Cardiology in the Young

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Pregnancy and early post-natal outcomes of fetuses with functionally univentricular heart in a low-and-middle-income country

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Abstract

Background: Care of children with functionally univentricular hearts is resource-intensive. *Objectives:* To analyse pregnancy and early post-natal outcomes of fetuses with functionally univentricular hearts in the setting of a low–middle-income country. *Methods:* A retrospective study was conducted during the period of January 2008–October 2019. Study variables analysed included gestational age at diagnosis, maternal and fetal comorbidities and cardiac diagnosis including morphologic type of single ventricle. Outcomes analysed included pregnancy outcomes, type of post-natal care and survival status on the last follow-up. *Results:* A total of 504 fetuses were included. Mean maternal age was 27.5 ± 4.8 years and mean gestational age at diagnosis was 25.6 ± 5.7 weeks. Pregnancy outcomes included non-continued pregnancies (54%), live births (42.7%) and loss to follow-up (3.3%). Gestational age at diagnosis was the only factor that impacted pregnancy outcomes (non-continued pregnancies 22.5 ± 3.5 vs. live births 29.7 ± 5.7 weeks; $p < 0.001$). Of the 215 live births, intention-to-treat was reported in 119 (55.3%) cases; of these 103 (86.6%) underwent cardiac procedures. Seventy-nine patients (36.7%) opted for comfort care. On follow-up (median 10 (1–120) months), 106 patients (21%) were alive. Parental choice of intention-to-.treat or comfort care was the only factor that impacted survival on follow-up. *Conclusions:* Prenatal diagnosis of functionally univentricular hearts was associated with overall low survival status on follow-up due to parental decisions on not to continue pregnancy or non-intention-to-treat after birth. Early detection of these complex defects by improved prenatal screening can enhance parental options and reduce resource impact in low-and-middle-income countries.

Introduction

Congenital heart disease (CHD) is one of the common forms of birth defects in newborn babies.[1] CHDs with univentricular circulation are defined as lesions where one of the two ventricles are too small to sustain the pulmonary or systemic circulation.[2] These occur at a prevalence of 4.4/10,000 live births.[3,4] Outcomes for these complex CHDs have significantly improved in recent years, though these require multiple-staged palliative procedures in the initial years of life.[4–6] Recent reports have indicated feasibility and good short-term outcomes with single ventricle palliation in low-and-middle-income countries.[7] Lifelong specialist cardiac review is required for these patients and additional neurodevelopmental and psychological issues cause further concern for longer-term survivors.[8,9] The medical and socio-economic challenges involved in the care of these complex CHDs may be very challenging for patients and their families in the setting of low-and-middle-income countries.[10,11]

Screening of the fetal heart is routinely offered as a part of the mid-trimester anomaly scan in all pregnancies in developed countries.[12–14] Inclusion of the four-chamber view in screening programs has shown a high sensitivity for the detection of complex CHDs like the functionally univentricular hearts.[15–17] Early prenatal diagnosis of complex CHDs gives more options to expectant families including the option of termination of pregnancy, thereby potentially reducing the post-natal prevalence of these defects.[18–20] Recent studies from developed countries reported longitudinal follow-up until Fontan operation after prenatal diagnosis of univentricular heart and identified risk factors for adverse perinatal outcomes in these patients.[21,22] However, despite the availability of guidelines for mid-trimester anomaly (18–20 weeks) scans in India, evaluation of the fetal heart is seldom performed in mass screening programs.[23] The Medical termination of pregnancy act of India was introduced in 1971 before the era of routine fetal ultrasound and it provides guidelines for termination of pregnancy in India until the gestational age limit of 20 weeks.[24] However, since many complex fetal anomalies including CHD are detected in the later stages of pregnancy, an amendment for this act has been proposed recently to increase the upper gestational age limit for termination of pregnancy.[25] Considering the

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challenges involved in the care and follow-up for complex CHDs in low-and-middle-income countries, prenatal diagnosis can potentially enhance parental decision-making options and this can impact the perinatal outcomes for these defects.

In this retrospective 10-year study, we analysed pregnancy and early post-natal outcomes of fetuses diagnosed with functionally univentricular heart in the setting of a low-and-middle-income country.

Methods

Study setting and design

This hospital-based retrospective study was conducted in the setting of a tertiary paediatric cardiac centre. The centre offers high-quality cardiac care accessible by the general population of Kerala, South India amounting to around 35 million. The annual number of live births in Kerala is around 500,000. All pregnant women in Kerala have universal access to antenatal care and most patients are offered a minimum of two ultrasound evaluations, either free of cost or at nominal rates (including a mid-trimester anomaly scan). A dedicated Fetal Cardiology division was initiated in our centre in 2008 with the specific goal of improving the availability of prenatal diagnosis of CHD in Kerala and provide counselling and options for prenatal and perinatal care. All fetuses with a diagnosis of functionally univentricular heart during the period of January, 2008–October, 2019 from our database were included in the analysis.

Inclusion and exclusion criteria

All fetuses with a diagnosis of functionally univentricular heart diagnosed during the study period were included in the analysis. Fetuses with borderline ventricle size were classified as hypoplastic when the ventricle length (measured from atrioventricular valve annulus to endocardium at apex) z-score was less than −2 and asymmetric when the z-scores where >−2; those with asymmetric ventricles were excluded from the analysis.[26]

Fetal echocardiography and counselling protocol

All patients underwent a detailed evaluation of fetal heart as per standard recommendations.[12–14] This included the standard imaging protocols in the transverse and sagittal planes along with the additional views as per indications and evaluation of the fetal heart rate and rhythm. Following the fetal diagnosis, the attending fetal cardiologist provided detailed counselling to the family about management options, expected outcomes in our centre, long-term concerns and expected costs of treatment including the hospital expenses for multi-staged surgical procedures, outpatient clinic visits and long-term medications. Our centre routinely performs all surgical procedures involved in the multi-staged palliation of all forms of single ventricle hearts, from the inception of the period of this study. The final decision regarding the management of pregnancy was taken by the respective families and the referring obstetrician based on family's preferences and the outcomes were reported retrospectively.

Study variables and groups

Since 2008, a dedicated fetal cardiology database was initiated including maternal variables, indication for referral, fetal variables, details of cardiac diagnosis, pregnancy outcomes and post-natal outcomes in the live-born fetuses. The maternal variables included in the analysis included maternal age, gravidity, gestational age at referral, indication for fetal echocardiography, associated comorbidities (diabetes mellitus, maternal infections like febrile illnesses in the first trimester, rubella and influenza, exposure to potential teratogenic drugs), mode of conception and consanguinity.[27] Fetal variables included the presence of hydrops, extra-cardiac anomalies, nuchal translucency and family history of CHD in previous children. Nuchal translucency values > 95th centile was taken as abnormal.[28] We included details about the socio-economic class by Modified Kuppuswamy Scale, type of family (nuclear or joint), religion and educational status of the parents in the prospective cohort subset of patients (January, 2017 onwards).[29]

Fetuses with a diagnosis of functionally univentricular heart were further sub-classified into the following sub-groups for analysis:

- Based on anatomical type – the anatomic cardiac diagnosis.
- Based on ventricular morphology – dominant left or right ventricle.
- Based on outflow tract anatomy – systemic outflow obstruction, pulmonary outflow obstruction or no outflow tract obstruction. The presence of obstruction was primarily assessed by the size of the respective outflow and calculation of the z-scores; values of < −2 were considered to be small and suggestive of obstruction.[26]

Outcome variables

The perinatal outcomes analysed in this study included pregnancy outcomes and early post-natal outcomes.

Pregnancy outcomes included the following:

- Non-continued pregnancies: This information was recorded as reported by the families by telephone enquiry. This included the termination of pregnancy and spontaneous intrauterine fetal death. Fetal autopsy for confirmation of the cardiac diagnosis was not performed.
- Live births.
- Lost to follow-up.

For the live-born babies, the details of the mode of delivery, birth weight, sex and presence of comorbidities (extra-cardiac anomalies, genetic syndromes, birth-related complications and neonatal sepsis) were noted. The attending paediatric cardiologist confirmed the cardiac diagnosis and provided a detailed counselling about prognosis and management options to the patient's families. Post-natal care was offered as per parental choices and was classified as intention-to-treat (if there was an intention to provide specialised cardiac care), comfort care (basic neonatal care with no specialised cardiac care) or no post-natal data. Decisions regarding comfort care were channelised through the palliative care services of our hospital after obtaining informed consent from the parents. In those with intention-to-treat, we recorded the details of the cardiac procedures performed (surgery or catheter-based) for initial palliation (Stage 1) as well as the subsequent stages in the single ventricle palliation (bidirectional Glenn shunt, one and a half ventricle repair and the Fontan procedure). The clinical status of the patient until the last available follow-up (alive, dead or lost to follow-up) was recorded.

The study was approved by the Institutional Review Board (date 18 February, 2020; IRB-AIMS-2020-095).

Statistical analysis

We summarised categorical variables as numbers (percentages) and continuous variables as mean, median (Interquartile range). Chi-square test was used to compare the categorical variables associated with pregnancy outcome and survival status on follow-up.

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Table 1. Baseline characteristics of patients included in the study (n = 504)

Variable	Number (percentage)
Mean maternal age (years)	27.5 ± 4.8
Mean gestational age at diagnosis (weeks)	25.6 ± 5.7
Indication for referral:	
Suspected CHD	485 (96.2)
Previous child with CHD	3 (0.6)
Maternal illness	4 (0.8)
Fetal arrhythmias	3 (0.6)
Extra-cardiac anomaly	4 (0.8)
Others	5 (1.0)
Consanguinity	11 (2.2)
Maternal risk factors:	
Diabetes mellitus	46 (9.1)
Exposure to teratogenic drugs	8 (1.6)
History of maternal infections	12 (2.4)
Nuchal translucency > 95th centile*	38 (7.5)
Extra-cardiac anomalies	57(11.3)
Hydrops#	8 (1.6)

*Nuchal translucency measurements were reported in only 217 patients (43.1%).
#In six cases, hydrops was related to the cardiac diagnosis (pulmonary atresia with intact ventricular septum with hypoplastic dysfunctional RV and severe tricuspid regurgitation in three, Heterotaxy in two and tricuspid atresia with restrictive foramen ovale in one). In two cases (complex double outlet RV with hypoplastic LV and Dextrocardia with double inlet LV), hydrops was due to non-cardiac reasons.

Table 2. Types of single ventricle based on anatomy, ventricular morphology and outflow tracts

Type of single ventricle	Number (percentage)
Anatomical subtype:	
Hypoplastic left heart	104 (20.6)
Tricuspid atresia	90 (17.9)
Heterotaxy syndromes #	110 (21.8)
Pulmonary atresia with intact ventricular septum	56 (11.1)
Others*	62 (12.3)
Complex double outlet right ventricle	41 (8.1)
Double inlet left ventricle	41 (8.1)
Ventricular morphology:	
Dominant left ventricle	223 (44.2)
Dominant right ventricle	281 (55.8)
Outflow tract anatomy:	
Systemic outflow obstruction	153 (30.4)
Pulmonary outflow obstruction	224 (44.4)
No obstruction	127 (25.2)

#Heterotaxy syndromes included complex CHD with unbalanced atrioventricular septal defect with associated intra-cardiac defects.
*Others – Left atrioventricular valve atresia with single ventricle – 30; Large ventricular septal defect amounting to single ventricle – 13, Hypoplastic right ventricle with VSD – 19.

Independent sample t-test was used to compare the continuous variables associated with pregnancy outcome and survival status. Multiple binary logistic (Forward conditional) regression analysis was used to estimate odds ratio with 95% CI of risk factor for non-continued pregnancy outcome and survival status on follow-up. Statistical analyses were conducted using SPSS Version 20.0 for Windows (IBM Corporation ARMONK, NY, United States of America).

Results

A total of 504 fetuses were diagnosed with functionally univentricular heart during the period of January, 2008–October, 2019. The mean maternal age was 27.5 ± 4.8 years. The mean gestational age at diagnosis was 25.6 ± 5.7 weeks. The most common reason for referral was suspicion of CHD in screening ultrasound (n = 485; 96.2%). Majority of the fetuses were singleton pregnancies (97.1%). Maternal risk factors included diabetes mellitus (46; 9.1%), exposure to teratogens (8; 1.6%) and intrauterine infections (12; 2.4%). Associated fetal anomalies included extra-cardiac anomalies (57; 11.3%) and hydrops fetalis (8; 1.6%). Nuchal translucency measurements were reported in 217 patients (43.1%) only; of these 38 fetuses (7.5%) had values > 95th centile. The baseline characteristics of the study patients are summarised in Table 1.

Types of single ventricle

The various types of functionally univentricular heart based on anatomical subtype are summarised in Table 2. Based on the ventricular anatomy, 281 fetuses (55.8%) had a dominant right ventricle while the rest (n = 223, 44.2%) had a dominant left ventricle. Pulmonary outflow obstruction was reported in 224 fetuses (44.4%), systemic outflow obstruction in 153 (30.4%) while 127 fetuses (25.2%) had no outflow obstruction.

Pregnancy outcomes

Of the total 504 fetuses, 272 (54%) had non-continued pregnancies including termination of pregnancy (n = 256, 50.8%) or intrauterine fetal death (n = 16; 3.2%). Live births were reported in 215 fetuses (42.7%) while 17 (3.3%) were lost to follow-up. On univariate analysis, gestational age at diagnosis, presence of hydrops and associated extra-cardiac anomalies impacted pregnancy outcomes (Table 3). However, on multivariate analysis, only gestational age at diagnosis had a significant association with the pregnancy outcomes. The mean gestational age at diagnosis was significantly lower in non-continued pregnancies compared with those with live births (22.5 ± 3.5 vs.29.7 ± 5.7; $p < 0.001$). Other factors like maternal age, cardiac diagnosis, type of ventricular morphology or outflow tract obstruction also did not influence the pregnancy outcomes.

In a prospective cohort of 57 fetuses (12.9%) included in this study after January, 2017, we had included a socio-economic questionnaire including the socio-economic class, type of family, religious background and educational status of the parents. Of these 57 cases, 18 (31.6%) had live births and the remaining 39 (68.4%) had non-continued pregnancies. None of the socio-economic or cultural factors had an impact on pregnancy outcomes (Table 3).

Neonatal and follow-up outcomes

Of the 215 live births, 98 (45.6 %) were delivered in tertiary cardiac centres, while the remaining (117; 54.4%) were delivered in

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Table 3. Univariate analysis of predictors of pregnancy outcome

Variables	Outcome: Live birth n = 215 (42.7%)	Outcome: Non-continued pregnancy n = 272(54.1%)	p-value
Maternal age (years)	27.4 ± 4.8	27.7 ± 4.7	0.392
Gestational age (weeks)	29.7 ± 5.7	22.5 ± 3.5	<0.001
Maternal diabetes			
No	193 (43.7)	249 (56.3)	0.501
Yes	22 (48.9)	23 (51.1)	
Hydrops			
No	202 (44.8)	249 (55.2)	0.011
Yes	0 (0)	8 (100)	
Extra-cardiac anomalies			
No	163 (42.2)	223 (57.8)	0.035
Yes	31 (57.4)	23 (42.6)	
Nuchal translucency			
Normal	85 (48.6)	90 (51.4)	0.136
Abnormal	13 (35.1)	24 (64.9)	
Anatomical subtype			
HLHS	34 (33.3)	68 (66.7)	0.077
Tricuspid atresia	39 (45.9)	46 (54.1)	
Heterotaxy syndromes	50 (46.7)	57 (53.3)	
PA/IVS	24 (44.4)	30 (55.6)	
Others*	34 (56.7)	26 (43.3)	
Complex DORV	13 (34.2)	25 (65.8)	
Double inlet left ventricle	21 (51.2)	20 (48.8)	
Ventricular morphology			
LV	100 (46.5)	113 (41.5)	0.272
RV	115 (53.5)	159 (58.5)	
Outflow obstruction			
Aortic	67 (44.7)	83 (55.3)	0.457
Pulmonary	99 (46.5)	114 (53.5)	
No obstruction	49 (39.5)	75 (60.5)	
Socio-economic status*			
Upper	2 (33.3)	4 (66.7)	0.995
Middle	11 (31.4)	24 (68.6)	
Lower	5 (31.3)	11 (68.8)	
Religion*			
Christian	6 (31.6)	13 (68.4)	0.502
Hindu	7 (25.9)	20 (74.1)	
Muslim	5 (45.5)	6 (54.5)	
Family type*			
Joint	11 (32.4)	23 (67.6)	0.879
Nuclear	7 (30.4)	16 (69.6)	

DORV = double outlet RV; HLHS = hypoplastic left heart syndrome; LV = left ventricle; PA/IVS = pulmonary atresia with intact ventricular septum; RV = right ventricle.
*This data is available in a cohort of 57 patients who were prospectively enrolled into this study from January, 2017 onwards.

Table 4. Comparison of variables between intention-to-treat and comfort care in live-born babies (n = 215)

Variables	Outcome: Intention-to-treat n = 119	Outcome: Comfort care n = 79	p-value
Weight	2.9 ± 0.28	2.89 ± 0.33	0.102
Co-morbidities present	4 (33.3)	8 (66.7)	0.053
Anatomical subtype			
HLHS	6 (18.8)	26 (81.3)	<0.001
Tricuspid atresia	33 (86.8)	5 (13.2)	
Heterotaxy syndromes	21 (48.8)	22 (51.2)	
PA/IVS	13 (56.5)	10 (43.5)	
Others*	19 (65.5)	10 (34.5)	
Complex DORV	11 (84.6)	2 (15.4)	
Double inlet left ventricle	16 (80.0)	4 (20.0)	
Ventricular morphology			
LV	73 (76)	23 (24)	<0.001
RV	46 (45.1)	56 (54.9)	
Outflow obstruction			
Aortic	22 (32.4)	46 (67.6)	<0.001
Pulmonary	73 (75.3)	24 (24.7)	
No obstruction	24 (57.1)	18 (42.9)	

DORV = double outlet right ventricle; HLHS = hypoplastic left heart syndrome; LV = left ventricle; PA/IVS = pulmonary atresia with intact septum; RV = right ventricle.
*Others – Left atrio-ventricular valve atresia with single ventricle 10; Large ventricular septal defect amounting to Single Ventricle – 10, Hypoplastic Right ventricle with VSD – 9.

non-cardiac units. The mean gestational age at delivery was 37.9 ± 1.2 weeks and the mean birth weight was 2.9 ± 0.3 kg; 113 (52.6%) babies were male. Twelve patients (5.6%) had associated comorbidities including genetic syndromes (n = 5), extra-cardiac anomalies (n = 4), prematurity or growth restriction (n = 2) or neonatal sepsis (n = 2).

Intention-to-treat and provision of cardiac care was the parental choice in 119 (55.3%) of the live-born babies. Eighty nine (74.8%) of these underwent surgical procedures; 14 (11.8%) required catheter-based interventions while the remaining 16 were continued on medications alone. Of these, 35 patients (16.2%) required Stage 1 palliative procedures (Table S1) in the neonatal period. Fifty-one patients (23.7%) underwent Stage 2 procedures including bidirectional Glenn shunt (n = 47; 21.9%) or "one and a half ventricle repair" for pulmonary atresia with intact septum (n = 4; 1.9%). Seventeen (7.9%) of the live-born infants completed Stage 3 Fontan procedure. In 79 patients (36.7%), the parents opted for comfort care, while in 17 infants (7.9%), no post-natal data was available. Cardiac diagnosis, ventricular morphology and type of outflow obstruction impacted the decision on the type of post-natal care offered (Table 4). Table S2 lists the cardiac diagnoses of patients undergoing staged procedures after birth.

On follow-up, median duration 10 (range 1–120) months, 106 (49.3%) of the 198 patients with post-natal data were alive; 85 (39.5%) died, while 7 (3.3%) were lost to follow-up. Ninety-five (79.8%) of the patients with intention-to-treat survived. Univariate analysis of predictors of survival on follow-up in live-born babies is summarised in Table 5. On multi-variate analysis, the only variable which impacted survival status on follow-up was intention-to-treat or

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Table 5. Univariate analysis of variables impacting survival status on follow-up in live-born infants

Variables	Follow-up status		p-value
	Alive 106 (49.3%)	Died 85 (39.5%)	
Birth weight (kg), mean ± SD	2.90 ± 0.29	2.90 ± 0.32	0.924
Cardiac diagnosis:			
HLHS	5 (15.6)	27 (84.4)	<0.001
Tricuspid atresia	26 (72.2)	10 (27.8)	
Heterotaxy syndromes	23 (56.1)	18 (4.9)	
PA/IVS	15 (65.2)	8 (34.8)	
Others*	14 (51.9)	13 (48.1)	
Complex DORV	9 (69.2)	4 (30.8)	
Double inlet left ventricle	14 (73.7)	5 (26.3)	
Ventricular morphology			
LV	63 (69.2)	28 (30.8)	<0.001
RV	43 (43.0)	57 (57.0)	
Outflow obstruction			
Aortic	22 (36.1)	39 (63.9)	<0.001
Pulmonary	63 (67.7)	30 (32.3)	
No obstruction	21 (56.8)	16 (43.2)	
Comorbidities			
No	103 (57.1)	76 (42.9)	0.038
Yes	3 (25.0)	9 (75.0)	
Type of treatment			
Intention-to-treat	95 (83.2)	19 (16.8)	<0.001
Comfort care	11 (14.3)	66 (85.7)	

DORV = double outlet right ventricle; HLHS = hypoplastic left heart syndrome; LV = left ventricle; PA/IVS = pulmonary atresia with intact septum; RV = right ventricle.

comfort care (survival 79.8% in intention-to-treat vs. 12.9% in comfort care group; $p < 0.001$).

Figure 1 depicts the flowchart of the pregnancy and post-natal outcomes of the patients included in this study.

Discussion

This retrospective study of 504 fetuses diagnosed with a functionally univentricular heart showed an overall low survival status of affected fetuses, both in pregnancy and in post-natal life. About half of the affected pregnancies were not continued to term and about a third of live-born babies did not have an intention-to-treat, resulting in an overall survival of about 20% on the last follow-up (Fig 1). Earlier gestational age at diagnosis significantly impacted pregnancy outcomes (Table 3). Amongst live births, cardiac diagnosis and ventricle morphology (systemic left ventricle) impacted parental decisions regarding intention-to-treat (Table 4). Most patients (>80%) with intention-to-treat underwent cardiac procedures (especially Stages 1 and 2); the final stage Fontan procedure was completed in 17 patients during the available follow-up period. Survival on follow-up was significantly impacted by parental decisions towards intention-to-treat or comfort care; about 80% of patients opting for specialised cardiac care were alive on the last follow-up (Table 5). Maternal or fetal comorbidities, socio-economic status, religion or educational status of the parents did not impact parental decision-making (Table 3).

Previous studies have reported higher prevalence of termination of pregnancy when the prenatal diagnosis of complex CHD is made in early gestation.[16–20] The first-trimester screening resulted in a lower prevalence of complex CHDs during the second trimester as well as post-natal period.[16] In a population-based analysis, Bull et al reported termination rates of 70 and 61% when a diagnosis of CHD was made before 19 and 23 weeks, respectively.[18] Beroukhim et al reported a higher rate of termination for fetuses with univentricular hearts when the diagnosis was made before 24 weeks.[21] Tararbit et al reported that of the 703 fetuses diagnosed with CHD, 46% were terminated, with 3.2 times higher odds of termination in those diagnosed before 22 weeks.[30] Other studies also have reported the lack of impact of factors like ventricular morphology, maternal age or other fetal comorbidities on pregnancy outcomes.[18–21] In the setting of a low-and-middle-income country, besides the gestational age at diagnosis, factors like economic burden, concerns about the long-term health and quality of life of a child with complex CHD and the potential impact of the affected child on the future of the family and other children might have influenced the pregnancy outcomes reported in this study.[5,6,8,9]

The overall low utilisation of cardiac care in the live-born babies in this study is different from reports from the developed world where the majority receive specialised cardiac care.[21,22] This is despite the fact that all palliative surgeries for univentricular heart were being performed in our centre from the inception of the study. A recent report had highlighted the feasibility of single ventricle palliations in the setting of low-and-middle-income countries with encouraging early outcomes.[7] We observed that intention-to-treat and cardiac procedures were more common in patients with systemic left ventricle, which has been shown to be associated with better long-term Fontan outcomes.[21,22] The medical costs of the staged single ventricle palliation pathway will consume about 5 times the average per capita annual income of a family in Kerala.[31] In addition, the annual clinic visits, evaluation and medications will exceed an average monthly income. Though government-funded schemes have been initiated for the care of children with CHD in Kerala and other states of India, the actual costs of care far exceed the support provided.[10,32] In the setting of a univentricular heart, where the threat of a failing Fontan pathway looms large with advancing years after the surgery, the overall impact on an average family can be devastating in most healthcare systems of the world, especially those in the low-and-middle-income countries.[33,34] The challenges of providing long-term care for the survivors of these complex CHDs may prove overwhelming for low-and-middle-income countries with an ever-increasing number of patients surviving tertiary cardiac care into adult life.[8–11,33–35] Policymakers and funding agencies need to develop strategies for providing extended support for follow-up care of these patients and not merely fund the cost of the surgical procedures in order to take care of complex CHDs feasible for affected families.[36]

The results of this study highlight the importance of early pregnancy screening of the fetal heart, especially in the low-and-middle-income countries. Most of the complex forms of CHD of the univentricular type can be suspected using the four-chamber view with a high degree of sensitivity.[15] In Kerala, the cost of an anomaly scan is very nominal in government hospitals (less than 500 Indian Rupees or approximately 7 US Dollars), especially for patients in the low-income groups. Fetal echocardiography in advanced centres cost around 3000 Indian Rupees (approximately 40 US Dollars). Compared to the long-term costs of care of a child with univentricular heart, the costs of prenatal diagnosis are thus

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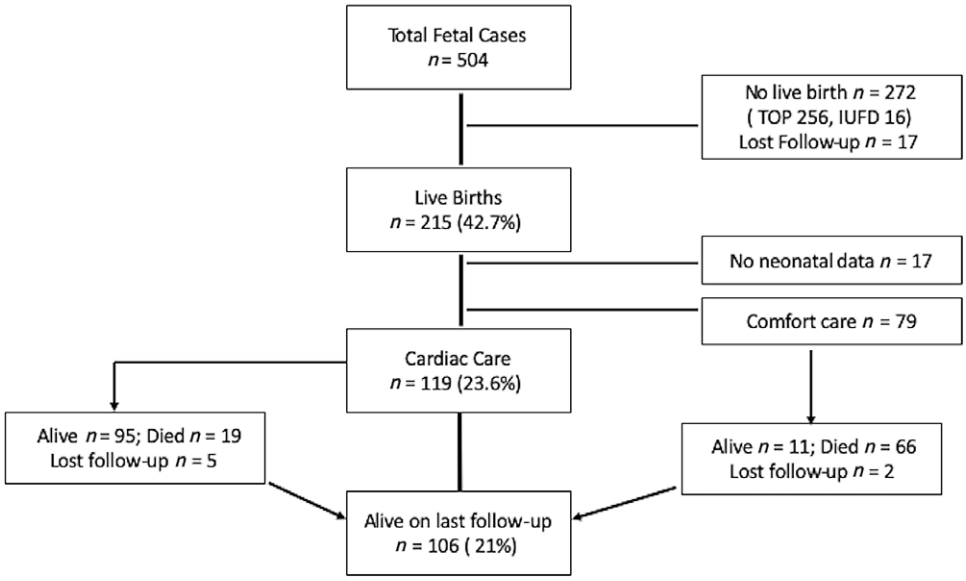

Figure 1. Flowchart describing study patients with pregnancy and post-natal outcomes. IUFD = intrauterine fetal death; TOP = termination of pregnancy.

quite nominal. Suspicion of a complex CHD on screening should initiate a downstream process of referral, detailed evaluation by a fetal cardiologist, counselling and enhanced parental options for decision-making. Early prenatal diagnosis by implementing a mandatory screening policy may a very cost-effective strategy for the care of children with CHD in low-and-middle-income countries by reducing the burden of complex CHDs, permitting more efficient utilisation of resources towards the care of more correctable CHDs.[37]

The strengths of the study include the large number of patients including the different anatomic subsets of functionally univentricular hearts and a near-complete pregnancy and early post-natal follow-up data. However, the limitations include inclusion of retrospective data and possibility of referral bias. Gestational age was calculated on the basis of the date of the last menstrual period alone and not based on ultrasound parameters. The role of socio-economic factors in deciding pregnancy outcomes and type of post-natal care was not comprehensively studied. A longer-term follow-up is needed to determine the further course of patients surviving in the intention-to-treat group until the completion of all stages of the single ventricle pathway and post-Fontan clinical outcomes.

In conclusion, prenatal diagnosis of functionally univentricular hearts was associated with an overall low survival status on follow-up. Early detection of these complex lesions by improved prenatal screening can enhance parental options and reduce resource impact in low-and-middle-income countries.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/S1047951120002929

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Aparna Vijayaraghavan conceptualised the study, collected and analysed the data, drafted the initial manuscript and revised the manuscript.

Stephy Thomas collected data, carried out the initial analyses and reviewed the manuscript.

Abish Sudhakar designed the data collection instruments, collected data, carried out the initial analyses and reviewed and revised the manuscript.

All the authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

What's already known about this topic?

Prenatal diagnosis of univentricular heart is associated with the overall high utilisation of post-natal specialised cardiac care in live-born infants in developed countries.

What does this study add?

In the setting of low-and-middle-income countries, prenatal diagnosis of functionally univentricular heart is associated with overall high rates of non-continued pregnancies and low utilisation of specialised cardiac care in live-born babies, despite the availability of tertiary paediatric cardiac services.

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