ORIGINAL ARTICLE

THE INCIDENCE AND MATERNAL AGE DISTRIBUTION OF ABDOMINAL WALL DEFECTS IN NORWAY AND ARKHANGELSKAJA OBLAST IN RUSSIA

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ABSTRACT

Objectives. To determine the foetal incidence of isolated anterior abdominal wall defects (gastroschisis and omphalocele) in the Arkhangelskaja Oblast (AO) in Russia and in Norway, as well as to study the maternal-age distribution of these defects.

Study Design. A register-based incidence study.

Methods. All registered foetuses and newborns with at least 12 weeks of gestation in the populations of AO (141,159) and Norway (293,708) were included. The data covered the period 1995–2004 in AO and 1999–2003 in Norway and were obtained from the malformation register in AO and the Medical Birth Registry of Norway.

Results. The majority of the outcomes with a defect were liveborn in Norway (65%), while in AO the majority were spontaneously or medically aborted (59%). The incidence of anterior abdominal wall defects was 5.4/10,000 (95% confidence limits: ±1.7) in AO and 5.1/10,000 (±0.8) in Norway, and the ratio of omphalocele to gastroschisis was 1.2 in AO vs. 0.9 in Norway. Gastroschisis was inversely associated with maternal age in Norway.

Conclusions. Despite a difference in maternal age distribution, there was no difference in the incidence of abdominal wall defects in AO and Norway. Gastroschisis was associated with young maternal age only in Norway, and the higher incidence in maternal age groups younger than 25 warrants further studies about aetiological factors associated with young maternal age.

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Keywords: birth defects, gastroschisis, maternal age, Norway, omphalocele, Russia
INTRODUCTION

Congenital defects continue to be a pressing challenge in both the paediatric and general health fields. These children eventually comprise a major part of the overall indicators concerning children’s health, such as disability, mortality, morbidity and hospitalization. The emphasis in prophylactic work for defects should be based on knowledge about the prevalence and distribution of newborn malformations in a population. Such knowledge is achieved through systematic population-based registration of information about all newborns and aborted foetuses, and by including information about the women who carry them.

Data on the prevalence of birth defects have mainly been provided by high-income countries, while more than 94% of all infants with a defect are born in middle- and low-income countries (1). In Russia, a middle-income country, systematic population-based computerized registration of all deliveries has been lacking, which has hampered the possibility for epidemiological studies concerning birth defects there. However, by 2006, 34 regions had put into place a computer program for population-based registration of newborns and foetuses with defects (2), but there have not been any published studies concerning the incidence or prevalence of severe congenital malformations in the northern regions of Russia.

Severe defects with a relatively high incidence include those of the abdominal wall, of which omphalocele and gastroschisis are the main and most common categories. The 2 have similar appearances, but are different defects. In omphalocele, the intestines and/or liver herniates into the proximal part of the intact umbilical cord. It evolves in the tenth week of gestation if the intestines fail to return to the abdominal cavity. In gastroschisis, the intestine herniates through a split in the abdominal wall due to an incomplete closure of the lateral body folds when the wall is formed during the fourth week of development (3). An association between these defects and stillbirth/spontaneous abortion has been reported (4,5), but most of the affected liveborn survive (6). The aetiology and incidence of these 2 defects differ (7); for gastroschisis, teratogens are implicated (8), whereas foetuses with omphalocele also tend to have other anomalies and abnormalities (4,5). A previous study of gastroschisis in Norway reported an increasing incidence at birth in the period 1967–1998 (9). There have been no internationally published studies concerning abdominal wall defects in north-west Russia.

The aim of this study was to determine the incidence of isolated anterior abdominal wall defects (gastroschisis and omphalocele) in the foetal and newborn populations of the AO (including Nenets Avtonomnyj Okrug) and Norway, and to study the maternal age distribution of these congenital defects.

MATERIAL AND METHODS

Both the AO and Norway are located in northern Europe, with most of their territories north of the 60th parallel. In 2003, the population in AO was 1.3 million, and in Norway 4.5 million. AO has a lower population density and more medical doctors per capita than Norway. Further details are presented elsewhere (10).

In Norway, it has been obligatory to submit a standard report about all newborns and abortions with at least 12 weeks gestation to
the national population-based birth registry since December 1998. Before that, medical abortions (granted elective terminations of pregnancy later than week 12 of gestation) were not reported to the registry. The Norwegian registry receives information about birth defects diagnosed up to one week after birth. Details about the data collection and registration in Norway have been described elsewhere (11,12). Termination of pregnancy beyond week 12 needed approval by a special committee. The further the gestation beyond week 12, the weightier the reasons for termination needed to be. According to the law, terminations were only granted after week 18 when the mother’s life was in danger or the foetus’ condition was not compatible with life (13). All pregnant women were offered one routine ultrasound examination, usually in week 18, but individual obstetricians may have had routines for doing this earlier. A medical abortion was rarely granted because of a detected gastroschisis and omphalocele.

In AO, pregnant women were examined by ultrasound in or around weeks 10 and 20 of pregnancy. When omphalocele or gastroschisis was evident, the women were informed by a specialist and could choose to terminate the pregnancy, but no later than week 22 of the pregnancy. There is no population-based birth registry in AO, but statistics about the total number of births, stillbirths and abortions are compiled by the AO Medical Information and Analytic Centre, which provided such data for this study. Since 1995, AO has had a system for collecting data about birth defects, birth rate and perinatal and infant mortality, and has since 1998 participated in a monitoring program based on legislative orders by the Federal Ministry of Health that includes compulsory notification and registration of congenital defects. A software program called Monitoring 2.5 was distributed for the purpose of registration and reports (2). The notification for registration was designed according to directions by the International Clearinghouse for Birth Defects (ICBD), but with adaptations to local conditions. The program has been connected to the federal population-based genetic register, which was focused on inherited diseases and anomalies (2,14). As a part of the above program, a regional registry of congenital defects was established in Moscow in 1999, and it became a member of the ICBD in 2001 (15).

In AO, all live newborns with severe defects were transferred to the main regional children’s hospital, which is located in the central city. Medical abortions were carried out in all larger hospitals. The central hospital received a report from the regional delivery clinics within AO about each malformed stillborn who had at least 12 weeks gestation, and there has been a systematic registration of newborns and medical abortuses with defects and/or anomalies. The following data were registered about each case: birth/abortion date; weight; alive/not alive; whether multiple delivery; diagnosis; gender; gestational age; place of delivery; and the mother’s age, parity and place of residence at the time of delivery. Spontaneous abortuses with defects were registered by the Centre of Medical Genetics.

In Russia, very pre-term newborns (gestational age <28 weeks, birth weight <1,000 grams, or length <35 cm) had to survive for 7 days before they were defined as live born. If death occurred before classification, they were counted and noted as spontaneous abortions. Details about Russian definitions and regula-
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tions concerning pregnancy termination and outcome have been described elsewhere (16).

The study population included all liveborn and stillborn infants, as well as foetuses that were aborted spontaneously or due to terminations after at least 12 weeks’ gestation. Data from the period 1995–2004 in AO were obtained from the P.G. Vyžletsova Clinical Children’s Hospital and the Centre of Medical Genetics in Arkhangelsk, while the data from Norway covered the period 1999–2003. The grouped data provided by the Medical Birth Registry of Norway for the study contained the frequencies of gastroschisis and omphalocele stratified by year and maternal age group within the pregnancy outcome categories medical abortions, live births and stillbirths (including spontaneous abortions with ≥12 weeks of gestation). The total number of pregnancy outcomes in the population in each of the strata was also given. In the present study, an induced termination after 12–27 weeks gestation was defined as a medical abortion, while births without life in this period were classified as spontaneous abortions. A stillbirth had at least 28 weeks of gestation. Newborns and foetuses registered with associated defects and chromosomal abnormalities were not included in the obtained frequencies of gastroschisis and omphalocele, which we have denoted with the term “isolated.” The study was approved by the Health Administration and the Clinical Hospital for Children in AO and Folkehelseinstituttet in Norway.

The analyses included the defect-specific incidence overall and in each maternal age group in the 2 populations; Wald confidence limits were used. If the maternal age was unknown, the cases were excluded in the age group-specific analyses. The incidence was estimated by dividing the number of foetuses/infants with gastroschisis or omphalocele (without any concurrent anomaly) in an age group by the total number of medical abortions, spontaneous abortions, stillbirths and live births in the same time period in the age group.

RESULTS

The study populations included 141,159 pregnancy outcomes in AO and 293,708 in Norway. There were a total of 76 (5.4 /10,000) (95% confidence limits: ±1.7) with the studied defects in AO and 150 (5.1 [±0.8]/10,000) in Norway. In Norway, 65% of abdominal wall cases were live-births, compared to 38% in AO. As presented in Table I, the majority of the foetuses with omphalocele (59%) and gastroschisis (60 %) in AO were medical or spontaneous abortuses (the obtained AO data did not provide for presenting medical and spontaneous abortuses separately). Information about pregnancy outcome was missing for 2 cases (3.0%) in Norway and for none in AO.

There was no defect-specific difference in incidence between the 2 populations, but the ratio of omphalocele to gastroschisis was 1.17 in AO and 0.92 in Norway. The delivering women in Norway were older than in AO. Forty-one percent in AO were in the age group 0–4, while the largest group in Norway was 25–29 years old (34.3%) (Fig. 1). Data about maternal age were missing for 113 subjects (0.04%) (59% of these were live births) in Norway and 133 (0.1%) in AO. The incidence of abdominal wall defects was associated with age group in Norway only, mainly due to an inverse association with gastroschisis (p<0.0001). Details about the age-group specific incidence are presented in Table II.
Table I. Frequency of anterior abdominal wall defects in Norway and the Arkhangelskaja Oblast based on pregnancy outcome.

| Defect      | Norway | Arkhangelskaja Oblast |
|-------------|--------|-----------------------|
|             | Live birth | Stillbirth | Abortion | Unknown | Live birth | Stillbirth | Abortion |
| Omphalocele | 38      | 53.5       | 3        | 4.2     | 30        | 42.2       | 0        | 0.0      | 16       | 39.0      | 1        | 2.4      | 24       | 58.6 |
| Gastroschisis| 59     | 74.7       | 2        | 2.5     | 16        | 20.3       | 2        | 2.5     | 13       | 37.7      | 1        | 2.9      | 21       | 60.0 |
| Total       | 97     | 64.7       | 5        | 3.3     | 46        | 30.7       | 2        | 1.3    | 29       | 38.2      | 2        | 2.6      | 45       | 59.2 |

a Live births constituted 98.3 % of the study population. 
b ≥ 28 weeks of gestation. 
c Include medical and spontaneous abortions with 12–27 weeks of gestation. 
d Live births constituted 92.8 % of the study population.

Figure 1. Maternal age distribution of the study population in the Arkhangelskaja Oblast (AO) and Norway.

The maternal age was unknown for 113 (0.04%) in Norway and 133 (0.1%) in AO.

Table II. Total and age-group specific incidence (95% confidence interval) of anterior abdominal wall defects per 10,000 abortuses and newborns in Norway and the Arkhangelskaja Oblast (AO).

| Age group | Gastrochisis | Omphalocele |
|-----------|--------------|-------------|
|           | Norway       | Oblast      | Norway       | Oblast      |
| <20       | 9.2 (±6.8)   | 3.9 (±4.4)  | 1.4 (±1.6)   | 2.4 (±2.1)  |
| 20–24     | 7.0 (±2.5)   | 3.2 (±1.6)  | 2.7 (±1.3)   | 3.6 (±1.5)  |
| 25–29     | 2.1 (±0.9)   | 2.1 (±0.9)  | 2.2 (±1.5)   | 1.7 (±1.3)  |
| 30–34     | 1.7 (±0.8)   | 1.7 (±0.8)  | 2.9 (±2.5)   | 1.2 (±1.6)  |
| ≥35       | 0.9 (±0.5)   | 3.8 (±1.8)  | 2.3 (±3.2)   | 4.7 (±4.6)  |
| Total     | 2.7 (±0.6)   | 2.4 (±0.6)  | 2.5 (±0.8)   | 2.9 (±0.9)  |

a Medical and spontaneous with ≥12 weeks of gestation. 
b In AO, information about maternal age was missing for 1 case of gastrochisis and 1 case of omphalocele. Hence, these cases were not included in the age-group specific rates.
DISCUSSION

An association between young maternal age and gastroschisis has also been observed in Norway for births previous to the time period of births in this study (9,17). Kazaura et al. (2004) also reported an increasing prevalence over time in the period 1967–1998, and an incidence at birth in the period 1995–1998 that was similar, both in total and across age groups, to what we found in the subsequent 5-year period (9). Thus, our findings showed that the prevalence of gastroschisis in Norway has remained high. An association with young maternal age has also been reported elsewhere (5,18–22), and the trend across age groups in the United States reported by Reefhuis and Honein (2004) was very comparable to the findings in the Norwegian population (20). The data obtained for our study were age-group specific, therefore the association with maternal age could not be analysed in more detail. The age group distribution (Fig. 1) showed that the average maternal age in AO was several years younger than in Norway, which was in accordance with that reported from a neighbouring region of AO in Russia (16). The age distributions within each age group were then also likely different in the 2 populations, with a younger age group-specific mean in AO in the youngest and oldest age groups.

The absence of such a trend in AO is an interesting finding. For misclassification of gastroschisis as omphalocele to be the explanation, the misclassification needs to have been relatively prevalent and associated with maternal age. This is not likely, and it would also imply that the true incidence of gastroschisis was very high and the incidence of omphalocele comparatively low. Thus, the risk factors for gastroschisis associated with young maternal age in Norway were not apparent in the incidence distribution in AO, but the age-group specific estimates for AO should be interpreted with care due to small numbers in the youngest and oldest age groups.

Some of the reports of a higher incidence of gastroschisis in the youngest maternal age groups have found an association with life-style factors, such as a more widespread use of different vasoactive agents, including smoking and drug abuse (5,23). Since the prevalence of gastroschisis has increased over time, Kazaura et al. suggested that the explanatory factor has not been introduced recently. Smoking has been relatively common amongst fertile Norwegian women, also during pregnancy, and especially amongst the youngest (24). However, in AO the age group-specific incidence of gastroschisis did not reflect the pattern of increasing prevalence of smoking amongst young women in Russia during the last decade (25,26).

Our investigation lacked the possibility to study factors associated with maternal age and the risk of the studied outcomes. Only the data registered in Norway contain comprehensive information about all deliveries and medical abortions, thus making future studies concerning the effects of multiple maternal factors possible. For the objectives of the present study, however, only stratified frequency data were requested.

A higher maternal age associated with omphalocele than with gastroschisis, as we found in Norway, has also been reported by other studies (4,9,18,19,21). In terms of
omphalocele, an implication of teratogens has not been conclusively reported, and isolated cases have been considered sporadic (7). When the risk of omphalocele has been associated with increasing maternal age, it has been related to a concurrent presence of certain chromosomal and genetic syndromes and other anomalies, just like the recurrence risk (5,7). The only vaguely apparent association with maternal age group in our 2 study populations was a slight U-shaped distribution, which was also reported by Kazaura et al. This fell in line with that reported by Reefhuis and Honein about an elevated risk of omphalocele in the age group 14–19 compared with the age group 25–29 (adjusted for parity) (20).

The ratio of omphalocele to gastroschisis appeared to be higher in AO than in Norway, but not as high as in EUROCAT (1.35) (27,28). Still, this finding was unexpected, considering the relatively young pregnant population in AO compared to in Norway. Misclassifications of gastroschisis as omphalocele in AO could be an explanation for the ratio difference (17,18). Since our study only included cases registered as isolated, under-diagnosing of anomalies co-occurring with omphalocele, such as heart defects (4), could also be an explanation. In central Norway, a study concerning prenatal diagnosis in the specialized National Centre for Foetal Medicine had a 100% detection rate and accuracy concerning gastroschisis at 17–20 gestational weeks (29), but this was presumably not the case in all maternity centres, and diagnostic misclassification has been reported in Norway (9). The inverse ratio in Norway evolved in the 1990s due to an increase in the prevalence of gastroschisis, while the prevalence of omphalocele did not change over time (9).

The mentioned systematic cultural differences in prenatal diagnosis routines and propensities to terminate a pregnancy confirm the importance of including abortuses in a study. Thus, it was a strength of our study that information about induced and spontaneous abortions from as early as 12 weeks’ gestation was available. Reported studies concerning severe birth defects in relation to maternal age usually did not include spontaneous abortuses with less than 20 or 24 weeks’ gestation (5,19,20,27,28); they only included medically induced abortuses (30), or abortuses were not included at all (18). Earlier studies of these defects in Norway did not include medical abortions and spontaneous abortuses with 12–16 weeks’ gestation (9,17,31). Such abortions were included in the registration of pregnancy outcomes in Norway from December 1998. We did not include Norwegian data for 2004 since the registration of abortions in 2004 was still in progress when the data were released to our study in December 2005 (Nilssen S, personal communication).

The Norwegian registration of births and abortuses was considered complete for the years 1999–2002 and almost complete for 2003 (Nilssen S, personal communication). However, as in AO, the completeness of ascertainment and reporting of infants and abortuses with the 2 defects has not been assessed (9). It is probable that some cases in AO are missing from 1995, when the registration was started. The registration of spontaneous abortuses has been less systematic than that of newborns and medical abortuses in both populations, and therefore
likely more under-ascertained. Although it is likely that the incidence in the 2 populations was underestimated, the observed associations with age group were not likely to have been influenced. In addition to an incomplete reporting of medical and spontaneous abortuses with defects, the probability of being prenatally diagnosed or aborting spontaneously must then have been related to maternal age.

In summary, the incidence of anterior abdominal wall defects was not different in Norway and AO, but the differences in proportional distribution of the defects in terms of maternal age, maternal age distribution, proportions of cases that were born alive, and in opportunity to terminate a pregnancy after a prenatal diagnosis inevitably contribute to differences between AO and Norway in perinatal and infant mortality, and the burden of abdominal wall defects on the health care systems.

In conclusion, this study revealed that the incidence of anterior abdominal wall defects was similar amongst foetuses in a northern population of Russia and in Norway, but the ratio of omphalocele to gastroschisis was lower in Norway. The incidence of gastroschisis was inversely associated with maternal age only in Norway. The high incidence in the maternal age groups younger than 25 warrants further studies about risk factors mediated by young maternal age in Norway.

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