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Influence of improved antenatal detection on the outcomes of complete atrioventricular block diagnosed in fetal-neonatal life and childhood periods – a single-centre experience in South Wales for 55 years

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Abstract

Objective: This study aimed to analyse the influence of improved antenatal detection on the course, contemporary outcomes, and mortality risk factors of the complete atrioventricular block during fetal-neonatal and childhood periods in South Wales. *Methods:* The clinical characteristics and outcomes of complete atrioventricular block in patients without structural heart disease at the University Hospital of Wales from January 1966 to April 2021 were studied. Patients were divided into two groups according to their age at diagnosis: I-fetal-neonatal and II-childhood. Contemporary outcomes during the post-2001 era were compared with historical data preceding fetal service development and hence earlier detection. *Results:* There were 64 patients: 26 were identified in the fetal-neonatal period and the remaining 38 in the childhood period. Maternal antibodies/systemic lupus erythematosus disease (anti-Ro/Sjögren's-syndrome-related Antigen A and/or anti-La/Sjögren's-syndrome-related Antigen B) were present in 15 (57.7%) of the fetal-neonatal. Fetal/neonatal and early diagnosis increased after 2001 with an incidence of 1:25000 pregnancies. Pacemaker implantation was required in 34 patients, of whom 13 were diagnosed in the fetal-neonatal group. Survival rates in cases identified before 2001 were at 96.3% (26/27), whereas it was 83.8% (31/37) in patients diagnosed after 2001 ($P > 0.05$). Other mortality risk factors comprised a lower gestational week at birth, maternal antibodies, and an average ventricular heart rate of < 55 bpm. *Conclusions:* Fetal diagnosis of complete atrioventricular block is still portends high fetal and neonatal mortality and morbidity despite significantly improved antenatal detection after 2001. Pacemaker intervention is needed earlier in the fetal-neonatal group. Whether routine antenatal medical treatment might alter this outcome calls for further prospective multicentre studies.

Highlights

What is already known on this topic

- Complete atrioventricular block is rare in children. There is limited contemporary national population data.

What this study adds

- Contemporary results show an increase in early fetal diagnosis of the complete atrioventricular block.
- Fetal diagnosis of complete atrioventricular block still portends into high fetal and neonatal mortality when associated with hydrops or lower junctional escape rates.
- The fetal onset of the complete atrioventricular block is important for the prediction of prognosis and the need for early pacemaker implantation.
- Prenatal treatment did not decrease the mortality in fetuses with severe decompensated heart failure and hydrops.
- Pacemaker implantation complications were seen mostly in the early implanted patients.

How this study might affect research, practice, or policy

- Whether routine antenatal medical treatment might alter this outcome calls for further prospective multicentre studies.

Complete atrioventricular block is rare in children and responsible for fewer than 2% of primary arrhythmias.[1,2] The incidence of the congenital complete atrioventricular block is approximately 1/15,000 to 1/20,000 of live-birth.[3,4]

Due to the dissimilarity of etiopathogenesis and increased risk of recurrence in future pregnancies, atrioventricular block is classified as congenital if diagnosed in utero, at birth, or within the first month of life. Therefore, childhood atrioventricular block is defined if the diagnosis is made between the first month and the 18th year of life.[1]

Maternal connective tissue disorders, systemic lupus erythematosus, and Sjögren syndrome are the leading causes of the fetal immune atrioventricular block.[5] Autoimmune-associated complete atrioventricular block may occur in 2–5% of the first pregnancies in the presence of high titres of anti-Ro/Sjögren's-syndrome-related Antigen A antibodies, with or without anti-La/Sjögren's-syndrome-related Antigen B antibodies, and it has a recurrence rate of 12–25% in subsequent pregnancies of the affected mothers.[6,7]

There is limited contemporary national population data on clinical manifestations, aetiological factors, therapeutic options, and outcomes of complete atrioventricular block.[6,8] This study was conducted to determine the clinical presentation, characteristics, management, and contemporary outcomes of patients with complete atrioventricular block in fetuses-neonates and children population in South Wales. The results of this review might form the basis for an international multicentre prospective trial for comparison purposes in our region and further afield.

Methods

This study was carried out at the University Hospital of Wales in Cardiff (which serves as the national paediatric cardiac centre for South Wales), by using the data collected between 1966 and 2021. Complete heart block, or third-degree complete atrioventricular block, is defined according to the published diagnostic criteria.[9,10] The exact diagnosis was confirmed through ECGs in all live cases including the ones detected by echocardiography during the fetal period. The age at first presentation was decided by the earliest documentation of a patient's symptoms correlating with ECG or fetal echocardiography evidence of complete atrioventricular block at the time of the first review in the paediatric cardiac centre.

The study information was collected from the departmental database and medical records of the patients, which included sex, age at diagnosis, first clinical presentation, outcomes, echocardiography findings, maternal history of autoimmune diseases, and maternal antibodies (including anti-Ro/SS-A and anti-La/SS-B), and pacemaker intervention ratios. These variables were analysed and compared for two age periods: antenatal – neonatal and childhood. The age cut-offs were defined as *"up to 28 days of age-corrected to the expected birth date for the fetal-neonatal group"*, and *"older than 28 days for the childhood group"*. For the fetal patients, the following information was also collected: gestation week at birth, mode of delivery, hydrops, and prenatal treatment.

In all fetuses, standard transabdominal fetal echocardiography was performed. Maternal lupus autoantibody titres, viral titres, and TORCH (toxoplasmosis, others, rubella, Cytomegalovirus, herpes simplex virus infections) screening were carried out. As a national screening programme, TORCH screening, autoantibodies, and viral titres screening have been carried out since 1990. In case of positivity, the results are recorded. Maternal ECGs were obtained to exclude long QT and other familial causes of bradycardia and heart block. Weekly ultrasound and Doppler scan surveillance were used to analyse fetal heart rate and rhythm, resolution of hydrops, cardiac function, fetal well-being, and the volume of amniotic fluid. Fetal heart rates were checked twice a week if they were always above 55/min. Beta-mimetic drugs like salbutamol, with or without dexamethasone, were only started in fetuses exhibiting heart rates below 55/min, associated with cardiac dysfunction, and elevated maternal anti-Ro and/or anti-La antibodies. In our protocol, the initial dose of dexamethasone is 4–8 mg/day for 2–4 weeks then 2 mg/day until delivery. When the heart rate is < 55 beats/min, β-sympathomimetic therapy combined with dexamethasone is given. Two widely used β2 adrenergic receptor agonists are oral salbutamol (10 mg every 8 h with a maximum dose of 30 mg/day) and terbutaline (2.5–7.5 mg every 4–6 h with a maximum dose of 30 mg/day). Intravenous immunoglobulin (400 mg/kg every 3 weeks from 12–24 weeks of gestation) with hydroxychloroquine has been considered when the lupus antibodies are positive and/or the mother is diagnosed as systemic lupus erythematosus, with the agreement of rheumatologists. Normal delivery was considered if there was no other obstetric or fetal concern.

The ECG tracings were re-analysed for rhythm, atrial and ventricular rates, degree of atrioventricular block, QRS duration, and corrected QT interval (QT_c).[11–14] For the echocardiographic dimensions, normal values were taken according to the paediatric scores.[15,16] Patients with atrioventricular block after a cardiac operation, with complex CHD, or who did not come to the follow-ups regularly, were excluded from the study.

The data before-after 2001 was compared with each other. This date as 2001 was chosen because of the changes in the treatment protocol of atrioventricular block following establishment of the fetal cardiac service for South Wales.[8]

Pacemaker therapy

The decision to pacemaker implantation was based on the published and standard guidelines in children.[17,18] In our institution for infants and very young children weighing less than 15 kg epicardial pacing systems with axillary or abdominal pacemaker pocket; for children between 15 kg and 12 years of age single chamber endocardial systems with submuscular pectoral pocket; and for children older than 12 years transvenous dual-chamber pacemaker systems with subcutaneous pectoral pocket were preferred.[19] Pacemaker programming was set in single chamber ventricular pacemaker (VVI) mode for neonates at a rate of 95–110 beat per minute (bpm) and beyond neonatal period and for young children up to 12 years of age in VVI mode at a rate of 60–75 bpm to prevent tracking of sinus tachycardia and causing pacemaker induced. Sleep rate was also set at 50 bpm for older children and at 75 bpm for neonates. Beyond 12 years of age, dual chamber pacemaker (DDD) or dual chamber rate modulated pacemaker (DDDR) modes were used at minimum tolerated rate of 60 bpm with and upper tracking rate of 175 bpm and sleep rate

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Table 1. Characteristics of the 64 diagnosed fetal-neonatal and childhood cases with CAVB.

	Fetal and neonatal (≤ 28 days of corrected postnatal age)	Childhood (>28 days of corrected postnatal age)	P-value
Number of cases	26	38	
Male/female*	11/13	17/21	>0.05
Age at diagnosis, months[δ]	Fetal: 10.5 weeks (0–33)	36 (1–204) months	
Cardiomyopathy	11	1	0.019
Maternal seropositivity/SLE diseases	14/15	3/3	<0.001
CAVB resolved	2	2	
PMI	13	21	
PMI at first year after diagnosis	10	4	>0.05
Mortality /number and ratio	6 (23%) 4 (15.3%) (after excluding fetal demise)	1 (2.6%)	<0.001
Total follow-up (years)[δ]	5 years (0–15)	25 years (16–32)	0.037
Pacemaker types (E/TV)	10/3	8/13	
Pacemaker indication (the most common ones)	Symptomatic bradycardia (n: 10)	Asymptomatic with a mean ventricular rate < 50 bpm (n: 13)	
Ventricular rate † (bpm)	60 (50–70)	56 (47–62)	0.514
Atrial rate † (bpm)	122 (103–135)	118 (101–131)	0.139

CAVB = complete atrioventricular block; CMP = cardiomyopathy; Bpm = beats per min; E = epicardial; PMI = pacemaker implantation; SLE = systemic lupus erythematosus; TV = transvenous.
Data are presented as median and range, or number or percentage.
*Gender unknown in 2 cases of intrauterine demise.
[δ]Median and range.
[†]Mean and range.

of 50 bpm. For children with CHD pacing rates were set at 10 to 20% higher ranges to prevent atrial or ventricular ectopy.

Statistical analysis

Data were expressed and defined as frequencies, numbers, median, range, and percentage, as appropriate. Normal distribution for variables was determined by the Shapiro–Wilks test. For comparisons of descriptive statistical methods and quantitative data between two groups, Student's t-test was used when the distribution of the variables was normal. If it was not normal, the Mann–Whitney U test was used. To compare the qualitative data, Fisher's Exact test, Fisher Freeman Halton test, and Continuity (Yates) correction were utilised. The variables 'survival outcome' and 'pacemaker implantation' were plotted as Kaplan–Meier survival curves using the Log Rank test. IBM SPSS Statistics for Windows 22.0 (SPSS Inc., Chicago, IL, USA) was employed to evaluate the results. A significant difference was defined as $P < 0.05$.

Results

Although complete atrioventricular block was identified in 73 patients, nine of them were excluded as they had complex congenital heart disease. Of those remaining 64 patients, 21 were diagnosed antenatally, and 5 were diagnosed in the neonatal period (26 were considered as congenital atrioventricular block). Totally, 38 were diagnosed in childhood age. This gave an incidence of 1 in 25 000 for congenital complete heart block among 525000 pregnancies between 2000 and 2021 in South Wales. Table 1 summarises the features of the patients.

Fetal and neonatal (congenital heart block) group

Three fetuses showed poor left ventricular function, hydrops fetalis, and signs of endocardial fibroelastosis. Despite the negativity of antibodies, one mother had signs and symptoms of systemic lupus erythematosus, and another mother developed Lupus 18 years after. Interestingly, one fetus born to a mother with lupus has developed lupus at age 19. All of the fetal characteristics, including maternal diseases and antibody status, are summarised in Table 2.

There were two fetal deaths of whom one is (4.7%) intrauterine termination with all exhibiting hydrops and severe cardiomyopathy. 19/21 (90.4%) were live-born. Four died immediately after birth in the neonatal period: all with severe bradycardia and cardiomyopathy and one from prematurity (29–30 weeks at birth) related complications of necrotising enterocolitis and respiratory distress.

During follow-up, the isolated complete atrioventricular block resolved in two patients, one before birth and other within the first year. A permanent pacemaker was implanted in 10 out of 15 (66.6%) live-birth patients and eight of these were younger than 1 year old. One child developed left ventricular dysfunction and pacemaker induced cardiomyopathy aged 2 years for which the patient required biventricular pacing and antifailure treatment. The child responded to atrioventricular synchronisation treatment, and at current follow-up, the patient's cardiac function normalised with restoration of age appropriate left ventricular dimensions.

Neonatal group

Complete atrioventricular block was identified in five patients in the neonatal period. Cardiomyopathy developed in three patients

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Table 2. Characteristics of the patients with a fetal diagnosis.

	Numbers /Percentage
Total number with fetal diagnosis	21
Gestational age at diagnosis	23 weeks (16–33)
Hydrops	7
Cardiomyopathy	8
Maternal SLE disease	15
Maternal antibody	14
Maternal diseases	
• SLE	13
• SLE + Sjögren syndrome	1
• Myasthenia gravis	1
Prenatal treatment	11
Fetal death	2 (1 demise, 1 termination)
Gestational week at birth	35 weeks (29–40)
Neonatal death	4
Postnatal survival	15
Pacemaker therapy	10
Freedom from pacemaker (median and range, years)	2 (0–4.5)
Current age (median and range, years)	7.75 (3.83–15.5)

SLE = systemic lupus erythematosus.
Values are shown as the median and range or ratio.

during the neonatal period, one of whom had dilated cardiomyopathy in their family history. A permanent pacemaker was implanted in three out of the five neonates (60%). There were no deaths in this group of the patients.

Childhood group

Complete atrioventricular block was identified in 38 patients. 16 patients were diagnosed before 12 months of age. Most of these patients presented with bradycardia-related symptoms.

The level of maternal antibody titres was measured in 14 mothers, three had anti-Ro/SS-A antibodies or anti-La /SS-B antibodies, of whom all were in the infant period and diagnosed in pre-2001.

Cardiomyopathy was seen in one patient when diagnosed at the age of 8 months.

The complete atrioventricular block was resolved in two patients who were both diagnosed at age 10; one recovered after one year of follow-up, and the other five years after the diagnosis. A permanent pacemaker was implanted in 21 (55.2%) of 38 patients at a median of five years (0–11 years) following the first diagnosis.

At a median follow-up of 25 years (range, 16–32 years), one patient with Down syndrome died at 22 years of age, and the death was related to the syndrome, and not of complete atrioventricular block.

Pacemaker therapy and follow-up results

A permanent pacemaker was implanted in 34 patients. The Kaplan–Meier test estimated the mean pacemaker implantation period was 20.08 ± 3.68 months (95% CI: 12.86–27.29) and 29.96 ± 2.1 months (95% CI: 25.85–34.08), in fetal-neonatal and childhood patients, respectively, with a significant difference (log-rank test P:0.023; $p < 0.05$) (Fig. 1). The patients diagnosed in the fetal-neonatal period had a pacemaker implantation earlier than the childhood group.

Follow-up and mortality

Altogether, seven deaths occurred, of which six were in the fetal and neonatal period (Fig. 2). 6 deaths occurred in the fetal/neonatal period were attributable to bradycardia and atrioventricular block-related heart failure. The one .death in the childhood period was associated with Down syndrome-related complications and not related to bradycardia/atrioventricular block solely. The Kaplan–Meier survival analysis (Fig. 3) showed a comparable survival rate of 96.3% [45.04 ± 0.94 years (95% CI: 43.20–46.88)] for the patients diagnosed before 2001. Survival rate was 83.8% [21.81 ± 1.72 years (95% CI: 18.44–25.17)] of the patients diagnosed after 2001. (log-rank test $P < 0.042$). There was not a significant difference between the two groups as only one patient had died in the pre-2001 group. The differences in mortality rates are not directly attributable to the care of children but could be explained with the higher number of sicker children being detected in fetal and neonatal period. It is plausible that in pre 2001 era very sick children might have died prior to coming to medical attention or being diagnosed.

The results of the factor analyses for the risk of death are given in Table 3.

Comparison of pre- and post-2001 era

The fetal and neonatal diagnosis was higher in the post-2001 era as a result of improved antenatal detection. Eleven patients belonging to the post-2001 era had intrauterine treatment and 7 survived. There were no patients that were given intrauterine treatment before 2001. Comparisons of pre-(group I) and post-2001 (group II) eras are summarised in Table 4.

Discussion

This study reports the first population incidence of congenital complete heart block in South Wales as 1 in 25,000 pregnancies. The aetiology and outcome of complete atrioventricular block are not the same between the fetal and childhood age groups with the immune mediated causes predominating in the former. Mortality rates are significantly higher in the fetal group, but this is a mere reflection of even sicker patients being detected prior to their demise in the post 2001 period. Other reasons could be due to differences in the management of complete heart block comprising fetal intervention with medication or over early delivery and implantation of early pacemaker.

When AVB is diagnosed early without any notable cause, it is still possible that the mother carries autoantibodies but at a level that is too low for measurement[20] or the connective tissue disease may become manifest later in the next 10–20 years as it happened in one of our cases.[21,22] In rare cases, heart block may also develop later during infancy or early childhood, or even later into young adulthood, therefore difficult to be certain of the true congenital complete heart block cases from the later-onset heart block.[23]

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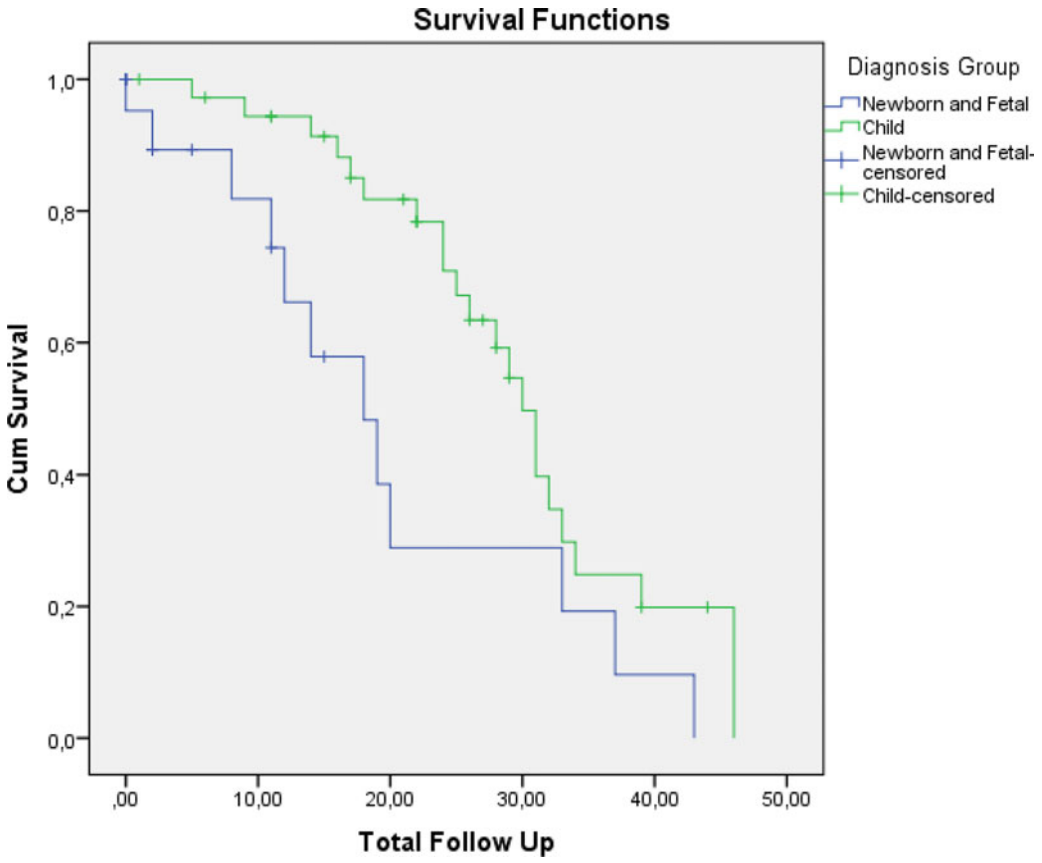

Figure 1. Kaplan–Meier PMI comparing fetal-neonatal, and childhood diagnosis of CAVB. CAVB = complete atrioventricular block, PMI = pacemaker implantation (*X* axis shows years, *Y* axis shows survival ratio).

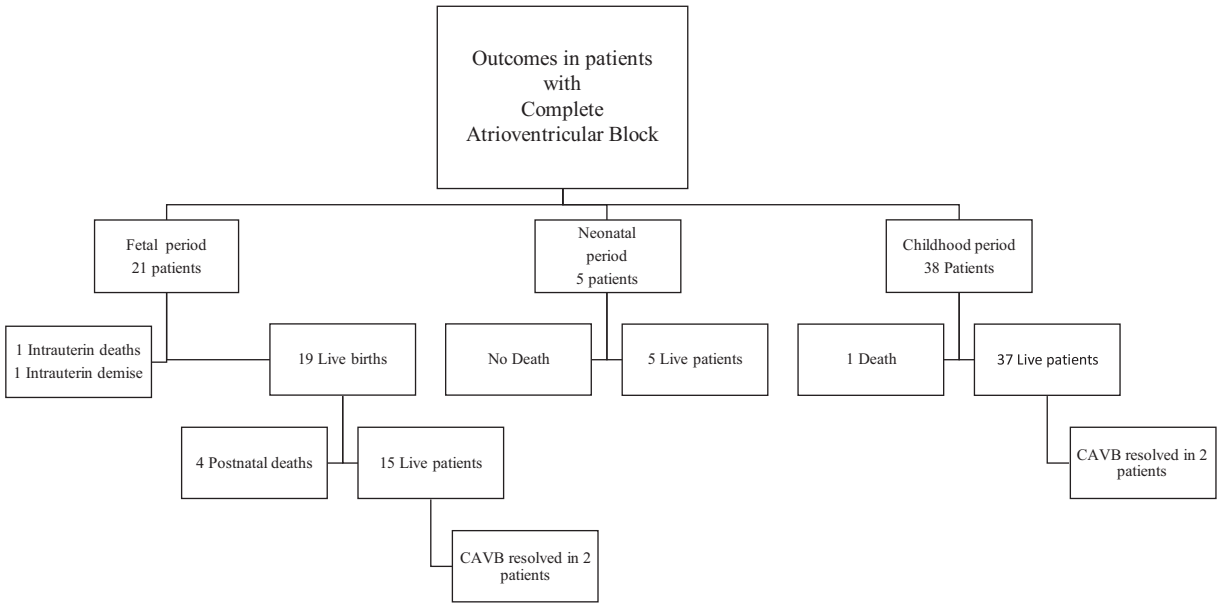

Figure 2. Outcomes in patients with complete atrioventricular block. CAVB = complete atrioventricular block.

Patients diagnosed in the fetal and neonatal period

Owing to improving antenatal screening policies, it has become more common to detect atrioventricular block in utero, as a result the number of antenatally diagnosed patients have been increasing through the years. The results of this study were reflective of this fact that most deaths occurred in patients diagnosed in the fetal period (6/64, 9.3%). It is plausible to think that in pre 2001 era, the sickest patients with complete atrioventricular block had died and only the ones with good heart rates and haemodynamics have survived. In keeping with this, the five patients died in group-2, from severe cardiomyopathy and endocardial fibroelastosis. The average fetal heart rate

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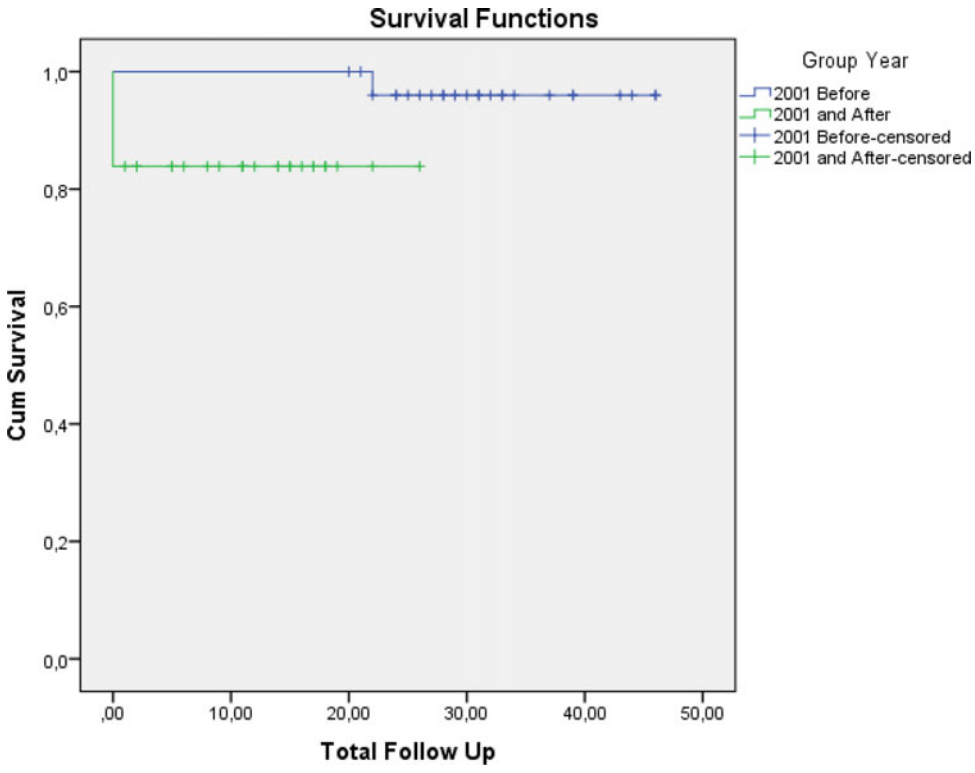

Figure 3. Kaplan–Meier survival of CAVB diagnosed pre and post-2001 periods. CAVB = complete atrioventricular block (*X* axis shows years, *Y* axis shows survival ratio).

was below 55 bpm in severe cases of complete atrioventricular block (n = 10), and the mortality rate was higher in this group ($P < 0.05$). Hydrops alone was also an important risk factor for mortality in fetal life that no patients survived after having developed hydrops ($P < 0.001$). Such patients would have died before the diagnosis in group 1 which is the most likely explanation for the lower mortality rates in older patients. These unfavourable outcomes in antenatally detected cases beg the need for developing more effective and earlier treatment strategies.

Maternal antibody positivity among most patients in this study is in keeping with the literature that the two-thirds of the pregnant women have elevated anti-Ro antibody titres.[22–25] Although many other studies have failed to establish a link between an increased risk of mortality and antibody-positivity in patients, such a risk was found to be significantly higher in our cases.[8,24] Since antibody positivity is more likely to be detected in the fetal-neonatal, and infant periods, the routine use of preventive and effective treatment strategies to improve patient outcomes should be searched and considered.[25] In our cohort, the maternal antibody positivity or symptomatic maternal connective tissue disease was significantly higher ($P < 0.001$) in the fetal-neonatal group as reported in earlier studies.[22]

Despite the lack of consensus, previous studies have suggested that intrauterine treatment with steroids could be favoured, especially in immune-mediated patients and/or patients with a low average heart rate.[26,27] In contrast, some studies have found no benefit from either steroid or intravenous immunoglobulin treatment.[28–30] The mortality rate of the patients treated antenatally was higher than the patients who were not treated (36.3–20%), but this difference is not meaningful due to sicker fetuses being selected more commonly for treatment.

In addition, a current study showed lower incidence of congenital complete heart block with antenatal use of hydroxychloroquine in mothers afflicted by Sjogren disease or Lupus.[31] After birth, there was also no significant difference in the development of cardiomyopathy between those treated as fetuses and those who were not. It could not be determined whether the transplacental therapy was ineffective because patients in the treatment group had a more severe clinical presentation, so it would be appropriate to test this hypothesis in a larger multicentre randomised control study which is in the way of being embarked on (personal communication with the Slow Heart Study Steering Group member OU and Edgar Jaeggi). These medications are mainly prescribed for those who are also strongly positive for antibodies associated with fetal hydrops, impaired cardiac function, or cardiomyopathy in order to reduce morbidity by preventing further cardiac cell destruction.[32]

Pacemaker therapy and follow-up of the patients

During the follow-up, it was found that the patients whose pacemaker was implanted early (in the first year of life) required multiple interventions compared with the patients diagnosed in childhood ($P < 0.001$). This can be due to the fact that subclinical impairment of heart function is more likely to occur in younger children with higher antibody load even when they are asymptomatic, hence early pacemaker implantation may help reduce mortality[9] in such cases. Nonetheless, more commonly implantation of pacemakers is undertaken in symptomatic and high-risk patients exhibiting bradycardia and/or symptoms of heart failure. Guidelines for pacemaker implantation have changed over time.[17] Although the transvenous route is a more preferred way in children with the improvement in pacing lead size and pacemaker properties, the epicardial route is still favoured in very small patients wighing less than 10–15 kg.[17] Thus, an epicardial approach is still mostly preferred in neonates/infants.

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Table 3. Mortality-related risk factors. Analyses of the mortality of CAVB diagnosed in the fetal-neonatal and childhood periods.

Number and ratio	Numbers	Mortality	Mortality in other patients	P-values
Fetal and neonatal diagnosis	26	6/26	1/38	<0.001
Cardiomyopathy + EFE	12	6/12	7/61	0.008
Hydrops fetalis	7	6/7	7/66	<0.001
Fetal heart rate<55 beats/min	10	6/10	4/17	<0.05
Maternal antibodies positivity	14 FET and N + 3 CHLD	6/17	1/19	0.021
PM implantation	34 PM implantation, FET: 10, N: 3, CHLD: 21	1/34	6/30	0.117
Prenatal treatment	11/21 fetal	4/11	2/10	0.051
PM implantation at first year after diagnosis	FET: 8, N: 2, CHLD: 4	1/14	0/20	>0.05

CAVB = complete atrioventricular block; CHLD = child; CMP = cardiomyopathy; EFE = endocardial fibroelastosis; FET = fetal; PM = pacemaker; N = neonatal.

Table 4. Pacemaker, mortality, diagnosis groups parameters, and treatment properties between the pre- and post-2001 eras.

		Before 2001 (27 patients)	2001 and After (37 patients)	*Total*	
		N (%)	N(%)	*n (%)*	p
Pacemaker Implantation	No	8 (%29,6)	22 (%59,5)	*30 (%46,9)*	**[1]0,035***
	Yes	19 (%70,4)	15 (%40,5)	*34 (%53,1)*	
Mortality	Dead	1 (%3,7)	6 (%16,2)	*7 (%10,9)*	**[2]0,223**
	Alive	26 (%96,3)	31 (%83,8)	*57 (%89,1)*	
Diagnosis Group	Neonatal and Fetal	4 (%14,8)	22 (%59,5)	*26 (%40,6)*	**[1]0,001***
	Childhood	23 (%85,2)	15 (%40,5)	*38 (%59,4)*	
Local treatment Protocols (Intrauterin treatment)	Fetal	None (%0)	11(%29.7)	11 (%17.1)	
Pacemaker Implantation Guidelines	Indication for all	Class ID: In an infant with a ventricular rate<50 to 55 bpm (18)	Class IC: In asymptomatic neonates or infants when the mean ventricular rate is<50 bpm (17)		

[1]Continuity (Yates) arrangement.
[2]Fisher's Exact Test.
*$p < 0.05$, n:number.

During the study period, complete heart block was resolved in four patients. The reason for this high degree recovery could be explained by the temporary nature of myocarditis related heart block in some children.[33] Recovery from complete heart block could be considered when the clinical status is much better, such as the absence of antibodies and no history of heart failure.

Limitations of the study

There are natural limitations relating to any observational, retrospective study such as this. However, this study represents a coherent approach to the treatment of complete atrioventricular block as all cases described were diagnosed and managed by a team in a single centre throughout the study period. The study also suffers from further limitations owing to the small number of patients being included (despite the 55-year observation period), but this reflects the rarity of the disease. In addition, the authors had access to only limited clinical and procedural data. Due to the fact that the study had a broad period, some data such as the serology of antibodies could not be measured in all patients presented in the pre-2001 period.

Conclusion

Contemporary results show a noticeable increase in early perinatal diagnosis of patients with complete atrioventricular block in the post-2001 era. As a result of sicker patients being diagnosed with complete atrioventricular block in the fetal period, there is an increased mortality risk due to fetal hydrops, a lower heart rate (< 55 bpm), cardiomyopathy, high titres of maternal antibody positivity, and early preterm delivery (≤ 30 weeks). Pacemaker implantation is equally required in all groups, but implantation may be required earlier (before 1 year of age) in patients diagnosed in the fetal period; hence, re-interventions and complications are higher in this group. Intrauterine treatment is reasonable in patients with immune-mediated complete atrioventricular block, severe bradycardia, and/or heart failure. Further multicentre prospective research studies with larger sample sizes are required to provide answers to the question of efficacy of hydroxychloroquine, steroid and beta mimetic treatment in the prevention of morbidity, and reducing mortality from this challenging condition.

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Author contribution. OU, as a fetal cardiologist had primary responsibility for the diagnosis of arrhythmia, RBB, CC, and OU in the treatment of the fetuses with complete atrioventricular block. RBB and CC as fetal medicine specialists were responsible for assessing the well-being of the pregnant women and the fetus (with OU) from the time of diagnosis to the delivery. RBB and CC were responsible for formulating investigations prior to embarking on medications. RBB, OU, DD, and GTS contributed to the collection and analysis of the data and writing of the manuscript. OU and RBB supervised DD and GTS in data collection and analysis of the results during her clinical attachment at the University Hospital of Wales as visiting research fellows. RBB, DD, GTS, and OU equally contributed to the paper in all stages by systematically organizing the data, critically appraising it, and writing the manuscript. AP, MC, GS, and MW were involved in the implantation of pacemakers and critically appraising the paper.

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Competing interests. None.

Ethics standard. Since the data were already collected and recorded as part of routine clinical work and for the purpose of the periodical service evaluation process, a specific ethical approval application was not considered necessary. Health Research Authority of the United Kingdom and South Wales Ethics Committee indicated that the reviews of this nature do not require ethics approval. The collected information was completely anonymized before retrospective analysis. DD had an official contract as a visiting research fellow with the University Hospital of Wales during the time of this review and analysis. All procedures relating to this review were carried out in accordance with the Declaration of Helsinki.

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