Impact of the 20-week scan
Fleurke-Rozema, Hanneke
Chapter 2

Impact of introduction of mid-trimester scan on pregnancy outcome of open spina bifida in The Netherlands

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ABSTRACT

Objective
To examine the impact of introduction of the mid-trimester scan on pregnancy outcome in cases of open spina bifida in two regions of The Netherlands.

Methods
This was a retrospective cohort study of 190 cases of open spina bifida diagnosed pre- or postnatally, with an estimated date of delivery between 2003 and 2011.

Results
With implementation of the mid-trimester scan the percentage of cases of open spina bifida detected before the 24th week of pregnancy increased from 43% to 88%. The rise in prenatal detection rate was associated with a significant increase in the number of terminated pregnancies and a decrease in the rate of perinatal loss; the percentage of children born alive did not change significantly. In the subgroup that underwent a scan between 18 and 24 weeks of pregnancy, cranial signs were present in 94.4% of cases.

Conclusion
Introduction of the mid-trimester scan has led to an increase in early identification of pregnancies complicated by open spina bifida. Pregnancies previously destined to end in perinatal loss are now terminated whilst pregnancies with a relatively good prognosis are frequently continued; the number of children with open spina bifida who are born alive has not changed significantly. Our study confirms that prenatal diagnosis is usually triggered by visualization of a lemon-shaped skull or a banana-shaped cerebellum.
INTRODUCTION

Open spina bifida (OSB) is a congenital malformation that occurs when the neural tube fails to close. It is well recognized that OSB is a serious condition associated with significant disability and mortality (1–3). Despite the availability of cerebrospinal fluid shunts which were introduced in the 1960s, the mortality rate has remained high and there is a wide range of outcomes in survivors, ranging from mild to severe disability (4,5).

Parents confronted with this condition face the choice between long-term care for a disabled child or termination of pregnancy (6). Prevention of OSB has been an important goal for a long time. The use of periconceptional folic acid, promoted for nearly 20 years, resulted in a reduction but not an elimination of spina bifida (7–9). The incidence of OSB in The Netherlands is currently estimated to be 1 in 2000. Because it is a serious condition and the ultrasound detection rate is high, a mid-trimester scan to allow early prenatal detection was introduced in 2007 in The Netherlands on advice of the Dutch Health Council. Prior to introduction of the mid-trimester scan, only pregnant women with risk factors were offered a mid-trimester scan.

The aim of our study was to assess the impact of introduction of the mid-trimester scan on the pregnancy outcome of OSB with special focus on gestational age at diagnosis and visualization of cranial features.

METHODS

In The Netherlands prenatal screening is organized by regional centers coordinated by eight Academic Centers. Ultrasound clinics performing the mid-trimester scan are affiliated with an academic center to which they refer suspected cases of anomaly for detailed ultrasound examination and further management in a fetal medicine unit. A retrospective cohort study was undertaken in the regions covered by the Foundation for Prenatal Screening, Amsterdam, referring to the Academic Medical Center in Amsterdam (AMC) in the northwest of The Netherlands and the Foundation for Prenatal Screening, Groningen, referring to the University Medical Center of Groningen (UMCG) in the northeast of The Netherlands.

A case list of all pre- and postnatally diagnosed cases of OSB in the catchment areas of the AMC and UMCG was compiled. Cases were included if the estimated date of delivery was between 1 January 2003 and 31 December 2011. Pregnancies were grouped according to estimated date of delivery, rather than actual date of birth, to ensure that terminated pregnancies were included in the year in which delivery would have taken place without intervention.
All fetuses with OSB were included in the study irrespective of presence or absence of additional congenital anomalies. To identify prenatally diagnosed cases, we searched the regional screening databases of the AMC and UMCG in which all detailed scan findings of anomalies are recorded. This provided a case list with information on gestational age at diagnosis, ultrasound findings and pregnancy outcome. The list was complemented with all postnatally diagnosed cases in collaboration with the pediatric spina bifida teams and data from the Dutch division of Eurocat (Eurocat, Northern Netherlands). Eurocat has kept track of congenital malformations in the three most northern provinces since the beginning of the 1980s.

To examine the prevalence of OSB the total number of pregnancies from which the cohort was derived was estimated using data from the screening registry. According to this registry approximately 16 000 (AMC area) and 26 000 (UMCG area) pregnant women were offered a mid-trimester scan each year, providing a denominator of 42 000. To assess the impact of introduction of the mid trimester scan on outcome of pregnancies complicated by OSB, data from the period 2003–2006 were compared with those from 2008–2011. Cases with an estimated date of delivery in the year 2007 were excluded, as this was a transitional year during which many, but not all, women were offered a mid-trimester scan.

Cranial signs associated with OSB were examined in a subgroup of pregnant women who underwent ultrasound examination between 18 and 24 weeks of pregnancy during the period 2008–2011. The first sign of interest was the appearance of scalloping of the parietal bones, producing a lemon-shaped skull. The second sign was posterior and downwards cerebellar displacement resulting in a banana-shaped cerebellum or an empty posterior fossa. The third sign was ventriculomegaly defined by an atrial width of the posterior ventricle of ≥10 mm. The chi-square test was used to examine whether there was a significant change in frequency of diagnosis before 24 weeks’ gestation and in outcome of affected pregnancies. Statistical analyses were made using IBM SPSS Statistics version 20.0 (Armonk, NY, USA). Differences were considered statistically significant if the P value was <0.05.

**RESULTS**

A total of 190 pregnancies complicated by OSB with an estimated date of delivery between 1 January 2003 and 31 December 2011 were registered. Using the estimated denominator of 42 000 pregnancies per year the prevalence of OSB was 5 in 10 000 pregnancies, comparable to 5.1 reported by Eurocat for the three northern provinces of The Netherlands and 5.3 based on data from the Dutch Perinatal Registry10–13.
The percentage of cases in which OSB was diagnosed before the 24th week of pregnancy increased significantly, from 43% before to 88% after introduction of the mid trimester scan (Table 1; P<0.001).

Table 1. Time of diagnosis of open spina bifida and pregnancy outcome in periods before (2003–2006) and after (2008–2011) implementation of the mid-trimester scan in The Netherlands

<table>
<thead>
<tr>
<th>Parameter</th>
<th>2003-2006 (n = 79)</th>
<th>2008-2011 (n = 85)</th>
<th>p *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• &lt; 24 weeks</td>
<td>34 (43)</td>
<td>75 (88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>• ≥ 24 weeks</td>
<td>23 (29)</td>
<td>5 (6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>• At birth</td>
<td>22 (28)</td>
<td>5 (6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• TOP</td>
<td>29 (37)</td>
<td>59 (69)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>• PND</td>
<td>24 (30)</td>
<td>6 (7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>• Alive</td>
<td>26 (33)</td>
<td>20 (24)</td>
<td>0.181</td>
</tr>
</tbody>
</table>

Data are given as n (%). TOP = termination of pregnancy; PND = Perinatal death; Intrauterine death and death before 28 days after birth.

*Comparison between patient groups before and after introduction of the mid-trimester scan.

Earlier diagnosis was associated with a significant increase in the percentage of elective terminations of pregnancy, from 37% to 69% (P<0.001). The increase in elective terminations in cases of suspected poor prognosis resulted in a significant decrease in perinatal death, from 30% to 7% (P<0.001). The percentage of children who survived the neonatal period between 2008 and 2011 was not significantly different from that between 2003 and 2006 (P=0.181).

Analysis of data from the subgroup of cases of OSB diagnosed after introduction of the mid-trimester scan demonstrated that 79/85 (92.9%) women opted for a scan before 24 weeks’ gestation. In 75/79 cases (94.9%) OSB was visualized. The four remaining cases showed no cranial signs at mid-trimester scan and diagnosis was made later in pregnancy (n=3) or at birth (n=1). In the group that did not opt for a mid-trimester scan (n=6) OSB was diagnosed late in pregnancy (n=2) or at birth (n=4).

To examine regional differences, data concerning pregnancy outcome of OSB in the AMC and UMCG areas are summarized in Table 2. Before introduction of the mid-trimester scan 65% of OSB cases in the AMC area were detected before the 24th week of gestation, compared to 32% in the UMCG area. In the AMC area detection of OSB rose to 97% and in the UMCG area to 82%. In the AMC area 96% of women participated in the mid-trimester scan, compared to 90% in the UMCG area. Following implementation of the mid-trimester scan, among cases
diagnosed before 24 weeks’ gestation, 76% (32/42) of women in the UMCG area and 82% (27/33) in the AMC area opted for termination of pregnancy.

Of the 79 women who underwent a scan before 24 weeks’ gestation, eight cases of OSB were diagnosed before 18 weeks. In 67/71 women (94.4%) who underwent an ultrasound scan between 18 and 24 weeks of pregnancy one or more cranial markers were registered (Table 3).

In four cases no markers were recorded. In one case cranial signs may have been present but were not registered since the pregnancy was complicated by multiple congenital anomalies and the parents opted for termination. In a second case there was no ventriculomegaly at mid-trimester scan but rapid progression of hydrocephaly was reported later and resulted in neonatal death. Another case was diagnosed at 21 weeks’ gestation because of isolated spinal abnormalities. This case as well as the remaining case of OSB without apparent cranial signs had small and low defects not affecting motor function of the lower limbs; both of these children are able to walk.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>UMCG area (n = 104)</th>
<th>AMC area (n = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dx &lt; 24 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOP</td>
<td>14 (26)</td>
<td>27 (79)</td>
</tr>
<tr>
<td>PND</td>
<td>1 (2)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Alive</td>
<td>2 (4)</td>
<td>4 (12)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>17 (32)</td>
<td>33 (97)</td>
</tr>
<tr>
<td>Dx &gt; 24 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOP</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PND</td>
<td>9 (17)^a</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Alive</td>
<td>9 (17)</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal</td>
<td>18 (34)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Dx at birth</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PND</td>
<td>7 (13)^a</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Alive</td>
<td>11 (21)</td>
<td>3 (12)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>18 (34)</td>
<td>4 (16)</td>
</tr>
<tr>
<td>Total</td>
<td>53 (100)</td>
<td>34 (100)</td>
</tr>
</tbody>
</table>

Data are given as n (%). Dx = diagnosis, TOP = termination of pregnancy, PND = Perinatal death; Intrauterine death and death before 28 days after birth.

^aIncluding one case of euthanasia. ^Pregnancy was terminated abroad where regulation concerning termination of pregnancy after 24 weeks differed from that in the Netherlands.
Table 3. Cranial signs facilitating prenatal diagnosis of open spina bifida in the subgroup that underwent ultrasound examination at 18–24 weeks of gestation, in comparison with previously reported data

<table>
<thead>
<tr>
<th>Sonographic sign</th>
<th>Present study (n=71)</th>
<th>Ghi et al.(^{17}) (n = 53)</th>
<th>Van den Hof et al.(^{18}) (n = 130)</th>
<th>D’Addario et al.(^{19}) (n = 49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lemon-shaped skull</td>
<td>80</td>
<td>100</td>
<td>98</td>
<td>53</td>
</tr>
<tr>
<td>Banana-shaped or absent cerebellum</td>
<td>73</td>
<td>100</td>
<td>72</td>
<td>96</td>
</tr>
<tr>
<td>Ventriculomegaly</td>
<td>58</td>
<td>64</td>
<td>-</td>
<td>81</td>
</tr>
<tr>
<td>Any of these features</td>
<td>94</td>
<td>100</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Data are given as %.

DISCUSSION

The first aim of this study was to assess the impact of introduction of the mid-trimester scan on the pregnancy outcome of OSB. Of all OSB cases for which a mid-gestational scan was performed, 94% were diagnosed before 24 weeks’ gestation which is the legal limit for termination of pregnancy in The Netherlands. The overall effect of timely diagnosis was associated with a significant decrease in perinatal mortality whilst the live birth rate did not change significantly. These findings indicate that multidisciplinary teams of perinatal experts are able to identify pregnancies destined to end in perinatal death and that, in these cases parents frequently opt for termination of pregnancy. The high detection rate of 94% is in line with the target set in the report of the Health Council of The Netherlands in 2007 (14).

Overall our findings confirm that ultrasound is an effective tool for detecting neural tube defects prenatally. Cranial signs, which often trigger suspicion of spinal defects, were present in 94.4% of the subgroup that underwent a scan between 18 and 24 weeks of pregnancy. These findings confirm observations of previous studies that reported the presence of one or more cranial markers in almost all affected pregnancies (15–19).

Our observed rate of cerebellar displacement was similar to that reported by van den Hof et al. (18) (73% compared to 72%). In contrast, the occurrence of a lemon-shaped skull (80%) and ventriculomegaly (58%) was lower than that reported in other studies: 98% for lemon-shaped skull as reported by van den Hof et al. (18); 100% for lemon-shaped skull and 64.2% for ventriculomegaly as reported by Ghi et al. (17); 81% for ventriculomegaly as reported by D’Addario et al. (19). The finding of a lower rate of ventriculomegaly and a higher rate of lemon-shaped skull in comparison to the study by D’Addario et al. (19) may be due to the fact that in our study gestational age ranged from 18 to 24 weeks, whilst in the study by D’Addario et al. (19) it ranged from 18 to 28 weeks. With progression of gestation the lemon sign disappears and the rate of ventriculomegaly increases.
When we compiled the dataset for our study we noted that details on cranial signs were not always recorded in the screening database, although they are described in the referral letter and at subsequent diagnostic ultrasound examination. This indicates that the mid-trimester scan is occasionally cut short upon finding a possible serious congenital defect after which women are referred immediately to a tertiary-care center. For monitoring purposes it is recommended that sonographers are made aware of the importance of recording the presence or absence of cranial signs to allow prospective monitoring of the predictive value.

Implementation of the mid-trimester scan was associated with a significant increase in cases in which OSB was diagnosed before 24 weeks’ gestation. In approximately 79% of these cases parents opted for termination of the pregnancy. These findings are comparable to those of a study by Boyd et al. which covered several European countries and showed that on average 89% of pregnancies complicated by neural tube defects are terminated (20). In contrast to reported uptake of first-trimester Down syndrome screening, participation in second-trimester screening for structural anomalies was not significantly different in the AMC and UMCG areas (21). This suggests that in The Netherlands parents are more concerned by structural anomalies than by Down syndrome.

According to our data the prevalence of OSB is 1 in 2000. This figure is in keeping with data reported by Eurocat and the Dutch Perinatal Registry. Small differences between reported prevalences may be due to differences in registration area, in in- or exclusion of cases with associated anomalies and in grouping strategy based on the date of diagnosis or estimated date of delivery.

The strength of this study is that the combination of data from several sources allowed for true population based statistics. The only affected pregnancies that may have been overlooked are those that ended in early spontaneous miscarriage before OSB was diagnosed and those in which the pregnant women opted for pregnancy care outside the study’s catchment area. Because the national screening program was introduced quite recently and relatively quickly (during 2007) The Netherlands is an ideal country in which to study the impact of the mid-trimester scan.

To summarize, introduction of the mid-trimester scan has led to increased rates of early identification of pregnancies complicated by OSB. Pregnancies previously destined to end in perinatal loss are now terminated whilst pregnancies with a relatively good prognosis are frequently continued; the number of children with OSB who are born alive has not changed significantly. Our study confirms that prenatal diagnosis is usually triggered by visualization of a lemon-shaped skull or a banana-shaped cerebellum.
ACKNOWLEDGMENTS

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REFERENCES


