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Comparison of spontaneous resolution of secundum atrial septal defects in term and preterm neonates

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ABSTRACT

BACKGROUND & OBJECTIVE: Atrial Atrial septal defects (ASDs) are among the most common congenital heart defects, with secundum ASD accounting for about 70% of cases. These often close spontaneously during infancy or early childhood, but the pattern and timing of closure may vary based on gestational age. This study aims to compare the spontaneous resolution of secundum ASDs in term versus preterm neonates to understand predictors of natural closure better and guide optimal neonatal interventions.

METHODOLOGY: This cohort study was conducted at the Pediatric Department of Hilal E Ahmar Hospital, Faisalabad, Pakistan, from December 2022 to March 2024. A total of 280 neonates diagnosed with secundum ASD within one month of birth were enrolled, including 140 preterm and 140 term infants. Newborns with major congenital heart defects were excluded. Spontaneous resolution was defined as a reduction in ASD size to less than 3 mm or complete closure without intervention. All patients were followed up regularly to monitor outcomes.

RESULTS: At baseline, mean ages were 4.44±1.86 days for term and 8.11±5.68 days for preterm neonates. Follow-up occurred at 13.57±6.56 months (term) and 14.16±6.87 months (preterm). Among preterm neonates, 77 (55%) were male, compared to 72 (51.4%) in the term group. ASD resolution occurred in 125 (89.3%) term infants and 104 (74.3%) preterm infants (p = 0.001).

CONCLUSION: Most ASDs in both term and preterm neonates resolve spontaneously. However, the resolution rate is significantly lower in preterm infants, indicating the need for closer monitoring and individualized management.

KEYWORDS: Atrial Septal Defect, Preterm, Congenital Heart Defects.

INTRODUCTION

The term "congenital heart defect" (CHD) refers to a structural defect of the heart and/or major vessels that exists from birth. It is the most common congenital deformity, making up around one-third of all significant congenital malformations. It also causes the majority of morbidity, mortality, and medical costs related to birth defects [1].Unexpectedly, the frequency of CHD rose from 11% to 57%, and the occurrence rate also shifted to 1-2 per 1000 live births, raising concerns for international health administrators [2].Ventricular septal defects (VSD) and atrial septal defects (ASD) accounted for 51% of all forms of CHD, with an increasing tendency over time [1]. There are various types of atrial septal defects (ASDs), including sinus venosus, ostium secundum, ostium primum, and coronary sinus ASDs [3]. With a 10% incidence, atrial septal defect is the most prevalent 40congenital cardiac condition [4].

One prevalent kind of congenital heart defect (CHD) is secundum atrial septal defect (ASD II). It has been reported that the birth prevalence is 164 per 100,000 live births, and it is proven to be significantly higher among preterm infants [5]. Nine to thirteen percent of all congenital heart abnormalities are associated with these problems [5]. For smaller, non-symptomatic ASD II cases, spontaneous closure is typical, and the majority of these children with ASD II remain asymptomatic throughout infancy. Patients with ASD have a greater long-term mortality rate than people in general [5]. The lack of cardiac tissue in the fossa ovalis region is the secondary cause of the ASDs.

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The sizes of the ASDs range from little to enormous. Usually, these are isolated defects,but occasionally, numerous defects or an atrial septum with multiple fenestration's are also seen. The right atrium (RA), right ventricle (RV), and pulmonary arteries enlarge as a consequence of left-to-right shunting via the ASD [3]. In the presence of a secundum atrial septal defect (ASD), left-to-right shunting of blood occurs due to the higher pressure in the left atrium compared to the right atrium. This abnormal flow results in volume overload of the right atrium (RA), right ventricle (RV), and pulmonary circulation. Over time, the increased volume leads to dilation of the RA and RV and enlargement of the pulmonary arteries due to increased pulmonary blood flow [3]. Hemodynamically, this volume overload may progress to elevated pulmonary artery pressures, and in prolonged cases, may contribute to pulmonary vascular remodeling and pulmonary hypertension. If left untreated, chronic right-sided volume and pressure load can lead to right ventricular dysfunction, arrhythmias, and eventually right heart failure. Early diagnosis and assessment of shunt severity are therefore critical to determine the need for intervention and prevent long-term complications.

Transthoracic echocardiography (TTE) is a highly valuable diagnostic tool for detecting atrial septal defects (ASDs) in both term and preterm neonates [6]. Preterm birth and congenital heart disease (CHD), including ASDs, are significant contributors to neonatal morbidity and mortality. Numerous studies have established an association between preterm delivery and an increased incidence of CHDs. Moreover, ASDs, particularly when large or associated with other complications, have been linked to increased mortality risk in neonates, especially in the preterm population. Early detection and regular follow-up through echocardiography are therefore critical for timely management and improved clinical outcomes. Preterm delivery is associated with CHD.

It most likely includes intricate interplay between genetic susceptibilities and various environmental exposures. It's possible that both could happen separately but have similar risk factors. Alternately, aberrant fetal hemodynamic profiles could be the cause of preterm birth in infants with CHD [7]. It is crucial to know which ASDs will eventually need intervention for counseling, to arrange the right kind of follow-up, and to use professional resources wisely in this population. The majority of research conducted thus far has focused on 53the natural history of secundum ASDs in term-born babies [6]. Data on the natural course of ASDs and how they resolve in Pakistani term and preterm newborns are scarce. This study was planned to compare the spontaneous resolution of secundum atrial septal defects among term and preterm neonates within their first two years of life.

METHODOLOGY

This cohort study was carried out at the Pediatric Department of Hilal E Ahmar Faisalabad, Pakistan, between December 2022 and March 2024. Following approval from the hospital's ethical review committee (1012/HAHF), the WHO sample size calculator was used to determine the sample size of 280 neonates (140 term and 140 preterm), taking into account the following factors: power of the study (80%), level of significance (5%), and the prevalence of spontaneous resolution in term (P1) and preterm (P2) neonates, respectively. Non-probability consecutive sampling was employed to get the sample size.

The first postnatal echocardiography, performed within the first month of life, provided the initial diagnosis and characterization of the atrial septal defect (ASD). Follow-up echocardiograms were conducted periodically until spontaneous closure occurred or the child reached two years of age. ASDs were classified into three categories based on their maximal diameter measured via echocardiography: small (<5 mm), moderate (5–8 mm), and large (>8 mm). Spontaneous resolution was strictly defined as complete anatomical closure of the defect without medical or surgical intervention. Mere reduction in ASD size regardless of final dimension was not considered a spontaneous resolution in this study. This classification allowed for consistent monitoring and assessment of the natural course of ASDs across different severities.

Data analysis was done with SPSS V-16. Shapiro-Wilk test was used to evaluate the normality of the data. The Mann-Whitney U test was used to analyze non-normally distributed data, and the Student's t-test was used to analyze normally distributed data. To analyze categorical data, the Fisher exact or the Chi-square test was used to analyze categorical data.The presentation of parametric continuous data was as mean ± standard deviation, whereas the presentation of nonparametric continuous variables were as median with interquartile range (IQR). A Kaplan-Meier curve for resolution of ASD was statistically analyzed with log-rank test using chi-square distribution. P-values less than 0.05 were regarded as significant.

Inclusion criteria:The study comprised newborns with secundum atrial septal defects greater than 3 mm that were identified within the first month of life. Cohorts were preterm neonates (gestational age < 37 weeks), while controls were term neonates (gestational age > 37 weeks) based on gestational age. Exclusion criteria:The study excluded neonates with major congenital heart defects, isolated bicuspid aortic valve, mitral valve prolapse without regurgitation, cardiac tumors, and trivial lesions such as aortic/pulmonary valve stenosis with a systolic pressure gradient less than 20 mm-Hg, patent foramen ovale, atrial septal defect <3 mm, and physiologic pulmonary artery branch stenosis.

RESULTS

A total of 280 newborns with secundum atrial septal defects were present; 140 (50%) of them were preterm,while another 140 (50%) were full- term. P-value = 0.0001 indicated a significant difference between preterm and term newborns regarding gestational age, age at baseline, and birth weight. In both groups, male newborns were more numerous

than female ones. Table-I provides baseline clinical and demographic information about the patients.

125 (89.3%) term neonates and 104 (74.3%) preterm neonates had spontaneous resolution of ASD; a statistically significant difference between the two groups was shown by the p-value of 0.001 (Table-II). 81 (75.7%) of the 107 preterm neonates with small defects had spontaneous resolution, while 73 (94.8%) of the 88 term neonates with small defects also showed spontaneous resolution. With a p-value of 0.001, there is a statistically significant difference between the two groups. There is no statistically significant difference in the spontaneous resolution of ASD between preterm and term newborns with moderate and major size defects(Table-III).

A log-rank test with a p-value of 0.057 indicated that there was no difference in the time to resolution between the term and preterm groups (Figure-I).

Table-II: Spontaneous resolution of ASD among term and preterm.

Spontaneous resolution of ASD	Preterm (n = 140)	Term (n = 140)	Total	P-value
Yes	104 (74.3)	125 (89.3)	229 (81.8)	0.001*
No	36 (25.7)	15 (10.7)	51 (18.2)	

ASD = Atrial septal defect, *chi-square test

Table-I: Baseline clinical characteristics of neonates.

Variables	Categories	Preterm (n = 140)	Term (n = 140)	P-value
Gestational age	Mean ±SD (weeks)	30.88±2.22	38.64±1.14	0.0001*
Age at baseline	Mean ±SD (days)	8.11±5.68	4.44±1.86	0.0001*
Age at follow up	Mean ±SD (months)	14.16±6.87	13.57±6.56	0.461*
Birth weight	Mean ±SD (kg)	1.62±0.51	3.16±0.4	0.0001*
ASD diameter	Mean ±SD (mm)	4.42±1.27	5.52±1.71	0.0001*
Gender	Male	77 (55)	72 (51.4)	0.549**
	Female	63 (45)	68 (48.6)	
Size of defect	Small	107 (76.4)	77 (55)	0.001**
	Moderate	29 (20.7)	54 (38.6)	
	Large	4 (2.9)	9 (6.4)	
Direction of flow	Left to right	127 (90.7)	129 (92.1)	0.931***
	Right to left	2 (1.4)	2 (1.4)	
	Bidirectional	11 (7.9)	9 (6.4)	
Patent duct arteriosus	Present	101 (72.1)	73 (52.1)	0.001**
	Absent	39 (27.9)	6747.9)	

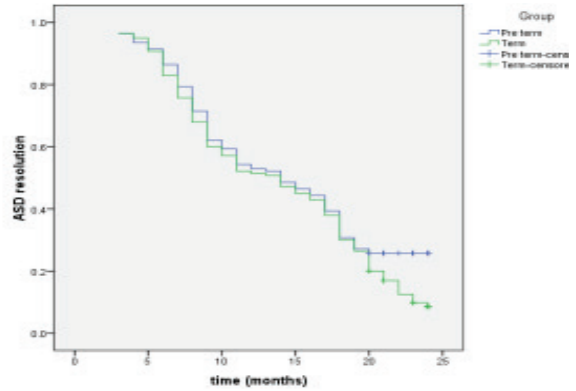
***t-test **chi-square test ***Fishers Exact test**

Table-III: Spontaneous resolution of ASD among term and preterm according to size of defect.

Size of defect	Spontaneous resolution of ASD	Preterm (n = 140)	Term (n = 140)	Total	P-value
Small	Yes	81 (75.7)	73 (94.8)	154 (83.7)	0.001**
	No	26 (24.3)	4 (5.2)	30 (16.3)	
Moderate	Yes	21 (72.4)	45 (83.3)	66 (79.5)	0.24**
	No	8 (27.6)	9 (16.7)	17 (20.5)	
Large	Yes	2 (50)	7 (77.8)	9 (69.2)	0.530*
	No	2 (50)	2 (22.2)	4 (30.8)	

****chi-square test, *Fishers Exact test**

Figure-I: ASD resolution as a function of time for term and preterm cohorts.



DISCUSSION

One of the most prevalent kinds of congenital heart abnormalities (CHDs) is a septal defect, which usually manifests as a left to right shunt. The extent of the defect, the volume and duration of shunting, and the reactivity of the pulmonary vascular bed are all factors that affect the consequences of such anomalies [8]. The main causes of ASD's clinical symptoms are volume overload-induced dilation of the right atrium (RA) and ventricle (RV) and continuously elevated pulmonary blood flow. Patients with ASD rarely experience

symptoms, even when their pulmonary blood flow is significantly elevated [9].

About half of congenital problems resolve on their own or can be managed medically or through pregnancy, while the remaining half need to be operated on or undergo cardiac catheterization[10]. It is best to seal asymptomatic atrial septal defects in children after they have reached the age of three to five years old. ASD results in a left-to-right shunt, which changes the structure and function of the heart and causes volume overload, enlargement of the right atrium and ventricle, and other problems[11]. A number of theories have been put out to explain spontaneous closure, including the fusing of valve-like holes, thrombotic plug creation, downward expansion of the septum secundum, and septal aneurysm formation[12]. Three to four preterm births are an independent risk factor for an ASD II diagnosis, indicating that this group of kids may require a new, systematic follow-up program with careful evaluation of the signs and symptoms when therapy is necessary[13].

Preterm and term newborns with a secundum atrial septal defect detected in the first month of life were included in this study. During the first two years of life, spontaneous resolution was observed on the echocardiograph. Our study's findings demonstrated that most ASDs in both term and preterm newborns resolve on their own in the early years without the need for treatment. The time to resolution is the same for neonates born on time and those born prematurely. These outcomes correspond with the findings of the earlier Canadian investigation [6]. Prior research has examined the rate of spontaneous closure of ASDs throughout the early stages of infancy. 53.4% of patients had spontaneous closure of ASD, according to a research by Ozceker [14]. Sixty percent of patients in another trial by Khalil et al showed spontaneous closure of ASD[15].

Prior research has demonstrated a strong correlation between the atrial septal defect's two-dimensional and color Doppler echocardiographic dimensions and its true anatomic size as determined by surgery. Depending on the anatomic form, atrial septal defects have different natural histories. It is not unusual for ostium secundum faults to spontaneously close [12]. In a retrospective study, 28% of the defects decrease to a diameter of 3 mm or less, and 34% of the defects closed on their own. The primary indicator of spontaneous closure was the initial diameter of the atrial septal defect [16]. Later, an Iranian study came to the conclusion that atrial septal abnormalities smaller than 6 mm usually repair on their own, while those larger than 6 mm in newborns and children may regress [17]. Spontaneous closure has been explained by a number of mechanisms, including the fusing of valve-like holes, thrombotic plug development, downward expansion of the septum secundum, and septal aneurysm formation [12].

According to research by Radzik et al.., ASDs detected before three months of age had a closure rate of 100% if the defect was less than three millimeters, while 3-5 mm, 5-8 mm, and > 8mm groups had closure rates of 87%, 80% , and 0% respectively [18]. ASD resolution happened in 95% of small (3-5 mm), 87% of moderate (5.1- 8mm), and 60% of large (>8mm) ASDs in TNs, according to another study. 80% of small ASDs, and 76% of moderate ASDs, and 67% of large ASDs among PNs resolved spontaneously [19] , consistent with our study's findings. It's interesting to note that PNs in our cohort had smaller absolute ASD sizes. Our results of low closure rate in PNs aligned with a prior work by Riggs et al.., that discovered preterm had a major influence on ASD closure rates[20].

The limitation of the current study is that the distribution of ASD sizes was narrow, with fewer bigger abnormalities being represented among preterm and term infants. On the other hand, if all ASDs with an initial size of less than 3mm had been included, it might have given more thorough insight on resolution patterns and recommendations for PN among low birth weight and extremely premature newborns.

CONCLUSION

Both preterm and term newborns who have secundum atrial septal abnormalities within the first month of life typically experience a spontaneous resolution. Term newborns with small size defects, however, do not require follow-up because they resolve on their own. Since most asymptomatic incidentally discovered ASDs fall into this size range, there would be less need to follow up with these individuals, which would save utilization of pediatric cardiac resources.

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Authors' Contribution:

Imtiaz Ahmad: Substantial contributions to the conception or design of the work.
Tanveer Ahmad: The acquisition and analysis of data for the work.
Imran Ahmad: Interpretation of data for the work.
Raheela Mukhtar: Drafting the work and reviewing it critically for important intellectual content.

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