Supplementary Materials

Neonatal Congenital Heart Defects at a Regional Referral Maternity in Western Romania, 2021–2022: Case Definition, Ascertainment, and the Antenatal Detection Gap

Supplementary Material S1. Classification Protocol

S1.1. Group definitions

Structural CHD group: any case containing at least one of the following, alone or combined with an interatrial communication (IAC) or patent ductus arteriosus (PDA): ventricular septal defect (VSD); tetralogy of Fallot; pulmonary artery stenosis; pulmonary atresia; Ebstein anomaly; hypoplastic left heart syndrome; congenital mitral insufficiency; dextrocardia; discordant atrioventricular connection; total anomalous pulmonary venous connection; aortopulmonary septal defect; other specified lesion coded ICD-10 Q20.8.

Transitional findings group: cases whose only findings were an isolated IAC, an isolated PDA, or the two together. This boundary is narrower than the EUROCAT case definition (EUROCAT Guide 1.4 and 1.5, Chapter 3.2): EUROCAT excludes the patent foramen ovale (PFO; Q21.11) and the PDA of infants born before 37 weeks, but registers the secundum atrial septal defect (ASD; Q21.10) and a PDA that is the only cardiac finding of a term infant. The primary structural group is therefore a conservative study definition, and a EUROCAT-aligned count is reported separately (S1.4).

S1.2. Echocardiographic criteria that were available

Lesion category per ICD-10 group (Q20–Q26); whether the lesion occurred isolated or in combination; gestational age at birth; birth weight; Apgar score at 1 minute; any antenatally documented anomaly notation transcribed into the obstetric record.

S1.3. Echocardiographic criteria that were not available

For interatrial communications: defect diameter, septal rim morphology or tissue deficiency, shunt direction, and follow-up or re-examination status. A PFO and a true secundum ASD are anatomically distinct, and the literature criteria for separating them (defect size with deficient septum secundum, left-to-right shunt beyond the physiologic window, persistence on follow-up) could not be applied retrospectively. All interatrial shunts are therefore reported as one undifferentiated IAC category.

For PDA: ductal diameter, hemodynamic significance, and persistence beyond the physiological window; gestational-age-specific interpretation was applied only through the preterm or term status at birth. For VSD: anatomic location (muscular versus perimembranous) and size. For pulmonary artery stenosis: pressure gradient or severity grade.

S1.4. Assignment rules and sensitivity handling

Assignment to the transitional group used a study convention, not per-case anatomy. Its consequences are bounded in the manuscript (Section 3.4). (a) EUROCAT-aligned count: adding the 23 term-born neonates whose findings included a PDA (20 isolated PDA, 3 PDA with an IAC) raises the structural frequency from 2.27% (66/2909) to 3.06% (89/2909; 95% CI 2.49–3.75). True secundum ASDs among the remaining 100 IACs (99 isolated, 1 preterm IAC with PDA) cannot be identified; at a birth prevalence of 1 to 2 per 1000, about 3 to 6 are expected, giving roughly 3.2% to 3.3%. (b) Extreme scenario: if all 100 were true secundum ASDs, the frequency would be 6.50% (189/2909; 95% CI 5.66–7.45). These analyses quantify the effect of classification assumptions; they do not establish the anatomical identity of any recorded lesion.

S1.5. AHA anatomic complexity mapping

Table S1. AHA anatomic complexity class assigned by the most complex lesion present in each case.

Lesion present (most complex per case)	AHA anatomic class
Hypoplastic left heart syndrome; pulmonary atresia; discordant atrioventricular connection; total anomalous pulmonary venous connection	III (great complexity)
Tetralogy of Fallot; Ebstein anomaly; congenital mitral insufficiency; aortopulmonary septal defect	II (moderate complexity)
VSD (isolated or with IAC and/or PDA only)	I (simple)
Pulmonary artery stenosis without severity grade; unspecified Q20.8 lesion; isolated dextrocardia without documented intracardiac disease	Not gradable

Severity in the hemodynamic sense (restrictive versus non-restrictive shunts, gradients, duct dependency) could not be graded from the available records; classes are anatomic only. "Critical CHD" is used only in the sense of the neonatal screening literature (duct-dependent or requiring intervention in the first weeks) and was not assignable from this database.

Table S2. Coding Audit Mapping

All 201 records were re-extracted and every lesion field was cross-checked against the echocardiographic report text. The table lists the original Romanian terminology of the source database, the initially assigned classification from an earlier translation step, the corrected classification, and the number of affected records. The audit validates coding against the written reports; the imaging itself was not re-read.

Original Romanian term (source database)	Initial mapping (earlier translation step)	Corrected classification	Records
Defect septal ventricular	Ventricular septal defect (Q21.0)	Confirmed	48
Defect septal atrial	Atrial septal defect (Q21.1)	Interatrial communication, ASD/PFO undifferentiated	119
Permeabilitate canal arterial	Patent ductus arteriosus (Q25.0)	Confirmed	42
Tetralogia Fallot	Tetralogy of Fallot (Q21.3)	Confirmed	6
Stenoza artera pulmonara	Pulmonary artery stenosis (Q25.6)	Confirmed; severity not graded	4
Comunicatia atrioventriculara discordanta	Discordant atrioventricular connection (Q20.5)	Confirmed	1
Boala Ebstein	Ebstein anomaly (Q22.5)	Confirmed	1
Sindromul inimii stangi hipoplazice	Hypoplastic left heart syndrome (Q23.4)	Confirmed	1
Insuficienta mitrala congenitala	Congenital mitral insufficiency (Q23.3)	Confirmed	1
Dextrocardia	Dextrocardia (Q24.0)	Confirmed	1
Conexiune venoasa pulmonara aberanta totala	Total anomalous pulmonary venous connection (Q26.2)	Confirmed	1
Atrezia arterei pulmonare	Pulmonary atresia (Q25.5)	Confirmed	1
Defect septal aorto pulmonar / alte malformatii (ambiguous free text)	**Aortopulmonary window (Q21.4) assigned to 36 records combined with ASD**	**Translation artifact. Corrected: 1 record aortopulmonary septal defect (Q21.4); 6 records with unspecified lesions retained under Q20.8 (next row); the remaining 29 records reassigned to the patterns documented in their reports (Table 2)**	**36 → 1 + 6 + 29**
Alte malformatii congenitale ale cavitatilor si orificiilor cardiace	Other congenital malformations of cardiac chambers and connections (Q20.8)	Confirmed as unspecified; no more specific anatomical diagnosis recoverable from the report text	6

The corrected counts reproduce Table 2 of the manuscript. The six Q20.8 records remain anatomically unspecified after audit because the underlying report text does not support a more specific label; forcing one would manufacture precision the data do not contain. These cases are labeled "not gradable" in the anatomic classification.

Table S3. Overlap with the Previously Published 2018–2022 Series

Item	Published series (Diagnostics 2024;14:1659)	Present study
Observation period	2018–2022 (five years)	2021–2022 (two years)
Births	10,113 births for 2018–2022, as published (the Methods of that paper describe the period as four years); no per-year breakdown or definition of the birth count (live births only, or all births) is given	2909 live births from the 2021–2022 birth register, about 1450 per year
Implied annual births	About 2000 per year if spread over five calendar years	About 1450 per year. The difference would require more births in 2018–2020 or a different denominator definition in the earlier paper; it cannot be verified from the published report
Cases	541 newborns with CHD labels	201 neonates with echocardiographic findings
Patient overlap	The 2021–2022 births analyzed here fall within the earlier ascertainment window; the 201 cases are expected to be a subset of the 541. Record-level linkage was not re-verified across extractions.	
Variables reused	Lesion categories, gestational age, birth weight, Apgar score, antenatal notations	Same fields, re-extracted and re-audited
Variables new here		Maternal conditions (including RT-PCR-confirmed SARS-CoV-2), per-case antenatal classification, coding audit fields
Case definition	All CHD labels counted together	Two-group split (structural versus transitional) plus AHA anatomic complexity grading
Detection definition	Permissive: any antenatal cardiac observation, counted against all 541 CHD labels, interatrial and ductal findings included: 151/541 (28%)	Strict: documented recognition concordant with the birth diagnosis, 3/66 structural cases (4.5%). The permissive rule applied to the present records gives 4/201 (2.0%) for any cardiac notation and 7/201 (3.5%) for any anomaly notation
Analyses unique to this study		Coding audit (Table S2); sensitivity bounds on the structural frequency; per-lesion zero-event expectations; class-level recognition
Endpoints	Incidence and antenatal detection	Case-mix composition, coding validity, documented recognition

No numerical result of the earlier publication is republished as a finding of this study. Where the earlier 28% figure appears, it is cited with its numerator and denominator (151 of 541), and the manuscript states that it cannot be reconstructed from the present extraction. Neither the annual number of births nor the antenatal detection figure of the two publications can be reconciled at record level, and the two series should not be read as a time trend.

Table S4. Lesion-by-Lesion Anatomic Classification and Documented Recognition

All 22 mutually exclusive presentation patterns. Group: S, structural; T, transitional. Recognition: documented antenatal cardiac diagnosis concordant with the index lesion at

birth. Neonatal intervention was not consistently coded in the source database and is therefore not reportable for any pattern (manuscript Section 3.8). AHA, American Heart Association; AV, atrioventricular; IAC, interatrial communication; n/a, not applicable; PDA, patent ductus arteriosus; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

Presentation pattern	n	Group	AHA class	Rationale	Recognized antenatally
Isolated interatrial communication	99	T	n/a	ASD/PFO undifferentiated; study convention; EUROCAT registers true secundum ASD	n/a (fetal structure patent)
Isolated VSD	32	S	I	Simple shunt lesion; size not recorded	1 (muscular VSD)
Isolated PDA	32	T	n/a	Study convention; EUROCAT registers term PDA; persistence not established	n/a (fetal structure patent)
VSD + IAC	8	S	I	VSD-based pattern	0
Tetralogy of Fallot, isolated	4	S	II	Conotruncal lesion	1
IAC + PDA	4	T	n/a	Study convention; EUROCAT registers term PDA	n/a
VSD + IAC + PDA	3	S	I	VSD-based pattern	1 (VSD recognized; co-lesions missed)
Pulmonary artery stenosis, isolated	3	S	Not gradable	Severity grade absent; class I if mild, II otherwise	0
Other Q20.8 lesion, isolated	3	S	Not gradable	Anatomy unspecified	0
IAC + TOF	1	S	II	Conotruncal lesion	0
IAC + VSD + TOF	1	S	II	Conotruncal lesion	0
Discordant AV connection + IAC + PDA	1	S	III	Complex connection anomaly	0
Ebstein anomaly	1	S	II	Per AHA listing	0
Hypoplastic left heart syndrome	1	S	III	Single-ventricle physiology	0
VSD + IAC + congenital mitral insufficiency	1	S	II	Valve disease beyond simple shunt	0
Q20.8 + VSD	1	S	Not gradable	Unspecified co-lesion	0
Dextrocardia, isolated	1	S	Not gradable	Cardiac malposition without documented intracardiac disease; deliberately not classed as severe	0
Total anomalous pulmonary venous connection	1	S	III	Per AHA listing	0
Q20.8 + pulmonary atresia	1	S	III	Pulmonary atresia governs	0
VSD + PDA	1	S	I	VSD-based pattern	0
Q20.8 + VSD + PDA + pulmonary stenosis	1	S	Not gradable	Unspecified co-lesion and ungraded stenosis	0
Aortopulmonary septal defect + IAC	1	S	II	Single audited case; see Table S2	0