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Live birth prevalence of atrioventricular septal defect after the implementation of new prenatal screening guidelines

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ABSTRACT

Introduction. In 2004, the Danish Health Authority implemented a new guideline on prenatal screening, offering all pregnant women in Denmark a foetal diagnostic ultrasound scan in the first and second trimester of their pregnancy. One of the diagnoses that may be diagnosed prenatally is congenital heart defect including atrioventricular septal defect (AVSD). AVSD is often associated with Down syndrome (DS). After a prenatal diagnosis of AVSD, parents are offered counselling on the impact of the diagnosis on their child's life. The aim of this study was to describe the impact of changes in prenatal screening programmes on the live birth prevalence of AVSD on the island of Funen, Denmark.

Methods. This was a registry-based descriptive analysis drawing on data from the EUROCAT Registry of Congenital Malformations for Funen County, Denmark. Cases of AVSD and DS from 1990 to 2018 were included.

Results. Out of 153,757 births, 60 cases of AVSD were registered, with a total prevalence at 3.9 per 10,000 births. Among all cases, 40% had an associated chromosomal diagnosis. The prenatal detection rate increased by 83% after implementation of the new screening programme. This was paralleled by an increase in the number of cases of termination of pregnancy following foetal anomaly (TOPFA) from 3% to 21% (p-value < 0.05) and a 21% reduction in live births among infants with AVSD.

Conclusions. A significant increase in the rate of TOPFA was found, with no difference in the distribution of chromosomal or non-chromosomal status, leading to a 21% reduction in liveborn infants with AVSD.

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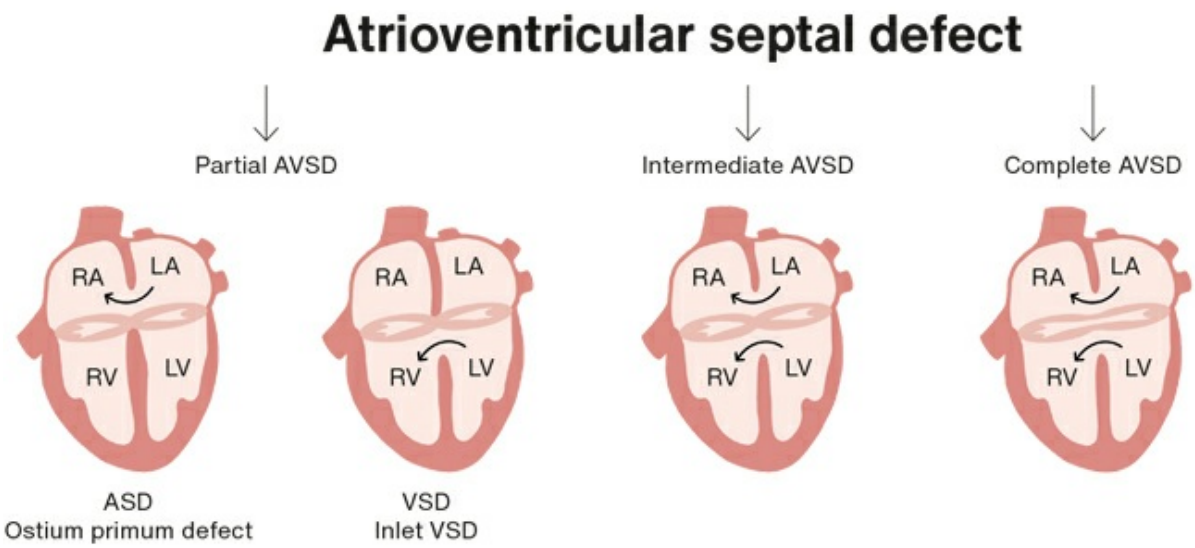
Atrioventricular septal defect (AVSD) is a congenital heart defect (CHD) characterised by the presence of a common atrioventricular valve combined with defects of the atrioventricular septum. This anomaly is also known as AV commune or common atrioventricular canal defect, and it is the ninth most common CHD lesion and the most common severe CHD [1].

Depending on the anatomy, AVSD may be classified as partial, transitional or complete (**Figure 1**). Partial AVSD includes an atrial septal defect (ASD) at the lower part of the atrial septum combined with the bridging leaflets being attached to the ventricular septum. In some patients, partial AVSD is seen as a ventricular septal defect (VSD).

FIGURE 1 Classification of atrioventricular septal defect.



ASD = atrial septal defect; AVSD = atrioventricular septal defect: LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle; VSD = ventricular septal defect.

Transitional AVSD is characterised by a primum ASD combined with a VSD, with two separate atrioventricular valves. Just like the transitional form, complete AVSD involves the combination of an ASD and a VSD, but with the valves fused into one common AV valve.

Patients with Down syndrome (DS) have a 1,000-fold increased risk of AVSD [2].

AVSD stands out as being the most common type of CHD among DS births, where 65% are diagnosed with complete AVSD, whereas partial AVSD is seen more often in non-chromosomal AVSD cases [3].

In 2004, the Danish Health Authority implemented a new guideline on prenatal screening [4]. The guideline recommends that all pregnant women in Denmark should be offered a combined first-trimester screening. The scan includes a risk assessment for chromosomal anomalies and its purpose is to obtain knowledge about the health of the foetus and to give the parents the best possible basis upon which to choose whether they want to continue or terminate the pregnancy in case of chromosomal abnormalities. In the second trimester, women are offered a second trimester scan which includes examination of the foetal organs, including the heart.

More than 97% of the pregnant women in Denmark choose both scans [5]. AVSD can be diagnosed prenatally by ultrasonography, and in those cases where AVSD is diagnosed prenatally, parents are offered counselling.

The aim of this study was to describe the impact of changes in prenatal screening programmes on the live birth prevalence of AVSD on the island of Funen, Denmark.

METHODS

This was a registry-based descriptive analysis based on data from the EUROCAT Registry of Congenital Malformations for Funen County, Denmark. EUROCAT is a European network of population-based registries for epidemiological surveillance of congenital anomalies. The EUROCAT central database includes data on births and termination of pregnancy covering 29% of the European birth population [6].

Data sources for the EUROCAT registry for Funen County were hospital records (obstetric and paediatric departments), birth and death certificates, post-mortem examinations and chromosomal data from the department of genetics. All live births, foetal deaths with a gestational age (GA) > 20 weeks and terminations of pregnancy at any GA were included in the registry.

For AVSD and DS, the following variables were extracted from the database: birth type (live birth, stillbirth, termination of pregnancy for foetal anomaly (TOPFA)), time of diagnosis (prenatally, after birth or unknown), GA at prenatal diagnosis, karyotype and one-week survival.

Data on AVSD and DS were divided into two periods;1990-2003 and 2004-2018.

Furthermore, data on AVSD were divided into partial and complete AVSD and compared on chromosomal status (chromosomal or non-chromosomal) and time of diagnosis.

The presence of associated major malformations among chromosomal and non-chromosomal cases was described with multiple malformations including cases defined as one or several associated non-cardiac malformations.

GA at the time of diagnosis was described for AVSD cases and compared with GA at the time of diagnosis among DS cases.

Statistical testing was made using the χ^2-test and Fisher's exact test with the level of significance set at 0.05.

The study is based on existing anonymised registry data and did not require ethical committee approval for access or publication.

Trial registration: none.

RESULTS

Patient characteristics

Sixty cases of AVSD were registered between 1990 and 2018. The total number of births in the same period was 153,757 and the corresponding total prevalence of AVSD was 3.9 per 10,000 births. Livebirths were registered in 50 cases (83%), stillbirths in one case (1.7%) and TOPFA in seven cases (11.7%). Furthermore, data showed that 24 cases (40%) had associated chromosomal anomalies, and 36 cases (60%) had no diagnosis of a chromosomal anomaly. Among all cases, 28% were diagnosed prenatally with an average GA at diagnosis of 23.5 weeks.

Prevalence of atrioventricular septal defect

The total prevalence of AVSD before and after 2004 was the same (3.9 per 10,000). Prenatally diagnosed cases increased by 83%, paralleled by an increase in TOPFA cases from 3% to 21% (p-value < 0.05). Cases of TOPFA included one chromosomal case before 2004 and six (three cases were chromosomal and three cases non-chromosomal) in 2004-2018 (**Table 1**).

TABLE 1 Atrioventricular septal defects on the island of Funen, Denmark, before and after implementation of the prenatal screening programme in 2004.

	Total births, n	Total AVSD cases, n	Chromosomal cases, n (%)	Non-chromosomal cases, n (%)	Total prevalence/ 10,000 births, n	Live births, n (%)	Stillbirths, n (%)	TOPFA, n (%)	Diagnosed prenatal, n (%)	Diagnosed after birth, n (%)	Time of diagnosis unknown, n (%)
1990-2003	79,701	31	14 (45)	17 (55)	3.9	29 (94)	1 (3)	1 (3)*	6 (19)	24 (77)	1 (3)
2004-2018	74,056	29	10 (34)	19 (66)	3.9	23 (79)	0	6 (21)*	11 (38)	18 (62)	0
Total	153,757	60	24 (40)	36 (60)	3.9	52 (86)	1 (2)	7 (12)	17 (28)	42 (70)	1 (2)

AVSD = atrioventricular septal defect; TOPFA = termination of pregnancy due to foetal anomaly.
*) $p < 0.05$ of changes during the study period.

From 1990 to 2003, 29 cases (94%) were live births, and one case (3%) was stillborn. From 2004, live births were present in 23 cases (79%) and no stillbirths were recorded (Table 1). However, statistical testing showed no significant decrease in live births between the two periods (p-value = 0.10).

Prevalence of Down syndrome

Between the two time periods, the total prevalence of DS increased from 16.2 to 26.3 per 10,000 births, with an average GA at the time of discovery of 13.7 weeks. Data showed a significant increase in prenatally diagnosed cases and TOPFA cases (p-value < 0.0001), leading to a 41% decrease in live births with DS (**Table 2**).

TABLE 2 Down syndrome on the island of Funen, Denmark, before and after implementation of the prenatal screening programme in 2004.

	Total births, n	Total Down syndrome cases, n	Total prevalence/ 10,000 births, n	Live births, n (%)	Stillbirths, n (%)	TOPFA, n (%)	Diagnosed prenatal, n (%)	Diagnosed after birth, n (%)	Time of diagnosis unknown, n (%)
1990-2003	79,701	129	16.2	75 (58)	9 (7)	45 (35)****	51 (40)****	75 (58)	3 (2)
2004-2018	74,056	195	26.3	44 (23)	2 (1)	149 (76)****	158 (81)****	37 (19)	0
Total	153,757	324	21.1	119 (37)	11 (3)	194 (60)	209 (64)	112 (35)	3 (1)

TOPFA = termination of pregnancy due to foetal anomaly.
****) p < 0.0001 of changes during the study period.

Atrioventricular septal defect and associated malformations

A total of 17 out of 36 (47%) cases with non-chromosomal AVSD had associated non-cardiac malformations; and among the chromosomal group, nine out of 24 cases (37%) had associated non-cardiac malformations besides AVSD. Cases with DS accounted for 21 out of 24 chromosomal cases. Other chromosomal cases included trisomy 18 (two cases) and trisomy 22 (one case); all with associated malformations.

Genetic and teratogenic syndromes

Genetic and teratogenic syndromes accounted for 12% of all AVSD cases and 19% of the non-chromosomal cases. With one syndrome as an exception, associated malformations were represented in all the remaining syndromes.

Chromosomal status and type of atrioventricular septal defect

Complete AVSD was the most common type; seen in 85% of all cases (51 cases). Among these, 28 cases (55%) were non-chromosomal and 23 cases (45%) were chromosomal. Infants with DS primarily suffered from complete AVSD and no other cardiac defects. Partial AVSD was present in eight cases (13%), one chromosomal and seven non-chromosomal; and 50% had associated malformations. One non-chromosomal case was categorised as other specified AVSD (**Table 3**).

TABLE 3 Distribution of the different types of atrioventricular septal defects (AVSD), Funen, Denmark 1990-2018.

	Total cases, n	Chromosomal cases, n (%)	Non-chromosomal cases, n (%)	Diagnosed prenatal, n (%)	Diagnosed prenatally in 1990-2003, n	Diagnosed prenatal in 2004-2018, n	Diagnosed after birth, n (%)	Time of diagnosis unknown, n (%)
Partial AVSD	8	1 (12.5)	7 (87.5)	1 (12.5)	1	0	6 (75)	1 (12.5)
Complete AVSD	51	23 (45)	28 (55)	16 (31)	5	11	35 (69)	0
Other	1	0	1 (100)	0	0	0	1 (100)	0

Prenatal detection rates

Between the two study periods, the detection rate for complete AVSD increased. From 1990 to 2003, 23 cases of complete AVSD were registered, and 22% were found prenatally. For comparison, 28 cases of complete AVSD were registered in the 2004-2018 period, and 39% were diagnosed prenatally. We found an average GA at

diagnosis of 23.5 weeks with a decrease from GA 30.3 to GA 19.8 between the two periods.

In relation to partial AVSD, seven cases were registered from 1990 to 2003, and one was diagnosed prenatally. From 2004 to 2018, one case of partial AVSD was registered, and this case was diagnosed after birth. No cases of transitional AVSD were found.

One-week survival

The majority of all liveborn infants with AVSD were still alive after one week, and the one-week survival rate among live births was 94%.

DISCUSSION

In the present study, we found that: i) after implementation of the new prenatal screening guidelines in 2004, prenatally diagnosed cases of AVSD increased by 83%, ii) TOPFA increased significantly after 2004, iii) half of the cases in which TOPFA was performed were chromosomal cases, iv) live births among infants with AVSD decreased by 21%, v) despite a 61% increase in the total prevalence of DS, the live birth prevalence decreased by 41% due to TOPFA.

In an increasing number of cases, the parents' decision included TOPFA. Data showed a significant increase in TOPFA cases, even though these results are limited due to several factors. First, along with other CHD, cases of AVSD may be missed and go undiagnosed in perinatal deaths without a full autopsy. Second, AVSD is highly associated with chromosomal anomalies, especially DS. Chromosomal anomalies are often diagnosed earlier in pregnancy, occasionally before a possible CHD, which means that an unknown number of AVSD cases will presumably never be diagnosed because of an increased number of early terminations de to the diagnosis of DS. Even though the prevalence of DS increased from 1990 to 2018, the prevalence of live births decreased due to a significant increase in prenatally diagnosed cases and cases of early TOPFA, which probably affected the prevalence of AVSD. The potentially undiagnosed cases of DS with AVSD will also have an impact on the recorded distribution of chromosomal and non-chromosomal cases with AVSD.

The increase in prenatally diagnosed cases may possibly be explained by the large screening participation of pregnant women in Denmark combined with the development of equipment and an opportunity allowing for more detailed anatomy screening over time. Even so, more than half of all AVSD cases between 2004 and 2018 were diagnosed after birth, which is consistent with the prenatal detection rate below 50% described by Allan [7]. The distribution of partial and complete AVSD may affect our results, since cases of partial AVSD were more difficult to diagnose by ultrasound, probably due to the less extensive change in anatomy and the varying level and degree of shunting.

We found no significant difference in the occurrence of chromosomal and non-chromosomal status among prenatally diagnosed cases, although a preponderance of chromosomal cases was expected. This may possibly be explained by TOPFA being performed in chromosomal cases prior to establishing the GA, where a full ultrasound may be performed for detection of associated anomalies. A European-based study showed a slightly larger proportion of prenatally diagnosed chromosomal cases, and Berg et al. also described AVSD with chromosomal anomalies as diagnosed significantly earlier in pregnancy [8, 9].

The overall prevalence of AVSD was 3.9 per 10,000 livebirths, which is lower than results previously published, but close to the findings by Miller et al. (3.7 per 10,000) [8, 10, 11]. Of note, several of the studies based their prevalence on live births only and are thus not directly comparable to the total prevalence reported herein, which included TOPFA and stillbirths.

In total, 17 out of 60 AVSD cases (28%) were diagnosed prenatally, which is similar to the findings by Heide et al. who reported 29.3% prenatally diagnosed cases [12]. Results from other studies have ranged from 67% to 91%, but the total number of AVSD cases in these studies was also considerably lower than in our study [13-15]. Since our study is based on data from Denmark, it should be taken into account that these studies are from other countries that may have different guidelines for prenatal screening.

A change in GA at the time of discovery was expected. Recent studies have described a GA at the time of diagnosis of 22-23 weeks, whereas earlier studies reported a GA of 26-27 weeks [7, 9, 11, 16]. Our average GA of 23.5 weeks corresponds well with the newest results, but the most interesting element in these outcomes is the decrease in GA at the time of diagnosis between the two time periods. The average GA from 1990 to 2003 was 30.3, which was higher than described in previous studies. However, the difference between this number and the average GA at the time of diagnosis after 2004 (19.8) is notable, since an earlier diagnosis is important for knowledge about the condition of the foetus. To our knowledge, no research has been conducted to determine whether an earlier diagnosis affects the parents psychologically and guides their choice as to terminating or carrying through a pregnancy.

Over time, the short- and long-term survival among infants with AVSD has increased; and today, more than 90% are still alive after ten years of life [17, 18]. The main reasons for this are improvement in surgical techniques, postoperative management and echocardiographic imaging. It is therefore important to consider the ethical aspects of the termination of non-chromosomal AVSD cases; in particular due to the enhanced possibility of a successful operation. The probability of associated malformations among non-chromosomal cases is high, and the severity of the malformations combined with possible complications and reoperation are worth considering.

Limitations

Despite the long duration of the study, our small sample size is an important limitation of the study as it questions the reliability of our results.

Furthermore, our results might be difficult to compare globally, since they are based on the Danish healthcare system, including free access to healthcare including screenings during pregnancy, and surgery, if necessary. Although the 2004 guidelines were rolled out nationally, it is important to underline that parental decision making may differ between geographical regions.

Finally, during the 28 years of study, significant improvements in the quality of echocardiographic imaging have been made, which is important for the comparability of data between the two periods. To confirm our results, a more comprehensive study based on a larger sample size is warranted.

CONCLUSIONS

As a result of the implementation of the prenatal screening programme in 2004, prenatally diagnosed cases of AVSD increased, although not statistically significantly so. A significant increase in cases of TOPFA was found with no difference in the distribution of chromosomal or non-chromosomal status, leading to a 21% reduction in liveborn infants with AVSD.

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