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ORIGINAL ARTICLE

Incidence of non-benign arrhythmia in neonatal intensive care unit: 18 years experience from a single center

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Abstract

Background: Non-benign arrhythmias, which require urgent recognition and care in neonatal intensive care unit (NICU) settings, are rare but can severely impact neonates. We aimed to clarify the epidemiology and characteristics of non-benign arrhythmias and their influence on neonates.

Methods: This single-center retrospective study included patients admitted to the NICU at Kurashiki Central Hospital between January 2001 and December 2019. Only patients with structurally normal hearts were included. The use of direct cardioversion (DC), antiarrhythmic agents, and the presence of risk factors was reviewed from medical records.

Results: Of the 8082 admissions, 2919 patients (36.1%) were low birth weight infants (LBWI) weighing less than 1500 g. There were 23 patients with arrhythmias (nine of them were LBWIs) with an incidence of 0.28%. There were 16 patients with tachyarrhythmia (eight supraventricular tachycardia [SVT] cases, three atrial flutters [AFL] cases, three ventricular tachycardia cases, two junctional ectopic tachycardia cases), and seven with bradyarrhythmia (all with complete atrioventricular [AV] block). For tachyarrhythmia cases, seven patients required DC, and eight were on antiarrhythmic agents at the time of discharge. Two patients (28.5%) with complete AV block required pacemaker implantation before discharge. The treatment strategy was dependent on the type of arrhythmia. All patients were discharged without significant morbidities.

Conclusions: The incidence of non-benign arrhythmias was as low as 0.28%. Arrhythmias can be managed successfully in neonates, yet risk factors related to mortality warrant further study.

KEYWORDS
arrhythmia, congenital AVB, LBWI, NICU, SVT

1 | INTRODUCTION

The incidence of neonatal arrhythmia is estimated to be 1%–5% during the first 10 days of life.[1] Meanwhile, the incidence of arrhythmias in the NICU ranges from 0.37% to as high as 10%, with most being benign arrhythmias, such as premature atrial contractions (PACs) and premature ventricular contractions (PVCs), which require no medical intervention.[2,3] While the incidence of non-benign arrhythmia is lower than that of benign arrhythmia, they require urgent recognition and treatment, as they lead to morbidity and potentially mortality.[4,5] As most previous reports included patients with congenital heart disease (CHD) who have a higher incidence of arrhythmias compared to the general population, we sought to investigate the incidence and characteristics of non-benign arrhythmias in patients with normal hearts in NICU settings.

2 | METHODS

A single-center retrospective study was conducted at the Kurashiki Central Hospital (Okayama, Japan). Among patients admitted to the NICU between January 2001 and December 2019, those with non-benign arrhythmias were included in this study. Our center serves as a tertiary center; therefore, most of the neonates with arrhythmias in surrounding areas are transferred to our center. As benign arrhythmias, such as PACs and PVCs, may be left unrecognized, we did not include patients exhibiting these signs because it is difficult to identify every patient and the incidence is likely to be underestimated. Patients with structural heart diseases, such as CHD or cardiac tumors, were excluded because they have a higher incidence of arrhythmias than patients without cardiac structural anomalies[6,7] and often require different treatment strategies.

Non-benign arrhythmias are defined as those requiring urgent recognition and management, such as supraventricular tachycardia (SVT), atrial flutter (AFL), ventricular tachycardia (VT), and junctional ectopic tachycardia (JET). SVT included atrioventricular reciprocating tachycardia, atrioventricular nodal reentrant tachycardia, and atrial tachycardia (AT). Congenital complete atrioventricular block (CAVB), sick sinus syndrome (SSS), and hereditary arrhythmias, such as long QT syndrome (LQTS), are considered non-benign. Patient characteristics such as gestational week, birth weight, sex, and Apgar—both 1- and 5-minute scores at birth were collected from the medical records. Some possible risk factors of arrhythmias, such as the placement of an umbilical catheter, application of nebulizer therapy, low blood sugar (blood sugar less than 50 mg/dL), and electrolyte disturbances,[3,5] were collected. The admission period and use of direct cardioversion (DC) or antiarrhythmic agents (AAs) were also reviewed. Statistical analysis was performed using SPSS ver. 26.0(IBM Corp.).

3 | RESULTS

During the study period, there were 8082 admissions to the NICU, of which 2919 (36.1%) were low birth weight infants (LBWIs) (those with birth weight less than 1500 g). Of these, 23 patients had non-benign arrhythmia (incidence = 0.28%) and nine patients with non-benign arrhythmia were LBWIs. Additionally, there were 16 patients with tachyarrhythmia and 7 patients with bradyarrhythmia. Patient characteristics are summarized in Table 1.

3.1 | Tachyarrhythmias

Of the 16 tachyarrhythmia cases, nine were males (9/16, 56.3%) and seven (7/16, 43.7%) had a prenatal diagnosis. Among the seven patients with prenatal diagnosis, six were born via emergency cesarean section due to non-reassuring fetal status caused by tachyarrhythmia. Tachyarrhythmias diagnoses were as follows: SVT, eight cases (50%); AFL, three cases (18.8%); VT, three cases (18.8%); JET, two cases (12.4%). A spontaneous resolution was achieved in three (13%) patients. DC was performed in seven cases (44%), which was successful in five cases (three AFL cases and two AT cases; success rate of 71% [5/7]). AA was prescribed in eight cases (8/16, 50%), including two patients who did not respond to DC. All patients were on AAs when they were discharged, and all but one patient with JET remained on AAs at the time of the latest follow-up. While there were two patients with congenital JET, one had a relatively stable course. This patient was treated with intravenous procainamide, which was converted slowly to oral flecainide. The other patient had fetal ascites, and the mother was administered digoxin. The patient required mechanical ventilation for respiratory failure caused by massive ascites. Drainage via peritoneal puncture was performed, and oral flecainide and intravenous landiolol were initiated. Landiolol was later converted to oral propranolol, and JET was managed successfully, after which ascites did not recur. The patient is currently aged

TABLE 1 Patient characteristics

Total number of patients	23
Incidence	23/8082(0.28%)
Gestational week	36.8 ± 3.0
Body weight (g)	2708 ± 673
Male	8/15(53.3%)
Apgar score at 1 and 5 min	7.5 ± 1.1/ 8.9 ± 0.7 (1 min/5 min)
Admission period(days)	31.7 ± 24.3
Low blood sugar	7/23(30.4%)
Smoking habit of the mother	2/23(8.7%)
Use of catecholamine	2/23(8.7%)
Use of SABA	0
Umbilical catheter	0
Electrolyte disturbance	0

Note: Patient background and possible risk factors related to tachyarrhythmia between normal and low birth weight infants.

Abbreviations: DC, direct cardioversion; LBWIs, low birth weight infants; NBWIs, normal birth weight infants, SABA, short-acting beta-agonist.

1.8 years and is on a flecainide and propranolol treatment regimen. Neither of the patients with congenital JET required extracorporeal membrane oxygenation. The types of AA and patient characteristics are shown in Table 2. All 16 patients were successfully discharged without any comorbidities.

3.2 | Bradyarrhythmia and other complications

There were seven patients with bradyarrhythmia, all with congenital CAVBs. There were no patients with SSS or LQTS. All patients had a prenatal diagnosis, and five patients (71%) were related to maternal anti-Ro/SSA or anti-La/SSB autoantibodies. Of the two patients with negative maternal anti-Ro/SSA or anti-La/SSB autoantibodies, normal sinus rhythm was recovered in one patient by day 5 and was maintained thereafter. Only one patient was treated with maternal dexamethasone (which was administered at a different hospital before the baby was transferred to our hospital after birth). Of the seven patients, two patients were delivered via emergency cesarean section because of fetal growth retardation caused by CAVB. All seven patients were discharged without any sequelae. Overall, four patients required pacemaker implantation (PMI). Two patients underwent PMI on the days they were born, as the ventricular rate did not increase despite the use of isoproterenol and exhibited signs of hemodynamic compromise. The other two patients were discharged from the NICU without any intervention yet required PMI later in life. One underwent PMI at 9 months of age due to failure to thrive, and the ventricular rate did not increase despite the initiation of 2 mg/kg/day of oral cilostazol. The other patient underwent PMI at 1.8 years of age due to left ventricular dysfunction. Among the three patients without PMI, one patient with spontaneously converted normal sinus rhythm was no longer under observation. The other two patients were aged 5.3 and 8.2 years, respectively, at the latest follow-up. Both were hemodynamically stable with sufficient psychomotor development. One patient who is currently 5.3 years of age without PMI has been treated with oral cilostazol since birth. Oral cilostazol administration was started on day seven at a dose of 4 mg/kg/day as the average ventricular rate decreased to <50. After initiation of cilostazol, the average ventricular rate increased to >50 and the same ventricular rate was maintained thereafter. The patient characteristics are described in Table 3.

4 | DISCUSSION

The incidence of tachyarrhythmia was 0.28% in our study, which is much lower than the general incidence of neonatal arrhythmia.[1] This disparity likely occurred because we included only patients with non-benign arrhythmias and excluded patients with structural heart disease. Moreover, as most LBWIs are likely to be discharged within 5 days in Japan, those who have arrhythmias after 5 days of birth are likely to be admitted to the general ward rather than to the NICU. Our center also manages the patients according to this timeline, which may have contributed to the discrepancy in the incidence of arrhythmias. However, the incidence at our institution was similar to that reported in some previous reports. Isik et al. reported the incidence of arrhythmia as 0.38%, including benign arrhythmias, such as PAC, with a block and a non-benign arrhythmia incidence of 0.20%.[2] The arrhythmia incidence reported by Kundak et al. was 0.70%, which included non-benign arrhythmia and patients with CHD[8]. When patients with CHD were excluded, the total incidence was 0.36%, which is not significantly different from that in our study, considering that Kundak et al. included non-benign arrhythmias as well. Badrawi reported the arrhythmia incidence to be as high as 10%, with the non-benign arrhythmia incidence being 1.5%.[3] This is because they performed Holter ECG to discover any arrhythmias that could be left unnoticed. Their report may reflect the true incidence of arrhythmias determined via Holter ECG, yet infrequent PACs or PVCs are arrhythmias that may have resolved spontaneously even when unidentified and untreated. While male infants are considered to have a higher incidence of arrhythmias,[3,8,9] we did not find any difference in incidence between male and female infants in our study (male, 48%).

SVT was the most common type of tachyarrhythmia, accounting for 50% of all arrhythmias. This is consistent with previous reports.[1,8] SVT can generally be managed well by medication, exhibiting a low recurrence rate after medications are discontinued.[9–11] The same finding was reflected in our study, as there was no recurrence in seven of eight patients with SVT (87%). Other arrhythmias such as AFL and VT also have excellent prognoses,[12–14] and are likely to resolve spontaneously early in life after treatment.[14] However, prompt recognition is warranted as arrhythmia may cause heart failure; AFL caused heart failure in more than 30% of neonates.[12] While most neonatal tachyarrhythmias have a favorable prognosis, congenital JET (defined as JET occurring within the first 6 months of birth) has a poor prognosis, with a mortality rate as high as 35%.[15,16] Two patients with congenital JET in our series were safely discharged. However, one patient had a difficult course, as mentioned previously. Congenital JET requires extra care among neonatal tachyarrhythmias.

In addition to tachyarrhythmias, only congenital CAVB was observed in our study. Congenital CAVB is the most common non-benign bradyarrhythmia that occurs in NICU settings,[5,8] with an incidence of 1 in every 15,000–20,000 live births.[17,18] The majority of congenital CAVB cases are caused by injury of the conduction system due to an inflammatory response triggered by the presence of anti-Ro/SSA or anti-La/SSB autoantibodies. Herein, five of seven cases (71%) were related to anti-Ro/SSA or anti-La/SSB autoantibodies. For those with positive anti-Ro/SSA or anti-La/SSB autoantibodies and without CAVB, there are no standardized follow-up protocols. Therefore, we usually follow them up on an outpatient basis for 1 year. It remains controversial if early detection of CAVB in the fetus and maternal treatment with dexamethasone results in a favorable prognosis,[19,20] as only one mother was treated with dexamethasone. The mortality rate of

TABLE 2 Characteristics of patients with tachyarrhythmia

Case	Body weight (g)	Arrhythmia type	HR of tachycardia	Prenatal diagnosis	Apgar score (1/5 min)	Risk factors	Clinical symptoms	Use of DC/ Successful termination	Antiarrhythmic agents	Admission period (days)	Medication discontinuation	Follow up period (years)	Outcomes
1	1572	AT	218	YES	8/9	Low blood sugar	Tachycardia only	YES/YES	None	41		4.8	No recurrence
2	2490	AT	206	YES	8/9	Low blood sugar	Tachycardia only	YES/YES	None	40		1.0	No recurrence
3	3004	AT	210	NO	9/10	None	Tachycardia only	YES/NO	Procainamide → Flecainide + Propranolol	24	By 2 years old	3.0	No recurrence
4	2560	AT	180	NO	8/9	Low blood sugar	Tachycardia only	NO	Digoxin + Flecainide + Propranolol	21	By 1 year old	3.0	No recurrence
5	2384	AT (short run)	NA	NO	6/10	None	Tachycardia only	NO	None	8		0.1	Spontaneous resolution
6	2786	PSVT	175	YES	7/9	Low blood sugar	Tachycardia only	NO	Procainamide + Propranolol	71	At 6 months old	1.0	No recurrence
7	2488	PSVT	250	NO	7/8	None	Tachycardia only	NO	Procainamide	20	At 5 years old	8.0	RFCA performed in other hospital at 11 years old
8	3232	PSVT	190	NO	8/9	None	Tachycardia only	NO	Digoxin + Verapamil	23	By 3 years old	4.5	No recurrence
9	3280	AFL	180	YES	8/9	None	Tachycardia only	YES/YES	None	10		1.3	No recurrence
10	3884	AFL	210	YES	7/8	None	Tachycardia only	YES/YES	None	17		0.5	No recurrence
11	3225	AFL	230	NO	8/9	None	Tachycardia only	YES/YES	None	6		2.3	No recurrence
12	1792	VT	NA	NO	6/9	Use of catecholamine	Hemodynamic compromise	NO	None	56		7.3	Spontaneous resolution
13	2778	VT	140	YES	9/10	Use of catecholamine	Poor feeding	YES/NO	Procainamide → Amiodarone	48	At 2 months old	4.5	No recurrence
14	3002	VT (short run)	197	NO	8/9	None	Tachycardia only	NO	None	11		1.2	Spontaneous resolution
15	3410	JET	167	YES	6/8	Smoking habit of mother	Massive ascitesRespiratory failure	NO	Flecainide + Landiolol → Flecainide + Propranolol	56	Under medication	2.3	No recurrence
16	3756	JET	214	NO	9/10	None	Poor feeding	NO	Propranolol → Procainamide → Flecainide	27	At 4 months old	0.3	Lost to follow up

Abbreviations: AT, atrial tachycardia; DC, direct cardioversion; HR, heart rate; JET, junctional ectopic tachycardia; NA, not available; RFCA, radiofrequency catheter ablation; SVT, supraventricular tachycardia; VT, ventricular tachycardia; WPW, Wolf-Parkinson-White syndrome.

TABLE 3 Characteristics of patients with complete atrioventricular block

Case	Body weight (g)	Prenatal diagnosis	Presence of anti SS-A/B antibody	Maternal use of Dexamethasone	Risk factors	Symptoms in NICU	Medication	Admission period (days)	PMI	Indication for PMI	Follow up period (years)
1	2734	Yes	Yes	Unknown	None	Hemodynamic compromise	Isoproterenol	18	At day 0	Heart failure	19.5
2	2126	Yes	No	No	None	Hemodynamic compromise	Isoproterenol	42	At day 0	Heart failure	15.9
3	2558	Yes	Yes	Yes	Low blood sugar	None	Oral cilostazol	30	No		5.3
4	2968	Yes	Yes	No	Low blood sugar	None	No	18	No		8.2
5	3086	Yes	No	No	Smoking habit of mother	Spontaneous resolution	No	16	No		4.5
6	2102	Yes	Yes	No	None	None	Oral cilostazol	16	At 9 months old	Failure to thrive	6.4
7	1084	Yes	Yes	No	Low blood sugar	None	No	110	At 1.8 years old	Ventricular dysfunction	5.8

Abbreviations: NICU, neonatal intensive care unit; PMI, pacemaker implantation.

congenital CAVB is reported to be as high as 20%,[21] with a higher mortality rate among neonates with ventricular rates less than 55.[22] PMI is necessary for patients exhibiting signs of heart failure, including failure to thrive; however, the optimal timing of PMI for asymptomatic patients remains controversial as well. While pacing sites in neonates or small infants tend to be the right ventricular wall via epicardial leads, long-term right ventricle pacing is associated with the risk of inducing dilated cardiomyopathy.[23,24] Thus, we attempted to defer the PMI whenever possible. While there are limited options for medical treatment for CAVB, we tried cilostazol, which is sometimes effective in increasing the ventricular rate.[25,26] It seemed to be effective in one of our patients, yet further investigation is warranted to determine the effects of cilostazol in infants or small children.

The overall mortality rate of neonatal arrhythmia could be as high as 23.6%[8]; however, mortality was not recorded in our study. This may be because we excluded patients with CHD and did not observe any concomitant electrolyte disturbances. Among the noted risk factors, electrolyte disturbance is strongly related to mortality.[8] While some types of arrhythmias, such as JET, need extra care in acute management, arrhythmias can be managed successfully when risk factors, such as electrolyte disturbance, are controlled.

This study has several limitations. First, it was a single-center retrospective study with a relatively small sample size. Second, because of the study's retrospective nature, we may have missed some cases with paroxysmal arrhythmias resolving spontaneously, such as short runs of AT or VT. While patients in the NICU are generally observed with a monitor ECG, it is difficult to interpret the waveform when the babies are crying, which may have overlooked some tachyarrhythmias. Thus, the true incidence may have been underestimated.

5 | CONCLUSIONS

The incidence of non-benign arrhythmias was as low as 0.28% in NICU settings. While neonates with non-benign arrhythmias had a favorable prognosis, further investigation is warranted to study the risk factors related to mortality.

CONFLICT OF INTEREST

The authors declare no conflict of interest for this article.

DECLARATIONS

Approval of the research protocol: This study was approved by the local Institutional Review Board.

Informed Consent: Need of individual informed consent was weaved by the local IRB for this was a retrospective study.

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