2D echocardiogram findings in neonates born with anorectal malformations in Sri Lanka

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Abstract

Introduction: Anorectal malformations (ARM) have an incidence of around 1 in every 5000 live births. They are associated with other anomalies, especially cardiac, which are more prevalent than in the general population. Cardiac anomalies affect the overall outcome of these patients.

Objectives: To describe the 2D echocardiogram findings of neonates born with ARM, who were referred to the Lady Ridgeway Hospital, Sri Lanka (LRH) for paediatric surgical management.

Method: A retrospective analysis was done of medical records of neonates with ARM who were referred to LRH between November 2015 and April 2019. Cardiac anomalies were categorized as major and minor according to their severity.

Results: There was a total of 60 patients with ARM: 48 with isolated ARM, 10 with ARM and oesophageal atresia (OA), 1 with ARM and duodenal atresia (DA) and 1 with ARM, OA and DA. The male to female ratio was 7:3. Associated congenital heart disease (CHD) was seen in 48 (80%) patients and it was commoner in patients with other associated gastrointestinal (GI) anomalies (92%) compared to patients with isolated ARM (77%). The common cardiac anomalies were combined atrial septal defect (ASD) and patent ductus arteriosus (PDA) (31.3%), isolated ASD (16.7%) and isolated PDA (16.7%). In those with cardiac defects, 43 (89.6%) had minor defects. In-hospital mortality rate was 13.3% (n=8). All 5 patients with major cardiac defects died due to cardiac complications. Commonest extra-intestinal manifestations were genitourinary, followed by musculoskeletal anomalies.

Conclusions: Majority of patients with ARM had associated minor cardiac anomalies, and their prevalence was higher in ARM associated with other GI anomalies compared to isolated ARMs. The commonest cardiac anomaly was combined ASD & PDA. All major cardiac anomalies in our cohort proved fatal.

(Key words**:** Anorectal malformations, Echocardiogram, Cardiac anomalies, Neonates, Sri Lanka)

Introduction

Anorectal malformations (ARM) are a spectrum of congenital malformations with an incidence of 1 in 1500 to 1 in 5000 live births with significant variations in prevalence between regions[1-5]. They are commoner in boys with a male to female ratio ranging from 1.2:1 to 2:1[1-9]. Associated anomalies are seen in 75% of neonates with ARM and their long-term prognosis is largely dependent on the presence and the severity of the associated anomalies rather than the ARM itself. Congenital heart defects (CHDs) are the commonest type of congenital abnormalities comprising 40% of all reported abnormalities[10-12]. The association of CHD with anorectal malformations is well known and the reported incidence ranges from 3.9% to 27%[7-9,13,14]. They occur in neonates as isolated ARM, a part of a recognizable syndrome or associated with other system malformations including gastrointestinal malformations. Detailed evaluation of patients with ARM for associated CHDs is therefore important as they influence the subsequent surgical management of the patients and may complicate perioperative care for these infants. In most centres, it is a routine practice to perform a 2-dimensional (2D) echocardiogram in all infants with ARM even if the clinical examination of cardiovascular system is normal to ensure that major cardiac defects are not overlooked.

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Objectives
The aim of our study was to evaluate the 2D echocardiogram findings of neonates with ARM who were managed surgically at Lady Ridgeway Hospital for Children (LRH), Colombo, the largest tertiary care referral centre for children in Sri Lanka.

Method
This is a retrospective study conducted in LRH analysing all cases referred for surgical management between November 2015 and December 2019. Medical records of sixty neonates with ARM were accessed and relevant findings, including 2D echocardiogram findings, were recorded. Two categories of CHDs were identified: minor and major. Atrial septal defect (ASD) >5 mm, patent ductus arteriosus (PDA) >2 mm with left ventricle volume overload, restrictive ventricular septal defect (VSD), and valvular aortic/pulmonary stenosis with gradients <25 mmHg, were classified as minor CHDs, whereas all other types were categorized as major CHDs[15]. Other variables included age, sex, gestational age at birth, type of ARM according to Krickenbeck classification and associated gastrointestinal and extra-gastrointestinal malformations.

Ethical issues: Approval for the study was obtained from the Ethics Review Committee of LRH (No. LRH/DA/05/2019). As it was a retrospective study informed consent was not feasible.

Results
Of the 60 neonates with ARM, 42 (70%) were males and 18 (30%) were females. Mean gestational age at birth was 37 weeks with 75% being term babies. Forty-eight (80%) neonates had isolated ARM. Twelve cases were found to have associated gastrointestinal (GI) anomalies that included 10 with oesophageal atresia (OA), one with duodenal atresia (DA) and one with DA and OA. Table 1 shows the incidence of types of ARM and associated CHDs.

Table 1: ***Incidence of types of anorectal malformations (Krickenbeck classification) and associated CHDs***

Type of anorectal malformation	Male	Female	Associated CHD
Perineal fistula	6	4	5 ASD+PDA 1 ASD 3 VSD
Recto-vestibular fistula	0	9	4 ASD+PDA 1 ASD 1 VSD 1 ASD+VSD+PDA
Recto-urethral (bulbar) fistula	10	0	3 ASD+PDA 1 ASD 1 PDA 1 TOF with PA
ARM without fistula	9	2	1 ASD+PDA 2 ASD 1 PDA 1 ASD+VSD+PDA
Cloacal anomaly	0	2	1 PDA 1 AS
Rectal atresia	1	1	1 VSD 1 Hypoplastic AA
Congenital pouch colon	3	0	1 ASD+PDA 1 PDA 1 VSD
Type not documented	7	0	1 ASD+PDA 1 ASD 2 PDA 1 ASD+VSD+PDA 1 DORV+PDA
Total	42	18	

CHD: congenital heart defect, ASD: atrial septal defect, PDA: patent ductus arteriosus, VSD: ventricular septal defect, TOF: tetralogy of Fallot, PA: pulmonary atresia, AS: aortic stenosis. AA: aortic arch, DORV: double outlet right ventricle, ARM: anorectal malformation

CHDs were present in 48 (80%) neonates. In those with cardiac defects 43 (89.6%) had minor defects and 5 (10.4%) had major defects. Cardiac anomalies were detected 11 (91.7%) of the 12 neonates with associated gastrointestinal anomalies compared to 37 of the 48 (77.1%) neonates with isolated ARM (Table 2).

Table 2: ***Distribution of CHDs in neonates with anorectal malformations (ARM)***

Type	Major CHD	Minor CHD	Normal	Total
Isolated ARM	04	33	11	48
ARM + OA	1	8	1	10
ARM + DA	0	1	0	01
ARM + OA + DA	0	1	0	01
Total	5	43	12	60

OA: oesophageal atresia, DA: duodenal atresia

Table 3 gives the distribution of the types of CHDs in neonates with ARM. PDA was the most common anomaly occurring in 33 (55%) of neonates. ASD was present in 27 (45%) neonates and VSD in 11 (18.3%) neonates.

Table 3: ***Distribution of types of congenital heart defects (CHDs) in neonates with ARM***

Type	Minor CHD						Major CHD
	ASD+PDA	Isolated ASD	Isolated PDA	VSD+PDA	Isolated VSD	Others	
Isolated ARM	14	5	6	4	1	3 (a)	4 (b)
ARM + OA	1	2	2	1	1	1 (c)	1 (d)
ARM + DA	-	-	-	-	1	-	-
ARM + OA + DA	-	1	-	-	-	-	-
Total	15	8	8	5	3	4	5

ASD: atrial septal defect, PDA: patent ductus arteriosus, VSD: ventricular septal defect, ARM: anorectal malformation, OA: oesophageal atresia, DA: duodenal atresia

(a): ASD+VSD+PDA (b): double outlet right ventricle + PDA 1, double outlet right ventricle + ASD 1, pulmonary atresia + PDA 1, hypoplastic aortic arch 1 (c): aortic stenosis (d): tetralogy of Fallot with pulmonary atresia

Excluding cardiac malformations, associated extra-gastrointestinal anomalies were grouped according to major organ systems. Extra-gastrointestinal anomalies were seen in 21 (35%) and was commoner in males (18/21). The data are shown in Table 4

Table 4: ***Associated extra-intestinal anomalies in neonates with anorectal malformation (ARM)***

Extra-intestinal anomaly	Number (%)
Genitourinary anomalies	12 (20.0)
Musculoskeletal anomalies	11 (18.3)
Respiratory anomalies	03 (05.0)
Chromosomal anomalies	03 (05.0)
Neurological anomalies	01 (01.7)
Integumentary anomalies	01 (01.7)

Ten (16.7%) neonates were complicated with multiple extra-intestinal anomalies (Table 3) and the commonest combination was genitourinary with musculoskeletal anomalies (n=5).

There were eight recorded mortalities before discharge from hospital following intervention comprising 4 (50%) patients with isolated ARM and 4 (50%) patients with ARM + OA. All eight neonates had associated cardiac lesions 62.5% being major CHDs and 37.5% being minor CHDs. All neonates who had major cardiac defects died due to cardiac complications. Of those 8 patients, associated extra-gastrointestinal malformations were present in 7 (87.5%) neonates with 5 of them having multiple malformations.

Discussion

Frequency of ARM ranges from 1 in 1500 to 1 in 5000 births in various studies[1-4]. The present study gives a male to female ratio of 2.3:1 which is slightly higher than previously reported ratios ranging from 1.2:1 to 2:1[1-3,5-9]. In patients with ARM, OA/tracheo-oesophageal fistula and DA are the common gastrointestinal (GI) associations mentioned in the literature and were the only lesions found in this study as well, coexisting with 20% of the study population. Incidence of associated GI anomalies was between 4% to 14.9% in various studies[1,5-8,9,13]. OA was found in 16.7% of neonates whilst DA and OA+DA were found in one neonate each. Incidence of OA in recent studies varied between 1.4% to 82.8% which could be attributed to the different study settings[1,5-8,14,16,17]. There is a paucity of data from the Southeast Asian region.

Frequency of different types of ARMs varies in different studies. In our study, however recto-urethral (prostatic and bulbar) fistula in males and recto-vestibular fistula in females were found to be the commonest. Levitt MA, *et al*[18] and vd Merwe *et al*[7] described similar results in their reviews. However, a European multicentre study contradicts these findings, showing perineal fistula to be the most frequent type in both males and females with 43% and 41% incidence respectively[6]. The

incidence of congenital pouch colon was higher (7.1%) which is comparable to the figures of North India which has the highest incidence globally[19,20]. Rare types of ARM were noted to be commoner in males (9.5%) compared to females (5.6%) in contrast to the findings of De Blaauw I, *et al*[6] which observed increased frequency in females. The discrepancy may be explained by the decreased detection of congenital pouch colon among females in the neonatal period which contributed to 60% of rare types in our study. There was a 4.8% incidence of cloacal anomaly similar to the previous literature reporting incidence between 3% to 10%[5-7].

The frequency of CHDs reported in association with ARM ranged from 3.9% to 27% compared to approximately 1% in the general population[3,5,6,13,21]. In our study, we found an incidence of 80% in our neonates with ARM, the majority being minor defects. In this study, incidence of cardiac anomalies was 91.7% in neonates with ARM associated with other GI malformations compared to neonates with isolated ARM, and a similar observation was made by Greenwood RD, *et al*[21].

Pattern of CHDs among neonates with ARM varies between studies and no single lesion has been found to have a predominant association[6]. A number of studies[5,7,9,21,24] have identified tetralogy of Fallot and VSD as the commonest anomalies while studies by Gokhroo RK, *et al*[22] and Örün UA, *et al*[23] have quoted ASD to be the commonest anomaly in ARM with 75% and 50% of the neonates respectively. However, in the Sri Lankan setting, we found the combination of PDA and ASD (31.3%) to be the most common anomaly followed by isolated ASD and isolated PDA which had an equal incidence of 16.7% The reason for the discrepancy in the frequency of CHDs needs to be evaluated in future large-scale studies.

In our series, apart from cardiac anomalies, 35% of neonates had extra-gastrointestinal anomalies. Multiple extra-gastrointestinal malformations were found in 16.7%. Among the multiple anomalies, genito-urinary (GU) and musculoskeletal anomalies were found to occur in 50%. This correlates with the findings of previous studies which showed higher frequency of GU anomalies with musculoskeletal anomalies[7,8]. The prevalence of the anomalies in this study was similar to that in previous reports where GU (20%) and musculoskeletal (18.3%) anomalies were found to be the most common associated anomalies. The figures are closer to the previous research showing the frequency of 22.4% to 62.8% of GU anomalies and 15.1% to 42.5% of musculoskeletal anomalies in patients with ARM[2,3,5,7,8,9,13,25-29]. The incidence of CHDs was greater in the presence of a GU anomaly where all the neonates with GU anomalies had CHDs.

Mortality rates of neonates with ARM in developing countries are estimated to be 15% with higher values in late presentation ranging from 26% to 58%[30-34]. Other studies have demonstrated mortality rates of 7% to 33%[7,21]. In our study, eight (13.3%) neonates demised which is closer to previous studies; 75% of these were males which was seen in ARM with associated anomalies which recorded 60% male predominance, which was noted by Merwe E, *et al*[7] as well. All 8 patients had CHDs. Neonates with major CHDs contributed to 62.5% of the deaths in the study population where all died due to cardiac complications. Our findings agree with those in the literature, which found CHD to be a major determinant factor in the mortality of patients with ARM, although there were studies that disputed this finding [7,21,23,35]. Seven (87.5%) out of eight deceased patients had associated extraintestinal anomalies. This contribution of extraintestinal anomalies to mortality was shown in previous studies as well [1-3,7]. Fifty percent of patients who died had ARM + OA. This negative impact of OA on mortality has also been established in previous research[30].

The most important limitation of the study is that it is a retrospective review lacking data about long term follow-up of patients. Other limitations include single-institutional experience with small number of patients lowering the ability to generalise it to the population and not including some patients with ARM who did not undergo surgery and who died soon after birth.

Patients with ARM should be investigated with 2D echocardiography prior to any attempt at surgical repair. Our study indicates the need for larger scale studies to determine the prevalence and pattern of CHD in patients with ARM in the Sri Lankan population, both for prognostic and surgical implications.

Conclusions

There was a high incidence of CHDs associated with ARM, even higher with associated gastrointestinal malformations. Majority of the CHDs were minor defects and ASD+PDA was found to be the most frequently occurring CHD. Common extraintestinal anomalies were related to genitourinary system and musculoskeletal system. Mortality rate of 13% was reported in this series and all major CHD resulted in demise of the neonates.

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