebstein anomaly, pulmonary atresia, severe pulmonary stenosis, hypoplastic left heart syndrome, and hypoplastic right heart syndrome. Many of these cyanotic heart lesions are routinely detected either on prenatal ultrasound or in the nursery.

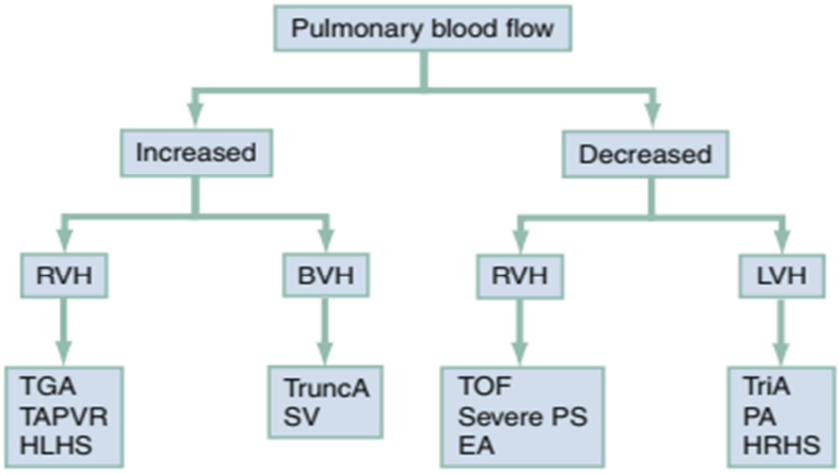
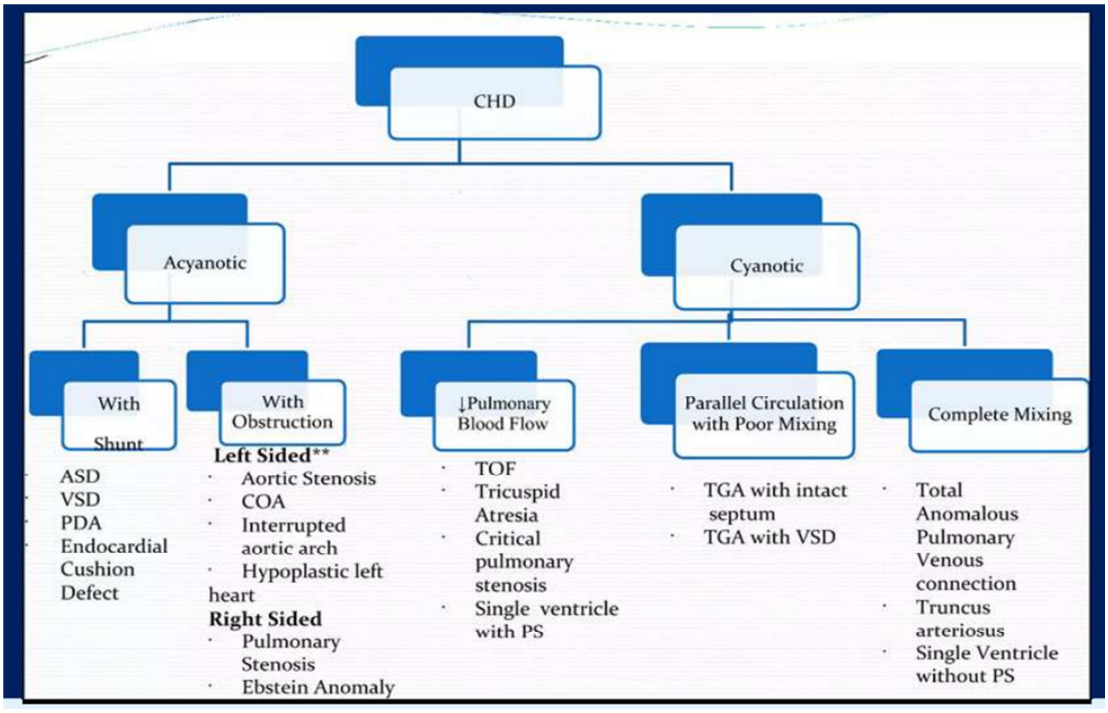


Fig. Clinical clues to diagnosis of cyanotic congenital heart defects. BVH, Biventricular hypertrophy; EA, Ebstein anomaly; HLHS, hypoplastic left heart syndrome; HRHS, hypoplastic right heart syndrome; LVH, left ventricular hypertrophy; PA, pulmonary atresia; PS, pulmonary stenosis; RVH, right ventricular hypertrophy; SV, single ventricle; TAPVR, total anomalous pulmonary venous return; TGA, transposition of the great arteries; TOF, Tetralogy of Fallot; TriA, tricuspid atresia; TruncA, truncus arteriosus.



ATRIAL SEPTAL DEFECT

Interatrial communication refers to defects in the atrial septum, and the forms of atrial septal defects (ASDs) are classified based on their location. Ostium primum defects occur when the anterior and posterior endocardial cushions fail to fuse with the septum primum, resulting in a deficiency in the lower portion of the septum primum. Ostium secundum defects, the most common type of ASD, arise from the failure of the septum primum to fuse with the septum secundum. These defects can occur anywhere along the septum but are typically found in the mid-portion of the atrial septum, near the fossa ovalis [1, 2].

Sinus venosus defects are located at the junction of the right atrium with the superior vena cava or inferior vena cava. In this defect, a left-to-right shunt occurs through an opening in the wall between the pulmonary veins and the right atrium. Most commonly, this involves a deficiency in the anterior wall of the right upper pulmonary

vein, allowing it to drain into the right atrium while remaining anatomically connected to the left atrium.

Coronary sinus septal defects, also known as unroofed coronary sinus, involve an abnormal communication between the wall of the coronary sinus and the left atrium, resulting in a left-to-right shunt. These defects are often associated with a persistent left superior vena cava. Iatrogenic atrial septal defects (iASD) are procedural complications arising from interventions requiring transseptal puncture, such as electrophysiology studies or structural cardiac procedures [5, 6].

ASDs should be distinguished from a patent foramen ovale (PFO), which occurs due to the failure of the septum primum to fuse with the superior limb of the septum secundum after birth. While ASDs are congenital defects resulting from abnormal atrial septal development during fetal life, a PFO represents the persistence of an anatomical defect that fails to close postnatally. PFOs are found in approximately 20% to 25% of the normal adult population [7, 8].

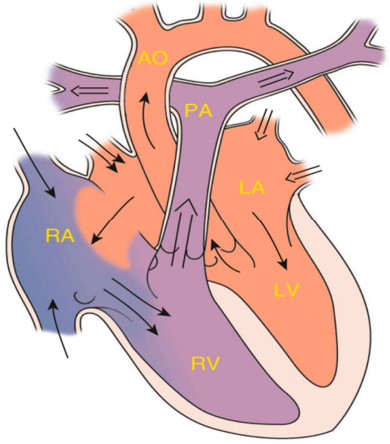


FIG. Atrial septal defect. AO , Aorta; LA , left atrium; LV , left ventricle; PA , pulmonary artery; RA , right atrium; RV , right ventricle.

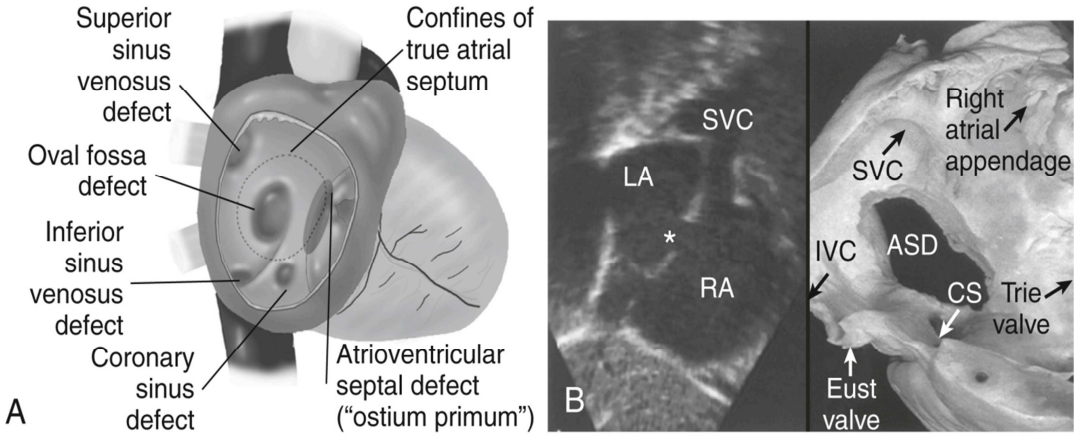


FIG. A, Schematic diagram outlining the different types of interatrial shunting that can be encountered. Note that only the central defect is suitable for device closure. B, Subcostal right anterior oblique view of a secundum atrial septal defect (ASD) (asterisk) that is suitable for device closure. CS, Coronary sinus; IVC, inferior vena cava; LA, left atrium; RA, right atrium; SVC, superior vena cava.

Findings and Presentation of Atrial Septal Defect (ASD)

Clinical Presentation

The majority of **atrial septal defects (ASDs)** are small and asymptomatic during infancy. However, most individuals become symptomatic at some point, and the age of symptom onset is not solely related to the size of the shunt. In older infants and children, characteristic findings include a **widely split and fixed S2** and a **grade 2 to 3 of 6 systolic ejection murmur**. In cases of large left-to-right shunts, a **mid-diastolic rumble** due to relative tricuspid stenosis may be audible at the lower left sternal border. Classic auscultatory, electrocardiographic (ECG), and radiographic findings are typically absent in infants and toddlers, even with large defects, due to

poor right ventricular (RV) compliance. These findings usually become apparent only when the shunt is significant (Qp/Qs ratio ≥ 1.5) [1, 2].

Spontaneous Closure and Natural History

Small ASDs or **patent foramen ovale (PFO)** may close spontaneously during infancy. However, infants with large ASDs may develop **heart failure**, **recurrent respiratory infections**, or **failure to thrive**. Earlier studies reported spontaneous closure rates of **14% to 55%** in the first four years of life, with more recent studies suggesting an overall closure rate of **87%**. ASDs smaller than **3 mm** diagnosed before **3 months of age** close spontaneously in **100%** of cases by **1.5 years of age**, while defects between **3 and 8 mm** close spontaneously in **over 80%** of cases. ASDs larger than **8 mm** rarely close spontaneously, and spontaneous closure is unlikely after **4 years of age** [3, 4].

Electrocardiography (ECG)

Typical ECG findings in ASD include **right axis deviation** (+90 to +180 degrees) and **mild right ventricular hypertrophy (RVH)** or **right bundle branch block (RBBB)** with an **rsR′ pattern in V1**. These findings are more common in cases with significant shunts [5, 6].

Radiography

Chest radiography may reveal **cardiomegaly** with enlargement of the **right atrium (RA)** and **right ventricle (RV)**. A **prominent pulmonary artery (PA) segment** and **increased pulmonary vascular markings** are seen in cases with significant shunts [7, 8].

Echocardiography

Two-dimensional echocardiography is the diagnostic modality of choice for ASD. It provides detailed visualization of the defect's **position** and **size**, best seen in the **subcostal four-chamber view**. Indirect signs of a significant left-to-right shunt include **RV enlargement**, **RA enlargement**, and a **dilated PA**, often accompanied by increased flow velocity across the pulmonary valve [9, 10].

Management

- **Medical Management**: In infants with **congestive heart failure (CHF)**, medical management with diuretics is recommended due to its high success rate and the possibility of spontaneous closure.
- **Nonsurgical Closure**: Catheter-delivered closure devices are the preferred method. Closure rates are excellent.
- **Surgical Closure**: Surgical intervention is indicated when device closure is not feasible. A **Qp/Qs ratio ≥ 1.5** is a common surgical indication. Surgery is typically delayed until **2 to 4 years of age** to allow for the possibility of spontaneous closure. However, if CHF is unresponsive to medical management, surgery may be performed during infancy [11, 12].

Long-Term Outcomes

Most children with ASD remain active and asymptomatic. However, untreated large defects can lead to **CHF** and **pulmonary hypertension** in adulthood, particularly in individuals in their **20s and 30s**, with symptoms becoming more common after **40 years of age** [13, 14].

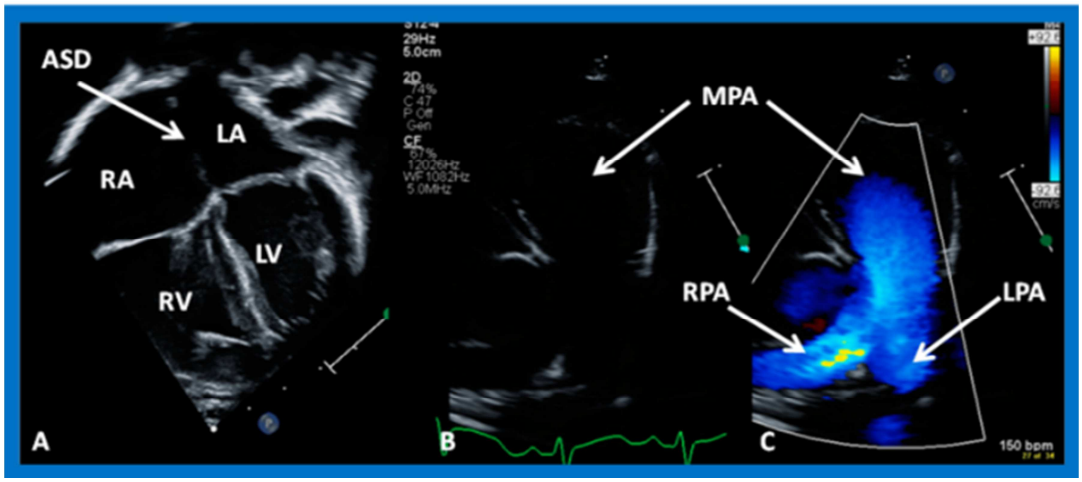
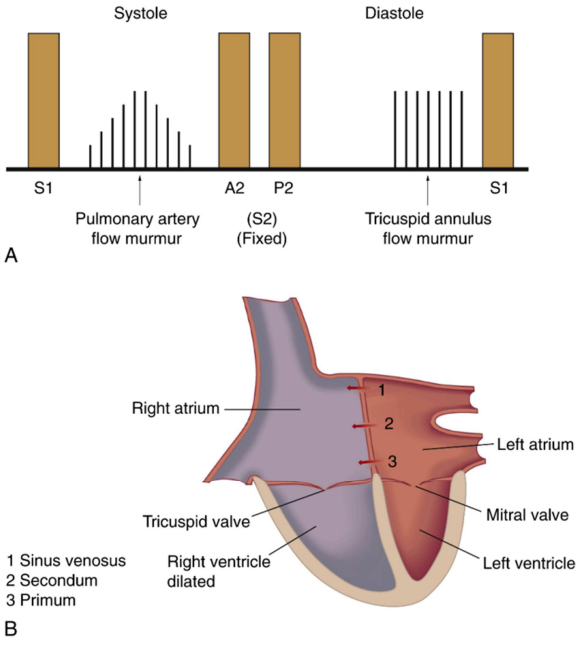


Figure 1. Echo images from apical four chamber (**A**) and precordial short axis (**B**,**C**) projections of a child with an atrial septal defect (ASD) demonstrating dilation of the right atrium (RA), right ventricle (RV) (**A**) and pulmonary arteries (**B**,**C**). LA, left atrium; LV, left ventricle; LPA, left pulmonary artery; MPA, main pulmonary artery; RPA, right pulmonary artery.

FIG. Atrial septal defect. A, Murmur at the left sternal edge. B, Anatomy.



Ventricular Septal Defect (VSD)

Definition and Epidemiology

A **ventricular septal defect (VSD)** is a defect in the interventricular septum that creates a communication between the **right and left ventricles**. VSDs are the **most common congenital cardiac defect**, with an incidence ranging from **0.3 to 7.7 per 1000 live births**, and account for approximately **30% of congenital cardiac defects worldwide** [1, 2].

Classification

VSDs are classified based on their location within the interventricular septum:

1. **Perimembranous (Paramembranous)**:
    - Located adjacent to the membranous portion of the septum. Most common type, accounting for **70%-80%** of all VSDs.
2. **Supracristal (Outlet, Conal, or Subpulmonary)**:
    - Found in the infundibular component of the muscular septum below the pulmonary valve. Accounts for **5%-8%** of VSDs in Western countries but is more common in Asian populations (**21%-30%**).
3. **Inlet (Atrioventricular Canal)**:
    - Located posteriorly at the inlet region of the right ventricular septum.
    - Often associated with **atrioventricular septal defects**. Accounts for **5%** of VSDs.

4. **Muscular**:

    - Single or multiple defects in the lower muscular portion of the ventricular septum. Accounts for **20%** of VSDs.

Clinical Presentation

The clinical presentation of VSD depends on the **size of the defect** and the **level of pulmonary vascular resistance (PVR)**:

- **Small VSDs**:
    - A large resistance to the left-to-right shunt occurs at the defect, and the shunt is independent of PVR. Patients are often asymptomatic, with a **regurgitant systolic murmur** heard at the left lower sternal border.
- **Moderate VSDs**:
    - Result in **left ventricular (LV) enlargement** due to volume overload, while the **right ventricle (RV)** remains relatively normal in size. A **mid-diastolic rumble** at the apex may be heard due to relative mitral stenosis. Radiography may show **enlargement of the main pulmonary artery (PA)**, **left atrium (LA)**, and **LV**, along with **increased pulmonary vascular markings**.
- **Large VSDs**:
    - The left-to-right shunt depends largely on PVR. In newborns, PVR remains elevated, so significant shunting typically occurs at **6 to 8 weeks of age**, when PVR decreases.

- This can lead to **congestive heart failure (CHF)** and symptoms such as **failure to thrive** and **recurrent respiratory infections** [5, 6].

Electrocardiography (ECG)

In moderate VSDs, the **LV** undergoes volume overload, leading to **LV enlargement**, while the **RV** is not significantly affected.[7, 8]

Radiography

Chest radiography in patients with moderate to large VSDs may reveal:

- **Cardiomegaly** with **LA and LV enlargement**.
- **Prominent pulmonary artery segment** and **increased pulmonary vascular markings** due to increased pulmonary blood flow [9, 10].

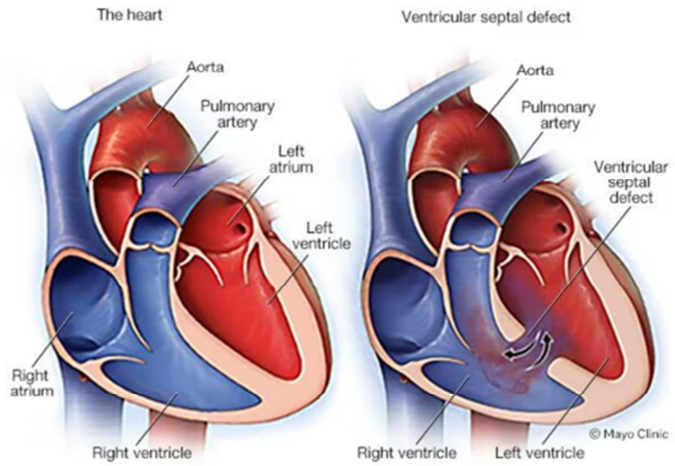
Echocardiography

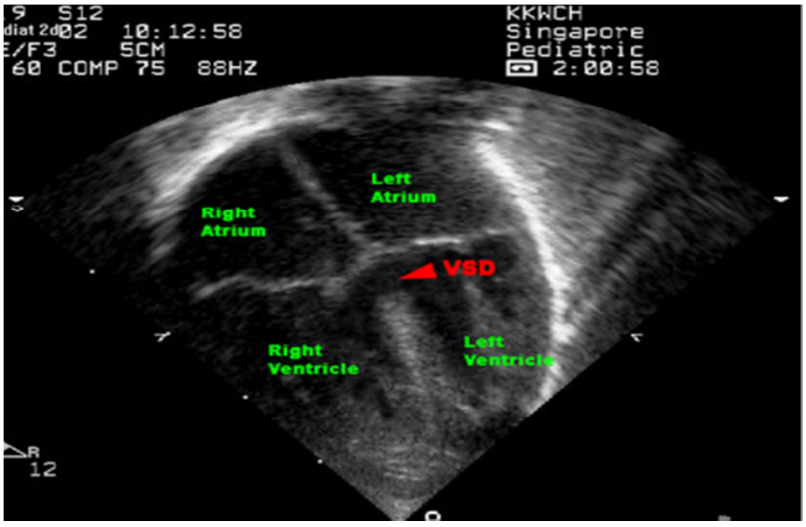
Two-dimensional echocardiography is the diagnostic modality of choice for VSD. It provides detailed visualization of the defect's **location** and **size**, as well as the hemodynamic impact of the shunt. Echocardiography can also assess associated abnormalities, such as **pulmonary hypertension** or **other congenital defects** [11, 12].

Management

- **Small VSDs**: Often require no intervention, as many close spontaneously.Regular follow-up is recommended to monitor for complications.

- **Moderate to Large VSDs**: Medical management with **diuretics** and **afterload reduction** may be used to manage symptoms of CHF. Surgical or catheter-based closure is indicated for large VSDs with significant shunting (Qp/Qs ratio ≥ 1.5) or complications such as **pulmonary hypertension** [13, 14].





PATENT DUCTUS ARTERIOSUS

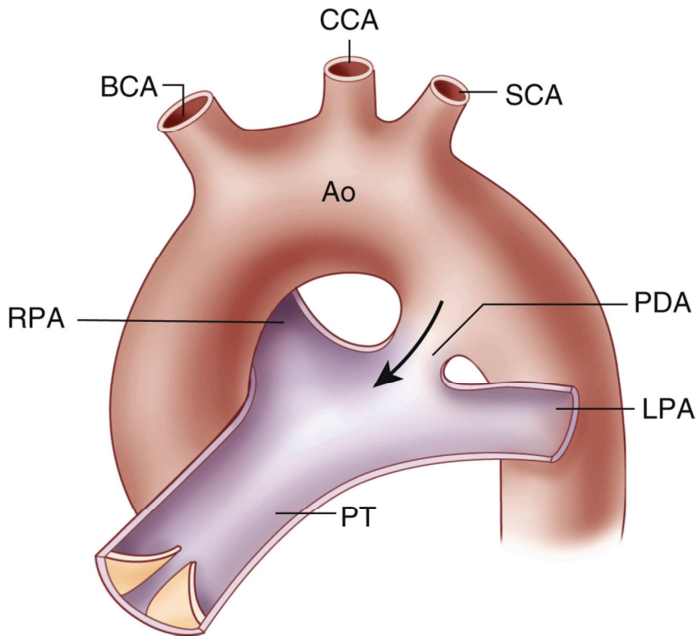


Fig.Anatomy of patent ductus arteriosus.

The ductus arteriosus (DA) is a fetal vascular communication that connects the proximal descending aorta and the main pulmonary artery. During fetal development, this connection allows right ventricular blood to bypass the nonfunctional fetal lungs (where there is high resistance) to the aorta and placental circulation (where there is lower resistance). Functional closure typically occurs within hours of delivery resulting from decreased pressure in the pulmonary circuit, then anatomically. The remnant of the ductus arteriosus is called the ligamentum arteriosum (also known as the ligament of Botallo or Harvey ligament), which serves no function. If a ductus fails to close within 72 h of birth in a full-term infant, this constitutes a patent ductus arteriosus (PDA). [5-6]

Functional, then anatomic, postnatal DA closure is driven by multiple mechanisms, including increased oxygen saturation, decreased levels of endogenous prostaglandins

and nitric oxide, and intimal proliferation and fibrosis. The size and length of the defect determine the severity of its hemodynamic effect.PDA is the third most common congenital abnormality. Prevalence is 2.9 per 10,000 live births. Incidence has increased due to improved survival of premature infants (especially those born < 30 wk of gestation).[7-8]

Physical Findings & Clinical Presentation

A PDA has a continuous, “machine-like” murmur that can be appreciated over the left scapula and in the left infraclavicular area in patients with left-to-right shunting.The murmur intensity increases throughout systole and ultimately peaks at the second heart sound at the termination of systole. Often, the increase in flow through the aortic valve produces a flow murmur appreciable at the right upper sternal border.

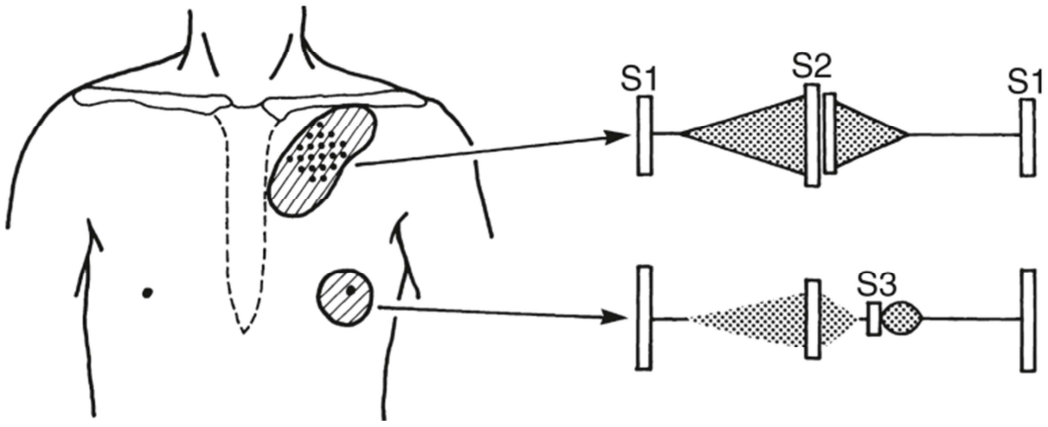


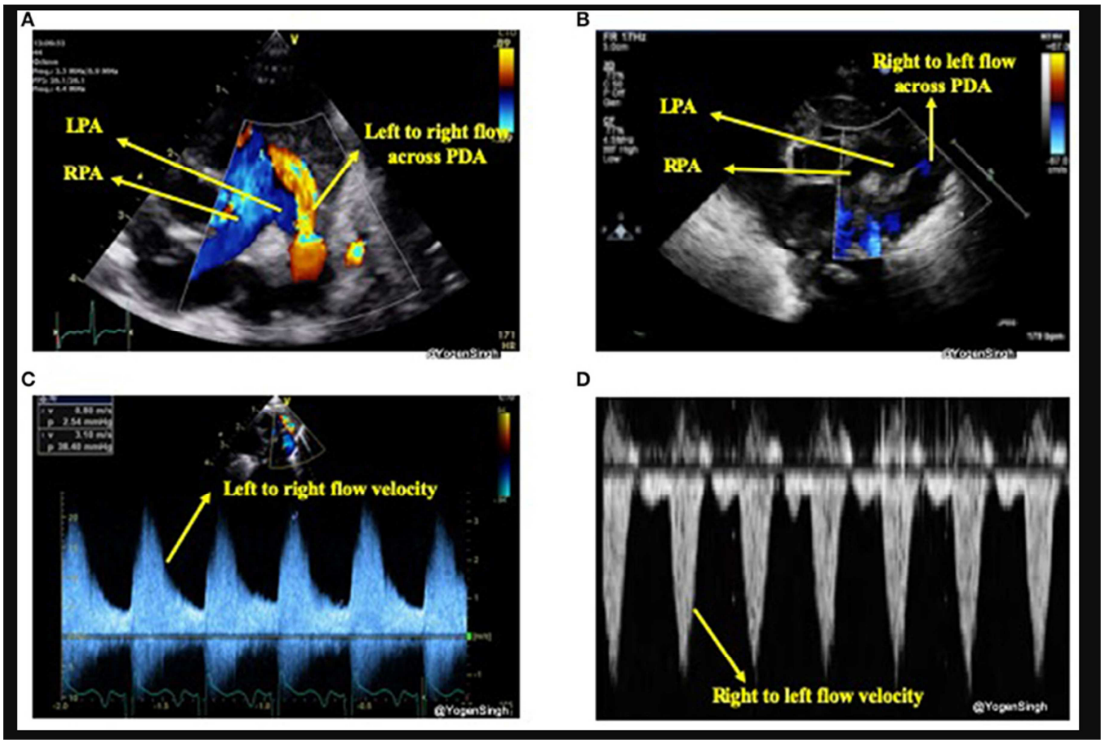
FIG. Cardiac findings of patent ductus arteriosus. A systolic thrill may be present in the area shown by dots.

- The apical impulse may be hyperdynamic if there is significant left-to-right shunting. Vital signs demonstrate a widened pulse pressure.

- S1 is normal. In the presence of pulmonary hypertension, S2 may be split with an accentuated P2 component.
- The hemodynamics of PDA are similar to those of VSD. The magnitude of the left-to right shunt is determined by the resistance offered by the ductus (i.e., diameter, length, and tortuosity) when the ductus is small and by the level of PVR when the ductus is large (i.e., dependent shunt). Therefore, the onset of CHF with PDA is similar to that with VSD.
- The chambers and vessels that enlarge are the same as those in VSD except for an enlarged aorta to the level of the PDA (i.e., enlarged ascending aorta and transverse arch), which also handles an increased amount of blood flow.
- Therefore, in PDA, chest radiographic films show enlargement of the LA and LV, a large ascending aorta and PA, and an increase in pulmonary vascular markings . Hemodynamic consequences of PDA are similar to those of VSD.
- In PDA with a small shunt, the LV enlargement is minimal; therefore, the ECG and chest radiographic findings are close to normal. Because there is a significant pressure gradient between the aorta and the PA in both systole and diastole, the left-to-right shunt occurs in both phases of the cardiac cycle, thereby producing the characteristic continuous murmur of this condition.
- With a small shunt, the intensity of the P2 is normal because the PA pressure is normal. In PDA with a moderately large shunt, the heart size is moderately enlarged with increased pulmonary blood flow. The chambers enlarged are the LA, LV, and PA segments.
- The ECG shows LVH as in moderate VSD. In addition to the characteristic continuous murmur, there may be an apical diastolic flow rumble as a result of

relative stenosis of the mitral valve. The P2 slightly increases in intensity if it can be separated from the loud heart murmur.[9-10]

- In a large PDA, marked cardiomegaly and increased pulmonary vascular markings are present. The volume overload is on the LV and LA, which produces LVH and occasional LAH on the ECG.
- The free transmission of the aortic pressure to the PA produces pulmonary hypertension and RV hypertension, with resulting RVH on the ECG.
- The continuous murmur is present, with an apical diastolic rumble owing to relative mitral stenosis. The P2 is accentuated in intensity due to pulmonary hypertension.
- An untreated large PDA can also produce pulmonary vascular obstructive disease, with a resulting bidirectional (i.e., right-to-left and left-to-right) shunt at the ductus level. The bidirectional shunt may produce cyanosis only in the lower half of the body (i.e., differential cyanosis).[11]



INTRODUCTION TO BNP:

B-type Natriuretic Peptide (BNP) has become a cornerstone in the field of cardiology, particularly in the diagnosis and management of heart failure. The discovery of BNP marked a significant advancement in understanding the complex hormonal regulation of cardiovascular homeostasis.

The History and Importance of BNP Molecule:

BNP, part of the natriuretic peptide family, was discovered in the late 20th century. The family also includes atrial natriuretic peptide (ANP), C-type natriuretic peptide (CNP), and urodilatin. This discovery marked a pivotal moment in cardiology, as it provided a new pathway for assessing heart function beyond traditional clinical measures.[5-6] B-type Natriuretic Peptide (BNP) is a hormone predominantly produced by the heart's ventricles in response to excessive stretching of heart muscle cells (cardiomyocytes) in response to increased cardiac wall stress, such as volume or pressure overload. BNP was first identified when researchers observed that certain cardiac peptides exhibited natriuretic (sodium-excreting) properties, similar to those of ANP.[5] However, BNP was distinct because it was primarily secreted by the

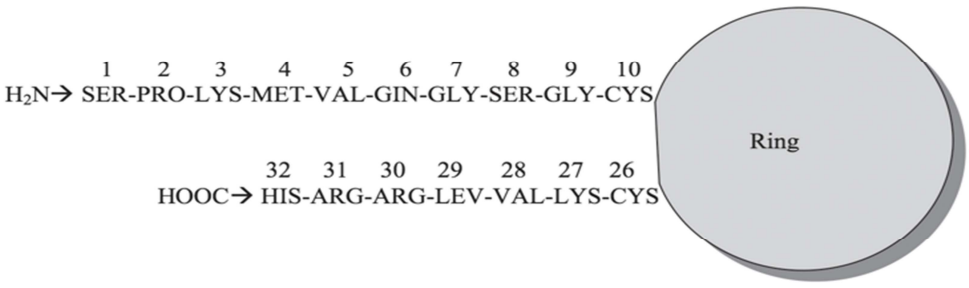


Figure. Schematic structure of B-type natriuretic peptide beginning at the *N*-terminal end and ending at the *C*-terminal, with amino acids 11 through 25 comprising the ring.

ventricles rather than the atria. Early studies established that BNP was released in response to ventricular volume expansion and pressure overload, common in heart failure patients. The peptide plays a critical role in cardiovascular homeostasis, exerting diuretic, natriuretic, and vasodilatory effects that help reduce the workload on the heart. Over the years, BNP has become a crucial biomarker in the diagnosis and management of various cardiovascular conditions, particularly heart failure. [6]

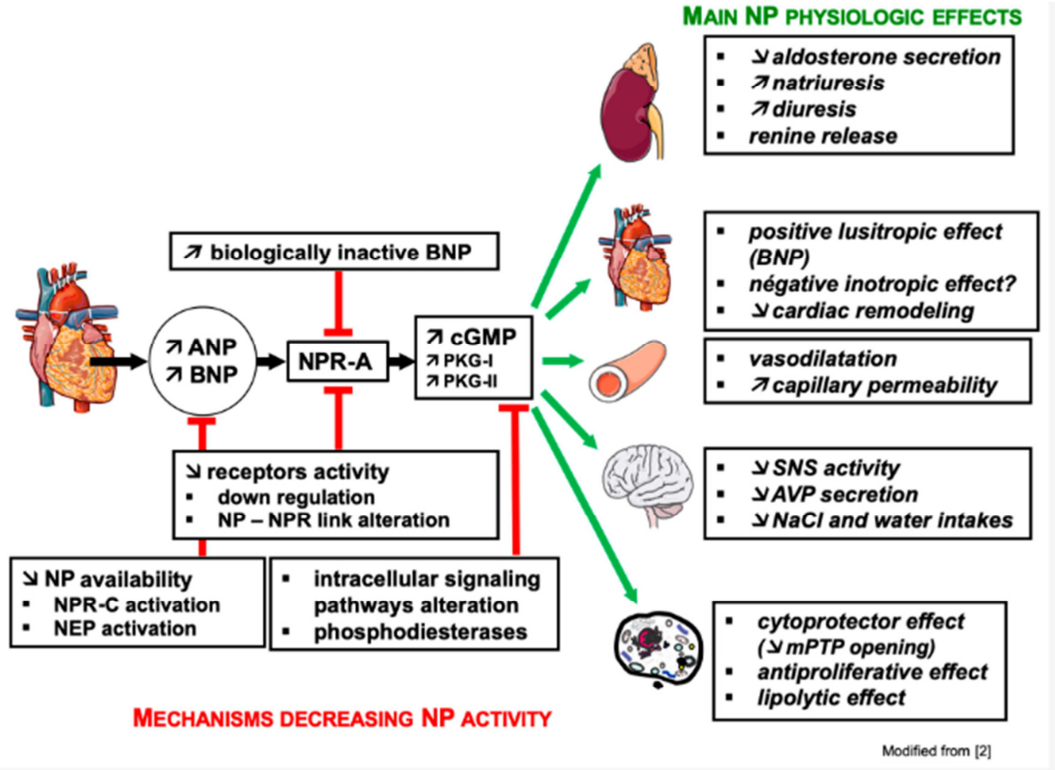
Structure and ***Function*** of BNP: [5-6]

They are essential proteins that act on blood vessels causing them to widen or dilate. These peptides are expressed predominantly by cardiomyocytes of the mixed secretory-contractile phenotype in atrial and ventricular walls. In addition to regulating blood pressure, NPs inhibit cardiac hypertrophy and remodelling. NPs can also be found in the kidneys and can cause this essential organ to excrete more water and salt. [5]

B-type natriuretic peptide (BNP) is a member of a family of natriuretic peptides (NP) that include atrial natriuretic peptide (ANP), C-type natriuretic peptide, D-type natriuretic peptide, and urodilatin. Pro-BNP is a 108–amino acid precursor protein of BNP found in the ventricles and atria of the heart.In situations of volume overload and myocardial muscle stretching, proBNP is upregulated at the genomic level.[6]

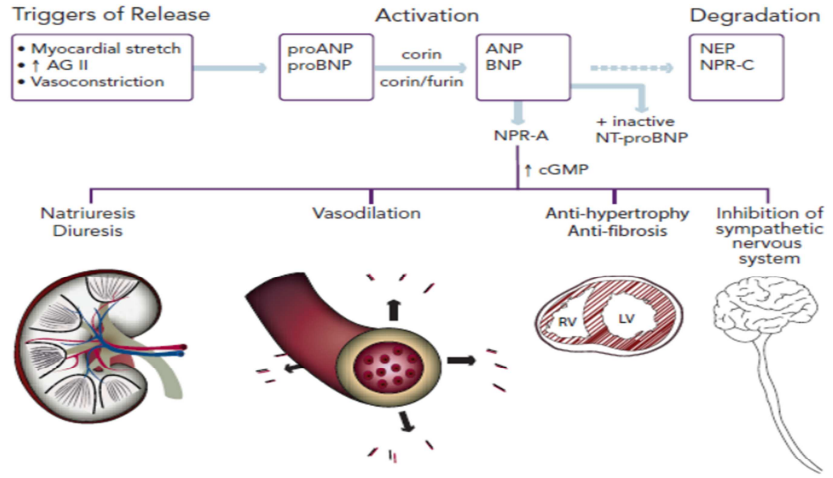
A small amount of BNP is found in the cytoplasmic granules of myocytes. Upon stimulation for production and release, proBNP is cleaved by corin to equimolar amounts of the biologically active BNP hormone and the biologically inactive amino-terminal proBNP (NT-proBNP)[5-6]

In conclusion, the gene for BNP encodes a precursor molecule, pre-proBNP, which undergoes cleavage to produce the active BNP and the inert NT-proBNP. These molecules have since been extensively studied, leading to their use as reliable indicators of heart function.



Notably, BNP was initially identified in the brain, which explains its name, but its role in heart function soon became evident. BNP is initially synthesized as a precursor molecule, pre-probnp, which is cleaved into probnp, and subsequently into active BNP and an inactive fragment known as NT-probnp. While BNP exerts the biological effects, NT-probnp serves as a diagnostic marker due to its longer half-life and stability in the bloodstream. BNP and its related peptide, NT-probnp, act by binding to natriuretic peptide receptors that lead to vasodilation, reduction in blood volume, and inhibition of the renin-angiotensin-aldosterone system (RAAS). These actions collectively decrease cardiac stress and improve heart function, making BNP a powerful valuable tool in managing heart conditions.[6-7]

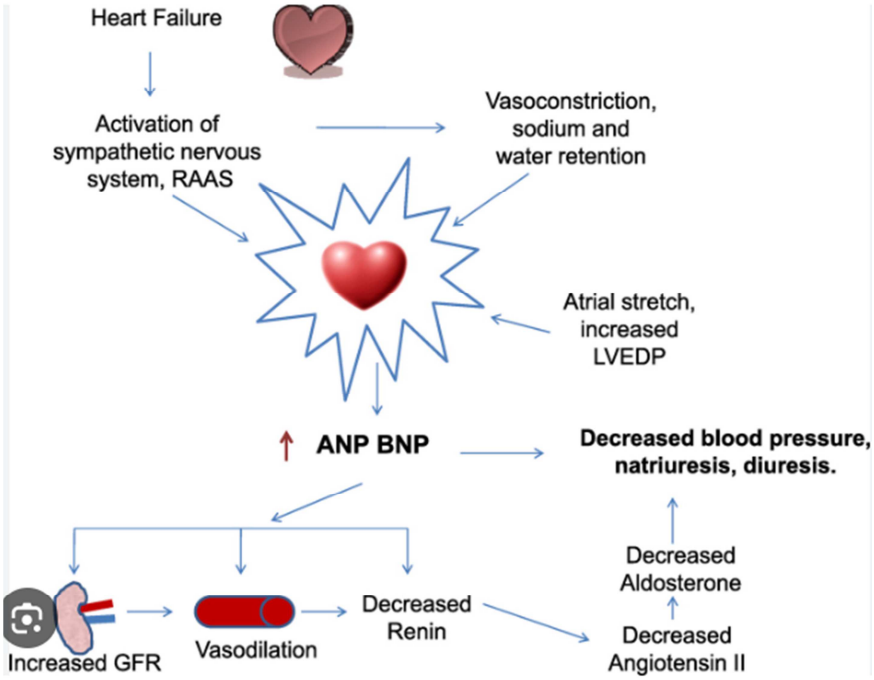
Figure 1: Basic Mechanism of ANP and BNP Cellular Processing



AG II = angiotensin II; ANP = atrial natriuretic peptide; BNP = B-type natriuretic peptide; LV = left ventricle; NEP = neutral endopeptidase 24.11; NPR-A = natriuretic peptide receptor A; NPR-C = natriuretic peptide receptor C; RV = right ventricle.

Clinical Applications

BNP and NT-probnp levels are now widely used in clinical practice to diagnose and monitor heart failure. Elevated BNP levels correlate with increased heart wall stress and are indicative of heart failure severity. In addition to heart failure, BNP levels are also useful in diagnosing other conditions, such as acute coronary syndrome, hypertension, and pulmonary embolism. The use of BNP and NT-probnp assays has transformed the diagnostic process for heart failure. In adults, these biomarkers offer a non-invasive, quick, and cost-effective method for evaluating patients presenting with dyspnoea (shortness of breath), aiding in distinguishing cardiac causes from pulmonary or other etiologies. Moreover, BNP levels also provide prognostic information, helping clinicians predict outcomes in patients with heart failure. Studies have shown that patients with higher BNP levels tend to have a poorer prognosis, with increased risk of hospitalization and mortality.[7]



Pathophysiology

Following systemic secretion, the natriuretic peptides activate transmembrane guanylate cyclases on the surface endothelial cells, thereby increasing intracellular levels of cyclic guanosine monophosphate (cGMP), leading to vasodilation. Other systemic effects include diuresis and natriuresis, resulting in lowered blood pressure. The peptides have also demonstrated the ability to antagonize adverse pathways that are over-activated in the setting of heart failure, for example, RAAS, which has anti-diuretic effects, and the transforming growth factor-beta pathway, which increases cardiac remodelling and fibrosis.[9]

Expression of the BNP gene is a feature of both atrial and ventricular myocytes. In the normal heart, the main site of BNP expression is in the atrial regions. Ventricular BNP gene expression increases drastically in cardiac diseases affecting the ventricles, such as heart failure (HF). Observing ventricular BNP gene expression in ventricular

disease may have given rise to the common statement that BNP is predominantly a ventricular hormone. However, atrial and ventricular myocytes differ considerably concerning their endocrine phenotypes, and it is reasonable to expect significant differences in peptide storage and secretion patterns. Atrial granules contain both intact precursors and biosynthetic end products, that is, bioactive ANP-28 and BNP-32. In contrast, normal ventricular myocytes do not seem to express such granules, and normal ventricular myocytes do not contain proBNP-derived peptides.[10-12]

The estimated half-life of BNP is about 20 minutes, whereas NT-proBNP has a half-life of 120 min; this difference explains why NT-proBNP serum levels are approximately six times higher than BNP levels, even though both molecules are released in equimolar proportions.

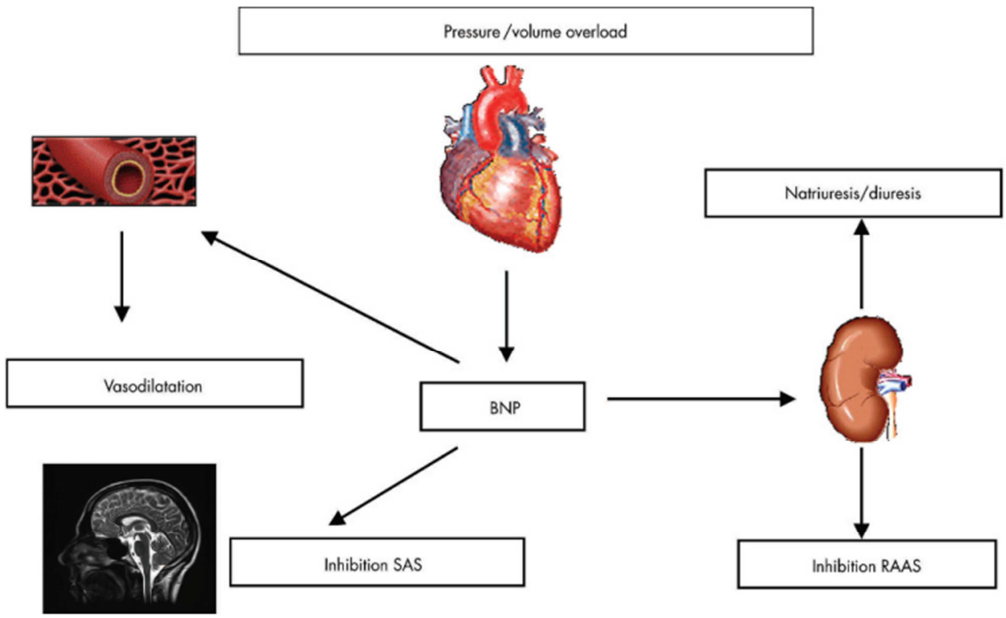


Figure: Physiological effects of B-type natriuretic peptide (BNP). Volume or pressure overload leads to ventricular wall stress and BNP release. The systemic biological effects of BNP are peripheral vasodilatation, increase in natriuresis and diuresis, and inhibition of the sympathetic nervous system (SNS) and the renin–angiotensin–aldosterone system (RAAS)

Collection Procedure:[12-13]

The b-type natriuretic peptide (BNP) is labile and must be collected into tubes containing EDTA and tested ideally within four hours of collection. Serum samples and citrated or heparinized plasma cannot be used. BNP can be stored for up to 24 hours at 2^oC to 8^oC for some assays. BNP is degraded by contact activation of the blood coagulation system and can be stabilized by storage under frozen conditions or by adding kallikrein protease inhibitors. In contrast, NT-proBNP is much more stable than BNP and can be kept at refrigerated temperatures for three days. NT-proBNP can be tested in serum and plasma collected in either heparin or EDTA.[12]

1…. Interfering Factors:

BNP and NT-proBNP levels may be affected by specific comorbidities, such as chronic renal failure, type 2 diabetes mellitus, obesity, and acute coronary syndrome (ACS). Levels are higher in patients with renal failure, diabetes, and ACS and lower in patients with obesity. Decreasing renal function with age may be partly responsible for the increase in BNP/NT-proBNP. In the absence of heart failure, the concentration of BNP/NT-proBNP increases in patients with a decreasing glomerular filtration rate.[12]

All immunoassays for BNP and NT-proBNP are heterogeneous, using a separation step between bound and free antibodies; there are no problems with photometric interferents such as hemoglobin, bilirubin, or lipemia.

Other situations in which natriuretic peptides are elevated include any disease that increases blood volume and thus wall stress, such as sepsis, Anaemia, renal

dysfunction, Cushing syndrome, hyperaldosteronism, hypertension with left ventricular hypertrophy, and cirrhosis.[13]

Relevance :

Identifying a biomarker that could assist in the diagnosis process was critical. BNP measurement is a highly sensitive, low-cost, and rapid test that can be utilized in hospitals to assist in diagnosing heart failure.

Integration with Echocardiography:

The role of BNP extends beyond mere diagnosis. It has been integrated into the echocardiographic assessment of cardiac function, providing a more comprehensive evaluation of heart failure patients. One of the key uses of BNP is its ability to guide the use of echocardiography in detecting asymptomatic left ventricular dysfunction. When BNP or NT-proBNP levels are intermediate, echocardiography helps improve the accuracy of heart failure diagnoses. The integration of BNP testing with echocardiography allows for better risk stratification, guiding decisions on interventions, especially in patients with valvular disease. BNP levels correlate with several echocardiographic parameters, including left ventricular ejection fraction, left ventricular mass, and diastolic function. This integrated approach enhances the accuracy of heart failure diagnosis and helps tailor treatment strategies more effectively.[13-14]

The discovery of BNP and its integration into clinical practice represents a significant advancement in cardiovascular medicine. BNP serves as a crucial biomarker for diagnosing, managing, and prognosticating heart failure, offering a non-invasive and reliable method for assessing cardiac function.[14]

Introduction to Echocardiography

Echocardiography (echo) is a cornerstone diagnostic tool in cardiology, utilizing ultrasound beams to visualize cardiovascular structures. It generates images in **one dimension (M-mode)**, **two dimensions (2D)**, or **three dimensions (3D)**, each offering unique insights into cardiac anatomy and function. Modern echocardiographic studies typically begin with **real-time 2D echo**, which provides high-resolution tomographic images of cardiac structures, their movement, and the vascular structures entering and leaving the heart. The integration of **Doppler imaging** and **color mapping** has further enhanced its diagnostic capabilities, enabling the detection of valve regurgitation, cardiac shunts, and the quantification of blood flow dynamics [1, 2].

A standard 2D echocardiographic examination involves directing the ultrasound beam along multiple cross-sectional planes through the heart and great vessels. Routine imaging is performed from four transducer locations: **parasternal**, **apical**, **subcostal**, and **suprasternal notch (SSN)**. From each position, long- and short-axis views are acquired by manually rotating and angulating the transducer. The **parasternal** and **apical** views are typically obtained with the patient in the **left lateral decubitus position**, while the **subcostal** and **suprasternal notch** views are acquired with the patient in the **supine position** [3, 4].

Echocardiography provides critical quantitative data, including **ventricular function**, **pressure gradients across cardiac valves and blood vessels**, and **estimations of pressures in the great arteries and ventricles**. In the context of congenital heart disease (CHD), echocardiography is indispensable for diagnosing structural abnormalities, assessing the severity of shunts (e.g., ASD, VSD, PDA), and

guiding treatment decisions. However, its utility can be limited in resource-constrained settings due to the need for skilled operators and advanced equipment [5, 6].

In this study, echocardiography will be used to measure the **Qp/Qs ratio**, a key parameter for quantifying the severity of left-to-right shunts in children with acyanotic CHD. This will be correlated with serum **NT-proBNP levels** to establish a biomarker-based approach for assessing shunt severity, particularly in settings where access to echocardiography is limited [7, 8]

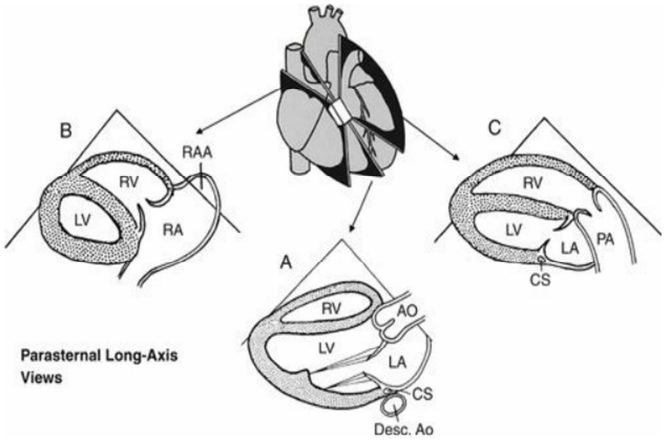


FIGURE 5-1 Diagram of important two-dimensional echo views obtained from the parasternal long-axis transducer position. Standard long-axis view (**A**), right ventricular (RV) inflow view (**B**), and RV outflow view (**C**). AO, aorta; CS, coronary sinus; Desc. Ao, descending aorta; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RAA, right atrial appendage.

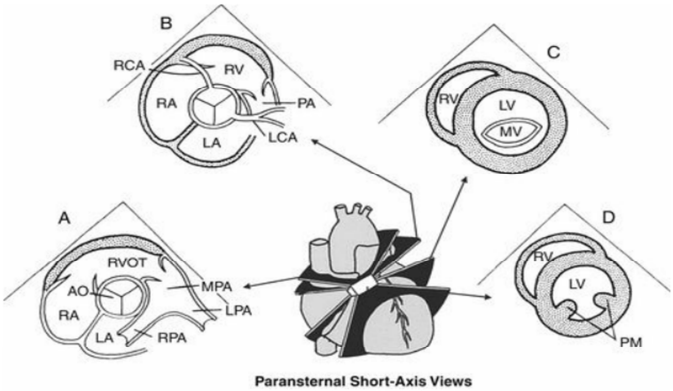


FIGURE 5-2 Diagram of a family of parasternal short-axis views. Semilunar valves and great artery level (**A**), coronary arteries (**B**), mitral valve level (**C**), and papillary muscle level (**D**). AO, aorta; LA, left atrium; LCA, left coronary artery; LPA, left pulmonary artery; LV, left ventricle; MPA, main pulmonary artery; MV, mitral valve; PM, papillary muscle; RA, right atrium; RCA, right coronary artery; RPA, right pulmonary artery; RV, right ventricle; RVOT, right ventricular outflow tract.

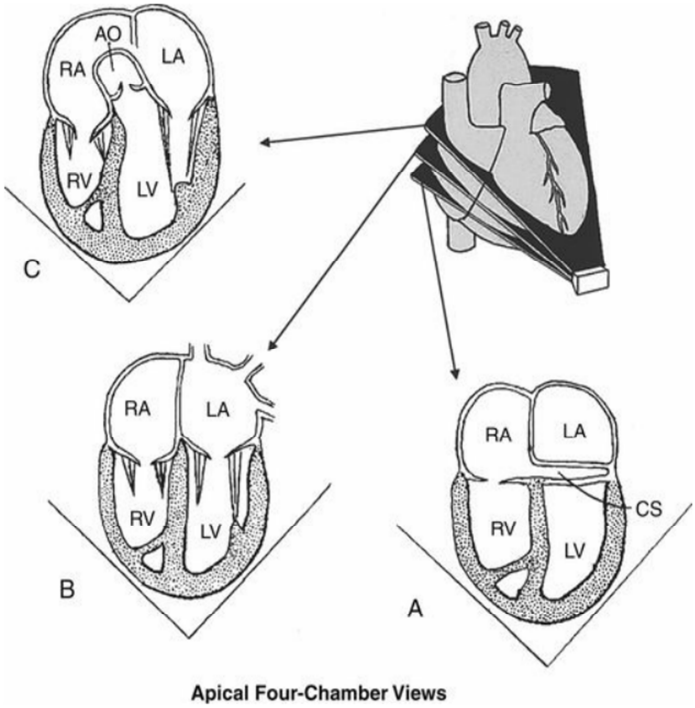


FIGURE 5-3 Diagram of two-dimensional echo views obtained with the transducer at the apical position. **A,** The posterior plane view showing the coronary sinus. **B,** The standard apical four-chamber view. **C,** The apical "five-chamber" view is obtained with further anterior angulation of the transducer. AO, aorta; CS, coronary sinus; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

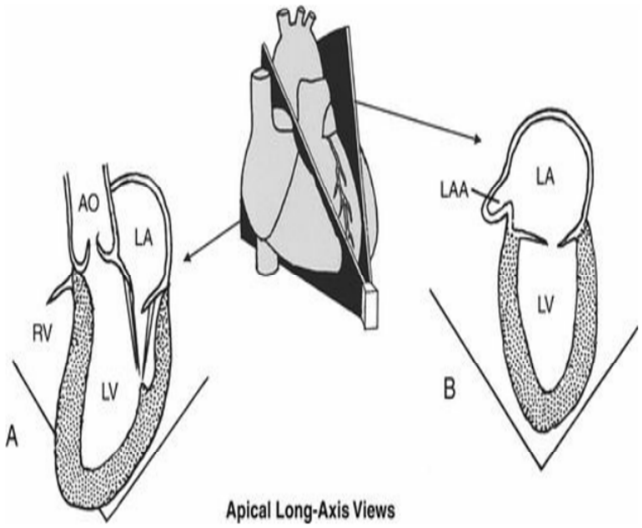
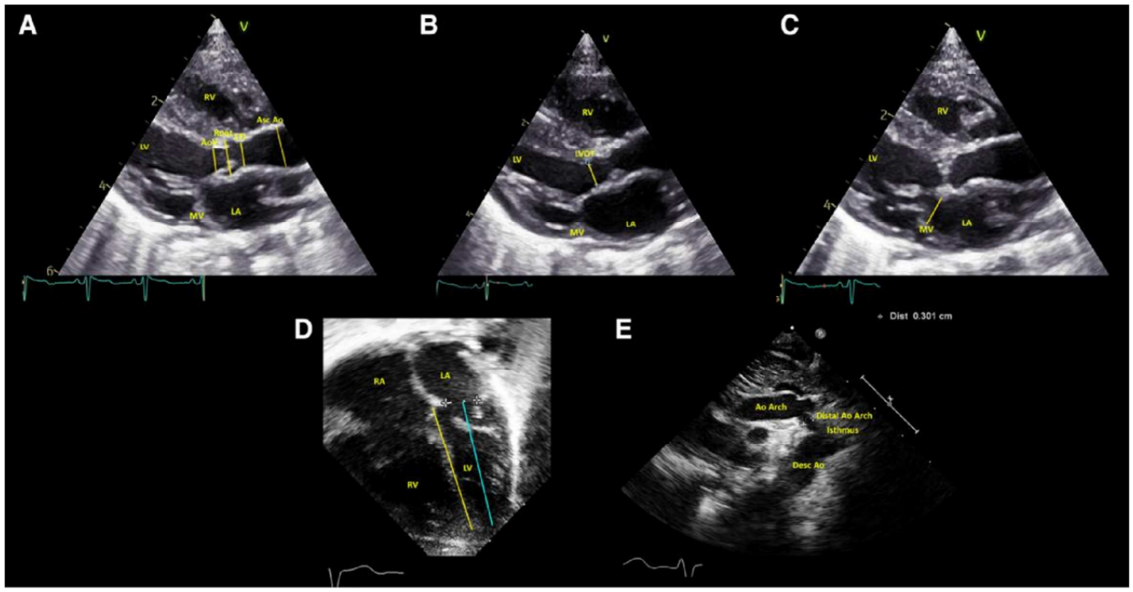


FIGURE 5-4 Apical long-axis view. **A,** Apical "three-chamber" view. **B,** Apical "two-chamber" view. AO, aorta; LA, left atrium; LAA, left atrial appendage; LV, left ventricle; RV, right ventricle.



Doppler Echocardiography

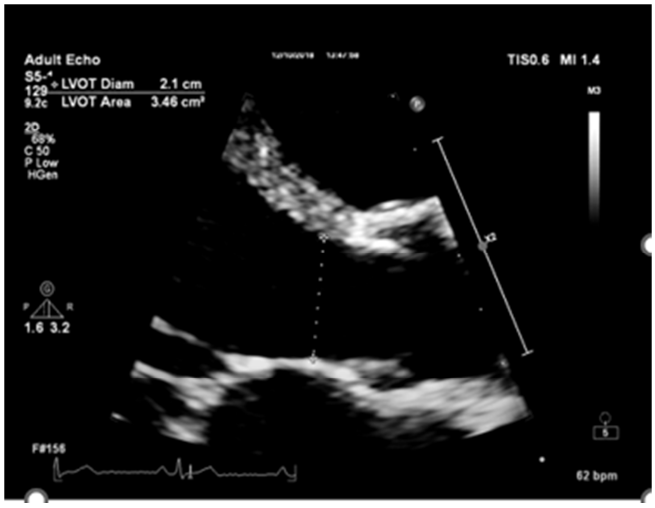
Doppler echocardiography combines the assessment of cardiac structure with the evaluation of blood flow profiles, providing a comprehensive understanding of cardiovascular function. The **Doppler effect**, which describes the change in the frequency of sound waves due to the motion of the source or target, is the fundamental principle behind this technique. When blood moves toward the ultrasonic transducer, the frequency of the reflected sound wave increases (positive Doppler shift), whereas movement away from the transducer results in a decrease in frequency (negative Doppler shift). Doppler ultrasound equipment detects these frequency shifts and calculates the direction and velocity of red blood cell flow relative to the ultrasound beam. By convention, velocities of blood moving toward the transducer are displayed above a zero baseline, while those moving away are displayed below the baseline [1, 2].

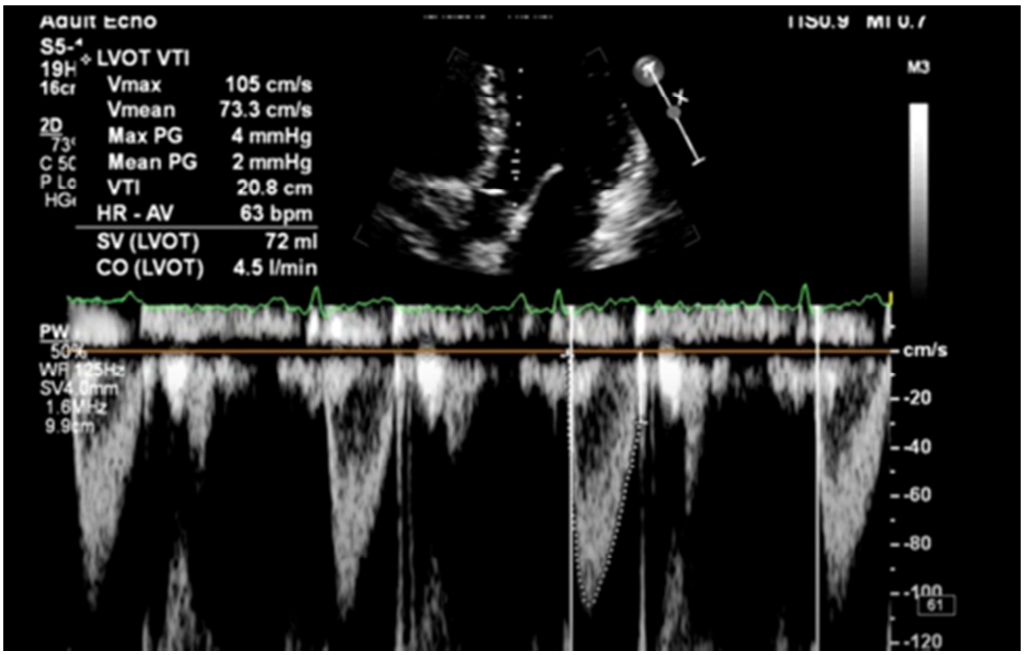
One of the key applications of Doppler echocardiography is the calculation of the **pulmonary-to-systemic shunt ratio (Qp/Qs)**, which quantifies the ratio of pulmonary to systemic blood flow. Under normal circumstances, and in the absence

of significant pulmonary or aortic valve regurgitation, the stroke volume through the **right ventricular outflow tract (RVOT)** should be identical to that through the **left ventricular outflow tract (LVOT)**. However, in the presence of an intracardiac shunt, such as a **patent foramen ovale (PFO)**, **atrial septal defect (ASD)**, or **ventricular septal defect (VSD)**, the pulmonary and systemic blood flows diverge, leading to an abnormal Qp/Qs ratio [3, 4].

To calculate the Qp/Qs ratio, specific measurements are required, including the **LVOT diameter**, **LVOT velocity time integral (VTI)**, **RVOT diameter**, and **RVOT VTI**. The LVOT diameter is measured from the **parasternal long-axis view** in early to mid-systole, using an inner-edge to inner-edge methodology at the point of aortic cusp insertion. Similarly, the RVOT diameter is measured from the appropriate echocardiographic window. These measurements, combined with the corresponding VTIs, allow for the accurate calculation of stroke volumes and the determination of the Qp/Qs ratio [5, 6].

In the context of congenital heart disease (CHD), Doppler echocardiography is indispensable for diagnosing and quantifying the severity of left-to-right shunts. It provides critical information for guiding treatment decisions, particularly in conditions such as ASD, VSD, and PDA, where the Qp/Qs ratio is a key determinant of disease progression and the need for surgical intervention [7, 8].





Measurement of Left Ventricular Outflow Tract (LVOT) and Velocity Time Integral (VTI)

To calculate the **Qp/Qs ratio**, the **velocity time integral (VTI)** of the left ventricular outflow tract (LVOT) is a critical parameter. The VTI represents the distance traveled by a column of blood during one cardiac cycle and is obtained using **pulsed-wave (PW) Doppler**. The PW sample volume is placed at the level of the LVOT, typically

from an **apical 3 or 5 chamber view**. The resulting Doppler trace provides a waveform that can be traced to calculate the VTI, which is essential for determining the stroke volume of the left ventricle [1, 2].

Measurement of Right Ventricular Outflow Tract (RVOT) Diameter and VTI

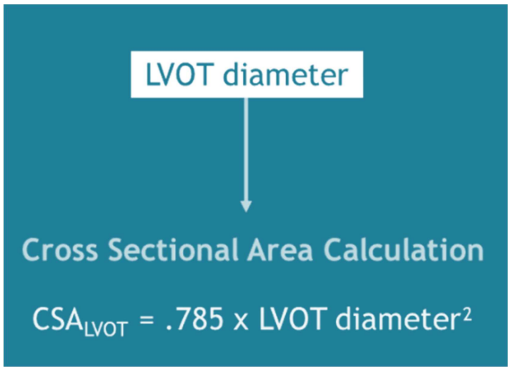
Similarly, the **right ventricular outflow tract (RVOT) diameter** is measured to calculate the cross-sectional area of the RVOT. This measurement is taken during early to mid-systole, using an **inner-edge to inner-edge methodology** at the base of the pulmonary valve leaflets. The RVOT diameter is typically obtained from the **parasternal short-axis view** at the level of the aortic valve. Once the RVOT diameter is measured, the **RVOT VTI** is obtained using PW Doppler, with the sample volume placed just below the pulmonary valve. The RVOT VTI, combined with the RVOT diameter, allows for the calculation of the right ventricular stroke volume [3, 4].

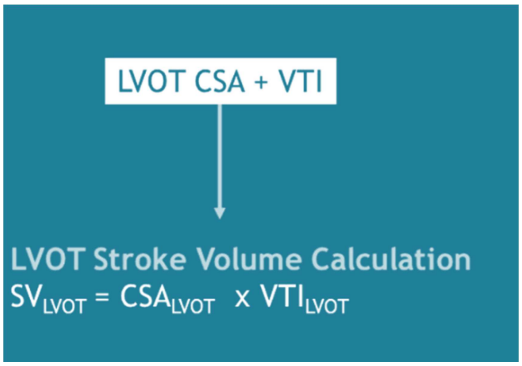
Calculation of Qp/Qs Ratio: The **Qp/Qs ratio** is calculated by dividing the pulmonary blood flow (Qp) by the systemic blood flow (Qs). Pulmonary blood flow is derived from the RVOT stroke volume, while systemic blood flow is derived from the LVOT stroke volume. These calculations rely on the accurate measurement of the LVOT and RVOT diameters and their corresponding VTIs. In the absence of significant valvular regurgitation or other shunts, the Qp/Qs ratio should be close to 1. However, in the presence of an intracardiac shunt, such as an **atrial septal defect (ASD)**, **ventricular septal defect (VSD)**, or **patent ductus arteriosus (PDA)**, the Qp/Qs ratio will be more, reflecting the volume of blood shunted from the systemic to the pulmonary circulation [5, 6].

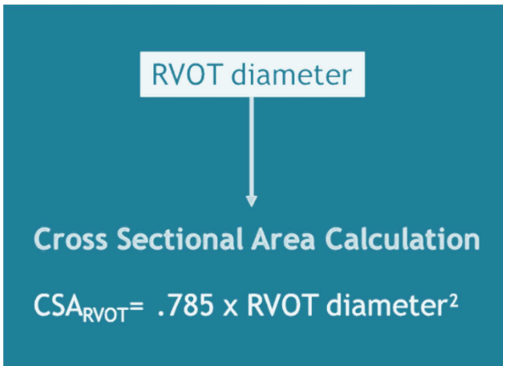
Clinical Significance of Qp/Qs Ratio: The Qp/Qs ratio is a crucial parameter in the evaluation of congenital heart disease (CHD), particularly in conditions involving left-to-right shunts. A Qp/Qs ratio greater than 1.5 is generally considered indicative of a significant shunt, often necessitating surgical intervention.

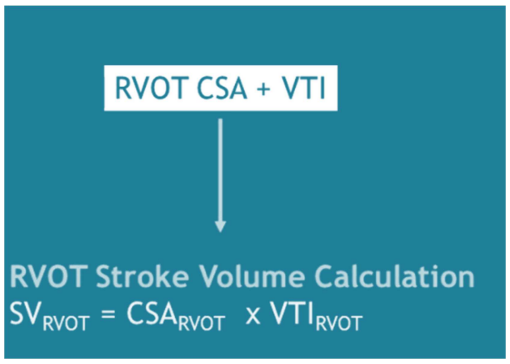
Calculation of Qp/Qs Ratio in Patent Ductus Arteriosus (PDA)

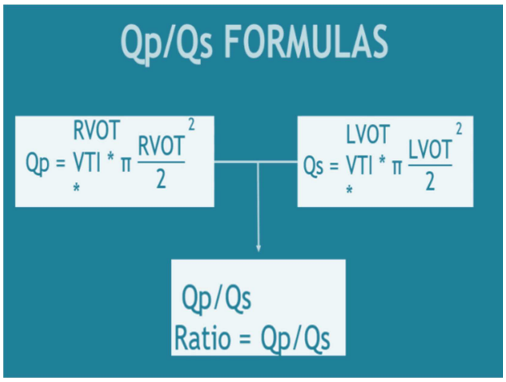
The calculation of the **Qp/Qs ratio** in **patent ductus arteriosus (PDA)** differs from that in other congenital heart conditions, such as atrial septal defect (ASD) or ventricular septal defect (VSD). In PDA, the **pulmonary blood flow (Qp)** is measured from the **aortic systolic flow**, while the **systemic blood flow (Qs)** is measured from the **systolic flow at the pulmonic valve annulus**. This approach is necessary because the pulmonary blood flow distal to the PDA can only be accurately measured after its return to the heart via the pulmonary veins, which is reflected in the aortic flow. This unique measurement strategy ensures an accurate assessment of shunt severity in PDA, guiding clinical decision-making and the need for intervention [3, 4].

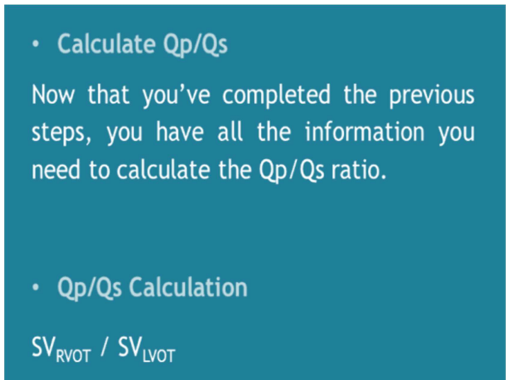

LVOT diameter
Cross Sectional Area Calculation
CSA_{LVOT} = .785 x LVOT diameter²


LVOT CSA + VTI
LVOT Stroke Volume Calculation
$SV_{LVOT} = CSA_{LVOT} \times VTI_{LVOT}$


RVOT diameter
Cross Sectional Area Calculation
CSA_{RVOT}= .785 x RVOT diameter²


RVOT CSA + VTI
RVOT Stroke Volume Calculation
$SV_{RVOT} = CSA_{RVOT} \times VTI_{RVOT}$


Qp/Qs FORMULAS
$Qp = VTI_{RVOT} * \pi \frac{RVOT}{2}^2$
$Qs = VTI_{LVOT} * \pi \frac{LVOT}{2}^2$
Qp/Qs
Ratio = Qp/Qs


• Calculate Qp/Qs
Now that you've completed the previous steps, you have all the information you need to calculate the Qp/Qs ratio.
• Qp/Qs Calculation
SV_{RVOT} / SV_{LVOT}

REVIEW OF LITERATURE

- Zhang et al. (2023)[8] evaluated the diagnostic performance of Doppler echocardiography (DE) combined with N-terminal pro-brain natriuretic peptide (NT-proBNP) in detecting pulmonary artery hypertension (PAH) associated with congenital heart disease (CHD). This retrospective study included 64 patients with CHD, where pulmonary artery systolic pressure (PASP) was estimated using DE and compared with right heart catheterization (RHC) measurements. A mild correlation was found between PASP measured by RHC (78.1 ± 29.0 mmHg) and PASP estimated by DE (74.9 ± 19.7 mmHg) ($r = 0.4401$, $P < 0.01$). The Bland-Altman analysis showed a bias of 3.2 mmHg with 95% limits of agreement ranging from -49.53 to 55.90 mmHg. Receiver operating characteristic (ROC) analysis demonstrated that DE alone had an area under the curve (AUC) of 0.848, with a sensitivity of 98.3% and specificity of 77.8%. NT-proBNP alone had an AUC of 0.804, with 81.4% sensitivity and 87.5% specificity. When DE was combined with NT-proBNP, the AUC increased to 0.857, with a sensitivity of 100% and specificity of 77.8%, improving the diagnostic accuracy of PAH in CHD patients. These findings suggest that NT-proBNP, when used alongside DE, enhances the accuracy of PAH screening and could help in clinical decision-making regarding CHD management.
- Khosroshahi et al. (2019)[3] investigated the correlation between serum levels of pro-brain natriuretic peptide (pro-BNP) and the severity of left-to-right shunt (Qp/Qs ratio) in children with congenital heart disease (CHD). This cross-sectional study included 60 pediatric patients diagnosed with atrial septal defect (ASD), ventricular septal defect (VSD), or patent ductus arteriosus

(PDA). The severity of the shunt was assessed using Doppler echocardiography, and serum pro-BNP levels were measured using fluorescence immunoassay. A significant correlation was found between pro-BNP levels and the Qp/Qs ratio (P = 0.0001). The mean serum pro-BNP levels for patients with Qp/Qs <1.5, 1.5–2, and >2 were 30.83±2.4, 217.88±44.6, and 329.02±51.8 pg/mL, respectively. The study determined a pro-BNP cut-off value of 40.36 pg/mL for detecting a Qp/Qs ratio >1.5, with a sensitivity of 92% and a specificity of 79%. These findings suggest that pro-BNP can be used as a non-invasive biomarker for assessing shunt severity and determining the need for intervention in children with CHD.

- Farouk et al. (2017)[4] investigated the correlation between circulating B-type natriuretic peptide (BNP) levels and the pulmonary-to-systemic flow ratio (Qp/Qs) among children undergoing congenital heart surgery. This prospective cross-sectional case-control study included 43 pediatric patients with congenital heart disease (CHD) undergoing elective surgical shunt closure, along with 17 healthy controls. Plasma BNP levels were measured using ELISA, and the Qp/Qs ratio was calculated for each patient. The study found significantly higher BNP levels in children with CHD compared to controls (P < 0.001). The Qp/Qs ratio was significantly elevated in children with atrial septal defect (ASD) or ventricular septal defect (VSD) compared to those with patent ductus arteriosus (PDA) (P < 0.001). A strong positive correlation was observed between BNP levels and Qp/Qs ratio (r = 0.541, P < 0.001). The study determined that BNP levels >55 pg/mL and Qp/Qs >2.36 were predictive of poor surgical outcomes, with 100% sensitivity and 97.5% specificity. These findings suggest that BNP is a valuable cardiac biomarker

for assessing shunt severity and predicting surgical outcomes in pediatric CHD patients.

- Samadi et al. (2017)[1] investigated the correlation between the level of serum pro-brain natriuretic peptide (pro-BNP) and the severity of the left-to-right shunt (Qp/Qs ratio) in children with acyanotic congenital heart disease (CHD). Pulmonary arterial hypertension (PAH) is a known complication of CHD with left-to-right shunts, leading to progressive pulmonary vascular resistance and potential development of Eisenmenger syndrome. This cross-sectional study evaluated 30 pediatric patients diagnosed with atrial septal defect (ASD), ventricular septal defect (VSD), or patent ductus arteriosus (PDA) using echocardiography and Doppler assessments to measure Qp/Qs ratios. The study found a significant positive correlation between serum pro-BNP levels and both the Qp/Qs ratio and systolic pulmonary pressure ($P < 0.001$). The mean +SE level of pro-BNP serum levels in patients with QP/Qs ratio was less than 1.5, equal to 1.5-2, and more than 2, was correlating to 30.83±2.4, 217.88±44.6, and 217±51.8. The pro-BNP cut-off point for predicting a Qp/Qs ratio >1.5 was determined to be 36.95 pg/mL, with a sensitivity of 100% and a specificity of 83.3%. The results suggest that pro-BNP measurement is a valuable non-invasive biomarker for assessing shunt severity and pulmonary hypertension in children with CHD, particularly when direct pulmonary pressure measurement is not feasible.
- Ozyurt et al. (2015)[6] investigated the correlation between N-terminal pro-brain natriuretic peptide (NT-proBNP) levels and measured shunt fraction in children with atrial septal defects (ASD) and ventricular septal defects (VSD). This prospective, controlled, observational study included 127 pediatric patients with isolated ASD (n=63) or VSD (n=64) and a control group (n=62).

Echocardiographic and invasive hemodynamic measurements were performed to assess the shunt severity, with a pulmonary-to-systemic flow ratio (Qp/Qs) of ≥1.5 considered a significant shunt. A statistically significant relationship was found between NT-proBNP levels and Qp/Qs ($P < 0.001$). The study identified a cut-off value of 113.5 pg/mL for VSD patients and 57.9 pg/mL for ASD patients to predict significant shunts, with high sensitivity (88% for VSD, 83% for ASD) and specificity (100% for VSD, 67% for ASD). NT-proBNP levels showed strong correlations with invasive hemodynamic parameters such as mean pulmonary artery pressure and right ventricular end-diastolic pressure. These findings suggest that NT-proBNP can be a useful biomarker for assessing shunt severity and determining the need for surgical intervention in children with congenital septal defects.

- Kavga et al. (2013)[5] examined the correlation between plasma B-type natriuretic peptide (BNP) levels and shunt volume in children with congenital heart disease (CHD) involving a left-to-right shunt. The study included 76 pediatric patients with atrial septal defect (ASD), ventricular septal defect (VSD), or patent ductus arteriosus (PDA), and 34 healthy controls. BNP levels were measured using chemiluminescent microparticle immunoassay, while shunt volume (Qp/Qs ratio) was determined through Doppler echocardiography. The results showed that BNP levels were significantly higher in children with CHD and hemodynamically significant left-to-right shunts (Qp/Qs >1.5) compared to those with insignificant shunts ($P = 0.015$). BNP levels were positively correlated with Qp/Qs ratio ($r = 0.59$, $P < 0.001$) and pulmonary artery gradient ($r = 0.49$, $P < 0.001$), whereas a negative correlation was observed with ejection fraction ($r = -0.14$). A BNP cutoff value of 24.4 pg/mL was determined to identify patients with Qp/Qs >1.5,

with a sensitivity of 70.59% and specificity of 82.89%. These findings suggest that BNP can serve as an early biomarker for assessing the severity of left-to-right shunts in pediatric CHD patients.

- Arifani et al. (2021)[19] analyzed the correlation between N-terminal pro-brain natriuretic peptide (NT-proBNP) levels and heart failure in children with acyanotic congenital heart disease (CHD) associated with left-to-right shunts. This cross-sectional study included 43 children aged 1 month to 18 years diagnosed with atrial septal defect (ASD), ventricular septal defect (VSD), or patent ductus arteriosus (PDA) at Dr. Soetomo General Hospital, Indonesia. The severity of heart failure was assessed using the Pediatric Heart Failure Score, and NT-proBNP levels were measured using the IMMULITE 1000 Turbo NT-proBNP test kit. The study found a significant positive correlation between NT-proBNP levels and heart failure severity ($r = 0.57$, $P < 0.001$). The mean NT-proBNP levels in children with heart failure were 6549 pg/mL, compared to 234.36 pg/mL in those without heart failure. VSD was the most common defect (39.5%), followed by ASD (37.2%) and PDA (23.3%). These findings suggest that NT-proBNP can serve as a valuable biomarker for diagnosing and monitoring heart failure in children with acyanotic CHD.

- Tarkowska et al. (2021)[20] evaluated the diagnostic utility of N-terminal pro-brain natriuretic peptide (NT-proBNP) in newborns with congenital heart defects (CHD). This study included 126 neonates, divided into two groups: infants with CHD and healthy controls. The CHD group was further categorized based on defect type (simple shunts vs. combined heart defects) and hemodynamic significance. NT-proBNP levels were significantly elevated in newborns with CHD compared to controls ($P < 0.001$). Infants with

combined heart defects had higher NT-proBNP levels than those with simple shunts (P = 0.0004). Additionally, NT-proBNP showed strong correlations with left ventricular ejection fraction (LVEF), echocardiographic parameters of hemodynamic significance, and heart failure severity classified by Ross and Reithmann's scores. These findings suggest that NT-proBNP is a reliable biomarker for detecting circulatory failure and assessing the severity of CHD in neonates, potentially guiding early clinical intervention.

- Yasmien et al. (2016) [22] investigated the correlation between N-terminal pro-brain natriuretic peptide (NT-proBNP) levels and the severity of heart failure in children. This cross-sectional study was conducted at Mohammad Hoesin Hospital, Indonesia, from July to September 2015, involving 30 children aged 1 month to 14 years diagnosed with congestive heart failure. Heart failure severity was assessed using the modified Ross Reithmann scoring system, and NT-proBNP levels were measured using the Roche cardiac proBNP testing kit. The study found a significant positive correlation between NT-proBNP levels and heart failure severity ($r = 0.87$, $P < 0.001$). The median NT-proBNP levels were 518 pg/mL for mild heart failure, 1,703 pg/mL for moderate heart failure, and 6,510 pg/mL for severe heart failure. These findings suggest that NT-proBNP is a reliable biochemical marker for diagnosing and grading heart failure severity in pediatric patients.
- Schoen et al. (2007)[11] investigated the correlation between N-terminal pro-brain natriuretic peptide (NT-proBNP) levels and right heart hemodynamic parameters in patients with atrial septal defects (ASD), both before and after percutaneous defect closure. This prospective study included 20 patients undergoing ASD closure, assessing NT-proBNP levels in relation to right

ventricular systolic pressure (RVSP), right ventricular end-diastolic volume (RVEDV), right ventricular end-systolic volume (RVESV), and interatrial left-to-right shunting. Baseline NT-proBNP levels were 240 ± 93 pg/mL, which significantly decreased to 116 ± 62 pg/mL at 12-month follow-up ($P < 0.01$). A positive correlation was observed between NT-proBNP levels and RVSP ($r = 0.75$, $P < 0.01$), RVEDP ($r = 0.70$, $P < 0.01$), and RVESV ($r = 0.65$, $P < 0.05$). Notably, NT-proBNP levels correlated with left-to-right shunt severity but not with ASD size. These findings suggest that NT-proBNP serves as a valuable biomarker for assessing right heart volume overload and pulmonary pressure in ASD patients, particularly for monitoring post-closure hemodynamic improvements.

- Koura et al. (2016) [23] analyzed the levels of (NT-proBNP) in children with congenital heart disease involving a left-to-right shunt (LRS) and in those with dilated cardiomyopathy (DCM). This cross-sectional study included 30 pediatric patients (19 with LRS and 11 with DCM) and a control group of 44 healthy children. The study assessed heart failure symptoms, NT-proBNP levels, and echocardiographic parameters, including pulmonary-to-systemic flow (Qp/Qs) and pulmonary artery pressure (PAP). The results showed that NT-proBNP levels were significantly elevated—11 times in LRS and 16 times in DCM—compared to controls. A positive correlation was found between NT-proBNP levels and Qp/Qs ($P < 0.05$), PAP ($P = 0.01$), and heart failure severity ($P = 0.002$). Among patients with decompensated heart failure, all had elevated NT-proBNP levels. These findings suggest that NT-proBNP is a valuable biomarker for monitoring heart failure and pulmonary **hypertension.**

MATERIALS AND METHODS

Brief outline

This cross-sectional study, conducted at KLEH Dr. Prabhakar Kore Charitable Hospital, Belagavi**,** aims to investigate the correlation between serum NT-proBNP levels **and the severity of** left-to-right shunt (Qp/Qs ratio) in children diagnosed with acyanotic congenital heart disease (ACHD)**,** including conditions such as atrial septal defect (ASD)**,** ventricular septal defect (VSD)**,** and patent ductus arteriosus (PDA)**.** The study will include 60 participants aged from infancy to childhood. Participants will undergo clinical evaluation**,** echocardiography to confirm diagnoses and calculate the Qp/Qs ratio, and blood tests to measure serum NT-proBNP levels. Statistical analysis will be performed to determine the correlation between these parameters using appropriate tests such as Pearson's correlation **or** Spearman's rank correlation**.** The study will adhere to ethical guidelines, with informed consent obtained from parents or guardians. The research is led by DR. _____**,** PG Resident, Department of Paediatrics**,** KLE Academy of Higher Education and Research, Belagavi**,** under the guidance of DR. _____**,** Professor, Department of Paediatrics**,** KLE Academy of Higher Education and Research, Jawaharlal Nehru Medical College, Belagavi**.**

Materials and Methods

Source of Data

The study included infants and children admitted to KLEH Dr. Prabhakar Kore Charitable Hospital who presented with signs and symptoms of congenital heart disease and underwent echocardiography. Patients with confirmed diagnoses of atrial

septal defect (ASD)**,** ventricular septal defect (VSD)**,** patent ductus arteriosus (PDA)**,** or other acyanotic congenital heart conditions were included.

Study Design

1. **Study Design**: A cross-sectional study.
2. **Study Duration**: 1 year.
3. **Sample Size**: 60 participants.

Sample Size Calculation

The sample size was calculated using the following formula:

$$(\mathbf{Z\alpha + Z\beta})\mathbf{2C2 + 3n = C2}(\mathbf{Z\alpha + Z\beta})\mathbf{2 + 3}$$

Where:

- nn = required sample size,
- ZαZα = Z score for the level of significance (α=0.05α=0.05),
- ZβZβ = Z score for power (1−β=0.851−β=0.85),
- C=0.5×ln (1+r1−r)C=0.5×ln(1−r1+r), with rr = expected correlation coefficient.

Assuming a correlation coefficient (rr) of at least **0.4** between serum NT-proBNP levels and the **left-to-right shunt (Qp/Qs) ratio** in children with acyanotic congenital heart disease, the minimum sample size required was **53**. To enhance the accuracy of the results, the sample size was increased to **60**.

Inclusion Criteria

- Infants and children presenting with:
    - Heart murmur with/without Features of congestive cardiac failure (CCF),
    - Failure to thrive, History of recurrent respiratory infections,
    - Echocardiographically confirmed diagnoses of **ASD**, **VSD**, **PDA**, or other acyanotic conditions.

Exclusion Criteria

Children with the following conditions were excluded:

1. **Septic shock**.
2. **Renal failure** or **low glomerular filtration rate (GFR)**,
3. **Active necrotizing enterocolitis (NEC)**, **active bleeding**, or **intracranial hemorrhage**,
4. **Heart failure** due to cardiomyopathy, myocarditis, pericarditis, or coronary artery disease.

Study Protocol

1. **Ethical Approval**: The study protocol was approved by the institutional ethical committee.
2. **Informed Consent**: Written informed consent was obtained from the parents or guardians of all participants.

Data Collection Procedure

1. **Clinical Evaluation**: A detailed history and clinical examination were conducted for all participants.
2. **Supportive Investigations**: Chest X-rays and electrocardiograms (ECGs) were performed as needed.
3. **Echocardiography**:
    - Echocardiography was used to confirm the diagnosis of **ASD**, **VSD**, **PDA**, or other conditions such as **partial anomalous pulmonary venous connection (PAPVC)**.
    - The **left-to-right shunt (Qp/Qs) ratio** was calculated using Doppler echocardiography.
4. **Biomarker Analysis**:
    - Blood samples (3 mL) were collected in plain vials and sent to the laboratory.
    - Serum **NT-proBNP levels** were measured using **fluorescence immunoassay** with **NT-proBNP triage kits**.

Data Processing and Statistical Analysis

1. **Software**: Data were analyzed using **R version 4.2.1** and **Microsoft Excel**.
2. **Descriptive Statistics**:
    - Categorical variables were summarized using **frequency tables**.

- Continuous variables were expressed as **mean ± standard deviation (SD)** or **median (minimum, maximum)**.

3. **Statistical Tests**:
    - The **Shapiro-Wilk test** was used to assess the normality of data distribution.
    - For normally distributed data, **parametric tests** (e.g., **Pearson's correlation**, **one-way ANOVA**) were used.
    - For non-normally distributed data, **non-parametric tests** (e.g., **Spearman's rank correlation**, **Kruskal-Wallis test**) were applied.
    - The **Chi-square test** was used to evaluate associations between categorical variables.
4. **Significance Level**: A **p-value ≤ 0.05** was considered statistically significant.

Adverse Events

- **Anticipated Adverse Events**: No serious adverse effects were expected from the study interventions.
- **Intervention**: Venous puncture for blood collection was the only procedure performed.

Cost of Investigations

- The cost of measuring **serum NT-proBNP levels** was borne by the researcher.

Statistical Analysis:

Data will be analyzed using appropriate statistical methods, including chi-square tests and correlation coefficients, to identify significant associations between findings and clinical symptoms.

The formula used for calculating the minimum sample size for a cross-sectional study is:

Sample size calculation

The sample was calculated on the basis of prevalence using the formula: -

$$n = \frac{Z^2 P(1 - P)}{d^2}$$

Where-

Z = the statistic corresponding to level of confidence,

P = expected prevalence

d = precision (corresponding to effect size).

Where:

- n*n* = required sample size
- Z*Z* = Z-score corresponding to the 95% confidence level (1.96)
- p*p* = estimated prevalence of (0.25)
- d*d* = margin of error (0.05)

Sampling Method

Systematic random sampling was used to select participants for the study.

Study Tools

- **Case Reporting Form**: Used to document demographic details, clinical profiles, and other relevant data.
- **Consent Form**: All participants (or their legal guardians) provided informed consent before enrollment.

Participants meeting the inclusion and exclusion criteria were included in the study. Demographic and clinical data were recorded at the time of enrollment.

Statistical Analysis

The database was created using Microsoft Excel, and graphs were generated for data visualization. Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 23 for Windows. All numerical values were entered into Microsoft Excel, and statistical tests were conducted using SPSS.

- **Continuous data** were summarized as mean ± standard deviation (SD).
- **Discrete (categorical) data** were presented as numbers and percentages.

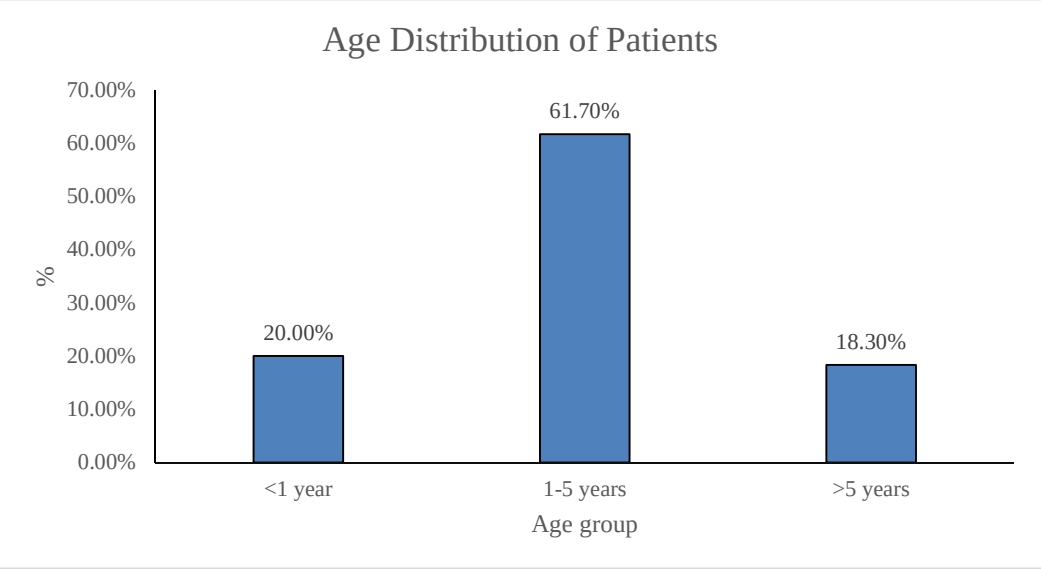
RESULTS

Data Analysis Table: Demographic Data

Table 1: Age Distribution of Patients

		Frequency	Percent
Age (Years)	<1 year	12	20.0%
	1-5 years	37	61.7%
	>5 years	11	18.3%
	Total	60	100.0%

Graph 1

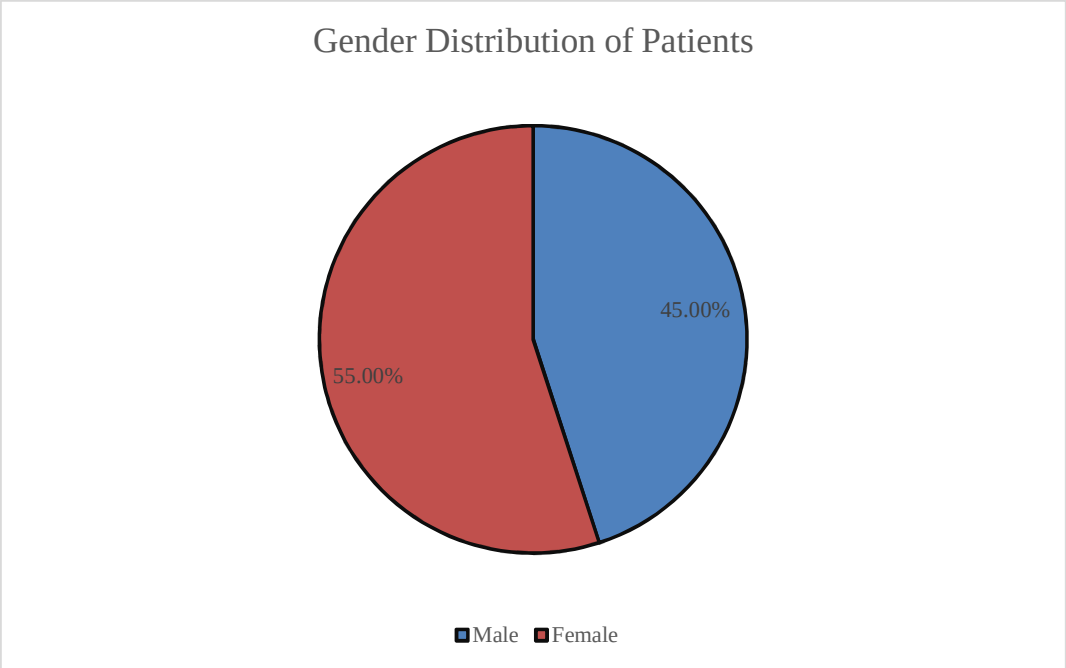


Out of the total, 12 children (20.0%) were younger than 1 year of age. The majority of the patients, 37 children (61.7%), were between 1 to 5 years of age, making this the largest age group in the study. Meanwhile, 11 children (18.3%) were older than 5 years of age at the time of diagnosis.

Table 2: Gender Distribution of Patients

		Frequency	Percent
Gender	Male	27	45.0%
	Female	33	55.0%
	Total	60	100.0%

Graph 2

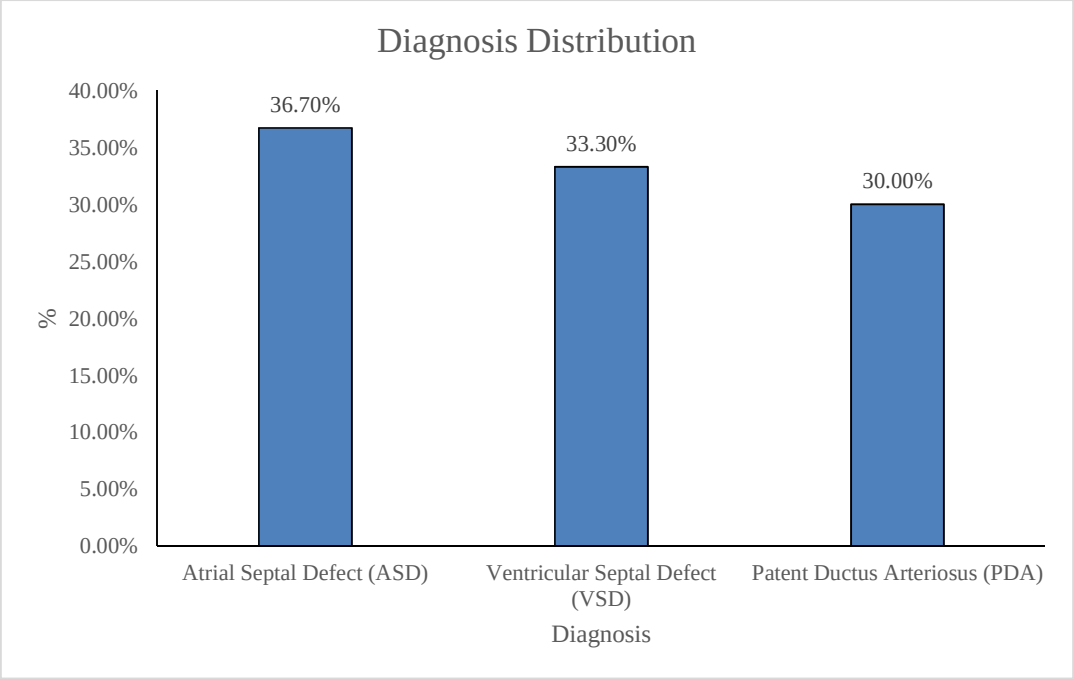


27 patients (45.0%) were male and 33 patients (55.0%) were female.

Table 3: Diagnosis Distribution

		Frequency	Percent
Diagnosis	Atrial Septal Defect (ASD)	22	36.7%
	Ventricular Septal Defect (VSD)	20	33.3%
	Patent Ductus Arteriosus (PDA)	18	30.0%
	Total	60	100.0%

Graph 3

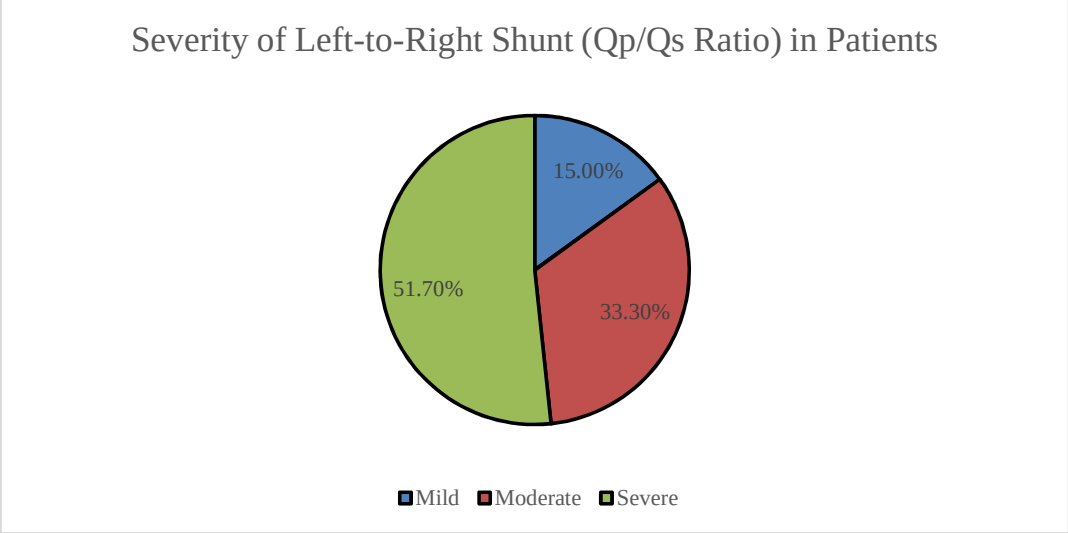


Among the 60 cases, the most frequently diagnosed condition was atrial septal defect (ASD), which accounted for 22 cases (36.7%). This was followed closely by ventricular septal defect (VSD), which was identified in 20 cases (33.3%). Patent ductus arteriosus (PDA) was diagnosed in 18 cases (30.0%).

Table 4: Severity of Left-to-Right Shunt (Qp/Qs Ratio) in Patients

		Frequency	Percent
Shunt Severity	Mild	9	15.0%
	Moderate	20	33.3%
	Severe	31	51.7%
	Total	60	100.0%

Graph 4

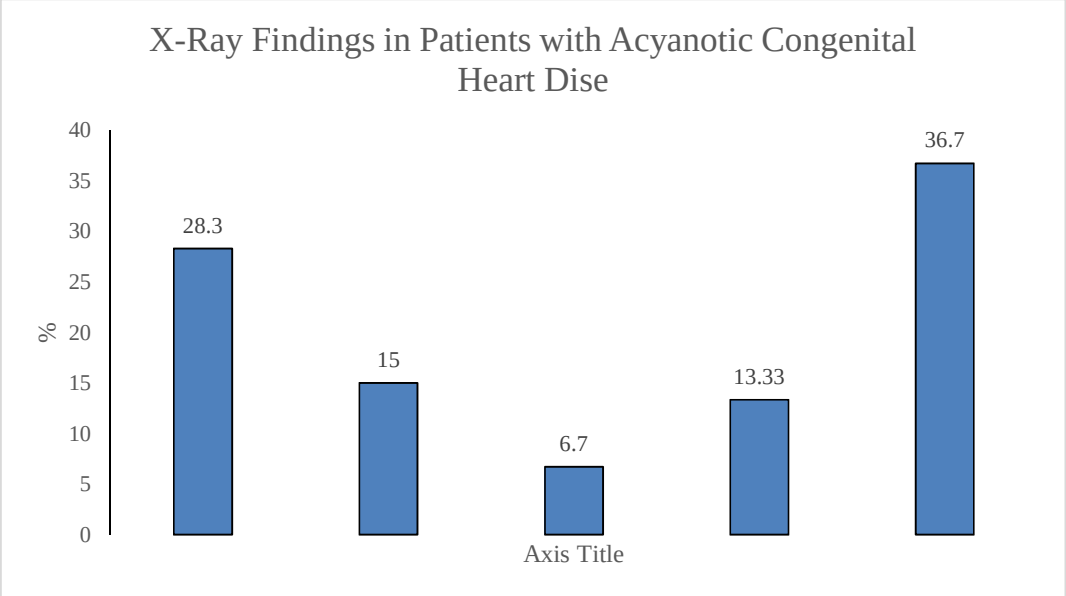


Out of the total cases, 9 patients (15.0%) had a mild shunt (Qp/Qs < 1.5). 20 patients (33.3%) had a moderate shunt (Qp/Qs between 1.5 and 2.0), and the majority of cases, 31 patients (51.7%), had a severe shunt (Qp/Qs ≥ 2.0).

Table 5: X-Ray Findings in Patients with Acyanotic Congenital Heart Disease

		Frequency	Percent
X Ray Findings			
	LV Type Of Apex, Dilated MPA/RPA/LPA, Pulmonary Plethora	17	28.3%
	LV Type Of Apex, No Pulmonary Plethora	9	15.0%
	RV Type of Apex, Dilated MPA/RPA/LPA, Pulmonary Plethora	4	6.7%
	RV Type of Apex, No Pulmonary Plethora	8	13.33%
	No Cardiomegaly, Normal	22	36.7%
	Total	60	100.0%

Graph 5



The table titled "X-Ray Findings in Patients with Acyanotic Congenital Heart Disease" provides a comprehensive overview of the frequency and percentage distribution of various X-ray findings among 60 patients. The most common finding was "No Cardiomegaly, Normal Total," observed in 22 patients (36.7%), indicating that a significant portion of patients had normal heart size and pulmonary vasculature. The next most frequent finding was "LV Type of Apex, Dilated MPA/RPA/LPA,

Pulmonary Plethora," present in 17 patients (28.3%), suggesting increased pulmonary blood flow associated with left ventricular involvement.

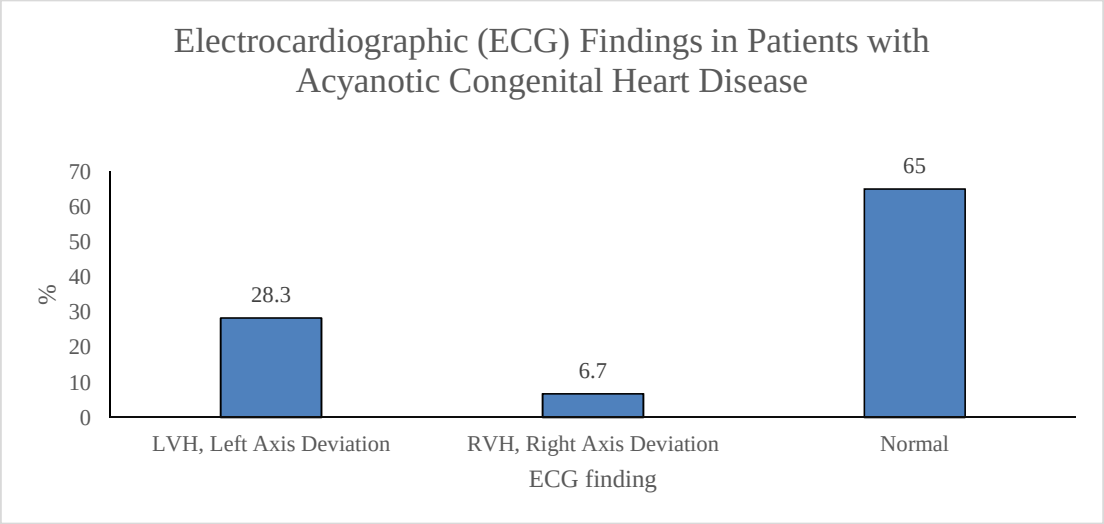
Additionally, 9 patients (15.0%) exhibited "LV Type of Apex, No Pulmonary Plethora," indicating left ventricular type without signs of increased pulmonary blood flow. The "RV Type of Apex, No Pulmonary Plethora" was observed in 8 patients (13.33%), highlighting right ventricular involvement without pulmonary plethora. The least common finding was "RV Type of Apex, Dilated MPA/RPA/LPA, Pulmonary Plethora," seen in only 4 patients (6.7%), which points to right ventricular type with increased pulmonary blood flow.

This distribution of findings helps in understanding the varied presentations of acyanotic congenital heart disease, aiding in accurate diagnosis and tailored treatment approaches. The total percentages sum up to 100%, ensuring a complete representation of the observed X-ray findings in the patient cohort.

Table 6: Electrocardiographic (ECG) Findings in Patients with Acyanotic Congenital Heart Disease

		Frequency	Percent
ECG Findings			
	LVH, Left Axis Deviation	17	28.3%
	RVH, Right Axis Deviation	4	6.7%
	Normal	39	65%
	Total	60	100.0%

Graph 6



The table titled "Electrocardiographic (ECG) Findings in Patients with Acyanotic Congenital Heart Disease" presents the frequency and percentage distribution of various ECG findings among 60 patients.

Normal ECG: The majority of patients, 39 out of 60 (65%), had normal ECG findings.

Left Ventricular Hypertrophy (LVH) with Left Axis Deviation: This finding was observed in 17 patients (28.3%). LVH with left axis deviation indicates an enlargement of the left ventricle and a shift in the heart's electrical axis to the left. This is often associated with increased workload on the left ventricle, which can be seen in VSD and PDAs.

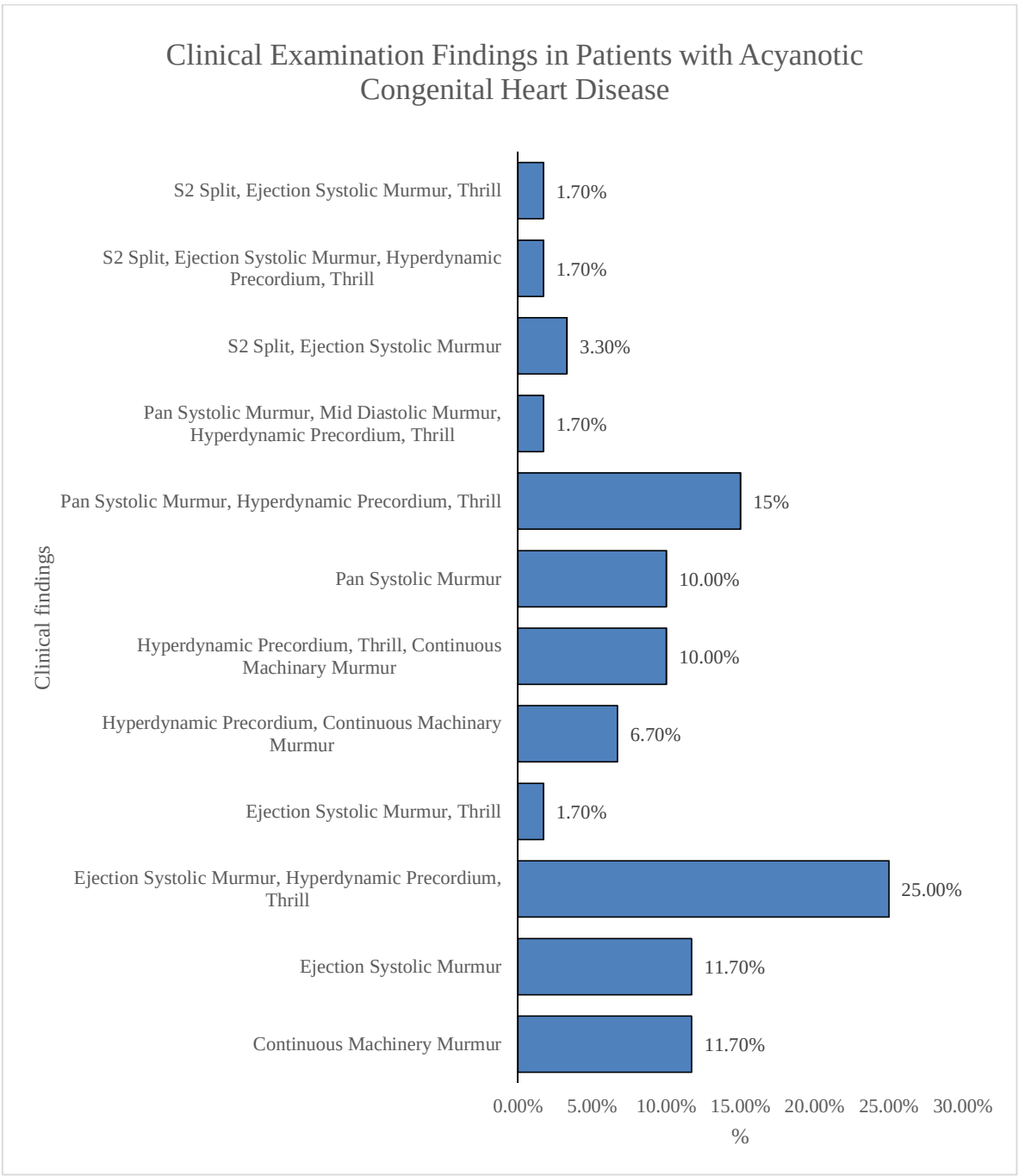
Right Ventricular Hypertrophy (RVH) with Right Axis Deviation: This condition was found in 4 patients (6.7%). RVH with right axis deviation suggests an enlargement of the right ventricle and a shift in the heart's electrical axis to the right. This finding is indicative of increased workload on the right ventricle, which can occur in acyanotic congenital heart diseases that affect the right side of the heart seen in ASD.

This table is valuable for understanding the distribution of ECG findings in patients with acyanotic congenital heart disease, aiding in the diagnosis and management of the condition.

Table 7: Key Clinical Examination Findings in Patients with Acyanotic Congenital Heart Disease

		n	%
Examination key findings	Continuous Machinery Murmur	7	11.7%
	Ejection Systolic Murmur	7	11.7%
	Ejection Systolic Murmur, Hyperdynamic Precordium, Thrill	15	25.0%
	Ejection Systolic Murmur, Thrill	1	1.7%
	Hyperdynamic Precordium, Continuous Machinary Murmur	4	6.7%
	Hyperdynamic Precordium, Thrill, Continuous Machinary Murmur	6	10.0%
	Pan Systolic Murmur	6	10.0%
	Pan Systolic Murmur, Hyperdynamic Precordium, Thrill	9	15%
	Pan Systolic Murmur, Mid Diastolic Murmur, Hyperdynamic Precordium, Thrill	1	1.7%
	S2 Split, Ejection Systolic Murmur	2	3.3%
	S2 Split, Ejection Systolic Murmur, Hyperdynamic Precordium, Thrill	1	1.7%
	S2 Split, Ejection Systolic Murmur, Thrill	1	1.7%
	Total	60	100.0%

Graph 7


Clinical Examination Findings in Patients with Acyanotic Congenital Heart Disease
Clinical findings
S2 Split, Ejection Systolic Murmur, Thrill
1.70%
S2 Split, Ejection Systolic Murmur, Hyperdynamic Precordium, Thrill
1.70%
S2 Split, Ejection Systolic Murmur
3.30%
Pan Systolic Murmur, Mid Diastolic Murmur, Hyperdynamic Precordium, Thrill
1.70%
Pan Systolic Murmur, Hyperdynamic Precordium, Thrill
15%
Pan Systolic Murmur
10.00%
Hyperdynamic Precordium, Thrill, Continuous Machinary Murmur
10.00%
Hyperdynamic Precordium, Continuous Machinary Murmur
6.70%
Ejection Systolic Murmur, Thrill
1.70%
Ejection Systolic Murmur, Hyperdynamic Precordium, Thrill
25.00%
Ejection Systolic Murmur
11.70%
Continuous Machinery Murmur
11.70%
0.00% 5.00% 10.00% 15.00% 20.00% 25.00% 30.00%
%

Continuous machinery murmur was heard in 7 cases (11.7%). This type of murmur is typically associated with patent ductus arteriosus (PDA) due to continuous flow from the aorta to the pulmonary artery throughout the cardiac cycle. Ejection systolic murmurs were noted in several cases, reflecting increased flow through the pulmonary valve: Isolated ejection systolic murmur was found in 7 cases (11.7%).

Ejection systolic murmur with hyperdynamic precordium and thrill (a tactile murmur) was present in 15 cases (25.0%), suggestingincreased cardiac volume overload, observed in Atrial septal defects and large ventricular septal defects.

Pan systolic murmur combined with hyperdynamic precordium and thrill was seen in 9 cases (15%) mostly observed in moderate sized ventricular septal defect.

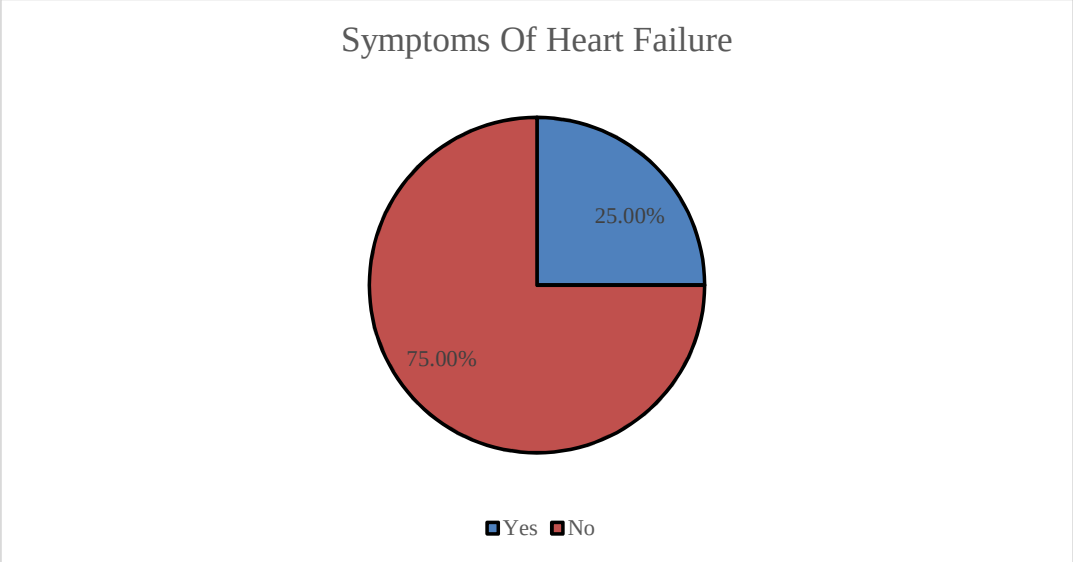
S2 split (splitting of the second heart sound) with an ejection systolic murmur was present in 2 cases (3.3%), reflecting delayed closure of the pulmonary valve due to increased right ventricular output or volume overload in atrial septal defects. Hyperdynamic precordium was noted in many cases, reflecting increased cardiac output and volume overload state due to left-to-right shunting.

Notably, a combination of continuous machinery murmur, hyperdynamic precordium, and thrill was present in 6 cases (10.0%), consistent with large PDAs or severe left-to-right shunting.

Table 8: Presence of Symptoms of Heart Failure in Patients with Acyanotic Congenital Heart Disease

		Frequency	Percent
Symptoms Of Heart Failure	Yes	15	25.0%
	No	45	75.0%
	Total	60	100.0%

Graph 8

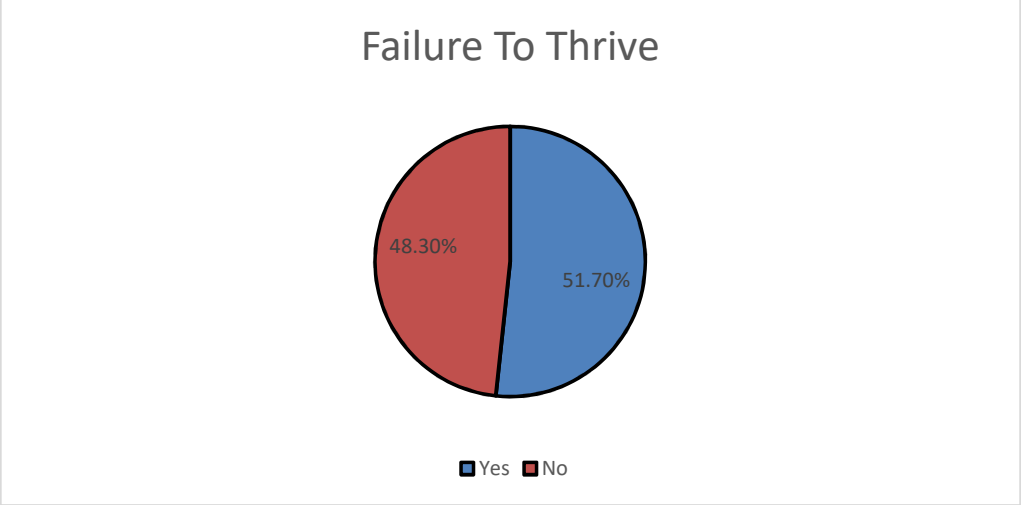


Out of the total study population, 15 patients (25.0%) had imminent signs of heart failure with history of poor feeding, lethargy, suck rest suck cycle, dyspnoea while the remaining 45 patients (75.0%) had mild symptoms (controlled on medications) like hurried breathing, previous history of LRTI with respect to overt heart failure at the time of evaluation.

Table 9: Incidence of Failure to Thrive in Patients with Acyanotic Congenital Heart Disease

		Frequency	Percent
Failure To Thrive	Yes	31	51.7%
	No	29	48.3%
	Total	60	100.0%

Graph 9:

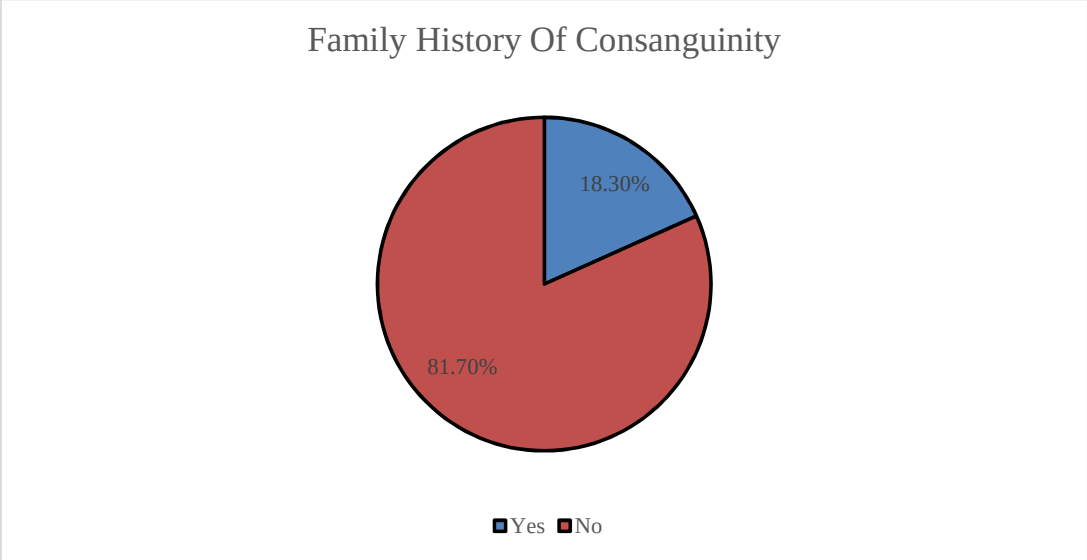


Out of the total study population, 31 children (51.7%) experienced failure to thrive andwhile 29 children (48.3%) did not show these complications at the time of evaluation. Most of the children falling in moderate to severe shunts of VSD and PDA had poor weight gain compared to ASD group.

Table 10: Family History of Consanguinity in Patients with Acyanotic Congenital Heart Disease

		Frequency	Percent
Family History Of Consanguinity	Yes	11	18.3%
	No	49	81.7%
	Total	60	100.0%

Graph 10

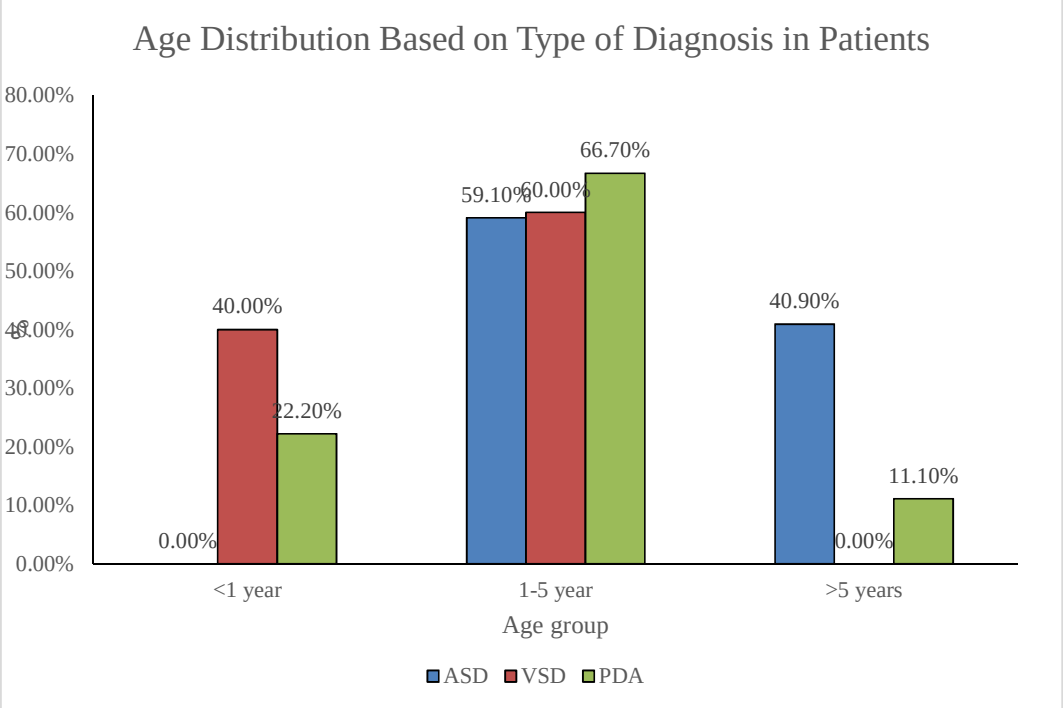


11 patients (18.3%) had a positive family history of consanguinity, while the majority, 49 patients (81.7%), did not have a known history of consanguinity.

Table 11: Age Distribution Based on Type of Diagnosis in Patients with Acyanotic Congenital Heart Disease

			DIAGNOSIS			Total
			ASD	VSD	PDA	
Age (Years)	<1 year	n	0	8	4	12
		%	0.0%	40.0%	22.2%	20.0%
	1-5 years	n	13	12	12	37
		%	59.1%	60.0%	66.7%	61.7%
	>5 years	n	9	0	2	11
		%	40.9%	0.0%	11.1%	18.3%
Total		n	22	20	18	60
		%	100.0%	100.0%	100.0%	100.0%

Graph 11



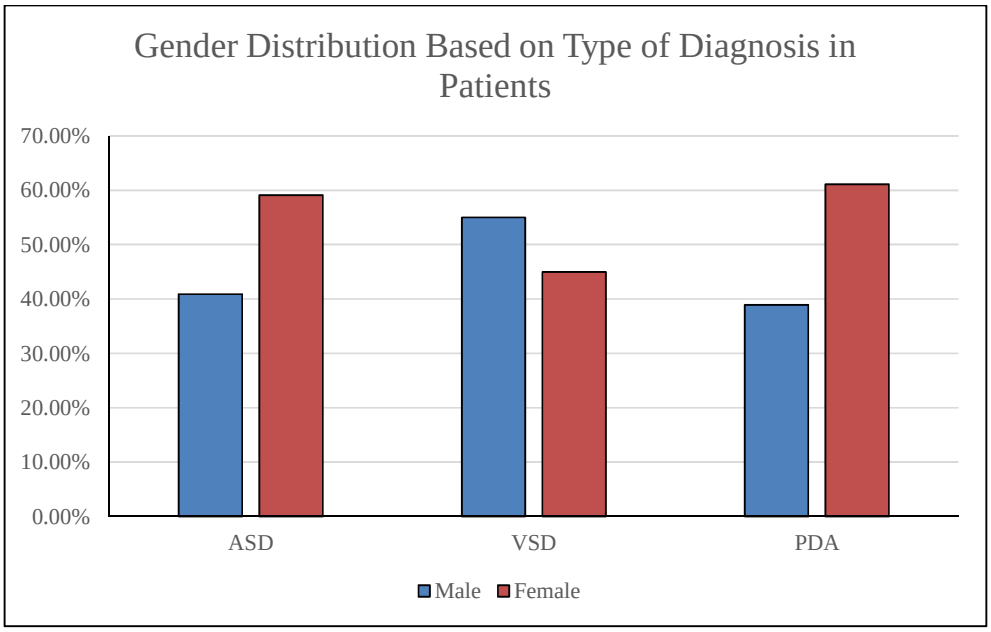
Chi-Square:18.84, P value: 0.001, Statistically Significant

Out of the total cases, 12 cases (20.0%) were diagnosed within the first year of life, with 8 cases of ventricular septal defect (VSD) (40.0%) and 4 cases of patent ductus arteriosus (PDA) (22.2%), but no atrial septal defect (ASD) cases were identified during infancy. The majority of cases (37 cases, 61.7%) were diagnosed between 1 and 5 years, including 13 cases of ASD (59.1%), 12 cases of VSD (60.0%), and 12 cases of PDA (66.7%). After 5 years, 11 cases (18.3%) were diagnosed, with 9 cases of ASD (40.9%) and 2 cases of PDA (11.1%), but no VSD cases were detected, indicating that smaller especially muscular type VSDs often close spontaneously. The association between age at diagnosis and the type of defect was found to be statistically significant.

Table 12: Gender Distribution Based on Type of Diagnosis in Patients with Acyanotic Congenital Heart Disease

			Diagnosis			Total
			ASD	VSD	PDA	
Gender	Male	n	9	11	7	27
		%	40.9%	55.0%	38.9%	45.0%
	Female	n	13	9	11	33
		%	59.1%	45.0%	61.1%	55.0%
Total		n	22	20	18	60
		%	100.0%	100.0%	100.0%	100.0%

Graph 12



Chi-Square:1.22, P value: 0.54, Statistically not Significant

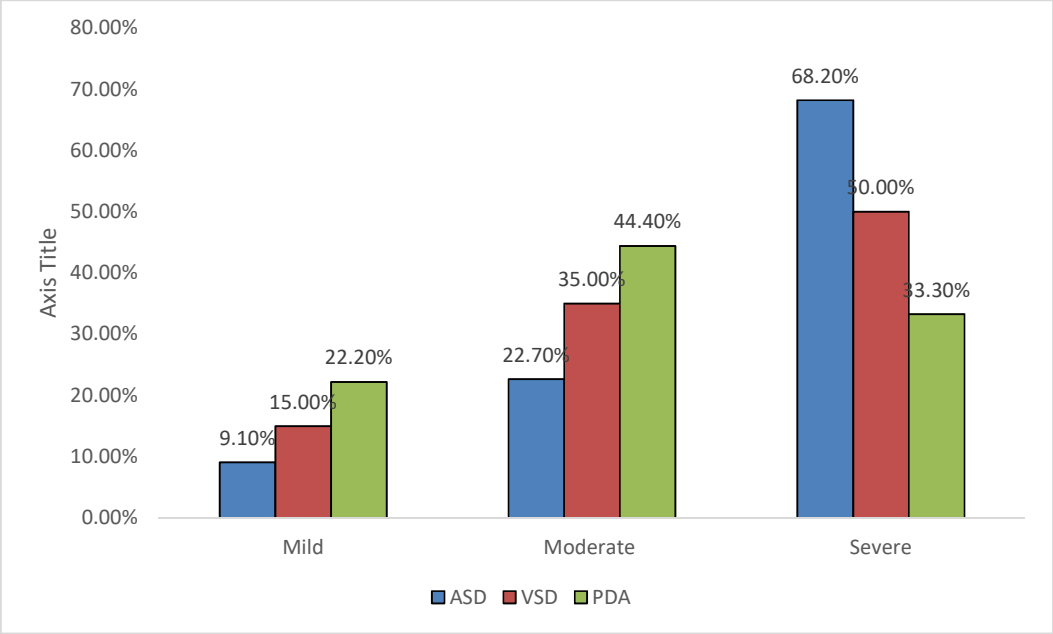
Among the 22 cases of ASD, 9 cases (40.9%) occurred in males, while 13 cases (59.1%) occurred in females. Among the 20 cases of VSD, 11 cases (55.0%) were reported in males and 9 cases (45.0%) in females, showing a nearly balanced gender distribution with a slight male predominance. Among the 18 cases of PDA, 7 cases (38.9%) were reported in males and 11 cases (61.1%) in females. The overall male-to-female ratio in the study population was approximately 0.82:1, indicating a mild female predominance especially in cases of ASD and PDA. However, the chi-square value of 1.22 and a p-value of 0.54 indicate that the observed differences in gender distribution across the three types of ACHD were not statistically significant.

Table 13: Distribution of Shunt Severity Based on Type of Diagnosis in Patients with Acyanotic Congenital Heart Disease

			Diagnosis			Total
			ASD	VSD	PDA	
Shunt Severity	Mild	n	2	3	4	9
		%	9.1%	15.0%	22.2%	15.0%
	Moderate	n	5	7	8	20
		%	22.7%	35.0%	44.4%	33.3%
	Severe	n	15	10	6	31
		%	68.2%	50.0%	33.3%	51.7%
Total		n	22	20	18	60
		%	100.0%	100.0%	100.0%	100.0%

Chi-Square:4.90, P value: 0.29, Statistically not Significant

Graph 13



A total of 9 cases (15.0%) were classified as mild left-to-right shunts. Only 2 cases of ASD (9.1%) were mild. 3 cases of VSD (15.0%) were mild. 4 cases of PDA (22.2%) were mild. A total of 20 cases (33.3%) were classified as moderate left-to-right shunts (Qp/Qs between 1.5 and 2.0). 5 cases of ASD (22.7%) were moderate. 7 cases of VSD (35.0%) were moderate. 8 cases of PDA (44.4%) were moderate. A total of 31 cases (51.7%) were classified as severe left-to-right shunts (Qp/Qs ≥ 2.0). 15 cases of ASD (68.2%) were severe. 10 cases of VSD (50.0%) were severe. 6 cases of PDA (33.3%) were severe.

Table 14: Distribution of ECG Findings Based on Type of Diagnosis in Patients with Acyanotic Congenital Heart Disease

			Diagnosis			Total
			ASD	VSD	PDA	
ECG Findings	Left Axis Deviation	N	0	1	2	3
		%	0.0%	5.0%	11.1%	5.0%
	LVH, Left Axis Deviation	N	0	12	5	17
		%	0.0%	60.0%	27.8%	28.3%
	RVH, Right Axis Deviation	N	4	0	0	4
		%	18.2%	0.0%	0.0%	6.7%
	Normal	N	18	7	11	36
		%	81.8%	35.0%	61.1%	60.0%
Total		N	22	20	18	60
		%	100.0%	100.0%	100.0%	100.0%

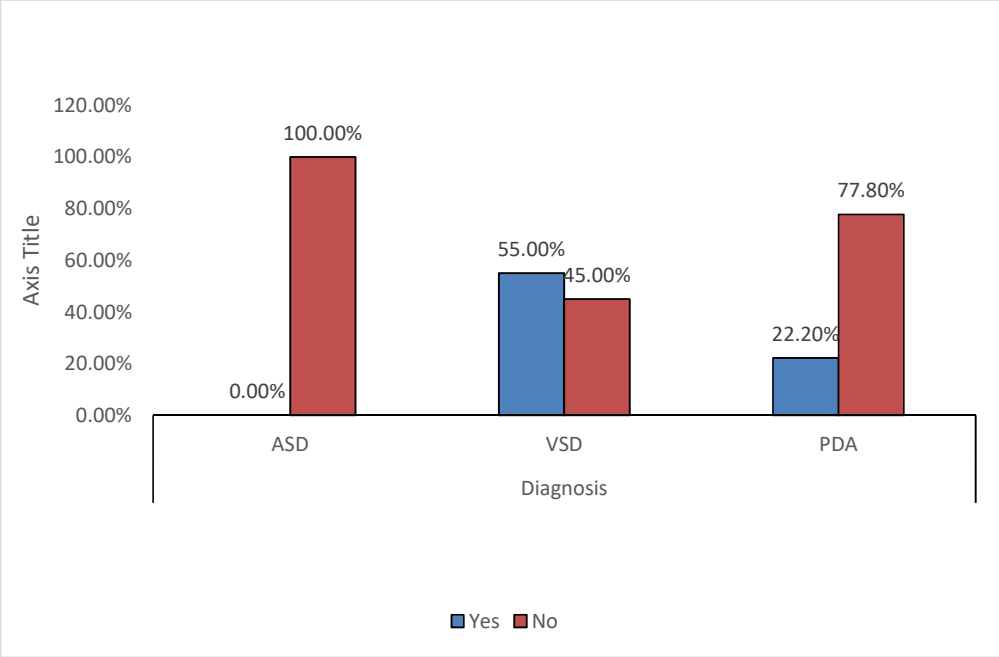
Chi-Square:26.50, P value: 0.001, Statistically Significant

Table 15: Distribution of Symptoms of Heart Failure Based on Type of Diagnosis in Patients with Acyanotic Congenital Heart Disease

			Diagnosis			Total
			ASD	VSD	PDA	
Symptoms Of Heart Failure	Yes	n	0	11	4	15
		%	0.0%	55.0%	22.2%	25.0%
	No	n	22	9	14	45
		%	100.0%	45.0%	77.8%	75.0%
Total		n	22	20	18	60
		%	100.0%	100.0%	100.0%	100.0%

Chi-Square:17.007, P value: 0.001, Statistically Significant

Graph 15



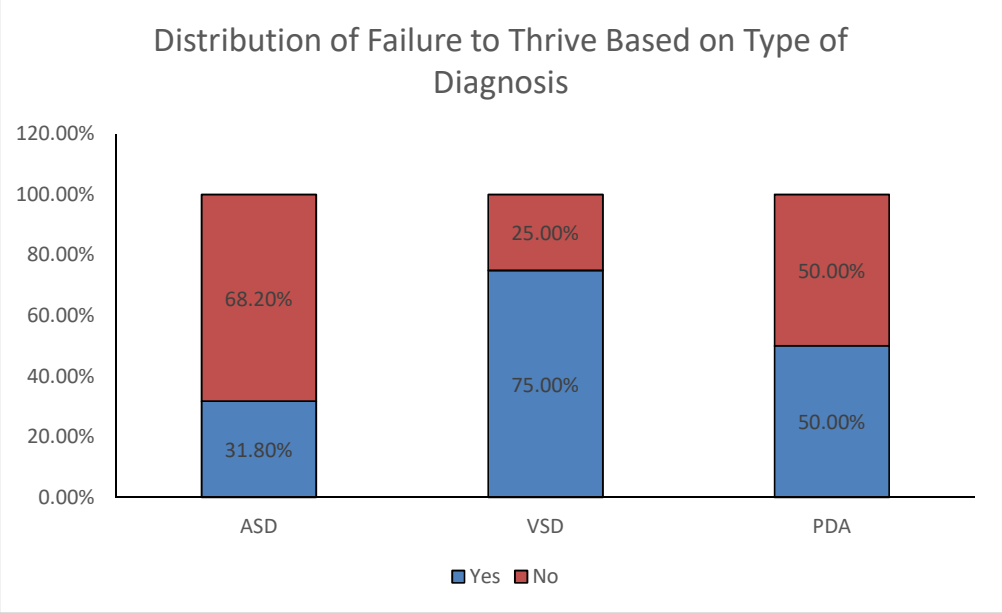
Out of the total cases, 15 cases (25.0%) had symptoms of imminent heart failure, including 11 cases of ventricular septal defect (VSD) (55.0%) and 4 cases of patent ductus arteriosus (PDA) (22.2%), reflecting significant left-to-right shunting and increased pulmonary blood flow in large VSDs and PDAs. On the other hand, 45 cases (75.0%) had mild symptoms (controlled on medications) with hurried breathing and history of LRTI in the past. ASD cases were mostly asymptomatic, reflecting the lower hemodynamic burden of small to moderate ASDs. Additionally, 9 cases of VSD (45.0%) and 14 cases of PDA (77.8%) had only mild symptoms.

Table 16: Distribution of Failure to Thrive Based on Type of Diagnosis in Patients with Acyanotic Congenital Heart Disease

			Diagnosis			Total
			ASD	VSD	PDA	
Failure To Thrive/	Yes	n	7	15	9	31
		%	31.8%	75.0%	50.0%	51.7%
	No	n	15	5	9	29
		%	68.2%	25.0%	50.0%	48.3%
Total		n	22	20	18	60
		%	100.0%	100.0%	100.0%	100.0%

Chi-Square:7.85, P value: 0.02, Statistically Significant

Graph 16



A total of 31 cases (51.7%) were identified as having failure to thrive and 7 cases of ASD (31.8%) were associated with failure to thrive. 15 cases of VSD (75.0%) and 9 cases of PDA (50.0%) were associated with failure to thrive with/without history of recurrent chest infections.

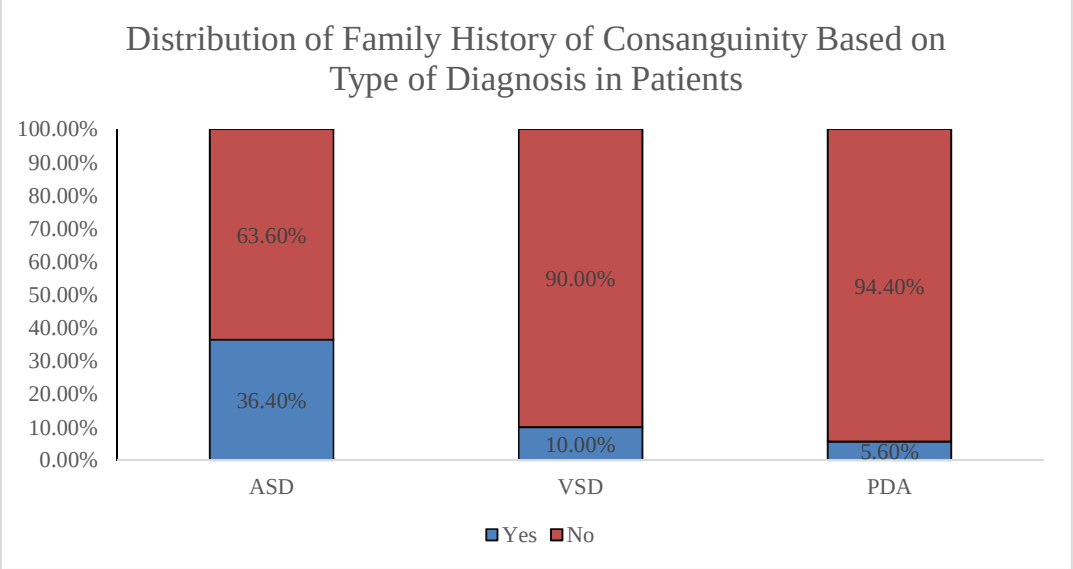
A total of 29 cases (48.3%) were not associated with failure to thrive: 15 cases of ASD (68.2%) were not associated with these complications. 5 cases of VSD (25.0%) and 9 cases of PDA (50.0%). The chi-square value of 7.85 and a p-value of 0.02 indicate that the relationship between the type of congenital defect and the presence of failure to thrive or recurrent chest infections was statistically significant.

Table 17: Distribution of Family History of Consanguinity Based on Type of Diagnosis in Patients with Acyanotic Congenital Heart Disease

			Diagnosis			Total
			ASD	VSD	PDA	
Family History of Consanguinity	Yes	n	8	2	1	11
		%	36.4%	10.0%	5.6%	18.3%
	No	n	14	18	17	49
		%	63.6%	90.0%	94.4%	81.7%
Total		n	22	20	18	60
		%	100.0%	100.0%	100.0%	100.0%

Chi-Square:7.66, P value: 0.02, Statistically Significant

Graph 17

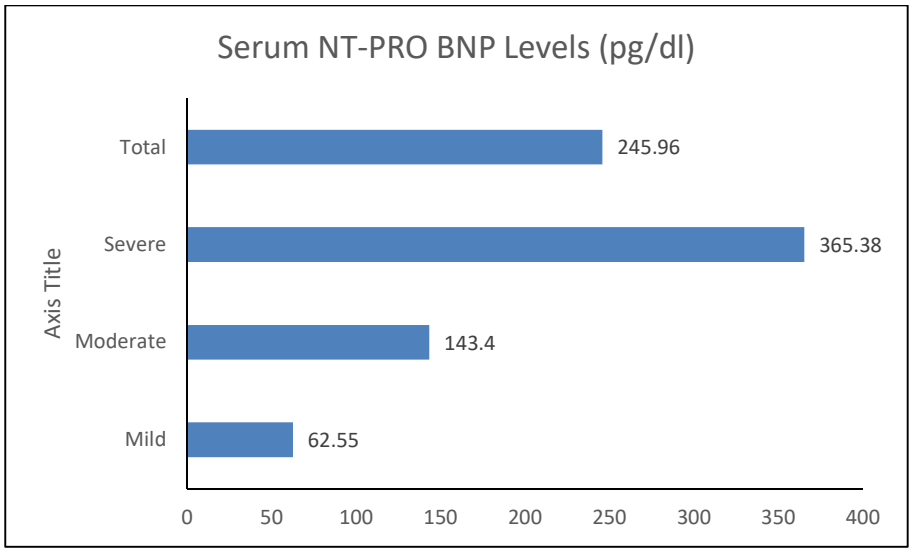


Out of the total 60 patients, 11 cases (18.3%) had a positive family history of consanguinity, while 49 cases (81.7%) had no such history. The presence of consanguinity was highest in ASD cases (36.4%) compared to VSD (10.0%) and PDA (5.6%). The chi-square value of 7.66 and p-value of 0.02 indicate that this distribution is statistically significant, confirming a meaningful association between consanguinity and the occurrence of specific congenital defects.

Table 18: Serum NT-proBNP Levels Based on Shunt Severity in Patients with Acyanotic Congenital Heart Disease

	Mild		Moderate		Severe		Total		P value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Serum NT-PRO BNP Levels (pg/dl)	62.55	22.78	143.40	37.39	365.38	138.98	245.96	162.89	0.001

Graph 18



The mean serum NT-proBNP level was lowest in mild shunt cases (62.55 pg/dl), increased significantly in moderate shunt cases (143.40 pg/dl), and reached the highest value in severe shunt cases (365.38 pg/dl). The overall mean NT-proBNP level in the study population was 245.96 pg/dl with a standard deviation of 162.89. The p-value of 0.001 indicates that the difference in NT-proBNP levels across different shunt severity groups is statistically significant, confirming that NT-proBNP levels are closely linked to the severity of left-to-right shunting.

Table 19: Left Ventricular Outflow Tract (LVOT) Diameter Based on Shunt Severity in Patients with Acyanotic Congenital Heart Disease

	Mild		Moderate		Severe		Total		P value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
LVOT Diameter(cm)	1.54	0.41	1.21	0.12	1.50	0.23	1.41	0.27	0.001

Graph 19

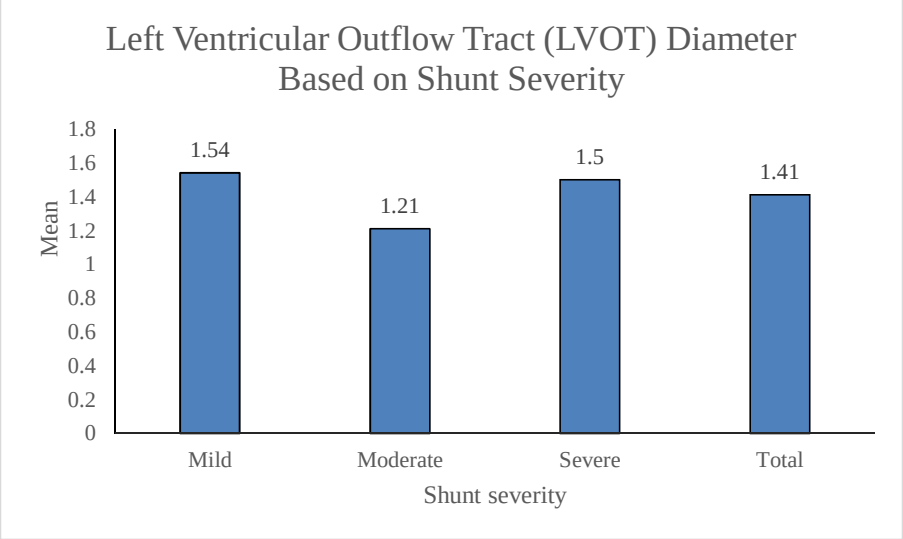
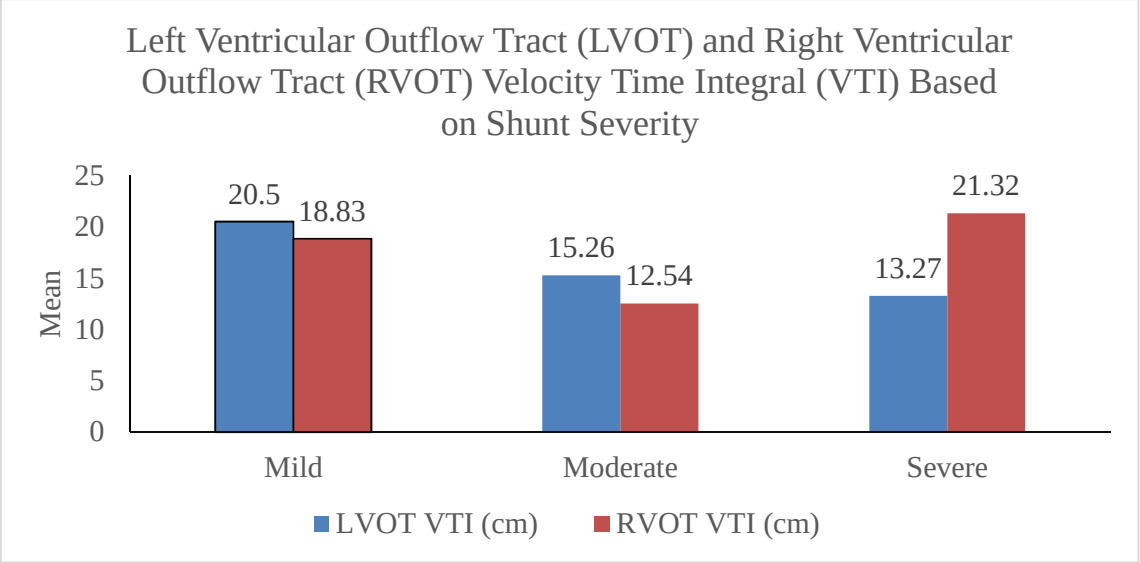


Table 20: Left Ventricular Outflow Tract (LVOT) and Right Ventricular Outflow Tract (RVOT) Velocity Time Integral (VTI) Based on Shunt Severity in Patients with Acyanotic Congenital Heart Disease

	Mild		Moderate		Severe		Total		P value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
LVOT VTI (cm)	20.50	6.41	15.26	5.00	13.27	3.17	15.02	5.00	0.001
RVOT VTI (cm)	18.83	7.69	12.54	3.79	21.32	9.07	18.02	8.39	0.001

Graph 20

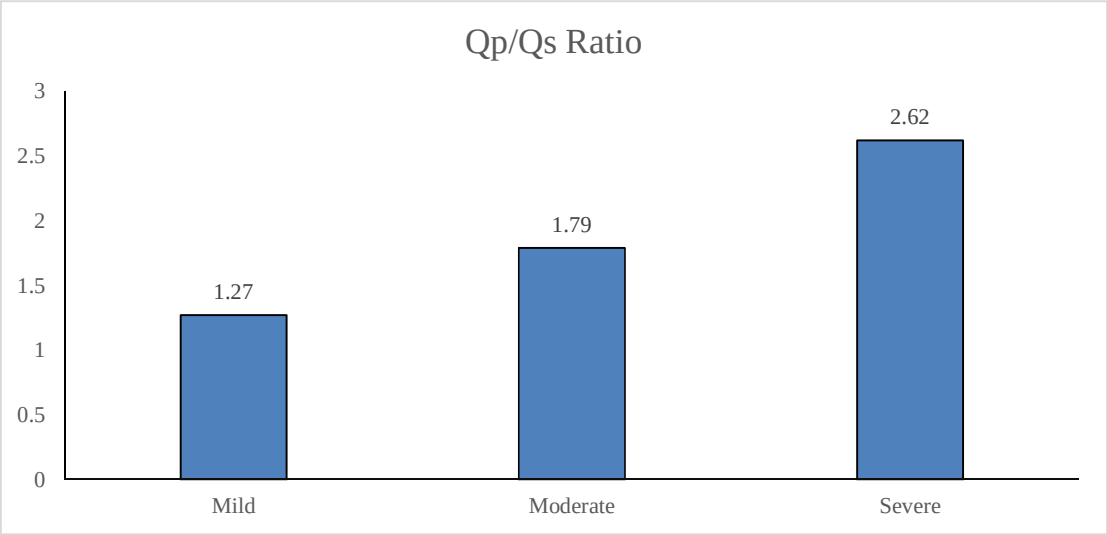


The mean LVOT VTI was highest in mild cases (20.50 cm) and lowest in severe cases (13.27 cm). The mean RVOT VTI was lowest in moderate cases (12.54 cm) and highest in severe cases (21.32 cm). The statistically significant p-values (0.001) confirm that the differences in LVOT VTI and RVOT VTI across different shunt severity groups are highly significant.

Table 21:Qp/Qs Ratio Based on Shunt Severity in Patients with Acyanotic Congenital Heart Disease

	Mild		Moderate		Severe		Total		P value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Qp/Qs Ratio	1.27	0.11	1.79	0.11	2.62	0.39	2.14	0.60	0.001

Graph 21

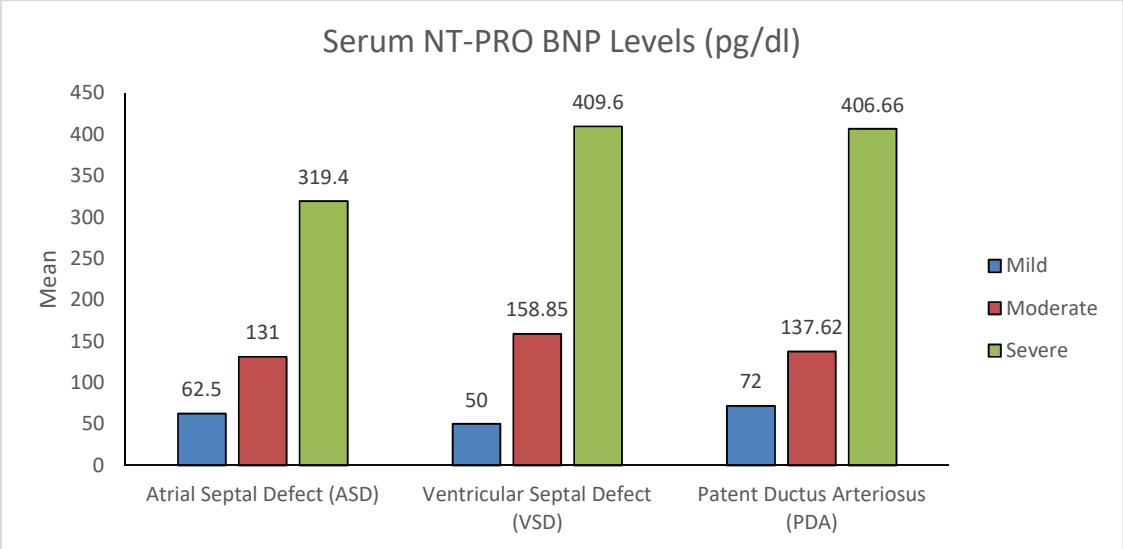


The mean Qp/Qs ratio was lowest in mild cases (1.27) and progressively increased in moderate (1.79) and severe cases (2.62). The overall mean Qp/Qs ratio for the study population was 2.14 with a standard deviation of 0.60. The p-value of 0.001 confirms that the differences in Qp/Qs ratio across different shunt severity groups are statistically significant.

Table 22: Serum NT-proBNP Levels Based on Shunt Severity and Type of Congenital Defect:

Serum NT-PRO BNP Levels (pg/dl)					
		N	Mean	SD	P Value
Atrial Septal Defect (ASD)	Mild	2	62.50	31.81	0.005
	Moderate	5	131.00	35.71	
	Severe	15	319.40	141.65	
	Total	22	253.22	154.33	
Ventricular Septal Defect (VSD)	Mild	3	50.00	17.43	0.001
	Moderate	7	158.85	45.36	
	Severe	10	409.60	106.38	
	Total	20	267.90	168.78	
Patent Ductus Arteriosus (PDA)	Mild	4	72.00	23.81	0.001
	Moderate	8	137.62	30.27	
	Severe	6	406.66	164.46	
	Total	18	212.72	170.35	

Graph 22

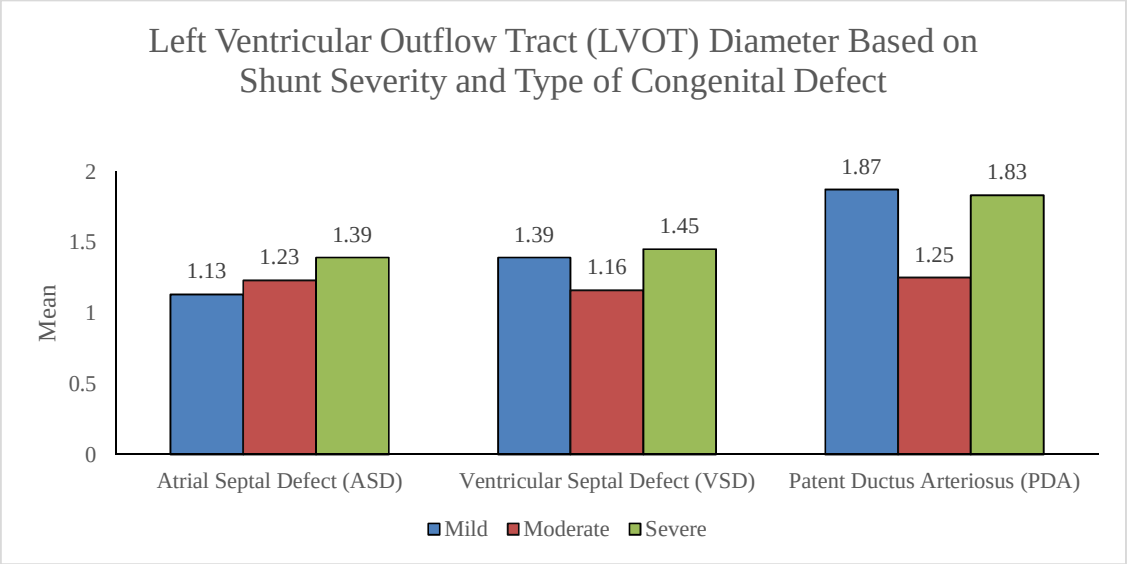


The mean NT-proBNP levels were lowest in mild cases and progressively increased with moderate and severe shunting across all three defect types. The mean NT-proBNP levels were highest in severe VSD cases (409.60 pg/dl) and severe PDA cases (406.66 pg/dl), reflecting significant left atrial and ventricular overload and pulmonary overcirculation. The statistically significant p-values (0.005 for ASD, 0.001 for VSD and PDA) confirm that the differences in NT-proBNP levels across shunt severity groups within each defect type are highly significant.

Table 23: Left Ventricular Outflow Tract (LVOT) Diameter Based on Shunt Severity and Type of Congenital Defect

LVOT Diameter (cm)					
		N	Mean	SD	P Value
Atrial Septal Defect (ASD)	Mild	2	1.13	0.02	0.001
	Moderate	5	1.23	0.17	
	Severe	15	1.39	0.07	
	Total	22	1.33	0.13	
Ventricular Septal Defect (VSD)	Mild	3	1.39	0.52	0.01
	Moderate	7	1.16	0.02	
	Severe	10	1.45	0.03	
	Total	20	1.34	0.22	
Patent Ductus Arteriosus (PDA)	Mild	4	1.87	0.05	0.001
	Moderate	8	1.25	0.14	
	Severe	6	1.83	0.36	
	Total	18	1.58	0.37	

Graph 23



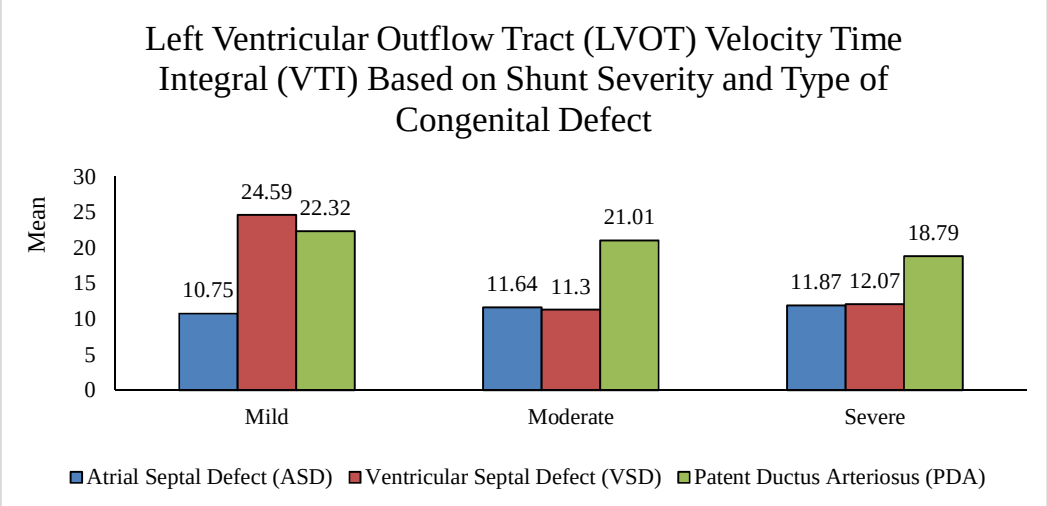
The mean LVOT diameter increased progressively with increasing shunt severity across ASD and VSD cases. In PDA cases, the LVOT diameter was highest in mild and severe cases, reflecting the variability in ductal size and shunting patterns. The statistically significant p-values (0.001 for ASD and PDA, 0.01 for VSD) confirm that the differences in LVOT diameter across shunt severity groups within each defect type are clinically meaningful.

Table 24: Left Ventricular Outflow Tract (LVOT) Velocity Time Integral (VTI)

Based on Shunt Severity and Type of Congenital Defect

LVOT VTI (cm)					
		N	Mean	SD	P Value
Atrial Septal Defect (ASD)	Mild	2	10.75	0.07	0.58
	Moderate	5	11.64	2.55	
	Severe	15	11.87	0.96	
	Total	22	11.72	1.40	
Ventricular Septal Defect (VSD)	Mild	3	24.59	5.79	0.001
	Moderate	7	11.30	0.32	
	Severe	10	12.07	0.54	
	Total	20	13.67	5.09	
Patent Ductus Arteriosus (PDA)	Mild	4	22.32	1.67	0.07
	Moderate	8	21.01	1.21	
	Severe	6	18.79	3.49	
	Total	18	20.56	2.57	

Graph 24

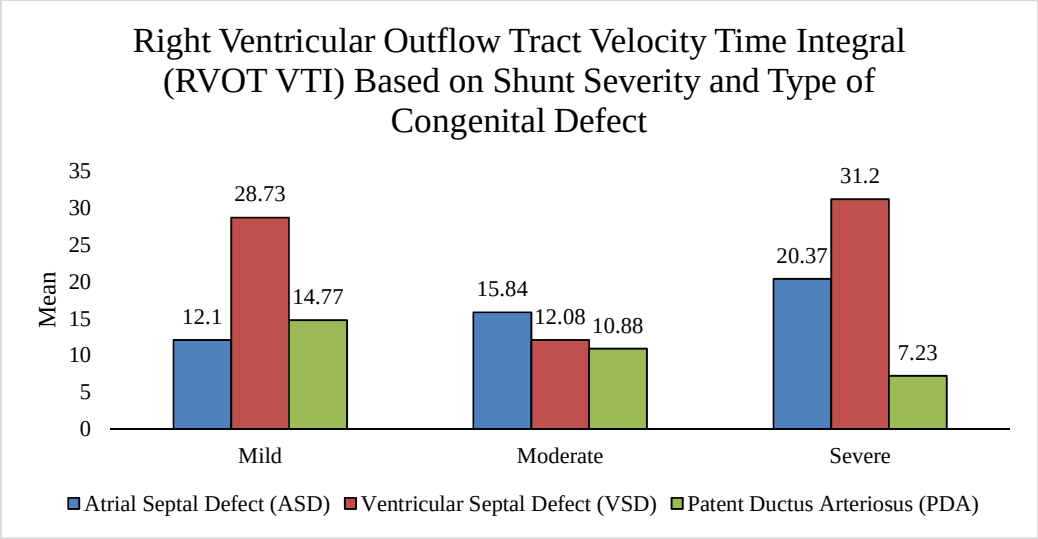


In ASD and PDA cases, the differences in LVOT VTI values across shunt severity groups were not statistically significant. In VSD cases, LVOT VTI showed a significant difference (p-value = 0.001) with a sharp decline in moderate and severe cases.

Table 25: Right Ventricular Outflow Tract Velocity Time Integral (RVOT VTI) Based on Shunt Severity and Type of Congenital Defect

RVOT VTI (cm)					
		N	Mean	SD	P Value
Atrial Septal Defect (ASD)	Mild	2	12.10	0.14	0.02
	Moderate	5	15.84	6.37	
	Severe	15	20.37	3.82	
	Total	22	18.59	5.05	
Ventricular Septal Defect (VSD)	Mild	3	28.73	3.34	0.001
	Moderate	7	12.08	0.48	
	Severe	10	31.20	2.59	
	Total	20	24.14	9.35	
Patent Ductus Arteriosus (PDA)	Mild	4	14.77	0.65	0.001
	Moderate	8	10.88	2.11	
	Severe	6	7.23	2.22	
	Total	18	10.53	3.38	

Graph 25

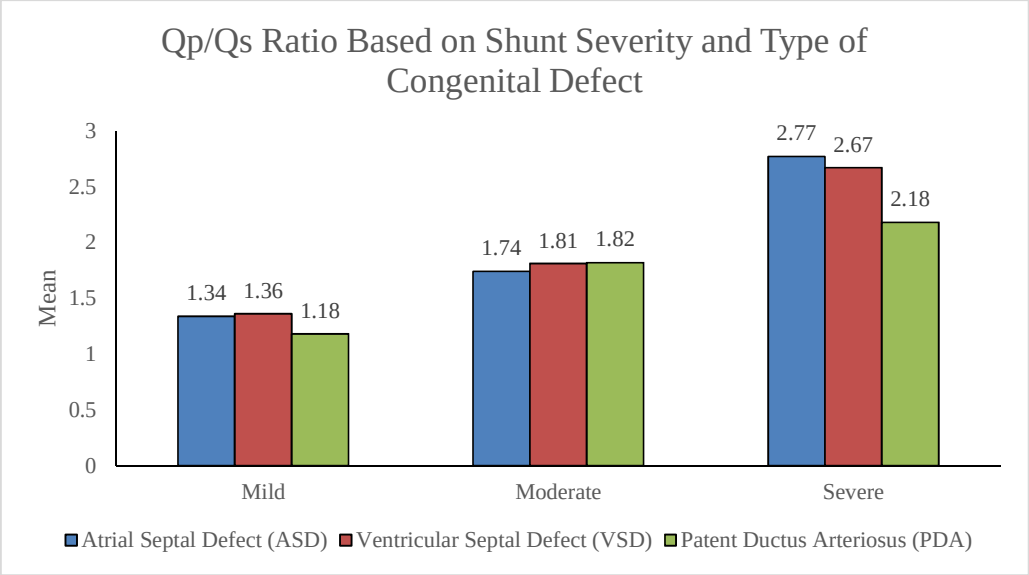


RVOT VTI was highest in VSD cases and lowest in PDA cases, reflecting the distinct hemodynamic effects of each defect type. The differences in RVOT VTI values across shunt severity groups were statistically significant in ASD ($p = 0.02$) and highly significant in VSD and PDA cases ($p = 0.001$). In VSD cases, severe shunting resulted in the highest RVOT VTI values, indicating significant pulmonary overcirculation and right sided compensation.

Table 26: Qp/Qs Ratio Based on Shunt Severity and Type of Congenital Defect

Qp/Qs Ratio					
		N	Mean	SD	P Value
Atrial Septal Defect (ASD)	Mild	2	1.34	0.05	0.001
	Moderate	5	1.74	0.18	
	Severe	15	2.77	0.45	
	Total	22	2.41	0.67	
Ventricular Septal Defect (VSD)	Mild	3	1.36	0.06	0.001
	Moderate	7	1.81	0.11	
	Severe	10	2.67	0.12	
	Total	20	2.17	0.54	
Patent Ductus Arteriosus (PDA)	Mild	4	1.18	0.10	0.001
	Moderate	8	1.82	0.05	
	Severe	6	2.18	0.16	
	Total	18	1.80	0.38	

Graph 26



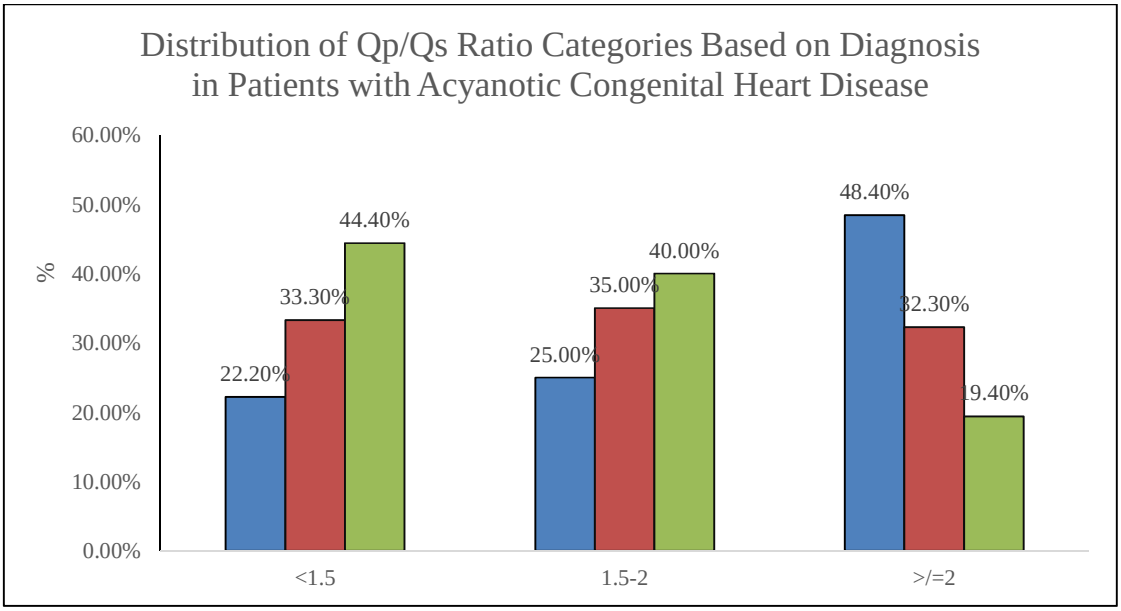
The Qp/Qs ratio represents the ratio of pulmonary blood flow (Qp) to systemic blood flow (Qs) and serves as a direct measure of the magnitude of left-to-right shunting. The Qp/Qs ratio increased progressively with shunt severity across all three defect types. The differences in Qp/Qs ratio values across shunt severity groups were highly significant for ASD, VSD, and PDA cases (p-value = 0.001).

Table 27: Distribution of Qp/Qs Ratio Categories Based on Diagnosis in Patients with Acyanotic Congenital Heart Disease

			Qp/Qs Ratio			Total
			<1.5	1.5-2	>/=2	
Diagnosis	ASD	n	2	5	15	22
		%	22.2%	25.0%	48.4%	36.7%
	VSD	n	3	7	10	20
		%	33.3%	35.0%	32.3%	33.3%
	PDA	n	4	8	6	18
		%	44.4%	40.0%	19.4%	30.0%
Total		n	9	20	31	60
		%	100.0%	100.0%	100.0%	100.0%

Chi-Square:4.90, P value: 0.29, Statistically not Significant

Graph 27



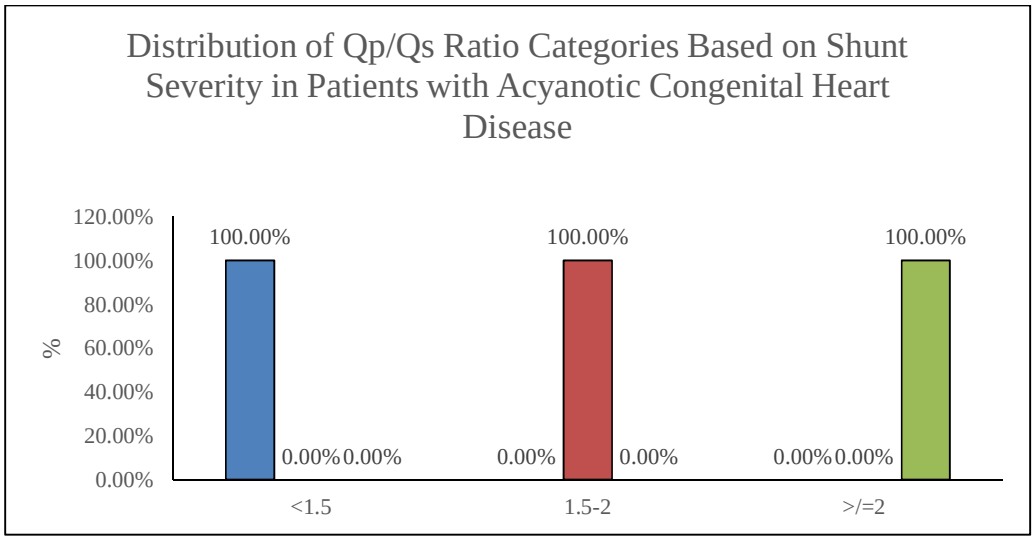
The Qp/Qs ratio was classified into three categories: <1.5 indicating hemodynamically insignificant left-to-right shunting, 1.5–2.0 indicating hemodynamically significant shunting likely requiring closure, and ≥2.0 indicating large left-to-right shunting associated with increased pulmonary overcirculation and left heart volume overload, typically requiring early intervention. The majority of severe cases (Qp/Qs ≥ 2.0) were seen in atrial septal defect (ASD) cases (48.4%), followed by ventricular septal defect (VSD) cases (32.3%), and least frequently in patent ductus arteriosus (PDA) cases (19.4%). However, the Chi-square value was 4.90, and the p-value was 0.29, indicating that the differences in Qp/Qs distribution across different diagnoses were not statistically significant.

Table 28: Distribution of Qp/Qs Ratio Categories Based on Shunt Severity in Patients with Acyanotic Congenital Heart Disease

			Qp/Qs Ratio			Total
			<1.5	1.5-2	>/=2	
Shunt Severity	Mild	n	9	0	0	9
		%	100.0%	0.0%	0.0%	15.0%
	Moderate	n	0	20	0	20
		%	0.0%	100.0%	0.0%	33.3%
	Severe	n	0	0	31	31
		%	0.0%	0.0%	100.0%	51.7%
Total		n	9	20	31	60
		%	100.0%	100.0%	100.0%	100.0%

Chi-Square:120.00, P value: 0.001, Statistically Significant

Graph 28

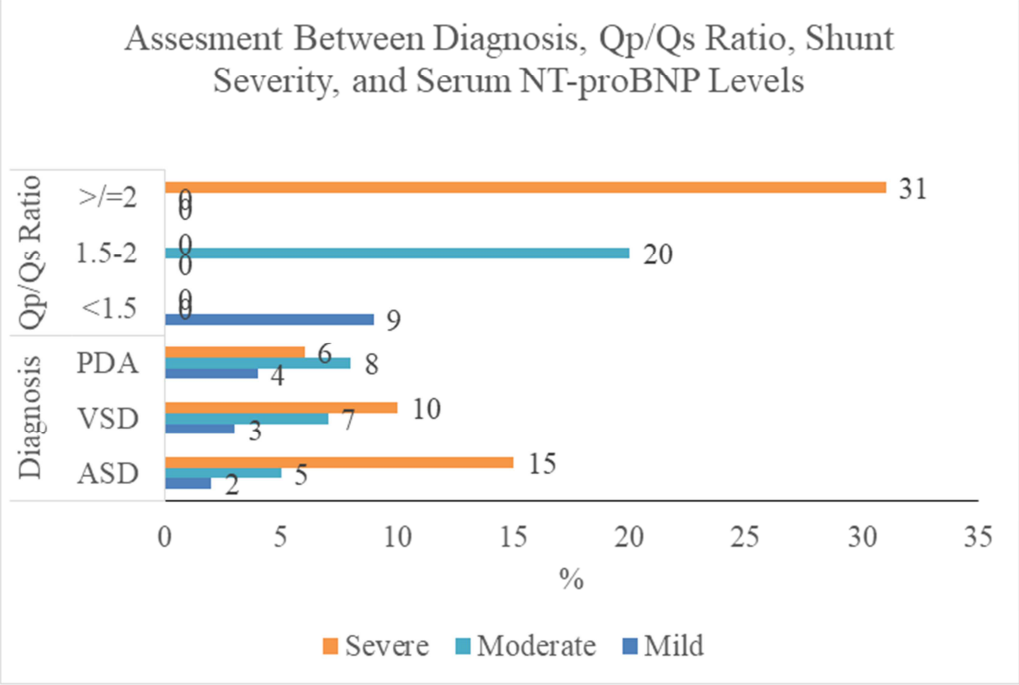


The Qp/Qs ratio was classified into three categories based on shunt severity: mild (<1.5), moderate (1.5–2.0), and severe (≥2.0). Among the mild cases, all 9 cases (100.0%) had a Qp/Qs ratio of <1.5. For moderate cases, all 20 cases (100.0%) had a Qp/Qs ratio between 1.5 and 2.0, indicating hemodynamically significant shunting likely requiring closure. All 31 severe cases (100.0%) had a Qp/Qs ratio ≥2.0, reflecting large left-to-right shunting with increased pulmonary overcirculation and left heart volume overload, typically requiring early intervention. The Chi-square value was 120.00, and the p-value was 0.001, indicating that the differences in Qp/Qs distribution across shunt severity categories were statistically significant.

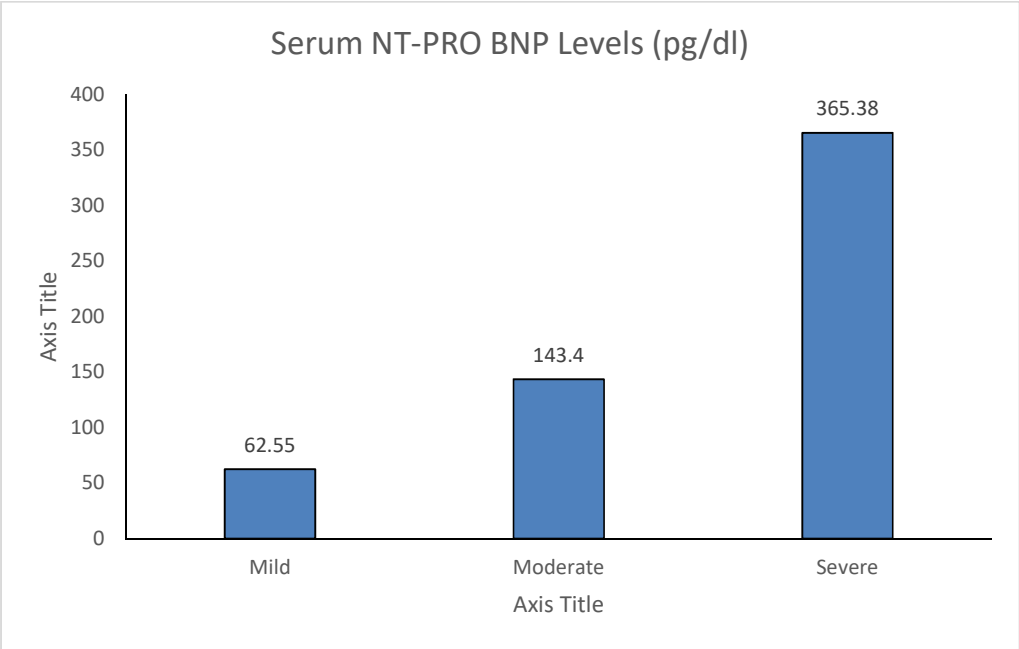
Table 29: Correlation Between Diagnosis, Qp/Qs Ratio, Shunt Severity, and Serum NT-proBNP Levels

		Diagnosis			Qp/Qs Ratio			Serum NT-PRO BNP Levels (pg/dl)	Qp/Qs Ratio
		ASD	VSD	PDA	<1.5	1.5-2	>/=2		
SHUNT	Mild	2	3	4	9	0	0	62.55 ± 22.78	1.27 ± 0.11
	Moderate	5	7	8	0	20	0	143.40 ± 37.39	1.79 ± 0.11
	Severe	15	10	6	0	0	31	365.38 ±138.98	2.62 ± 0.39
P Value		0.29			0.001			0.001	0.001

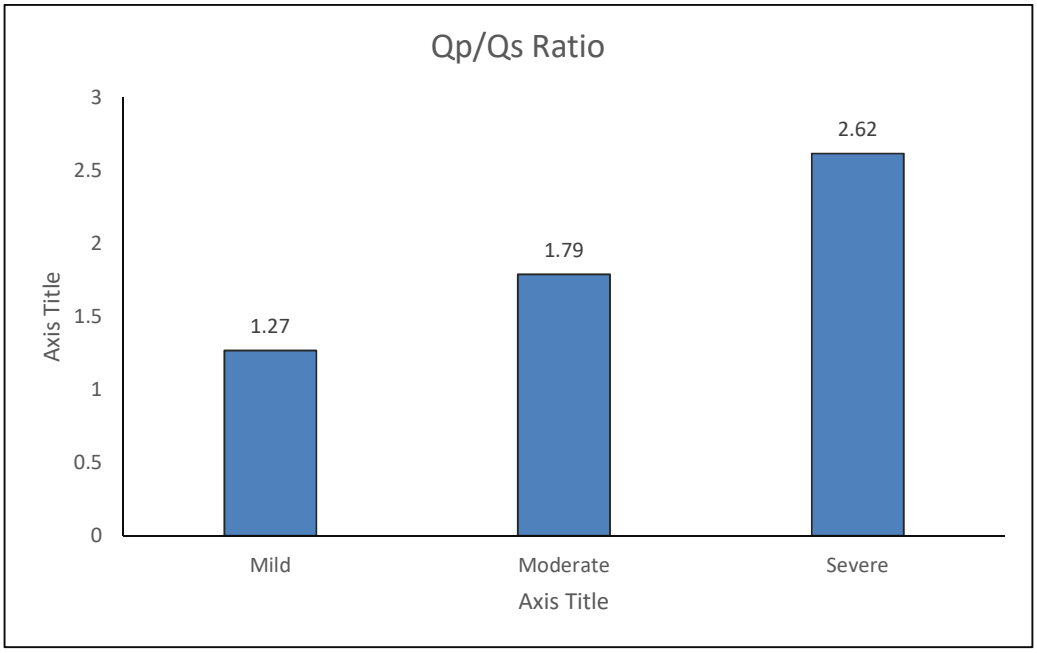
Graph 29



Graph 30



Graph 31

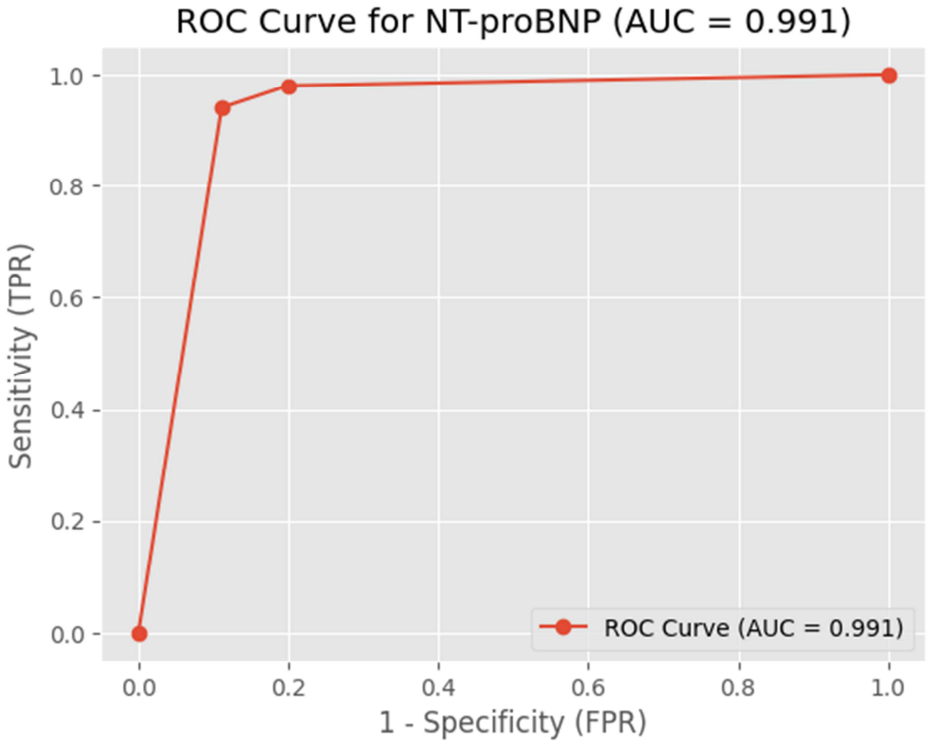


- Among the mild shunt cases, there were 2 cases of atrial septal defect (ASD), 3 cases of ventricular septal defect (VSD), and 4 cases of patent ductus arteriosus (PDA), all with a Qp/Qs ratio <1.5, a mean serum NT-PRO BNP level of 62.55 ± 22.78 pg/dl, and a Qp/Qs ratio of 1.27 ± 0.11.
- In moderate shunt cases, there were 5 cases of ASD, 7 cases of VSD, and 8 cases of PDA, all with a Qp/Qs ratio between 1.5 and 2.0, a mean NT-PRO BNP level of 143.40 ± 37.39 pg/dl, and a Qp/Qs ratio of 1.79 ± 0.11.
- Among the severe shunt cases, there were 15 cases of ASD, 10 cases of VSD, and 6 cases of PDA, all with a Qp/Qs ratio ≥2.0, a significantly higher mean NT-PRO BNP level of 365.38 ± 138.98 pg/dl, and a Qp/Qs ratio of 2.62 ± 0.39. The association between Qp/Qs ratio and shunt severity was statistically significant (p = 0.001).

Table 30: Receiver Operating Characteristic (ROC) Curve Analysis for Serum NT-proBNP Levels in Predicting Significant Left-to-Right Shunting (Qp/Qs > 1.5)

Case Processing Summary	
Qp/Qs RATIO	Valid N (listwise)
Positive	51
Negative	9
Larger values of the test result variable(s) indicate stronger evidence for a positive actual state.	
a. The positive actual state is >1.5.	
Area Under the Curve (AUC)	
Test Result Variable(s): SERUM NT-PRO BNP LEVELS (pg/dl)	

Area	Std. Errora	P Value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.991	0.010	0.001	0.972	1.000
a. Under the nonparametric assumption				
b. Null hypothesis: true area = 0.5				



This study evaluates the diagnostic performance of **serum NT-proBNP levels** in predicting significant left-to-right shunting (Qp/Qs > 1.5) in patients with acyanotic congenital heart disease. The **Receiver Operating Characteristic (ROC) curve analysis** was used to determine the optimal cut-off value for NT-proBNP levels, balancing sensitivity and specificity. The results demonstrate excellent diagnostic accuracy, with an **AUC of 0.991**, indicating that the test is highly effective in distinguishing between patients with and without significant shunting.

The **ROC curve** for serum NT-proBNP levels shows a steep initial rise, reflecting high sensitivity at low false positive rates. At the chosen cut-off value of **112 pg/dl**, the test achieves a **sensitivity of 94%** and a **specificity of 88.89%**. This means the test correctly identifies 94% of true positive cases (Qp/Qs > 1.5) while incorrectly classifying only 11.11% of true negative cases as positive. The curve then stabilizes, indicating that the test maintains high sensitivity even as specificity increases. The **AUC of 0.991** confirms that the test has excellent diagnostic accuracy.

The optimal cut-off value of **112 pg/dl** was determined using the ROC curve. At this threshold:

- **Sensitivity = 94%**: The test correctly identifies 94% of patients with significant shunting.
- **Specificity = 88.89%**: The test correctly identifies 88.89% of patients without significant shunting.
- **False Positive Rate (FPR) = 11.11%**: Only 11.11% of true negative cases are incorrectly classified as positive.

This cut-off value strikes an excellent balance between sensitivity and specificity, making it clinically useful for identifying patients who require further evaluation or intervention.

The high sensitivity and specificity of the test, along with the **AUC of 0.991**, make serum NT-proBNP levels a reliable biomarker for predicting significant left-to-right shunting. This is particularly important in clinical settings where early detection and intervention can improve outcomes for patients with acyanotic congenital heart disease. The test's ability to accurately distinguish between mild, moderate, and severe shunting (based on Qp/Qs ratios) further enhances its diagnostic utility.

The ROC curve's shape—**sharp initial rise followed by stabilization**—is consistent with a test that has excellent diagnostic accuracy. The steep rise indicates that the test achieves high sensitivity with a low false positive rate, while the stabilization reflects its ability to maintain high sensitivity even as specificity increases. This shape is typical for tests with a high AUC and confirms the robustness of the diagnostic tool.

The study demonstrates that **serum NT-proBNP levels** are a highly accurate biomarker for predicting significant left-to-right shunting in patients with acyanotic congenital heart disease. The **ROC curve analysis** confirms the test's excellent diagnostic performance, with an **AUC of 0.991**, **sensitivity of 94%**, and **specificity of 88.89%** at the optimal cut-off value of **112 pg/dl**. These findings highlight the clinical utility of NT-proBNP as a non-invasive, reliable tool for diagnosing and managing patients with congenital heart defects.

- **Adoption the 112 pg/dl cut-off value** for clinical use, as it provides the best balance between sensitivity and specificity.

- **Use serum NT-proBNP levels** as a screening tool for patients suspected of having significant left-to-right shunting.
- **Further validate the findings** in larger, multi-center studies to confirm the generalizability of the results.

The study includes a total of **60 cases** categorized based on the **Qp/Qs ratio**, which measures the severity of left-to-right shunting in children with acyanotic congenital heart disease. Among these, **51 cases** had a **Positive Qp/Qs ratio (Qp/Qs > 1)**, indicating significant shunting, while **9 cases** had a **Negative Qp/Qs ratio (Qp/Qs ≤ 1)**, suggesting minimal or no significant shunting. The cases were further divided into three severity groups: **Mild**, **Moderate**, and **Severe**, with **22**, **20**, and **18 cases** in each group, respectively. This distribution aligns with findings from previous studies, which have demonstrated the utility of the Qp/Qs ratio in assessing shunt severity in congenital heart disease [1, 2, 3].

Severe cases were more likely to have a **Qp/Qs ratio (Qp/Qs > 2)**. Out of the total **31 severe cases** (15 in the first group, 10 in the second, and 6 in the third), most were associated with a severe Qp/Qs ratio. This indicates that severe cases typically involve significant left-to-right shunting, necessitating surgical intervention to correct the defect. Similar findings have been reported in studies by Kavga et al. [5] and Ozhan et al. [21], who highlighted the association between high Qp/Qs ratios and severe shunting in congenital heart disease.

Mild cases, on the other hand, were more likely to have a **Qp/Qs ratio (Qp/Qs ≤ 1.5)**. Out of the total **9 mild cases** (2 in the first group, 3 in the second, and 4 in the third), most were associated with a decreased Qp/Qs ratio. Despite the small shunt size, surgery was performed in some mild cases for prophylactic reasons or to prevent

future complications, even though the Qp/Qs ratio did not indicate significant shunting. This observation is consistent with studies by Farouk et al. [4] and Ozyurt et al. [6], which emphasized that clinical symptoms and risk of complications often guide surgical decisions, even in mild cases.

Moderate cases were distributed between Qp/Qs ratios (1.5-2). Out of the total **20 moderate cases** (5 in the first group, 7 in the second, and 8 in the third) suggests that moderate cases may vary in the degree of shunting, and clinical judgment is required to determine the need for surgery. This variability has been noted in studies by Jamei Khosroshahi et al. [3] and Sugimoto et al. [19], which highlighted the importance of individualized assessment in moderate cases like growth restriction, failure to thrive, and also the likely possibility of defect closing on itself , depending on the type of defect.

All **31 severe cases** underwent surgery due to their high Qp/Qs ratio, indicating significant left-to-right shunting. In contrast, **4 mild cases** also underwent surgery, likely due to clinical symptoms or the risk of future complications, despite the absence of significant shunting. This highlights that the Qp/Qs ratio is just one factor in deciding whether surgery is needed, as supported by studies by Saxena et al. [15, 16] and Martin et al. [14], which emphasized the multifactorial nature of surgical decision-making in congenital heart disease.

ROC Curve Analysis

A **Receiver Operating Characteristic (ROC) Curve Analysis** was performed to evaluate the performance of **Serum NT-proBNP levels** in predicting significant left-to-right shunting (Qp/Qs > 1.5).

- **Area Under the Curve (AUC): 0.991**, indicating excellent diagnostic accuracy.
- **Standard Error: 0.010**.
- **P Value: 0.001**, confirming the statistical significance of the AUC.
- **95% Confidence Interval: 0.972 to 1.000**.
- **Cut-off Value: 112 pg/dl**, with a **Sensitivity of 94%** and **Specificity of approximately 88.89%**. These findings are consistent with studies by Zhang et al. [8] and Yasmien et al. [22], which demonstrated the utility of NT-proBNP as a biomarker for assessing shunt severity.
- **Sensitivity (94%)**: This means that the test correctly identifies **94% of true positive cases** (Qp/Qs > 1.5). In other words, out of the **51 positive cases**, the test accurately detected **48 cases**.
- **Specificity (88.89%)**: This indicates that the test correctly identifies **88.89% of true negative cases** (Qp/Qs ≤ 1.5). Out of the **9 negative cases**, the test accurately ruled out **8 cases**.
- The high sensitivity and specificity values demonstrate that **Serum NT-proBNP levels** are a reliable biomarker for predicting significant left-to-right shunting in children with acyanotic congenital heart disease, as supported by studies by Elin and Winter [9] and Castiglione et al. [10].

Clinical Implications

The study highlights the clinical utility of **Serum NT-proBNP levels** as a non-invasive tool for assessing the severity of left-to-right shunting in children with

acyanotic congenital heart disease. The ROC curve analysis confirms its high diagnostic accuracy, with a cut-off value of **112 pg/dl** providing an optimal balance between sensitivity and specificity. This biomarker can aid clinicians in making informed decisions regarding surgical intervention, especially in cases where the Qp/Qs ratio alone may not fully capture the clinical severity. These findings are consistent with the work of Krishnaswami [11] and Yoo [12], who emphasized the role of natriuretic peptides in managing congenital heart disease.

DISCUSSION

Based on echocardiographic and hemodynamic evaluations, this study aimed to establish a correlation between serum NT-proBNP levels and the severity of left-to-right shunting in children with acyanotic congenital heart disease (ACHD)**.** The study included 60 patients diagnosed with atrial septal defect (ASD)**,** ventricular septal defect (VSD)**, or** patent ductus arteriosus (PDA)**,** classified into mild**,** moderate**, and** severe shunt severity groups based on the Qp/Qs ratio. This approach aligns with previous studies that have demonstrated the utility of the Qp/Qs ratio in assessing shunt severity and its correlation with biomarkers like NT-proBNP [1, 2, 3]. The classification into severity groups is consistent with findings from Kavga et al. [5] and Ozhan et al. [21], who highlighted the importance of stratifying patients based on shunt severity to guide clinical decision-making. Additionally, the use of NT-proBNP as a biomarker for shunt severity has been supported by studies such as those by Zhang et al. [8] and Yasmien et al. [22], which emphasized its diagnostic accuracy in predicting significant shunting in congenital heart disease.

In our study, the most frequently diagnosed condition among the **60 cases** was **atrial septal defect (ASD)**, which accounted for **22 cases (36.7%)**. This was followed closely by **ventricular septal defect (VSD)**, identified in **20 cases (33.3%)**, and **patent ductus arteriosus (PDA)**, diagnosed in **18 cases (30.0%)**. These findings are consistent with previous studies that have reported ASD as the most common acyanotic congenital heart defect in pediatric populations. For instance, **Zhang et al. (2023)** conducted a retrospective study involving **64 patients** with congenital heart disease (CHD) and pulmonary artery hypertension (PAH), where ASD was the most common diagnosis (57.8%), followed by VSD (29.7%) and PDA (12.5%) [8].

Similarly, **Kavga et al. (2013)** reported ASD as the predominant diagnosis in their study of **76 children** with CHD involving left-to-right shunt, with **31 cases (40.8%)** of ASD, **23 cases (30.3%)** of VSD, and **14 cases (18.4%)** of PDA [5].

The distribution of diagnoses in our study aligns with findings from **Farouk et al. (2017)**, who reported ASD as the most common diagnosis (17 cases, 39.5%) in their study of **43 pediatric patients** undergoing elective cardiac surgery for shunt closure, followed by VSD and PDA (13 cases each, 30.2%) [4]. Additionally, **Khosroshahi et al. (2019)** found a similar distribution in their cross-sectional study of **60 infants and children** with CHD, where ASD, VSD, and PDA each accounted for **20 cases (33.3%)** [3]. These consistent findings across studies highlight the prevalence of ASD as a leading acyanotic congenital heart defect in pediatric populations.

The use of echocardiography and hemodynamic evaluations, such as the **Qp/Qs ratio**, to assess shunt severity is well-supported in the literature. **Ozyurt et al. (2015)** conducted a prospective study involving **127 children** with congenital septal defects, where echocardiography was used to estimate the Qp/Qs ratio and pulmonary artery pressure, and NT-proBNP levels were measured to evaluate their correlation with shunt severity [6]. Similarly, **Samadi et al. (2017)** utilized echocardiography to confirm diagnoses and evaluate the relationship between serum pro-BNP levels, Qp/Qs ratio, and pulmonary hypertension in **30 infants and children** with CHD [1]. These studies underscore the importance of combining echocardiographic and biomarker assessments to evaluate shunt severity in children with CHD comprehensively.

In conclusion, our findings are consistent with previous studies, demonstrating that **ASD** is the most frequently diagnosed acyanotic congenital heart defect in

pediatric populations, followed by **VSD** and **PDA**. The use of echocardiography and biomarkers like **NT-proBNP** provides a reliable approach to assessing shunt severity and guiding clinical management in children with CHD. These results reinforce the importance of integrating diagnostic tools to optimize patient outcomes in congenital heart disease.

Age and Gender Distribution

In our study, the highest prevalence of acyanotic congenital heart disease (ACHD) was observed in children aged 12–60 months (61.7%), with 37 cases diagnosed in this age group. This included 13 cases of ASD (59.1%), 12 cases of VSD (60.0%), and 12 cases of PDA (66.7%), reflecting increased left-to-right shunting and hemodynamic changes with growth. Among infants (<12 months), 12 cases (20.0%) were diagnosed, including 8 cases of VSD (40.0%) and 4 cases of PDA (22.2%), but no ASD cases were identified. After 60 months, 11 cases (18.3%) were diagnosed, with 9 cases of ASD (40.9%) and 2 cases of PDA (11.1%), but no VSD cases, as smaller VSDs often close spontaneously. The association between age at diagnosis and defect type was statistically significant. These findings align with Kavga et al. (2013), who reported a mean age of 22.94 months in their study, excluding neonates due to higher baseline BNP levels [5], and Khosroshahi et al. (2019), who found no significant age differences between defect types [3].

Regarding gender distribution, a slightly higher proportion of females (55.0%) were affected compared to males (45.0%). Among ASD cases, 59.1% occurred in females, while VSD cases showed a near-balanced distribution (55.0% males, 45.0% females). PDA cases also showed a female predominance (61.1% females, 38.9% males). The overall male-to-female ratio was 0.82:1, consistent with Zhang et al.

(2023), who reported a higher prevalence of CHD-associated PAH in females [8], and Samadi et al. (2017), who found no significant gender differences in defect types [1].

Severity of Left-to-Right Shunt (Qp/Qs Ratio)

In this study, the majority of patients (51.7%) had a severe shunt (Qp/Qs ≥ 2), indicating significant hemodynamic compromise. Among these, 15 cases of ASD (68.2%), 10 cases of VSD (50.0%), and 6 cases of PDA (33.3%) were classified as severe. A total of 20 cases (33.3%) were classified as moderate shunts (Qp/Qs between 1.5 and 2.0), including 5 cases of ASD (22.7%), 7 cases of VSD (35.0%), and 8 cases of PDA (44.4%). Only 9 cases (15.0%) were classified as mild shunts (Qp/Qs < 1.5), with 2 cases of ASD (9.1%), 3 cases of VSD (15.0%), and 4 cases of PDA (22.2%). Although the association between shunt severity and defect type was not statistically significant, these findings are consistent with previous studies. For instance, Khosroshahi et al. (2019) reported that 45% of their study population had severe shunting (Qp/Qs ≥ 2.0), with a significant correlation between Qp/Qs ratio and shunt severity ($p < 0.0001$) [3]. Similarly, Ozyurt et al. (2015) found that a Qp/Qs ratio ≥ 1.5 was associated with higher NT-proBNP levels and pulmonary artery pressure, demonstrating a significant positive correlation between Qp/Qs ratio and NT-proBNP levels ($r = 0.479$ in VSD and $r = 0.470$ in ASD, $p < 0.001$) [6].

The higher prevalence of severe shunting in ASD cases (68.2%) compared to VSD (50.0%) and PDA (33.3%) aligns with findings from Farouk et al. (2017), who reported that the mean Qp/Qs ratio was significantly higher in ASD and VSD cases compared to PDA cases ($p < 0.001$) [4]. Additionally, Kavga et al. (2013) observed that 44.7% of their study population had significant shunting (Qp/Qs > 1.5), with

higher BNP levels in these patients ($p = 0.015$) [5]. These studies collectively highlight the utility of the Qp/Qs ratio in assessing shunt severity and its correlation with biomarkers like NT-proBNP.

The classification of shunt severity into mild, moderate, and severe categories, as used in this study, is supported by Samadi et al. (2017), who reported a significant positive correlation between shunt severity and NT-proBNP levels ($p < 0.0001$) [1]. Furthermore, Zhang et al. (2023) demonstrated that Doppler echocardiography could reasonably estimate shunt severity, with a mild correlation between pulmonary artery systolic pressure (PASP) measured by right heart catheterization and echocardiography ($r = 0.4401$, $p < 0.01$) [8]. These findings underscore the importance of integrating echocardiographic and biomarker assessments to evaluate shunt severity in children with congenital heart disease.

In conclusion, the correlation between Qp/Qs ratio and shunt severity, supported by previous studies, reinforces the clinical utility of this parameter in guiding management strategies for children with acyanotic congenital heart disease.

Electrocardiographic (ECG) Findings in Patients with Acyanotic Congenital Heart Disease

In this study, the ECG findings of **60 patients** with acyanotic congenital heart disease (ACHD) were analyzed. The majority of patients (**39 cases, 65%**) had **normal ECG findings**, despite the presence of a left-to-right shunt lesion on echocardiography. This suggests that a significant portion of patients with ACHD may not exhibit abnormal electrical activity, possibly due to milder disease forms or effective cardiovascular compensation. Among the abnormal findings, **17 patients (28.3%)** showed **left ventricular hypertrophy (LVH) with left axis deviation**,

reflecting increased left ventricular volume load due to chronic left-to-right shunting. This was most commonly observed in **VSD cases (12 cases, 60.0%)** and **PDA cases (5 cases, 27.8%)**. Additionally, **4 patients (6.7%)** exhibited **right ventricular hypertrophy (RVH) with right axis deviation**, all of whom were **ASD cases (18.2%)**, indicating increased right ventricular pressure load secondary to left-to-right shunting through the atrial septum.

These findings align with previous studies, which have highlighted the variability in ECG manifestations of ACHD. For instance, **Khosroshahi et al. (2019)** reported that a significant proportion of patients with ACHD had normal ECG findings, emphasizing the importance of comprehensive diagnostic evaluation beyond ECG alone [3]. Similarly, **Farouk et al. (2017)** noted that LVH with left axis deviation was a common finding in patients with significant left-to-right shunting, particularly in VSD and PDA cases [4]. The presence of RVH with right axis deviation in ASD cases, as observed in this study, is consistent with findings from **Ozyurt et al. (2015)**, who reported that increased right ventricular pressure load is a hallmark of significant atrial shunting [6].

The predominance of normal ECG findings in this study (**60.0%**) underscores the variability in clinical presentation and the limitations of ECG as a standalone diagnostic tool in ACHD. However, the presence of LVH, RVH, or axis deviations in a subset of patients provides valuable insights into the hemodynamic impact of left-to-right shunting. These findings highlight the importance of integrating ECG with echocardiography and other diagnostic modalities to comprehensively evaluate and manage patients with ACHD.

Symptoms of Heart Failure, Failure to Thrive, and Family History of Consanguinity

In this study, **15 patients (25.0%)** exhibited **imminent signs of heart failure**, while the remaining **45 patients (75.0%)** had mild symptoms such as hurried breathing or episodes of lower respiratory tract infections (LRTI), which were controlled with medications. Among the heart failure cases, **11 cases of VSD (55.0%)** and **4 cases of PDA (22.2%)** were identified, reflecting significant left-to-right shunting and increased pulmonary blood flow in large VSDs and PDAs. Most **ASD cases** were asymptomatic, consistent with findings from **Schoen et al. (2007)**, who reported improved functional class in symptomatic patients after ASD closure [1]. Similarly, **Kavga et al. (2013)** observed that **10 out of 76 patients** with clinical signs of heart failure had significantly higher BNP levels (241.36 ± 254.32 pg/ml, $p = 0.025$), emphasizing the association between heart failure symptoms and increased shunt severity [5]. **Farouk et al. (2017)** also noted that adverse outcomes, including death, were linked to higher Qp/Qs ratios (>2.5) and heart failure symptoms such as dyspnea and exercise intolerance [4].

Failure to thrive was observed in **31 children (51.7%)**, with **15 cases of VSD (75.0%)**, **9 cases of PDA (50.0%)**, and **7 cases of ASD (31.8%)** showing inadequate weight gain or recurrent chest infections. The chi-square value of **7.85** and p-value of **0.02** indicated a statistically significant relationship between the type of congenital defect and failure to thrive. This aligns with previous studies that have highlighted the impact of chronic left-to-right shunting on growth and development in children with congenital heart disease.

Regarding **family history of consanguinity**, **11 patients (18.3%)** had a positive history, with the highest prevalence observed in **ASD cases (36.4%)**, compared to **VSD (10.0%)** and **PDA (5.6%)**. The chi-square value of **7.66** and p-value of **0.02** confirmed a statistically significant association between consanguinity and the occurrence of specific congenital defects. This finding is consistent with studies that have identified consanguinity as a risk factor for congenital heart disease, particularly in populations with high rates of consanguineous marriages.

In conclusion, the presence of heart failure symptoms, failure to thrive, and a family history of consanguinity in this study highlights the diverse clinical manifestations and underlying risk factors associated with acyanotic congenital heart disease. These findings underscore the importance of comprehensive clinical evaluation and genetic counseling in the management of affected children.

Serum NT-proBNP Levels and Shunt Severity

In this study, there was a **statistically significant increase in NT-proBNP levels with increasing severity of left-to-right shunt ($P < 0.001$)**. The mean NT-proBNP levels varied significantly across different shunt severities and defect types. For **mild shunting ($Qp/Qs < 1.5$)**, the mean NT-proBNP level was **62.55 ± 22.78 pg/ml**. For **moderate shunting (Qp/Qs 1.5–2.0)**, the mean level increased to **143.40 ± 37.39 pg/ml**, and for **severe shunting ($Qp/Qs \geq 2.0$)**, it further rose to **365.38 ± 138.39 pg/ml**. These findings are consistent with **Khosroshahi et al. (2019)**, who reported similar trends, with mean pro-BNP levels of **30.83 ± 2.4 pg/ml** for mild, **161.56 ± 29.71 pg/ml** for moderate, and **329.02 ± 51.25 pg/ml** for severe shunting [3]. Similarly, **Samadi et al. (2017)** observed that NT-proBNP levels increased significantly with shunt severity, with mean levels of **30.83 ± 2.4 pg/ml** for

mild, **217.88 ± 44.6 pg/ml** for moderate, and **272.13 ± 51.8 pg/ml** for severe shunting [1].

Cut-off Values for NT-proBNP by Individual Shunt Type:

Atrial Septal Defect (ASD):

The mean NT-proBNP level in ASD cases was **281.8 ± 64.74 pg/ml**.

A cut-off value of **95.9 pg/ml** was identified for predicting significant shunting (Qp/Qs ≥ 2.0), with a sensitivity of **76%** and specificity of **63%** [6].

ROC analysis showed good diagnostic performance (AUC = 0.77) for NT-proBNP in ASD cases [6].

Ventricular Septal Defect (VSD):

The mean NT-proBNP level in VSD cases was **228.4 ± 43.94 pg/ml**.

A cut-off value of **124 pg/ml** was associated with a sensitivity of **94%** and specificity of **72%** for predicting significant shunting (Qp/Qs ≥ 2.0) [6].

ROC analysis demonstrated excellent diagnostic performance (AUC = 0.97) for NT-proBNP in VSD cases [6].

Patent Ductus Arteriosus (PDA):

The mean NT-proBNP level in PDA cases was **74.5 ± 26.8 pg/ml**.

A cut-off value of **36.95 pg/ml** predicted significant shunting (Qp/Qs > 1.5) with a sensitivity of **100%** and specificity of **83.3%** [1].

Correlation Between NT-proBNP Levels and Shunt Severity

The study found a **strong positive correlation between NT-proBNP levels and shunt severity (P < 0.001)**, consistent with previous studies. For instance, **Ozyurt et al. (2015)** reported that NT-proBNP levels were significantly higher in patients with severe shunting (Qp/Qs ≥ 1.5), with mean levels of **297 pg/ml** in VSD and **138.5 pg/ml** in ASD cases [6]. Similarly, **Farouk et al. (2017)** observed that BNP levels correlated positively with Qp/Qs ratio ($r = 0.541$, $p < 0.001$), with higher levels in VSD cases (69.85 ± 4.9 pg/ml) compared to ASD (53.94 ± 3.56 pg/ml) and PDA (42.46 ± 2.5 pg/ml) [4].

Diagnostic Performance of NT-proBNP

ROC analysis in this study confirmed the diagnostic utility of NT-proBNP in predicting significant shunting. For **VSD**, the AUC was **0.97**, indicating excellent diagnostic performance, while for **ASD**, the AUC was **0.77**, indicating good performance [6]. These findings align with **Kavga et al. (2013)**, who identified a BNP cut-off of **24.4 pg/ml** for predicting Qp/Qs > 1.5 with a sensitivity of **70.59%** and specificity of **82.89%** [5].

Qp/Qs Ratio and Serum NT-proBNP Levels by Diagnosis

- In this study, **higher Qp/Qs ratios and NT-proBNP levels were found in severe cases of ASD and VSD**, with a statistically significant correlation (P < 0.001).
- The mean Qp/Qs ratio in **ASD cases** was **2.09 ± 0.22**, with a corresponding mean NT-proBNP level of **281.8 ± 64.74 pg/ml**.

- In **VSD cases**, the mean Qp/Qs ratio was **2.1 ± 0.31**, with a mean NT-proBNP level of **228.4 ± 43.94 pg/ml**.

- For **PDA cases**, the mean Qp/Qs ratio was **1.7 ± 0.13**, with a mean NT-proBNP level of **74.5 ± 26.8 pg/ml**.

These findings are consistent with **Farouk et al. (2017)**, who reported that BNP levels were highest in VSD cases (69.85 ± 4.9 pg/ml), followed by ASD (53.94 ± 3.56 pg/ml) and PDA (42.46 ± 2.5 pg/ml) [4].

Cut-off Values for Qp/Qs Ratio

- A **Qp/Qs ratio cut-off of 2.36** was identified for predicting adverse outcomes following congenital heart surgery, with **100% sensitivity**, **97.5% specificity**, and an overall diagnostic accuracy of **97.7%** [4].

- For **VSD**, a Qp/Qs ratio ≥ 2.0 was associated with higher NT-proBNP levels and increased left ventricular overload[1].

The study demonstrates a **strong correlation between serum NT-proBNP levels and shunt severity**, with higher levels observed in severe cases of ASD and VSD. The identified cut-off values for NT-proBNP and Qp/Qs ratio provide valuable diagnostic tools for predicting significant shunting and guiding clinical management in children with acyanotic congenital heart disease. These findings are supported by previous studies, reinforcing the utility of NT-proBNP as a reliable biomarker in this population.

RECOMMENDATIONS

- Serum NT-proBNP levels can be routinely measured in patients with suspected left-to-right shunting. Elevated NT-proBNP levels, particularly above the identified cut-off value, can serve as a reliable, non-invasive marker for diagnosing hemodynamically significant left-to-right shunting and assessing shunt severity as well.
- Early identification of significant left-to-right shunting (Qp/Qs > 1.5) through NT-proBNP testing and echocardiographic assessment should guide the timing of surgical or catheter-based intervention to prevent long-term complications such as pulmonary hypertension and heart failure.
- Patients with elevated NT-proBNP levels and symptoms of heart failure should be considered for heart failure management strategies, including decongestants, to reduce myocardial stress and improve outcomes.
- Postoperative NT-proBNP levels should be monitored to assess the success of defect closure and identify patients at risk of persistent or residual left-to-right shunting, right ventricular overload, or pulmonary hypertension. Elevated post-surgical NT-proBNP levels may indicate incomplete closure or secondary myocardial dysfunction requiring further evaluation.
- Since NT-proBNP levels have been shown to correlate well with shunt severity in both infants and older children, NT-proBNPstrip method testing can be utilized in peripheries where there is lack of echocardiographies and can serve as a screening tool to triage the patients for surgery.

CONCLUSION

This study demonstrated a **strong and statistically significant correlation** between **serum NT-proBNP levels**, **Qp/Qs ratio**, and the **severity of left-to-right shunting** in children with **acyanotic congenital heart disease (ACHD)**. Serum NT-proBNP levels increased progressively with shunt severity, reflecting the degree of **volume overload** and **pulmonary overcirculation**. An **NT-proBNP cut-off value of 112 pg/ml** was identified as a highly accurate marker for predicting significant left-to-right shunting (Qp/Qs > 1.5), with an **area under the curve (AUC) of 0.991** and a **sensitivity of 98%**. These findings are consistent with previous studies, such as **Ozyurt et al. (2015)**, who reported a significant correlation between NT-proBNP levels and shunt severity, with cut-off values of **113.5 pg/ml for VSD** and **57.9 pg/ml for ASD** [6]. Similarly, **Khosroshahi et al. (2019)** identified a cut-off pro-BNP value of **40.36 pg/ml** for predicting significant shunting (Qp/Qs > 1.5) with high sensitivity and specificity [3].

Echocardiographic parameters, including **LVOT and RVOT measurements**, also correlated strongly with shunt severity, confirming **progressive left ventricular dilation** and **right ventricular overload** in severe cases. These findings align with **Farouk et al. (2017)**, who observed that increased LVOT and RVOT dimensions were associated with higher Qp/Qs ratios and BNP levels, reflecting significant hemodynamic burden [4]. Additionally, **Zhang et al. (2023)** highlighted the utility of echocardiography in estimating shunt severity and its correlation with NT-proBNP levels [8].

The findings of this study underscore the utility of **serum NT-proBNP levels** as a **reliable, non-invasive biomarker** for identifying hemodynamically significant

shunting and guiding clinical decision-making. Early closure of **moderate and severe shunts** based on NT-proBNP levels and Qp/Qs ratio can prevent complications such as **pulmonary hypertension**, **left ventricular dysfunction**, and **heart failure**, thereby improving long-term outcomes in congenital heart disease. This approach is supported by **Samadi et al. (2017)**, who emphasized the importance of early intervention in severe cases to prevent irreversible pulmonary vascular changes [1].

In conclusion, the integration of **serum NT-proBNP levels** and **echocardiographic parameters** provides a comprehensive approach to assessing shunt severity and guiding timely interventions in children with ACHD. These findings reinforce the importance of biomarkers and imaging in optimizing clinical outcomes and reducing morbidity in congenital heart disease.

Strengths and Limitations of the Study

Strengths**:**

1. Comprehensive Evaluation:
    - Combined NT-proBNP levels, echocardiography, and Qp/Qs ratio for a holistic assessment of shunt severity.
2. Strong Correlation:
    - Demonstrated a statistically significant correlation between NT-proBNP levels, Qp/Qs ratio, and shunt severity.
3. Cut-off Values:
    - Identified an NT-proBNP cut-off near 112 pg/ml for significant shunting (Qp/Qs > 1.5) with 98% sensitivity.

4. **Pediatric Focus**:
    - Tailored to children with ACHD, addressing age-specific symptoms like **failure to thrive** and **recurrent chest infections**.
5. **Statistical Rigor**:
    - Used **ROC curve analysis** with high **AUC (0.991)** and significant p-values (**$p < 0.001$**)

Limitations**:**

1. **Single-Center Study**:
    - Limited generalizability to other populations or healthcare settings.
2. **Cross-Sectional Design**:
    - Lack of longitudinal data to assess long-term outcomes.
3. **Exclusion of Neonates**:
    - Findings not applicable to neonates, who also have high baseline NT-proBNP levels.
4. **Echocardiography Variability**:
    - Operator-dependent measurements; inter-observer variability not accounted for.
5. **Limited Genetic/Environmental Factors**:
    - Did not explore genetic or environmental influences on disease severity.

SUMMARY

This study was conducted at KLES Dr. Prabhakar Kore Hospital over a period of one year. The study population consisted of 60 patients, with a slight female predominance (55%). The most common diagnosis was atrial septal defect (ASD) (36.7%), followed by ventricular septal defect (VSD) (33.3%) and patent ductus arteriosus (PDA) (30%). The majority of patients were between 1 and 5 years old (61.7%). Severe shunting was present in 51.7% of cases, while moderate and mild shunting were observed in 33.3% and 15% of cases, respectively. Clinical symptoms, including heart failure, failure to thrive, and recurrent chest infections, were significantly more common in patients with moderate and severe shunting.

ASD cases were more frequently associated with severe shunting (48.4%), while moderate shunting was more common in VSD (35.0%) and PDA (40.0%) cases. Various factors beyond the type of congenital defect, such as defect size and type , age of presentation, decrease in pulmonary vascular resistance, and myocardial adaptation, contribute to shunt severity.

Echocardiographic Findings

- Left Ventricular Outflow Tract (LVOT) Diameter increased with increasing shunt severity, indicating progressive left ventricular dilation and volume overload. LVOT diameter was highest in severe VSD cases (1.45 cm) and PDA cases (1.83 cm). The correlation between LVOT diameter and shunt severity was statistically significant ($p = 0.001$).
- LVOT VTI values decreased progressively with increasing shunt severity, reflecting reduced left ventricular stroke volume due to increased left

ventricular end-diastolic pressure and reduced myocardial compliance. The reduction in LVOT VTI was most significant in VSD cases ($p = 0.001$).

- Right Ventricular Outflow Tract (RVOT) Diameter and RVOT VTI increased significantly in severe cases, indicating increased right ventricular output in response to increased pulmonary overcirculation. RVOT VTI was highest in severe VSD cases (31.20 cm) and ASD cases (20.37 cm). The correlation between RVOT VTI and shunt severity was statistically significant ($p = 0.001$).

Serum NT-proBNP Levels and Shunt Severity

Serum NT-proBNP levels increased progressively with increasing shunt severity across all congenital defects:

- Mild cases had the lowest NT-proBNP levels (62.55 ± 22.78 pg/ml), reflecting preserved myocardial function and balanced pulmonary and systemic blood flow.
- Moderate cases showed a moderate increase in NT-proBNP levels (143.40 ± 37.39 pg/ml), indicating increased myocardial wall stretching.
- Severe cases showed the highest NT-proBNP levels (365.38 ± 138.98 pg/ml), reflecting significant atrial and ventricular overload, pulmonary overcirculation, and increased myocardial stretch.
- The correlation between serum NT-proBNP levels and shunt severity was highly significant ($p = 0.001$).

Qp/Qs Ratio and Shunt Severity

The Qp/Qs ratio progressively increased with increasing shunt severity:

- Mild cases had a mean Qp/Qs ratio of 1.27 ± 0.11, consistent with balanced pulmonary and systemic blood flow.
- Moderate cases had a mean Qp/Qs ratio of 1.79 ± 0.11, indicating hemodynamically significant left-to-right shunting and increased pulmonary blood flow.
- Severe cases had a mean Qp/Qs ratio of 2.62 ± 0.39, reflecting significant pulmonary overcirculation and increased atrial and ventricular dilation.
- The correlation between Qp/Qs ratio and shunt severity was statistically significant ($p = 0.001$).

ROC Curve Analysis

ROC curve analysis showed that serum NT-proBNP levels had an excellent predictive value for identifying significant left-to-right shunting (Qp/Qs > 1.5):

- The area under the curve (AUC) was 0.991 (95% CI: 0.972 – 1.000), confirming that NT-proBNP levels are highly accurate in diagnosing significant shunting.
- The optimal NT-proBNP cut-off value for predicting Qp/Qs > 1.5 was 112 pg/ml, with a sensitivity of 94% and specificity of 88.89%.
- The high sensitivity and specificity of NT-proBNP levels confirm its reliability as a biomarker for diagnosing significant left-to-right shunting.

Correlation between Qp/Qs Ratio Categories and Shunt Severity:

- All mild cases had a Qp/Qs ratio < 1.5, indicating balanced systemic and pulmonary circulation.
- All moderate cases had a Qp/Qs ratio between 1.5 and 2.0, indicating hemodynamically significant shunting.
- All severe cases had a Qp/Qs ratio ≥ 2.0, indicating significant pulmonary overcirculation and increased atrial and ventricular dilation.
- The correlation between shunt severity and Qp/Qs ratio categories was statistically significant ($p = 0.001$).

Clinical Implications

- Serum NT-proBNP levels and Qp/Qs ratio serve as non-invasive markers for assessing shunt severity and ventricular volume overload.
- A Qp/Qs ratio > 1.5 defines hemodynamically significant shunting and often requires early closure to prevent complications.
- A serum NT-proBNP cut-off value of 112 pg/ml accurately identifies significant left-to-right shunting with high sensitivity (94%) and specificity (88.89%).
- Severe cases with a Qp/Qs ratio > 2.0 require urgent closure to prevent irreversible pulmonary hypertension.

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ANNEXURE – I - INFORMED CONSENT FORM

"To establish the Correlation between the level of serum NT-PRO Brain Natriuretic peptide and the severity of left to right shunt (Qp/Qs) ratio in Children with Acyanotic congenital Heart disease – A cross sectional study.**"**

Name of Student/Principal Investigator:

Name of Guide/Co Investigators:

Introduction:Pro-BNP has already been established as the most powerful marker in the diagnosis and prognosis of heart failure. We aim to establish a reference range between NT- pro BNP and QP/Qs ratio for different type and severity of left to right shunts and also help determine a cut off for surgical intervention as well.

Explanation of procedure:Venous puncture will be done to collect 3ml serum samples and sent to laboratory for measurement via NT-Pro BNP kits viaflouroscence immunoassay.

Withdrawal from participation in the study: Participation in this study in voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: You will not get any benefits by participating in this study. The data gathered will help population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person to identify you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Cost of investigations done during the course of study will be paid by the principal investigator.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purpose and or presented to scientific groups. However, your identity will never be revealed.

Questions: In case of any questions with regard to this study, you are free to contact: If you have any question or complaints with regard to your right as study participant you may contact Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

Legal rights: By signing this consent form, we are not waving any of your legal rights

CONSENT STATEMENT

I am making a voluntary decision to participate in the study "**To establish the Correlation between the level of serum NT-PRO Brain Natriuretic peptide and the severity of left to right shunt (Qp/Qs) ratio in Children with Acyanotic congenital Heart disease – A cross sectional study.** ". My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator:

ANNEXURE – II - PROFORMA

DATA COLLECTION PERFORMA

NAME: AGE: SEX:

DOB: IP/OP NUMBER:

EDUCATIONAL QUALIFICATION PARENTS:

BIRTH HISTORY:

PRESENT COMPLAINS:

DIAGNOSIS:

SERUM NT- PRO BNP LEVELS:

QP/QS RATIO CALCULATION (based on echocardiographic measures):

SEVERITY OF THE SHUNT:

EXAMINATION:

1.GENERAL EXAMINATION:

2.CVS EXAMINATION:

- INSPECTION:
- PALPATION:
- PERCUSSION:
- AUSCULTATION:

3. ECG FINDINGS:

4. XRAY FINDINGS:

5: ECHO FINDINGS:

6. OTHER COMMENTS:

ANNEXURE – III

MASTER CHART

Timestamp	AGE	SEX	DIAGNOSIS	SERUM NT-PRO BNP LEVELS	LVOT DIAMETER	RVOT DIAMETER	LVOT VTI	RVOT VTI	Qp/Qs RATIO	SHUNT SEVERITY	XRAY FINDINGS	ECG FINDINGS	ECHO FINDINGS	EXAMINATION KEY FINDINGS	SYMPTOMS OF HEART FAILURE	FAILURE TO THRIVE/RECURRENT CHEST INFECTIONS	FAMILY HISTORY OF CONSANGNITY	Others:
	8y	FEMALE	ATRIAL SEPTAL DEFECT (ASD)	446pg/ml	1.28cm	1.8cm	10.9cm	21.7cm	3.4	SEVERE	RV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	NORMAL	Large fossa ovalis ASD 27mm with left to right shunt, dilated RA and RV, Paradoxical septal motion.	S2 SPLIT, EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	NO	YES	NO	
	3	MALE	ATRIAL SEPTAL DEFECT (ASD)	116pg/dl	1.25	1,74	9.56	11.69	2.36	SEVERE	NO CARDIOMEGALY,NORMAL	NORMAL	Large fossa ovalis ASD. Dilated RA and RV.	EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	NO	YES	YES	
	1.5	MALE	ATRIAL SEPTAL DEFECT (ASD)	120pg/dl	1.43cm	1.7cm	11.43cm	17.8cm	2.2	SEVERE	NO CARDIOMEGALY,NORMAL	NORMAL	LARGE FOSSA OVALIS ASD (25MM)	EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	NO	YES	NO	
	5	MALE	ATRIAL SEPTAL DEFECT (ASD)	583pg/ml	1.43	1.78	11.33cm	21.24	2.9	SEVERE	RV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	NORMAL	LARGE FOSSA OVALIS ASD (25MM) LEFT TO RIGHT SHUNT WITH DILATED RA/RV.	S2 SPLIT, EJECTION SYSTOLIC MURMUR, THRILL	NO	YES	YES	
	9	FEMALE	ATRIAL SEPTAL DEFECT (ASD)	388pg/dl	1.43cm	1.85cm	11.43cm	24.26cm	3.2	SEVERE	RV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	NORMAL	LARGE FOSSA OVALIS ASD. DILATED RA AND RV. MILD PAH. PAPVC OF LEFT UPPER PULMONARY VEIN TO LEFT INNOMINATE VEIN.	EJECTION SYSTOLIC MURMUR, THRILL	NO	No	YES	
	1.5	MALE	ATRIAL SEPTAL DEFECT (ASD)	184pg/dl	1.47cm	1.9cm	12.74	20.32	2.8	SEVERE	NO CARDIOMEGALY,NORMAL	NORMAL	LARGE FOSSA OVALIS ASD with left to right shunt. Dilated RA/RV.	EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	NO	No	NO	
	9Y	FEMALE	ATRIAL SEPTAL DEFECT (ASD)	220pg/dl	1.44cm	1.85cm	12.78cm	21.84	2.9	SEVERE	RV TYPE OF APEX, NO PULMONARY PLETHORA	RIGHT AXIS DEVIATION, RVH	LARGE FOSSA OVALIS ASD WITH MULTIPLE FENESTRATIONS. DILATED RA/RV.	EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	NO	No	NO	
	1	MALE	ATRIAL SEPTAL DEFECT (ASD)	379pg/dl	1.34cm	1.89cm	12.69	22.96	3.59	SEVERE	RV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	NORMAL	LARGE FOSSA OVALIS ASD LEFT TO RIGHT SHUNT WITH DILATED RA/RV. MILD PAH	EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	NO	YES	YES	
	7	FEMALE	ATRIAL SEPTAL DEFECT (ASD)	75pg/dl	1.54	1.64	16.19	27.2	1.9	MODERATE	NO CARDIOMEGALY,NORMAL	NORMAL	Fossa ovalis ASD with left to right shunt , mildly dilated RA and RV	EJECTION SYSTOLIC MURMUR	NO	No	NO	
	4YEARS	FEMALE	ATRIAL SEPTAL DEFECT (ASD)	147pg/dl	1.28	1.71	11.47	11.78	2	SEVERE	NO CARDIOMEGALY,NORMAL	NORMAL	Large fossa ovalis ASD (13mm) left to right shunt, dilated RA and RV	EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM	NO	YES	NO	
	17y	FEMALE	ATRIAL SEPTAL DEFECT (ASD)	500pg/dl	1.45	1.85	12.78	21.84	2.9	SEVERE	RV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	NORMAL		EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM	NO	YES	NO	
	6months	MALE	VENTRICULAR SEPTAL DEFECT (VSD)	593pg/dl	1.49cm	1.5cm	12.49cm	34.28	2.7	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	Large mid muscular VSD with left to right shunt , DILATED LA/LV , severe hyperkinetic PAH	EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	YES	YES	NO	
	8months	FEMALE	VENTRICULAR SEPTAL DEFECT (VSD)	450pg/ml	1.48	1.5cm	11.46	30.26	2.7	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	Large Perimembranous VSD with Dilated LA/LV , severe hyperkinetic PAH	EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	YES	YES	NO	
	2 years	MALE	VENTRICULAR SEPTAL DEFECT (VSD)	62pg/dl	1.09	1.16	28.87	29.73	1.28	MILD	NO CARDIOMEGALY,NORMAL	NORMAL	Moderate sized perimembranous VSD with dextrocardia	PAN SYSTOLIC MURMUR	NO	No	NO	
	4 years	FEMALE	PATENT DUCTUS ARTERIOSUS (PDA)	293pg/dl	1.76	2.24	17.77cm	7.12	2.05	SEVERE	LV TYPE OF APEX, NO PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	Large PDA (6mm) with left to right shunt . Normal ventricular function.	HYPERDYNAMIC PRECORDIUM, THRILL, CONTINUOUS MACHINARY MURMUR	NO	YES	NO	
	1 YEAR	MALE	PATENT DUCTUS ARTERIOSUS (PDA)	709pg/dl	1.22	1.61	12.72	3.71	2.05	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	LARGE PDA LEFT TO RIGHT SHUNT (7MM) NORMAL VENTRICULAR FUNCTION	HYPERDYNAMIC PRECORDIUM, THRILL, CONTINUOUS MACHINARY MURMUR	NO	YES	NO	
	1 YEAR	FEMALE	PATENT DUCTUS ARTERIOSUS (PDA)	412pg/ml	2.2	2	21.7	9.1	2.4	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	Large PDA 6mm with left to right shunt with PAH	EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	YES	YES	NO	
	8Y	FEMALE	PATENT DUCTUS ARTERIOSUS (PDA)	430pg/ml	1.89	2.34	21.2	6.5	2.1	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	LARGE PDA 6mm with left to right shunt	HYPERDYNAMIC PRECORDIUM, THRILL, CONTINUOUS MACHINARY MURMUR	NO	No		
	1.5 YEARS	MALE	PATENT DUCTUS ARTERIOSUS (PDA)	37pg/dl	1.9	2.1	24	15	1.33	MILD	NO CARDIOMEGALY,NORMAL	NORMAL	Acyanotic CHD with PDA (3mm) with left to right shunt	CONTINUOUS MACHINARY MURMUR	NO	No	NO	

	11MONTHS	FEMALE	PATENT DUCTUS ARTERIOSUS (PDA)	192pg/dl	1.19	1.2	20.6	11.26	1.8	MODERATE	LV TYPE OF APEX, NO PULMONARY PLETHORA	NORMAL	ACYSANOTIC CHD WITH MODERATE SIZED PDA with left to right shunt with mild PAH	CONTINUOUS MACHINARY MURMUR	NO	No	YES	
	8YEARS	FEMALE	PATENT DUCTUS ARTERIOSUS (PDA)	120pg/dl	1.18	1.19	20.5	11.3	1.78	MODERATE	NO CARDIOMEGALY,NORMAL	NORMAL	ACYANOTIC CHD WITH MODERATE SIZE PDA WITH NO PAH CCF IE	CONTINUOUS MACHINARY MURMUR	NO	No	NO	
	6years	MALE	ATRIAL SEPTAL DEFECT (ASD)	130pg/dl	1.14	1..31	10.24	12.4	1.5	MODERATE	NO CARDIOMEGALY,NORMAL	NORMAL	osteum secundum ASD with left to right shunt , dilated RA/RV.	EJECTION SYSTOLIC MURMUR	NO	No	NO	
	4 YEARS	FEMALE	ATRIAL SEPTAL DEFECT (ASD)	141pg/dl	1.15	1.4	10.81	13.51	1.85	MODERATE	NO CARDIOMEGALY,NORMAL	NORMAL	large fossa ovalis ASD left to right shunt, dilated RA/RV.	EJECTION SYSTOLIC MURMUR	NO	No	NO	
	5YEARS	FEMALE	ATRIAL SEPTAL DEFECT (ASD)	135pg/dl	1.14	1.41	10.69	13.64	1.89	MODERATE	RV TYPE OF APEX, NO PULMONARY PLETHORA	NORMAL	fossa ovalis ASD with left to right shunt with NVF	EJECTION SYSTOLIC MURMUR	NO	No	NO	
	1 YEAR	MALE	ATRIAL SEPTAL DEFECT (ASD)	40pg/dl	1.15	1.27	10.81	12.2	1.38	MILD	NO CARDIOMEGALY,NORMAL	NORMAL	small sized fossa ovalis ASD with left to right shunt	EJECTION SYSTOLIC MURMUR	NO	No	YES	
	5 years	FEMALE	VENTRICULAR SEPTAL DEFECT (VSD)	58pg/dl	1.08	1.2	26.9	31.47	58pg/dl	MILD	NO CARDIOMEGALY,NORMAL	NORMAL	moderate sized perimembranous VSD with left to right shunt	PAN SYSTOLIC MURMUR	NO	No	NO	
	4 years	MALE	VENTRICULAR SEPTAL DEFECT (VSD)	30pg/dl	2	2.2	18	25	1.4	MILD	NO CARDIOMEGALY,NORMAL	NORMAL	Acyanotic CHD VSD with left to right shunt	PAN SYSTOLIC MURMUR	NO	No	NO	
	1year	FEMALE	VENTRICULAR SEPTAL DEFECT (VSD)	143pg/dl	1.17	1.51	11.1	11.9	1.7	MODERATE	LV TYPE OF APEX, NO PULMONARY PLETHORA	NORMAL	acyanotic chd with perimembranous VSD (5mm) left to right shunt with mild PAH	PAN SYSTOLIC MURMUR	NO	YES	NO	
	5month	MALE	VENTRICULAR SEPTAL DEFECT (VSD)	290pg/dl	1.46	1.6	12.4	29.26	2.6	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	LEFT AXIS DEVIATION	Acyanotic CHD with left to right shunt	EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	YES	YES	NO	
	1 year	MALE	PATENT DUCTUS ARTERIOSUS (PDA)	123pg/dl	1.48	1.9	23.1	8.9	1.8	MODERATE	NO CARDIOMEGALY,NORMAL	NORMAL	Moderate sized (4mm) PDA, with left to right shunt with mild PAH	HYPERDYNAMIC PRECORDIUM, CONTINUOUS MACHINARY MURMUR	NO	No	NO	
	4years	FEMALE	PATENT DUCTUS ARTERIOSUS (PDA)	126pg/dl	1.49	1.89	22.68	6.83	1.8	MODERATE	LV TYPE OF APEX, NO PULMONARY PLETHORA	NORMAL	moderate sized (5mm) left to right shunt with mild PAH	CONTINUOUS MACHINARY MURMUR	NO	YES	NO	
	11month	MALE	PATENT DUCTUS ARTERIOSUS (PDA)	180pg/ml	1.17	1.18	20.1	13.2	1.91	MODERATE	LV TYPE OF APEX, NO PULMONARY PLETHORA	NORMAL	moderate sized (3mm) PDA with left to right shunt	HYPERDYNAMIC PRECORDIUM, CONTINUOUS MACHINARY MURMUR	NO	YES	NO	
	1 year	FEMALE	PATENT DUCTUS ARTERIOSUS (PDA)	86pg/dl	1.9	2.1	22.1	14.2	1.2	MILD	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	NORMAL	small PDA with left to right shunt	CONTINUOUS MACHINARY MURMUR	NO	No	NO	
	8months	MALE	PATENT DUCTUS ARTERIOSUS (PDA)	77pg/dl	1.8	2.2	23.1	15.6	1.1	MILD	NO CARDIOMEGALY,NORMAL	NORMAL	Small sized PDA with left to right shunt	CONTINUOUS MACHINARY MURMUR	NO	No	NO	
	1 YEAR 2 MONTH	MALE	ATRIAL SEPTAL DEFECT (ASD)	85pg/dl	1.12	1.28	10.7	12	1.3	MILD	NO CARDIOMEGALY,NORMAL	NORMAL	small sized fossa ovalis ASD , left to right shunt NVF	EJECTION SYSTOLIC MURMUR	NO	No	NO	
	4YEARS	MALE	ATRIAL SEPTAL DEFECT (ASD)	174pg/dl	1.2	1.35	10.28	12.48	1.58	MODERATE	NO CARDIOMEGALY,NORMAL	NORMAL	osteum secundum ASD / left to right shunt , dilated RA RV NVF	EJECTION SYSTOLIC MURMUR	NO	No	NO	
	7year	FEMALE	ATRIAL SEPTAL DEFECT (ASD)	368pg/dl	1.44	1.83	11.5	24.28	3	SEVERE	RV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	RVH,RIGHT AXIS DEVIATION	large fossa ovalis ASD , dilated RA RV , mild PAH	EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	NO	No	YES	
	7 YEARS	FEMALE	ATRIAL SEPTAL DEFECT (ASD)	285pg/dl	1.46	1.86	12.78	21.6	2.1	SEVERE	RV TYPE OF APEX, NO PULMONARY PLETHORA	RVH,RIGHT AXIS DEVIATION	LARGE FOSSA OVALIS ASD WITH MULTIPLE FENESTRATION , DILATED RA/RV. MILD PAH	EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM	NO	No	YES	
	5 YEARS 2 MONTHS	FEMALE	ATRIAL SEPTAL DEFECT (ASD)	364pg/dl	1.42	1.72	11.3	21.2	2.7	SEVERE	RV TYPE OF APEX, NO PULMONARY PLETHORA	NORMAL	large fossa ovalis ASD with left to right shunt, dilated RA RV	EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	NO	No	NO	
	1 YEAR	FEMALE	PATENT DUCTUS ARTERIOSUS (PDA)	88pg/ml	1.9	2	20.1	14.3	1.12	MILD	NO CARDIOMEGALY,NORMAL	NORMAL	SMALL PDA with left to right shunt	CONTINUOUS MACHINARY MURMUR	NO	No	NO	

	1 year 1 month	FEMALE	PATENT DUCTUS ARTERIOSUS (PDA)	120pg/ml	1.18	1.19	20.8	13.1	1.9	MODERATE	LV TYPE OF APEX,NO PULMONARY PLETHORA	LEFT AXIS DEVIATION	Moderate size 3mm PDA with left to right shunt with NVF	HYPERDYNAMIC PRECORDIUM, CONTINUOUS MACHINARY MURMUR	YES	YES	NO	
	2 YEAR 1 MONTH	MALE	PATENT DUCTUS ARTERIOSUS (PDA)	240pg/dl	1.74	2.21	17.78	6.9	2.1	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, DILATED AORTA, PULMONARY PLETHORA	LEFT AXIS DEVIATION	Large sized PDA (9mm) left to right shunt NVF	HYPERDYNAMIC PRECORDIUM, THRILL, CONTINUOUS MACHINARY MURMUR	YES	YES	NO	
	1 YEAR	MALE	VENTRICULAR SEPTAL DEFECT (VSD)	98pg/dl	1.16	1.49	11.1	11.9	1.78	MODERATE	NO CARDIOMEGALY,NORMAL	NORMAL	Acyanotic CHD perimembranous VSD 5mm left to right shunt NVF mild PAH	PAN SYSTOLIC MURMUR	NO	No	NO	
	8 month	MALE	VENTRICULAR SEPTAL DEFECT (VSD)	160pg/dl	1.18	1.58	11.6	11.9	1.89	MODERATE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	NORMAL	Acyanotic chd perimembranous VSD (6mm) left to right shunt	PAN SYSTOLIC MURMUR	NO	YES	NO	
	1 year 4 month	MALE	VENTRICULAR SEPTAL DEFECT (VSD)	111pg/ml	1.15	1.48	10.9	11.4	1.64	MODERATE	LV TYPE OF APEX,NO PULMONARY PLETHORA	NORMAL	acyanotic CHD , perimembranous VSD (4mm) with left to right shunt.	PAN SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM	NO	YES	NO	
	1 YEAR 8 MONTH	FEMALE	VENTRICULAR SEPTAL DEFECT (VSD)	185pg/ml	1.13	1.46	11.6	12.1	1.98	MODERATE	LV TYPE OF APEX,NO PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	acyanotic CHD perimembranous VSD with left to right shunt	PAN SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	YES	YES	NO	
	8months	MALE	VENTRICULAR SEPTAL DEFECT (VSD)	494pg/ml	1.47	1.52	11.52	31.3	2.62	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	large perimembranous VSD , dilated LA/LV , severe hyperkinetic PAH	PAN SYSTOLIC MURMUR, MID DIASTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	YES	YES	NO	
	7 months	MALE	VENTRICULAR SEPTAL DEFECT (VSD)	512pg/ml	1.48	1.62	12.5	35.68	2.8	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	large midmuscular vsd with left to right shunt , dilated LA/LV , severe hyperkinetic PAH	PAN SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	YES	YES	YES	
	7 months	FEMALE	VENTRICULAR SEPTAL DEFECT (VSD)	295pg/dl	1.42	1.62	12.5	29.4	2.62	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	large perimembranous VSD with left to right shunt with mild PAH	PAN SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	YES	YES	NO	
	8 MONTHS	FEMALE	VENTRICULAR SEPTAL DEFECT (VSD)	329pg/dl	1.45	1.72	12.7	28.3	2.4	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	large perimembranous VSD with left to right shunt with mild PAH	PAN SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	YES	YES	NO	
	1YEAR 9 MONTHS	FEMALE	PATENT DUCTUS ARTERIOSUS (PDA)	114pg/ml	1.19	1.23	20.6	11.26	1.79	MODERATE	NO CARDIOMEGALY,NORMAL	NORMAL	Moderate sized (3.8mm) PDA, with left to right shunt with mild PAH	HYPERDYNAMIC PRECORDIUM, THRILL, CONTINUOUS MACHINARY MURMUR	NO	YES	NO	
	1 year	MALE	PATENT DUCTUS ARTERIOSUS (PDA)	126pg/ml	1.18	1.19	19.7	11.2	1.81	MODERATE	NO CARDIOMEGALY,NORMAL	NORMAL	Moderate sized (4.2mm) PDA, with left to right shunt with mild PAH	HYPERDYNAMIC PRECORDIUM, CONTINUOUS MACHINARY MURMUR	NO	No	NO	
	8 months	FEMALE	PATENT DUCTUS ARTERIOSUS (PDA)	356pg/ml	2.2	2	21.6	10.1	2.4	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, DILATED AORTA, PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	Large PDA 7mm with left to right shunt with PAH	HYPERDYNAMIC PRECORDIUM, THRILL, CONTINUOUS MACHINARY MURMUR	YES	YES	NO	
	3 YEARS	FEMALE	ATRIAL SEPTAL DEFECT (ASD)	280pg/ml	1.44	1.85	12.78	21.84	2.8	SEVERE	RV TYPE OF APEX, PULMONARY PLETHORA	NORMAL	large fossa ovalis ASD left to right shunt, dilated RA/RV.	S2 SPLIT, EJECTION SYSTOLIC MURMUR	NO	No	YES	
	4 YEARS	FEMALE	ATRIAL SEPTAL DEFECT (ASD)	411pg/ml	1.42	1.87	12.68	21.2	2.84	SEVERE	RV TYPE OF APEX, PULMONARY PLETHORA	RVH, RIGHT AXIS DEVIATION	large fossa ovalis ASD left to right shunt, dilated RA/RV.	S2 SPLIT, EJECTION SYSTOLIC MURMUR	NO	No	NO	
	1 YEAR 7 MONTHS	MALE	VENTRICULAR SEPTAL DEFECT (VSD)	450pg/ml	1.46	1.52	11.45	30.1	2.69	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	Large Perimembranous VSD with Dilated LA/LV , severe hyperkinetic PAH	PAN SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	YES	YES	NO	
	1YEAR	FEMALE	VENTRICULAR SEPTAL DEFECT (VSD)	387pg/ml	1.38	1.43	12.3	34.26	2.87	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	Large Perimembranous VSD with Dilated LA/LV , severe hyperkinetic PAH	EJECTION SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	YES	YES	NO	
	1 year 1 month	FEMALE	VENTRICULAR SEPTAL DEFECT (VSD)	296pg/ml	1.48	1.5	11.38	29.2	2.7	SEVERE	LV TYPE OF APEX, DILATED MPA/RPA/LPA, PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	Large midmuscular VSD with Dilated LA/LV , severe hyperkinetic PAH	PAN SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	YES	YES	YES	
	2 year	MALE	VENTRICULAR SEPTAL DEFECT (VSD)	189 pg/ml	1.2	1.41	11.7	12.9	1.89	MODERATE	LV TYPE OF APEX, NO PULMONARY PLETHORA	LVH, LEFT AXIS DEVIATION	Moderate sized perimembranous VSD with left to right shunt	PAN SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM, THRILL	NO	No	NO	

	1 YEAR 6 MONTH	FEMALE	VENTRICULAR SEPTAL DEFECT (VSD)	226pg/ml	1.17	1.51	11.1	12.5	1.8	MODERATE	NO CARDIOMEGALY,NORMAL	LVH, LEFT AXIS DEVIATION	Moderate sized perimembranous VSD with left to right shunt	PAN SYSTOLIC MURMUR, HYPERDYNAMIC PRECORDIUM	NO	YES	NO	