Impact of the 20-week scan
Fleurke-Rozema, Hanneke

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Timing of detection of anencephaly in the Netherlands

J.H. FLEURKE-ROZEMA
L. VAN LEIJDEN*
K. VAN DE KAMP*
E. PAJKRT
C.M. BILARDO
R.J.M. SNIJDERS

* These authors contributed equally to the manuscript

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ABSTRACT

Objective
To assess the gestational age at detection and prevalence of anencephaly in the North of the Netherlands over a five year period.

Methods
A case-list of all cases of anencephaly from two Fetal Medicine Units was compiled. Cases were included if the estimated due date was between August 1, 2008 and July 31, 2013.

Results
Overall prevalence of anencephaly was 5.4 per 10,000 pregnancies (n=110). The majority of cases (69%) were detected before 18 weeks’ gestation. Factors determining successful early diagnosis were competence level of the sonographers, with a significantly higher detection rate when scans were performed by a sonographer licensed by the FMF for nuchal translucency measurement (p=0.001), and gestational age at or beyond 11 weeks of gestation (p=0.024).

Conclusion
Improving detection of anencephaly in the first trimester requires ultrasound screening at or after 11 weeks of gestation, performed by experienced sonographers trained in recognizing fetal anomalies. Sonographers should be instructed that the goal of the first trimester scan is not only to measure nuchal translucency thickness but also to exclude major anomalies.
INTRODUCTION

Anencephaly (Greek word for ‘absence of brain’) is the end stage of a neural tube defect that starts with (partial) absence of the cranial vault (acrania). Initially the fetal brain is located outside the skull in the amniotic fluid (exencephaly); due to traumas and bleeding it degenerates (anencephaly). In about 12% of the cases, anencephaly is associated with other structural anomalies (1) and in 0.7 to 5.6% of cases a chromosome abnormality is diagnosed (2). Prenatal detection rates have been reported to be as high as 96%-100% (3-6). Anencephaly is fatal; affected children usually die immediately after birth (7), but longer survival has been documented (8). Reported prevalence of anencephaly in the Netherlands varies from 1.3 based on data from the Dutch Perinatal Registry (PRN) to 3.7 per 10,000 births based on data from the Eurocat registry of congenital anomalies in three provinces in the North of the Netherlands (9).

In 2007, the policy of prenatal screening in the Netherlands was modified to ensure that not only women with an a-priory increased risk but all women can opt for screening for chromosome defects in the first trimester and screening for neural tube defects in the second trimester of pregnancy. At the same time, the policy for dating of pregnancies was adjusted to dating based on an early ultrasound scan rather than last menstrual period.

Dating scans can be performed by all sonographers who completed basic ultrasound training. Screening scans can only be performed by sonographers who have been specifically trained according to the guidelines of the national screening program. The regional centers monitor the quality of screening scans and provide regular targeted training.

The uptake of first trimester screening is relative low. The main reasons for this are a relative positive attitude towards Down syndrome and a negative attitude towards termination of pregnancy (10). In addition, women under 36 years of age have to pay for first trimester screening and parents are not routinely informed that the scan can reveal major structural anomalies. The costs of second trimester screening are covered by the National Health Insurance. Parents are counseled that the aim of the second trimester scan is to detect major structural anomalies. Based on the yearly number of scans and data from the national birth registry the uptake is about 95%.

Aim of the present study was to assess the prevalence and timing of prenatal detection of anencephaly with the new screening policy.

METHODS

A prospective cohort study was undertaken in the two regions covered by the Foundation for Prenatal Screening Amsterdam, referring to the Academic Medical Centre in Amsterdam (North West) with about 15,000 mid-trimester scans per year and the Foundation for Prenatal
Screening Groningen, referring to the University Medical Centre of Groningen (North East) with an average of 24,000 mid-trimester scans per year. A case-list of all diagnosed cases of anencephaly was compiled. Cases were included if the estimated due date was between August 1, 2008 and July 31, 2013. For each case, details regarding the diagnosis were collected from the regional screening databases of the AMC and UMCG. Outcome measures were gestational age (GA) at diagnosis, presence or absence of additional (chromosomal) anomalies and pregnancy outcome.

**Statistical analysis**

Statistical analysis was performed with SPSS version 20 for Windows (IBM SPSS Software, Netherlands). To analyze whether timing of detection had changed significantly during the five-year period, a Kruskall-Wallis test was performed. To compare differences between groups, the chi-square test was used. A p-value of < 0.05 was considered significant.

**RESULTS**

During the study period 110 cases of anencephaly were diagnosed; 43 in the North West and 67 in the North East (Table 1). Additional structural anomalies, such as spina bifida, polycystic kidney disease, caudal regression syndrome, short limbs, and abnormal position of the hands, ventricular septum defect, and omphalocele were reported in 27 cases (24.5%). In the group with associated anomalies, cytogenetic karyotype was examined in 16 cases and was abnormal in 6 cases, all of these showing multiple congenital abnormalities. Of the 83 isolated cases (75.5%), karyotyping was performed in 24 fetuses (28%) and all had normal chromosomes.

<table>
<thead>
<tr>
<th>Type</th>
<th>N (110)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated</td>
<td>83</td>
<td>75.5</td>
</tr>
<tr>
<td>• No karyotyping</td>
<td>59</td>
<td>53.6</td>
</tr>
<tr>
<td>• Normal karyotype</td>
<td>24</td>
<td>21.8</td>
</tr>
<tr>
<td>Associated anomalies</td>
<td>27</td>
<td>24.5</td>
</tr>
<tr>
<td>• No karyotyping</td>
<td>11</td>
<td>40.7</td>
</tr>
<tr>
<td>• Normal karyotype</td>
<td>10</td>
<td>37.0</td>
</tr>
<tr>
<td>• Abnormal karyotype^</td>
<td>6</td>
<td>22.2</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Termination of pregnancy</td>
<td>96</td>
<td>87.3</td>
</tr>
<tr>
<td>• Intrauterine death</td>
<td>4</td>
<td>3.6</td>
</tr>
<tr>
<td>• Death during or within 28 days after birth</td>
<td>10</td>
<td>9.1</td>
</tr>
</tbody>
</table>

^ Trisomy 18 (n=4), 69XXY (n=1), 47XY+12[11]/46,XY[19] (n=1)
In this study 14 affected pregnancies (12.7%) continued beyond 24 weeks of gestation; two resulted in intra-uterine death and two were terminated at 24 and 25 weeks’ gestation, respectively. Of the births, all 10 infants died during delivery or within one week after birth. Prevalence of anencephaly over the 5-year period was calculated on a total of 205,000 pregnancies, based on the number of mid-trimester scans in both regions and assuming an uptake of the mid-trimester scan of 95%. Overall prevalence of anencephaly was 5.4 per 10,000 pregnancies. From 18 weeks’ gestation prevalence dropped to 1.7 per 10,000 pregnancies.

Mean gestational age at time of detection during the study period was 14.7 weeks and did not change significantly over the study period (p=.535). Overall, 69% of the cases were detected before 18 weeks’ gestation (table 2).

<table>
<thead>
<tr>
<th>Gestational age at detection</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;17 weeks</td>
<td>76 (69)</td>
</tr>
<tr>
<td>18-23 weeks</td>
<td>33 (30)</td>
</tr>
<tr>
<td>&gt;24 weeks</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Total</td>
<td>110</td>
</tr>
</tbody>
</table>

In the group where an early scan was performed by a sonographer licensed by the FMF for nuchal translucency measurement 86.4% of the cases were diagnosed before the mid-trimester scan, compared to 58.5% in the group where the early scan was performed by a sonographer with basic ultrasound training (table 3, p=0.001). In the group where the first trimester scan was performed before 11 weeks’ gestation, 56% of the cases were diagnosed before 18 weeks’ gestation. In contrast, of the group that had an ultrasound scan at or after 11 weeks’ of gestation, 77% was diagnosed before 18 weeks’ gestation (p = 0.024).

<table>
<thead>
<tr>
<th>Sonographer training</th>
<th>Timing of diagnosis (N/%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal Medicine Foundation 11-14 week scan</td>
<td>38 (86.4)</td>
</tr>
<tr>
<td>Basic Ultrasound Training</td>
<td>38 (58.5)</td>
</tr>
<tr>
<td>Total</td>
<td>76 (69.7)</td>
</tr>
</tbody>
</table>

* One women did not found out she was pregnant until the second trimester and this case was not included in the table.
DISCUSSION

This study shows that in a country where first trimester ultrasound at 11-14 weeks gestation is not performed routinely, many cases of anencephaly remain undetected until the mid-trimester scan. In our study late diagnosis occurred in almost a third of the cases. Moreover, our findings indicate that an important determinant for early diagnosis is a sonographers’ competence in identifying fetal anomalies. Sonographers who attended training from the Fetal Medicine Foundation, which includes early detection of fetal anomalies, identified significantly more cases in the first trimester than sonographers who only had basic ultrasound training. Our observation confirms the findings of Johnson et al. that awareness of the variable appearance of anencephaly at different gestational ages is essential for early diagnosis (11). The finding that anencephaly is missed even if the scan is performed by a trained sonographer may be related to the fact that the focus of first trimester scan is not primarily to look for anomalies.

In addition to targeted training, our results demonstrate that the timing of the first trimester scan is of importance; if the early scan was performed before 11 weeks’ gestation, anencephaly was significantly less often diagnosed before the mid-trimester scan. This may be due to the fact that ossification of the skull normally occurs at or after 11 weeks of gestation (7). Before that time the fetal brain is still visible and it is only at later stages that, as a result of traumas and bleeding, it progressively degenerates resulting in the typical appearance in the second trimester.

The prevalence of anencephaly in the present study (5.4 per 10,000) is higher than reported by Eurocat (3.7 per 10,000 births) and the Dutch Perinatal Registry (1.3 per 10,000 births). This indicates that cases may not be included in registries if the pregnancy is terminated at a very early stage of pregnancy. In addition, cases may not be classified as anencephaly if there are multiple defects. Our findings support the observation of Johnson et al. that an increasing frequency of prenatal diagnosis and termination of pregnancy have important implications for the interpretation of results from epidemiological studies of birth defects (11).

In present study the percentage of cases where anencephaly was associated with other defects was 25.5% compared to 11%-19% in previous studies (1,5,12). A possible explanation for the higher rate of associated defect is that in the Netherlands all pregnancies where anencephaly is suspected are referred to a fetal medicine unit for an advanced ultrasound scan. Sonographers who perform the advanced scans are experienced in detecting congenital anomalies and they may recognize defects that are otherwise missed.

For the cases where a scan was performed by a sonographer licensed for the 11-14 week scan by the Fetal Medicine Foundation, 86% of the cases were detected before the mid-trimester scan. Sonographers should be instructed that the goal of the first trimester scan is not only to measure nuchal translucency thickness but also to exclude major anomalies. The value of
first trimester screening for major anomalies is that this enables timely diagnosis, providing more and valuable time to consider options at a stage were termination of pregnancy is less traumatic (13). Given the fact that first trimester screening for aneuploidies in the Netherlands is chosen by less than 30% of pregnant women, second trimester screening remains important for the detection of anencephaly.

ACKNOWLEDGEMENTS

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What’s already known about this topic?

- Anencephaly is a fatal neural tube defect which can be detected by ultrasound examination during pregnancy.

What does this study add?

- Early detection of anencephaly requires that scans are performed by sonographers experienced in recognizing fetal anomalies.
- The 20 week anomaly scan remains important for the detection of anencephaly if the uptake of first trimester screening is low.
REFERENCES


