First symptoms of prenatally undetected heart defects

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Abstract

Background: Severe or critical congenital heart defects (CHDs) are 35% of those detected only after birth. The aim of the study was to measure the incidence of these CHDs, identify their clinical symptoms, and determine individual risk periods for CHD manifestation.

Methods: This retrospective cohort study was conducted from 2009 to 2018 in a population of 175,153 live births. Occurrence of the first symptoms of CHD was noted as early neonatal (0–7 days), late neonatal (8–28 days), in early infancy (1–6 months), or in late infancy (6–12 months). The first symptom for which the child was referred to a pediatric cardiologist was defined as a symptom of CHD.

Results: There were 598 severe CHDs diagnosed (3.3 cases/1000), and 70% were isolated anomalies. A concomitant genetic disorder was diagnosed in 20%, and extracardiac pathology with a normal karyotype was present in 10%. Of the total, 53% of CHDs were detected prenatally and excluded. The remaining 47% developed CHD symptoms postnatally. Of these, 74% were diagnosed as early neonates, 16% as late neonates, and 10% as infants. Defects requiring repeated operations manifested significantly earlier than those with requiring one primary correction. The most common symptoms leading to the diagnosis of CHD were heart murmur and cyanosis. Conclusions: Despite the effectiveness of prenatal diagnosis, some children will be born with undiagnosed major heart defects. Assessment of symptoms and early detection of the defect is crucial.

Background

Congenital heart defects (CHDs) are the most frequently observed congenital defects in the human population, representing up to 40% of all congenital malformations [1, 2]. The incidence of CHD varies from 4 to 50 cases per 1000 live births, but when minor ventricular septal defects are also included, the incidence rises to 75 cases per 1000 live births [3]. The etiology of CHDs is complex, as known genetic and environmental factors play a part [3] but a multifactorial etiology is likely for most of these defects [4, 5]. Approximately 20–25% of CHDs are associated with a precise genetic cause [4, 6]. Most CHDs can be prenatally detected, and the overall success of prenatal CHD diagnoses has generally improved. Fetal echocardiography has displayed high sensitivity and specificity for detecting major CHDs [7, 8]. However, some children are born with prenatally undetected CHDs that are diagnosed only after birth. Of the total number of CHDs, 35% are considered severe or critical, and these defects can be health- and life-threatening. It is crucial to diagnose these defects as soon as possible. Symptoms of heart disease may develop slowly or very rapidly, and worsen in the maternity hospital or in the home. In critical and severe CHDs, the most common symptom is the development of hypoxemia and heart failure. In other defects, the most common is pulmonary symptomatology, failure to thrive, or murmur. CHDs have an incidence of 2–75 per 1000 live births, gathered from many studies [1, 3, 6, 9, 10]. The first manifestations of CHDs associated with the different stages of childhood are studied less frequently, but this information is very important for pediatricians.

The aim of this work was to study the incidence of critical and severe CHDs, identify their clinical symptoms, and determine the individual risk periods for CHD manifestation.

Methods

This study was conducted between 2009 and 2018 at the Department of Pediatric and Prenatal Cardiology, University Hospital Ostrava, Czech Republic, and at the Department of Pediatrics, Palacky University Hospital, Olomouc, Czech Republic. These centers are tertiary referral centers for pediatric cardiology and offer prenatal care and care for critical and severe CHDs. They serve a population of about 1,830,000 inhabitants, with 18,200 live births per year.

The echocardiograph ultrasound systems used were the GE Vivid 7, Vivid 9, Voluson E8, and Voluson E10. These systems were equipped with multifrequency wide-bandwidth transducers: a C2-9 single crystal abdominal convex 2.3–8.4 MHz.
transducer, 6S phased-array 2.4–8.0 MHz transducer, 5S phased-array 3.0–9.0 MHz transducer, and M5Sc active matrix single crystal phased array 1.5–4.6 MHz transducer. The echocardiograph system provided basic 2D imaging, M-mode and anatomical M-mode, color Doppler imaging, and pulse wave and continuous wave Doppler imaging.

Only critical and severe CHDs were included in this study. The category of severe defects included severe illnesses in the newborn period or early infancy, which typically required postnatal heart surgery or a catheterization procedure during the first year of age. Cases with complex cardiac abnormalities were classified according to the dominant heart lesion. For instance, atrioventricular septal defects were a primary diagnostic lesion for all of the complex heart lesions reported in the study. A double-outlet right ventricle diagnosis was made if more than 50% of the aorta or the pulmonary trunk overrode the ventricular septal defect. A single ventricle was classified as a univentricular atrioventricular connection with a double inlet or a common atrioventricular valve. When an atrioventricular connection was absent, the diagnosis of either tricuspid or mitral atresia was made. Hypoplastic left heart syndrome was defined as a heart with a small left ventricle and flow reversal in the aortic arch. Coarctation of the aorta with a ventricular septal defect was classified as a coarctation of the aorta [11, 12].

For the purpose of this study, and to understand the course of CHDs, two groups of CHDs were defined, based on severity and management (Table 1). The authors used their knowledge regarding the postnatal course of heart defects and the outcomes from their management in the Czech Republic [9]. Group A consisted of defects that are, despite possible critical manifestations, mostly managed with a primary surgical correction or catheterization, without any further significant complications; however, reoperation or re-catheterization is possible. In this group, residual findings tend to be less significant and are mostly well tolerated. Group B included defects that can be associated with certain clinical complications (hypoxic events, arrhythmias, late progression of residual findings) and a higher probability of reoperation, repeated surgical procedure, or re-catheterization.

The occurrence of the first symptoms of CHD was monitored in the following defined periods of childhood: early neonatal (0–7 days), late neonatal (8–28 days), early infancy (1–6 months), and late infancy (6–12 months).

The first clinical manifestation for which the child was referred to a pediatric cardiologist was defined as a symptom of CDH.

The study was approved by the local Ethics Committee (Ethics Committee the University Hospital and the Faculty Medicine Palacky University Olomouc). The patients were enrolled in the study after giving informed consent signed either by themselves or their parents.
Table 1 Classification and definition of CHD groups and abbreviations

| Group A: probable primary correction, biventricular circulation |
|---------------------------------------------------------------|
| AS                | Aortic stenosis   |
| AVSD              | Atrioventricular septal defect |
| CoA               | Coarctation of aorta |
| IAA               | Interruption of the aortic arch |
| PDA               | Persistent ductus arteriosus |
| PS                | Pulmonary stenosis |
| TAPVR             | Total anomalous pulmonary venous return |
| TGA               | Transposition of the great arteries |
| VSD               | Ventricular septal defect |

| Group B: surgery/repeated surgery, possible complications, biventricular or single-ventricle circulation |
|---------------------------------------------------------------|
| CAT                | Common arterial trunk |
| CTGA              | Corrected transposition of the great arteries |
| DORV              | Double outlet right ventricle |
| EBST              | Ebstein's anomaly |
| HLH               | Hypoplastic left heart syndrome |
| PAIVS             | Pulmonary atresia with intact ventricular septum |
| PAVSD             | Pulmonary atresia with ventricular septal defect |
| SV                | Single ventricle |
| TA                | Tricuspid atresia |
| TOF               | Tetralogy of Fallot |

Statistical analysis

The data obtained were stored and processed using Microsoft Excel. The same program was used for descriptive statistics. Results are presented in tables as numbers and percentages. The Chi-square test was used for other comparisons. The level of significance $\alpha$ for the probability of a type-I error ($p$ or $p$ value) was set at 0.05 for all tests. Analyses were performed using IBM SPSS software v. 25.

Results

Basic evaluation

A total of 598 severe heart defects were diagnosed in the study population of 175,153 live births between 2009 and 2018 (3.3 cases/1000). The CHDs mostly (70%, 419/598) manifested as isolated anomalies. A concomitant genetic disorder was diagnosed in 20% (120/598) of cases, and extracardiac pathology with a normal karyotype was present in 10% (59/598) of cases. In the monitored period, 53% (316/598) of CHDs were detected prenatally (Table 2). These CHDs were excluded from the study. In this group of prenatally diagnosed CHDs, 49% of families decided to terminate the pregnancy and 51% of
families continued the pregnancy. In cases of prenatally diagnosed CHDs and continued pregnancy, the newborn was examined shortly after delivery and we did not wait for the first symptoms to occur.

In the study region, 47% (282/598) of CHDs were prenatally undetected; these children developed CHD symptomatologies postnatally and these cases were included in the study. Data from the perinatal period of these defects are listed in Table 3. The most common CHD was a ventricular septal defect, and the least common was a single ventricle. On average, children with CHDs were not born prematurely except in cases of persistent ductus arteriosus. The incidence and severity of this defect were influenced by the prematurity of the newborns. Most children with CHDs were born vaginally and there was no significant perinatal asphyxia, even in cases with critical defects.
Table 2 The incidence and prenatal detection of CHDs, in absolute numbers

| CHD                                      | N   | I   | Prenatally detected | Prenatally undetected |
|------------------------------------------|-----|-----|----------------------|------------------------|
|                                          |     |     | %                    | %                      |
| Ventricular septal defect                | 100 | 0.56| 28 (28)              | 72 (72)                |
| Atrioventricular septal defect           | 65  | 0.36| 46 (71)              | 19 (29)                |
| Coarctation of aorta                    | 57  | 0.31| 24 (42)              | 33 (58)                |
| Transposition of the great arteries      | 55  | 0.31| 31 (56)              | 24 (44)                |
| Tetralogy of Fallot                     | 54  | 0.31| 34 (63)              | 20 (37)                |
| Persistent ductus arteriosus            | 46  | 0.25| -                    | 46                     |
| Hypoplastic left heart syndrome          | 45  | 0.25| 41 (91)              | 4 (9)                  |
| Pulmonary stenosis                      | 39  | 0.22| 22 (56)              | 17 (44)                |
| Double outlet right ventricle            | 37  | 0.2 | 23 (62)              | 14 (38)                |
| Aortic stenosis                         | 32  | 0.17| 20 (63)              | 12 (38)                |
| Pulmonary atresia with ventricular septal defect | 12 | 0.07| 9 (75)               | 3 (25)                 |
| Common arterial trunk                   | 11  | 0.06| 6 (55)               | 5 (45)                 |
| Ebstein's anomaly                       | 11  | 0.06| 6 (55)               | 5 (45)                 |
| Tricuspid atresia                       | 10  | 0.06| 8 (80)               | 2 (20)                 |
| Single ventricle                        | 8   | 0.04| 7 (88)               | 1 (12)                 |
| Pulmonary atresia with intact ventricular septum | 6 | 0.03| 6 (100)              | 0 (0)                  |
| Interruption of the aortic arch         | 4   | 0.02| 2 (50)               | 2 (50)                 |
| Corrected transposition of the great arteries | 3 | 0.02| 3 (100)              | 0 (0)                  |
| Total anomalous pulmonary venous return | 3   | 0.02| 0 (0)                | 3 (100)                |
| Total                                   | 598 | 3.3 | 316 (53)             | 282 (47)               |

CHD: congenital heart defect; I: incidence, N/1000 live births

Table 3 Prenatally undetected CHDs in the perinatal period (N = 282)

| CHD                                      | N   | delivery | AS in 5 min | weight in g | length in cm | week of delivery |
|------------------------------------------|-----|----------|-------------|-------------|---------------|-----------------|
|                                          |     | V/SC     | median (range) | median (range) | median (range) | median (range)  |
| VSD                                      | 72  | 51/21    | 10 (7–10)   | 2800 (1180–4520) | 49 (34–51)     | 39 (30–42)     |
| PDA                                      | 46  | 16/30    | 9 (3–10)    | 940 (540–4320)  | 35 (26–53)     | 27 (24–40)     |
| COA                                      | 33  | 20/13    | 10 (6–10)   | 2980 (960–3790)  | 48 (35–53)     | 38 (29–41)     |
| TGA                                      | 24  | 19/5     | 8 (1–10)    | 3000 (1770–4370) | 47 (44–52)     | 38 (33–42)     |
| TOF                                      | 20  | 14/6     | 10 (7–10)   | 3010 (1880–4050) | 49 (41–51)     | 38 (37–42)     |
| Condition | Incidence | Prenatal Detection | Incidence | Apgar Score | Incidence |
|-----------|-----------|--------------------|-----------|-------------|-----------|
| AVSD      | 19        | 11/8               | 9 (5–10)  | 3195 (1870–4100) | 49 (44–52) | 39 (34–41) |
| PS        | 17        | 12/5               | 10 (6–10) | 2880 (2300–3960) | 48 (45–52) | 39(35–42) |
| DORV      | 14        | 10/4               | 10 (8–10) | 2990 (1450–4470) | 47 (40–53) | 39 (36–40) |
| AS        | 12        | 7/5                | 10 (7–10) | 2800 (1900–3900) | 48 (35–51) | 38 (35–40) |
| CAT       | 5         | 4/1                | 10 (7–10) | 2600 (1300–3050) | 45 (40–49) | 36 (34–38) |
| EBST      | 5         | 3/2                | 10 (7–10) | 2900 (2680–3390) | 49 (48–52) | 39 (38–41) |
| HLH       | 4         | 3/1                | 9 (8–10)  | 3550 (3180–4100) | 50 (48–52) | 40 (37–41) |
| PAVSD     | 3         | 2/1                | 9 (7–10)  | 2930 (1740–2320) | 49 (42–51) | 40 (33–40) |
| TAPVR     | 3         | 2/1                | 10 (9–10) | 3650 (3130–4620) | 50 (46–52) | 40 (39–40) |
| IAA       | 2         | 1/1                | 9 (8–10)  | 3700 (3500–3900) | 50 (49–51) | 40 (39–41) |
| TA        | 2         | 2/0                | 9 (8–10)  | 2500 (1500–3500) | 47 (40–53) | 37 (32–41) |
| SV        | 1         | 0/1                | 4         | 1690         | 42  | 35 |

Abbreviations are defined in Table 1. CHD: congenital heart defect, V: vaginal, SC: sectio caesarea, AS: Apgar score

Time of diagnosis

A total of 74% (209/298) of children with CHD were diagnosed as early neonates, usually during their stay in the maternity hospital (Table 4). In 100% of cases, the following defects occurred at this early age: transposition of the great arteries, tetralogy of Fallot, common arterial trunk, interruption of the aortic arch, hypoplastic left heart syndrome, pulmonary and tricuspid atresia, and single ventricle. Coarctation of the aorta and Ebstein's anomaly were the least frequent diagnoses in the earliest period, these defects were manifested in the late neonatal period, when the newborn is released from the maternity hospital, in one third of cases. Ventricular septal defect, pulmonary stenosis, coarctation of the aorta and Ebstein's anomaly had the highest (10–20%) risk of late manifestations in infancy. With the exception of isolated cases of ventricular septal defect and persistent ductus arteriosus, all defects were diagnosed by 6 months of age. Defects requiring repeated operations (group B) manifested significantly earlier than those requiring one primary correction (Table 5, Fig. 1).
Table 4. Time of diagnosis of CHDs, according to the absolute numbers

| CHD   | N   | Newborn 0–7 days | Newborn 8–28 days | Infant 1–6 months | Infant 7–12 months |
|-------|-----|-------------------|--------------------|-------------------|-------------------|
|       | N (%) | N (%) | N (%) | N (%) | N (%) |
| Group A |       |       |       |       |       |
| VSD   | 72  | 50 (69) | 7 (10) | 13 (18) | 2 (3) |
| PDA   | 46  | 29 (63) | 14 (31) | 2 (4) | 1 (2) |
| COA   | 33  | 15 (46) | 13 (39) | 5 (15) | 0 (0) |
| TGA   | 24  | 24 (100) | 0 (0) | 0 (0) | 0 (0) |
| AVSD  | 19  | 15 (79) | 3 (16) | 1 (5) | 0 (0) |
| PS    | 17  | 12 (70) | 3 (18) | 2 (12) | 0 (0) |
| AS    | 12  | 10 (83) | 2 (17) | 0 (0) | 0 (0) |
| TAPVR | 3   | 3 (100) | 0 (0) | 0 (0) | 0 (0) |
| IAA   | 2   | 2 (100) | 0 (0) | 0 (0) | 0 (0) |
| Group B |       |       |       |       |       |
| TOF   | 20  | 20 (100) | 0 (0) | 0 (0) | 0 (0) |
| DORV  | 14  | 13 (93) | 0 (0) | 1 (7) | 0 (0) |
| CAT   | 5   | 5 (100) | 0 (0) | 0 (0) | 0 (0) |
| EBST  | 5   | 2 (40) | 2 (40) | 1 (20) | 0 (0) |
| HLH   | 4   | 4 (100) | 0 (0) | 0 (0) | 0 (0) |
| PAVSD | 3   | 3 (100) | 0 (0) | 0 (0) | 0 (0) |
| TA    | 2   | 2 (100) | 0 (0) | 0 (0) | 0 (0) |
| SV    | 1   | 1 (100) | 0 (0) | 0 (0) | 0 (0) |
| Total | 282 | 209 (74) | 45 (16) | 25 (9) | 3 (1) |

Abbreviations are defined in Table 1. CHD: congenital heart defect

Table 5. Time of diagnosis of CHDs, according to severity of defect

| Group | N   | Newborn 0–7 days | Newborn 8–28 days | Infant 1–12 months |
|-------|-----|-------------------|--------------------|-------------------|
|       | N   | %     | N   | %   | N   | %   |
| A     | 160 | 70%   | 42  | 19% | 25  | 11% |
| B     | 50  | 93%   | 2   | 4%  | 2   | 4%  |

p = 0.003

Figure 1
Symptoms leading to diagnosis
The most common symptoms leading to the diagnosis of CHD were heart murmur and cyanosis (Table 6). Heart murmur was the most common symptom in Group A in ventricular and atrioventricular septal defects, coarctation of the aorta, and pulmonary and aortic stenosis; and in Group B, in double outlet right ventricle and Ebstein's anomaly. Cyanosis was the most common symptom in Group A in transposition of the great arteries, total anomalous pulmonary venous return, and interruption of the aortic arch; and in Group B in tetralogy of Fallot, common arterial trunk, hypoplastic left heart syndrome, and pulmonary and tricuspid atresia. Cyanosis occurred significantly more in Group B (Table 7).

Circulatory instability and circulatory shock were most common in PDA cases, due to immaturity and neonatological complications. Respiratory complications were the main symptom in 10–20% of cases with coarctation of the aorta, aortic stenosis, total anomalous pulmonary venous return, and common arterial trunk. The highest rate of failure to thrive (15%) in the diagnosis of CHD was in coarctation of the aorta. In this defect, finding of a weakened pulse on the femoral arteries contributed to diagnosis in only 9% of cases.

Stigmatization due to genetic abnormalities contributed most (26%) to the diagnosis of CHD in atrioventricular septal defect. Rarely, a diagnosis of CHD was made in the follow-up for other organ pathologies, most notably in cases of double-outlet right ventricle.

Except for cyanosis and circulatory instability, the incidence of symptoms did not differ significantly between group A and group B (Table 7). The occurrence of symptoms in relative numbers in both groups is shown in Fig. 2.
Table 6 Symptoms of CHD leading to diagnosis.

(shaded boxes show the most common symptom for each CHD)

| CHD   | N  | cyanosis | dyspnoea | failure | murmur | tachypnoea | to thrive | stigmatisation | weakened | circulator. | other   | disability |
|-------|----|----------|----------|---------|--------|------------|-----------|----------------|----------|-------------|---------|------------|
|       | N (%) |          |          |         |        |            |           |                |          |             |         |            |
|       |      |          |          |         |        |            |           |                |          |             |         |            |
| Group A |     |          |          |         |        |            |           |                |          |             |         |            |
| VSD   | 72  | 3 (4)    | 3 (4)    | 2 (3)   | 60 (83)| 2 (3)      | 0 (0)     | 0 (0)          | 2 (3)    |             |         |            |
| PDA   | 46  | 0 (0)    | 0 (0)    | 2 (4)   | 21 (46)| 0 (0)      | 0 (0)     | 23 (50)        | 0 (0)    |             |         |            |
| COA   | 33  | 8 (24)   | 4 (12)   | 5 (15)  | 10 (31)| 1 (3)      | 3 (9)     | 1 (3)          | 1 (3)    |             |         |            |
| TGA   | 24  | 24 (100)| 0 (0)    | 0 (0)   | 0 (0)  | 0 (0)      | 0 (0)     | 0 (0)          | 0 (0)    |             |         |            |
| AVSD  | 19  | 4 (21)   | 0 (0)    | 1 (5)   | 9 (48) | 5 (26)     | 0 (0)     | 0 (0)          | 0 (0)    |             |         |            |
| PS    | 17  | 1 (6)    | 1 (6)    | 0 (0)   | 15 (88)| 0 (0)      | 0 (0)     | 0 (0)          | 0 (0)    |             |         |            |
| AS    | 12  | 0 (0)    | 2 (17)   | 0 (0)   | 10 (83)| 0 (0)      | 0 (0)     | 0 (0)          | 0 (0)    |             |         |            |
| TAPVR | 3   | 2 (67)   | 1 (33)   | 0 (0)   | 0 (0)  | 0 (0)      | 0 (0)     | 0 (0)          | 0 (0)    |             |         |            |
| IAA   | 2   | 2 (100)| 0 (0)    | 0 (0)   | 0 (0)  | 0 (0)      | 0 (0)     | 0 (0)          | 0 (0)    |             |         |            |
| Group B |     |          |          |         |        |            |           |                |          |             |         |            |
| TOF   | 20  | 13 (65)  | 0 (0)    | 0 (0)   | 7 (35) | 0 (0)      | 0 (0)     | 0 (0)          | 0 (0)    |             |         |            |
| DORV  | 14  | 2 (14)   | 0 (0)    | 0 (0)   | 9 (65) | 1 (7)      | 0 (0)     | 0 (0)          | 2 (14)   |             |         |            |
| CAT   | 5   | 4 (80)   | 1 (20)   | 0 (0)   | 0 (0)  | 0 (0)      | 0 (0)     | 0 (0)          | 0 (0)    |             |         |            |
| EBST  | 5   | 1 (20)   | 0 (0)    | 0 (0)   | 4 (80) | 0 (0)      | 0 (0)     | 0 (0)          | 0 (0)    |             |         |            |
| HLH   | 4   | 4 (100)| 0 (0)    | 0 (0)   | 0 (0)  | 0 (0)      | 0 (0)     | 0 (0)          | 0 (0)    |             |         |            |
| PAVSD | 3   | 3 (100)| 0 (0)    | 0 (0)   | 0 (0)  | 0 (0)      | 0 (0)     | 0 (0)          | 0 (0)    |             |         |            |
| TA    | 2   | 2 (100)| 0 (0)    | 0 (0)   | 0 (0)  | 0 (0)      | 0 (0)     | 0 (0)          | 0 (0)    |             |         |            |
| SV    | 1   | 0 (0)    | 0 (0)    | 0 (0)   | 0 (0)  | 1 (100)    | 0 (0)     | 0 (0)          | 0 (0)    |             |         |            |
| Total | 282 | 69 (24)  | 12 (4)   | 10 (4)  | 149 (53)| 10 (4)     | 3 (1)     | 24 (8)         | 5 (2)    |             |         |            |

Abbreviations are defined in Table 1. CHD: congenital heart defect
### Table 7 Symptoms of heart defects: occurrence in groups A and B

| Symptoms                  | Group A | Group B | p-value |
|---------------------------|---------|---------|---------|
|                           | N   | %   | N   | %   |         |
| Cyanosis                  | 44  | 19% | 25  | 46% | < 0.001 |
| Murmur                    | 125 | 55% | 24  | 44% | 0.169   |
| Failure to thrive         | 10  | 4%  | 0   | 0%  | 0.217   |
| Dyspnoea, tachypnoea      | 11  | 5%  | 1   | 2%  | 0.473   |
| Weakened aa. femorales    | 3   | 1%  | 0   | 0%  | 1.000   |
| Stigmatization            | 8   | 4%  | 2   | 4%  | 1.000   |
| Other organ disability    | 3   | 1%  | 2   | 4%  | 0.245   |
| Circulator instability    | 24  | 11% | 0   | 0%  | 0.006   |

Figure 2

**Discussion**

CHDs are the most frequently observed morphological defects in human populations and most can be diagnosed prenatally. Although fetal echocardiography is a precise method for detecting cardiac malformations in the fetus and has excellent results, some defects are not detected fetally and a child with an unrecognized heart defect is born. The heart defect is then manifested by different symptoms at different times. The main findings of this study were as follows: (i) despite the effectiveness of prenatal screening, half of severe CHDs were undetected at birth; (ii) heart defects had no perinatal major complications; (iii) three quarters of the children with prenatally unrecognized CHDs were symptomatic in the early neonatal period; and (iv) the most common symptoms of CHD were cyanosis and heart murmur.

The worldwide success rate of prenatal CHD diagnostics has generally improved [13], but the rates have varied among individual countries [14]. During this study, 57% of severe CHDs (persistent ductus arteriosus excluded) were detected fetally, and the success rate has increased continuously. Currently, the prenatal care system is very effective, and for some types of defects (single ventricle, hypoplastic left or right heart syndrome) the detection rate is 90–100%. Some families decided to terminate the pregnancy after receiving a prenatal CHD diagnosis, but the aims of prenatal diagnostics are a more detailed examination of pathological pregnancies and correct counseling. Prior studies have provided different results on the beneficial effects of fetal diagnostics on morbidity and mortality in newborns and children [13, 15–17], but in the authors’ opinion, fetal transport “in utero” for delivery at an adequate hospital is important. In these cases, late diagnosis of a heart defect is not inevitable, and a child with CHD is stabilized and treated immediately after delivery.

Despite the fact that the basic clinical signs of critical and severe heart defects are hypoxemia (cyanosis) and manifestations of heart failure, in our study newborns with CHDs were without moderate or severe perinatal symptoms [9]. Newborns with CHDs had mostly normal Apgar scores after delivery, and symptoms of the defect developed later. Clinical stability was probably positively influenced by the presence of fetal shunts. Stable neonates are not routinely screened with a pulse oximeter on the first day in the study region, but this method would have good specificity and sensitivity to detect critical defects [18]. In children with CHDs, there was also no higher tendency towards premature birth or hypotrophy. The exception was children with an persistent ductus arteriosus; this diagnosis was due to their immaturity [19].

The diagnosis of CHD was established in three quarters of children in the early neonatal period, that is, at the time when the child is usually hospitalized in the neonatology department. Clinical signs were dominant, but currently we expect higher detection of CHDs under hospitalization with the introduction of routine pulse oximetry [20]. The number of surgical
procedures depends on the severity of the defect [21]. In our study, in the early neonatal period, CHDs requiring multiple future operations were significantly more frequently diagnosed.

The authors consider the late neonate stage as a risky period: this is when a newborn with unrecognized CHD is discharged from the maternity hospital and severe or moderate CHD becomes apparent when fetal shunts close. In these newborns, the worse pre-operative condition and the critical course of the disease are more frequent [22]. In this study, the CHDs with the highest risks in this period were coarctation of the aorta and Ebstein’s anomaly. Ebstein’s anomaly is rare, but coarctation of the aorta has a significant incidence in the population. It is reported that up to 30% of coarctation cases are not diagnosed in newborns after delivery [23]; in our study it was 50%. Ventricular septal defect was most commonly detected in infants, although only severe and operated defects were included in this study. This defect is recommended for surgery at high flow and in symptomatic children early in infancy [24].

The most common symptoms in CHD were murmur and cyanosis. Heart murmur is common in healthy and asymptomatic children, but may also indicate a serious heart defect [25]. Newborns with heart murmur are at higher risk, as most asymptomatic newborns with heart murmur have a structural defect [26, 27]. In our study, ventricular septal defect and aortic and pulmonary stenosis were most often manifested by murmur. These defects are usually manifested by systolic murmur in asymptomatic patients [25]. Cyanosis is most often seen in the first weeks of life in children with CHD, when circulation is dependent on arterial ductus [28]. In our patients, cyanosis was a major sign of critical defects that required repeated surgical corrections. Of well-operable defects, transposition of the great arteries was typically manifested by cyanosis, mostly on the first day of life [29]. The largest share of circulatory instability was seen in persistent ductus arteriosus. This, however, was influenced by the immaturity of neonates and neonatological complications. The direct relevance of persistent ductus arteriosus to hemodynamic instability is still unclear [30, 31]. In other CHDs, circulatory collapse was less frequent, and the defects were detected according to clinical signs before severe alteration of circulation. This may indicate the quality of pediatric care in the monitored region. The clinical course of a child with CHD and beginning heart failure may imitate respiratory diseases, particularly dyspnea and cough [32]. Other possible symptoms of CHD are poor feeding and failure to thrive. These were a rare symptoms in our patients, and most commonly found in children with aortic and aortic arch defects. Sometimes stigmatization and suspected genetic abnormality indicated cardiological examination of the child. This was evident in atrioventricular septal defects, which in half of the cases were associated with a genetic impairment, especially trisomy 21 [33]. Surprisingly, coarctation of the aorta was rarely detected by examination of femoral artery pulsation in the study region. This examination is a screening test and the gold standard for the clinical detection of this defect [34]. Coarctation is the most common CHD that may not be diagnosed until adolescence or adulthood [35]. This should improve with better education of pediatricians and more focused attention during preventive examinations throughout childhood.

**Conclusion**

In conclusion, despite the effectiveness of prenatal diagnosis, some children will be born with undiagnosed major heart defects. Assessment of symptoms and early detection of the defect is crucial. Most children with CHD are diagnosed as neonates. The most common symptoms of CHD are heart murmur and cyanosis.

**Abbreviations**

CHD  
Congenital heart defects

**Declarations**

**Acknowledgments**

Not applicable.
Authors’ contributions

JP conceptualized and designed the study and was responsible for manuscript writing, JP and EK were investigators for fetal echocardiography and collected fetal data, AP and RS were investigators in obstetrics, collected data, mainly during fetal screening and extra-cardiac fetal findings, SK and AMP were consultants for post-natal heart diseases and collected postnatal data, TG critically reviewed the manuscript from the overall pediatric viewpoint and was responsible for final approval. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Ethics approval

The study was approved by the local Ethics Committee (Ethics Committee the University Hospital and the Faculty Medicine Palacky University Olomouc). The patients were enrolled in the study after giving informed consent signed either by themselves or their parents.

Consent for publication

Not applicable.

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Figures

**Fig. 1. Time of diagnosis of CHDs, according to severity of defect**

![Figure 1](image-url)
Figure 2

Symptoms of CHDs in relative numbers: group A (a) and group B (b) Abbreviations are defined in Table 1. CHD: congenital heart defect