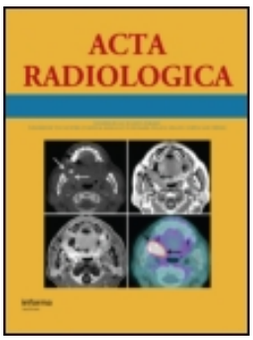

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Antenatal Ultrasound and Postnatal Autopsy Findings in Terminations after 12 Weeks' Gestation due to Fetal Abnormality: Population-Based Study in Western Norway, 1988–2002

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Background: Ultrasound screening has been part of antenatal care for several decades, and warrants high expertise to meet the criteria for a worthwhile screening program. In particular, the rate of false positives should be low.
Purpose: To examine time trends of pregnancy terminations for fetal abnormality after 12 weeks' gestation, and to assess the agreement between antenatal ultrasound and post-termination autopsy findings for the main pathologies leading to termination.
Material and Methods: During the period 1988 to 2002, 198 pregnancies were terminated for fetal abnormality after 12 weeks' gestation. We reviewed the case notes for those 151 who were autopsied (male/female/undetermined = 91/56/4). Annual rates of live births and stillbirths were retrieved from the Medical Birth Registry of Norway.
Results: Antenatal ultrasound provided a correct diagnosis of the major abnormality in 149/151 cases (99%), based on post-termination autopsy findings. The annual rate of terminations after 12 weeks' gestation varied between 0.6 and 3.4 (mean 1.8) per 1000 live births, with a trend toward higher rates over the study period ($P = 0.001$, chi-square test for linear-by-linear association).
Conclusion: The specificity of antenatal ultrasound for major abnormalities was high, as compared to postnatal autopsy findings. The mean annual rates of termination after 12 weeks' gestation tended to increase over the 14-year study period.

Key words: Abnormalities; antenatal; autopsy; ultrasound; screening; termination

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Antenatal diagnostic procedures and pregnancy termination are controversial. National legislation and the attitudes of health professionals differ within and between countries (1). When mid-trimester ultrasound was introduced in the early 1980s, the primary aims were to 1) to refine term dating, 2) to detect multiple pregnancies, and 3) to determine placental site. Technical improvements have enabled clinicians to visualize the fetus earlier and in greater detail. Several medical conditions, both lethal and non-lethal, can now be detected as early as 10–12 weeks (2, 3). Thus, in practice, the indications for antenatal ultrasound have changed to also include screening for fetal abnormality (4). Approximately 94% of all pregnant women in Norway attend ultrasound screening (midwife, obstetrician, or both) at around 18 weeks' gestation (5). Norway legalized termination by choice in the first 12 gestational weeks in 1978. After 12 weeks, approval by a committee of medical and law

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professionals is mandatory. Approval is generally granted in cases of lethal fetal abnormality or serious handicap, severe maternal disease, or grave social circumstances.

Up until 1999, the Medical Birth Registry of Norway did not collect data on the indications for termination for fetal abnormality (6). We therefore aimed at assessing indications as well as time trends for such terminations in a population-based cohort. Secondly, we examined the agreement between antenatal ultrasound and autopsy findings for the main pathologies leading to termination.

Material and Methods

This was a retrospective case-note study. Data protection and ethical approval of the study was obtained prior to data collection.

During the period 1988 to 2002, 198 fetuses from mothers residing in two counties (Hordaland and Sogn og Fjordane, population approximately 600,000), for which our institution was the sole referral center in cases of termination for fetal abnormality, were terminated due to antenatal diagnostics at Haukeland University Hospital. Decisions were based on an extended ultrasound examination by one of three experienced obstetricians, amniocentesis, or specific intrauterine blood tests, as appropriate. Because of a rigid referral practice and no private healthcare providers in the above-mentioned regions, the study group was considered population based.

An autopsy, including a skeletal survey, was part of the routine postnatal diagnostic workup, whilst chromosomal analyses were performed when indicated.

We reviewed the case notes, including the autopsy reports, for those 151 who had an autopsy performed. Data on gender, gestational age, and indication for termination were collected from specific departmental notes held for all the terminations performed for fetal abnormality throughout the study period. Additional data were retrieved from the case notes whenever needed.

The annual rates of live and stillbirths in the counties of Hordaland and Sogn og Fjordane were retrieved from the Medical Birth Registry of Norway. Differences in annual rates of late terminations were examined using a chi-square test for linear-by-linear association. P values less than 0.05 were considered statistically significant. All reported P values are two tailed. The statistical analyses were performed using the program SPSS (version 14; SPSS, Inc., Chicago, Ill., USA).

Results

One hundred ninety-eight fetuses (male/female/undetermined sex = 117/67/14) were terminated based on antenatal findings. Gestational age ranged from 13 to 29 weeks (mean 18.6 weeks), with only two fetuses being older than 24 weeks' gestation (27 and 29 weeks, respectively). Maternal age ranged between 16 and 45 years (mean 30.7 years). In 154/198 cases (77.8%), the medical decision was based on ultrasound findings alone, in 40 cases (20.2%) on amniocentesis alone, and in two cases (1.0%) a combination of ultrasound and amniocentesis or other chromosomal analysis was necessary. One pregnancy was terminated due to maternal high-dose epilepsy medication and one due to fetal mucopolysaccharidosis type II (Hunter's disease) diagnosed on intrauterine blood testing due to a family history. The terminations were based on abnormalities involving the central nervous (CNS; $n = 75$), musculoskeletal ($n = 20$), urogenital ($n = 17$), or the cardiovascular ($n = 6$) systems, whilst 54 were terminated due to chromosomal aberrations and 21 due to a variety of other diagnoses, including hydrops fetalis, omphalocele, hypoplastic lungs, VATER syndrome, growth retardation, and Meckel-Gruber syndrome.

The most common indications for termination were anencephaly (37 fetuses; 18.7%) (Fig. 1), trisomy 21 ($n = 32$; 16.2%), and severe myelomeningocele ($n = 16$; 8.1%). The remaining diagnoses were seen in numbers varying from eight to one.

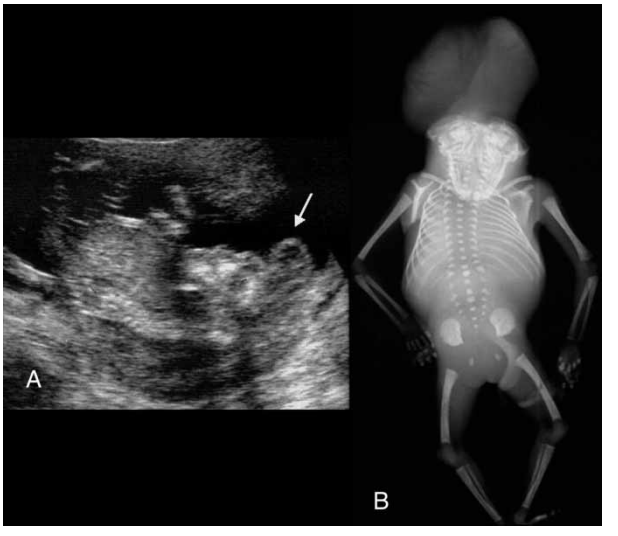

Fig. 1. Anencephaly in a fetus at 16 weeks' gestation, diagnosed on antenatal ultrasound, shows an absent cranium (A, short arrow) and otherwise unremarkable findings. The diagnosis was verified on a postmortem skeletal survey (B).

Table 1. Total numbers of births, terminations up to and including the 12th week of gestation (data from the Medical Birth Registry of Norway), and numbers of terminations following 12 weeks' gestation (study data) in two counties in western Norway (Hordaland and Sogn og Fjordane) during the years 1988–2002.

Year	Total no. of births (live and still)	Terminations ≤12 weeks' gestation (per 1000 births)	Terminations >12 weeks' gestation (per 1000 births)	Autopsied terminations >12 weeks' gestation
1988	7535	1595 (211.6)	11 (1.5)	8
1989	7892	1589 (202.5)	5 (0.6)	5
1990	7971	1588 (199.2)	18 (2.3)	17
1991	8061	1547 (191.9)	10 (1.2)	9
1992	7771	1427 (183.6)	11 (1.4)	10
1993	7802	1452 (186.1)	14 (1.8)	11
1994	8043	1376 (171.5)	16 (2.0)	11
1995	7787	1342 (172.3)	9 (1.2)	9
1996	8046	1443 (179.3)	16 (2.0)	15
1997	7629	1351 (177.1)	15 (2.0)	12
1998	7483	1378 (184.2)	11 (1.5)	8
1999	7505	1466 (195.3)	16 (2.1)	7
2000	7772	1466 (188.6)	21 (2.7)	15
2001	7319	1412 (192.9)	25 (3.4)	14
Total	108616	20412 (187.9)	198 (1.8)	151

The annual rates of late terminations varied between 0.6 and 3.4 per 1000 (mean 1.8) (Table 1), with a trend toward increasing rates throughout the period ($P = 0.001$, chi-square test for linear-by-linear association).

One hundred fifty-one of the 198 fetuses were autopsied (male/female/undetermined sex = 91/56/4). Table 2 lists the 35 major diagnoses identified on postmortem examinations as well as the antenatal diagnosis. Full agreement was reached for all fetuses, with major disorders affecting the CNS, the urogenital, and the cardiovascular systems. Most fetuses with severe musculoskeletal disorders had descriptive, nonspecific antenatal diagnoses such as short, bent long bones, narrow chest, fixed flexion, and fractures. One case of osteogenesis imperfecta type II was correctly diagnosed on ultrasound. Thanatophoric dysplasia in two fetuses and chondroectodermal dysplasia in one fetus were suggested by ultrasound and confirmed postmortem. In all fetuses with skeletal dysplasia, postnatal radiography provided a final specific diagnosis (Table 2).

Additional autopsy findings were demonstrated in 29 of the 151 fetuses (19%), of which the following were seen in two or more cases: limb deformities (nine cases), ventricular septal defect (VSD; seven cases), horseshoe kidney (four cases), cleft palate (four cases), pulmonary hypoplasia (four cases), adrenal hypoplasia (two cases), esophageal atresia (two cases), anal atresia (two cases), and absent ears (two cases) (Table 3). Gastroschisis was missed in one fetus with bilateral renal agenesis.

In one fetus terminated at 16 weeks' gestation because of possible damage due to anti-epilepsy medication, no pathological findings were found on ultrasound, radiography, or postmortem examinations.

Discussion

The agreement between ante- and postnatal fetal diagnosis in this study was high for major abnormalities leading to termination. The detection of additional, minor pathologies was less accurate, but would not have influenced the decision to terminate. The rates of induced abortions after 12 weeks due to prenatal diagnostics varied between 0.6 and 3.4 per 1000 births, with increasing rates toward the end of the study period. Although the figures should be read with some caution due to the retrospective nature of the data set, routines for referrals and registration of the patients remained unchanged throughout the period, reducing the risk for selection bias. Except for a few women who preferred to have their terminations performed outside the two counties under surveillance, and the possibility of erroneous registration of patients within both the hospital information system and the special departmental lists administrated by the midwives, the data set is likely to represent a population-based survey. Unfortunately, autopsy was undertaken in only 76% of the fetuses, leaving 151 for a detailed comparison between antenatal ultrasound and postnatal autopsy. The reduced autopsy rate was due to difficulties in internal hospital routines as well as non-consenting parents. However, since full agreement between ante- and postnatal diagnosis was reached for almost all of the

Table 2. Agreement between antenatal and postmortem main diagnosis for 151 fetuses terminated after 12 gestational weeks

Postmortem diagnoses (based on radiological and autopsy findings)	Number (% of total)	Concordance between prenatal and postnatal diagnosis (number of cases)
1. *Central nervous system*	*58 (38.2%)*	
Anencephaly	29	29
Myelomeningocele	14	14
Arnold-Chiari malformation	7	7
Dandy-Walker malformation	6	6
Severe congenital hydrocephalus	2	2
2. *Musculoskeletal*	*18 (11.8%)*	
Osteocartilaginous dysplasias (13):		
Thanatophoric dysplasia	5	2*
Osteogenesis imperfecta type II	3	1 certain, 2*
Achondrogenesis	2	2*
Asphyxiating thoracic dysplasia		1*
Chondroectodermal dysplasia	1	1*
Skeletal dysplasia, type Rosendahl	1	1*
Other musculoskeletal (5):		
Arthrogryposis multiplex congenita	3	3*
Lethal multiple pterygium syndrome	1	1*
Sirenomyelia (caudal regression syndrome)	1	1*
3. *Urogenital*	*15 (9.9%)*	
Renal dysplasia	5	5
Potter disease sequence	4	4
Renal agnesis	3	3
Obstructive uropathy	3	3
4. *Chromosoma*l	*38 (25%)*	
Trisomy 21	21	21
Trisomy 18	8	8
Trisomy 13	5	5
Unbalanced chromosomal dislocations	3	3
47, XXY (Klinefelter's syndrome)	1	1
5. *Cardiac*	*4 (2, 6%)*	
Hypoplastic left heart	4	4
6. *Miscellaneous*	*19 (12.5%)*	
Hydrops fetalis	3	3
Omphalocele	3	3
Pulmonary hypoplasia	2	2
VATER syndrome	2	2
Growth retardation	2	2
Meckel-Gruber syndrome	1	1
Hunter's disease	1	0
Amniotic bands	1	1
No abnormality detected	1	1
Several semi-severe diagnoses†	3	3

* Nonspecific findings on antenatal ultrasound, suggesting skeletal dysplasia.
† Combination of disorders, which alone would not have led to termination, but which combined were considered to increase the long-term morbidity of the fetus (such as a small VSD and Meckel diverticle, or small omphalocele and a Dandy-Walker cyst).

151 autopsied fetuses, we assumed that the prenatal ultrasound diagnoses were correct for the rest of the cohort as well and as such provide accurate data as to fetal diagnosis.

The mean termination rate found in the present 14-year survey is slightly lower than the annual rates of around 2.5 per 1000 live births reported from two national (Norwegian) surveys during the periods 1996 and 1997 (7) and 1999–2002 (6), although rates for specific years such as 1996–1997 and 2000–2001 are concordant. The differences may reflect different attitudes toward termination due to fetal abnormalities among health professionals as well as cultural differences and availability of medical services. The

Table 3. Additional autopsy findings in 29 of 151 fetuses terminated due to antenatal pathology as assessed by ultrasound

	Major findings on antenatal ultrasound	Additional findings on autopsy
1. *Central nervous system*		
1	Anencephaly	Adrenal hypoplasia
2	Anencephaly,?enlarged kidneys	Choanal atresia
3	Anencephaly	Bilateral renal agnesis, unilateral pulmonary hypoplasia
4	Anencephaly	Adrenal and pulmonary hypoplasia
5	Anencephaly	Deformities right lower limb, cleft palate
6	Anencephaly	Spina bifida
7	Anencephaly, open thorax and abdomen	Scoliosis, 4 fingers and 4 toes bilaterally, short upper left limb
8	Anencephaly	Cleft palate, adrenal and pulmonary hypoplasia
9	Myelomeningocele, renal dysplasia	Horseshoe kidney, deformities both feet, contractures of the lower limbs
10	Dandy-Walker malformation, omphalocele	VSD
11	Severe congenital hydrocephalus, ASD, VSD	Cleft palate
12	Severe congenital hydrocephalus, complex cardiac defect, polydactyly	Omphalocele, horseshoe kidney
2. *Musculoskeletal*:		
13	Deformities right femur, bilateral radial aplasia	Hydrocephalus
14	Short limbs	VSD, Meckel diverticulum, cleft palate
15	Spinal defects, agenesis right lower limb	Esophagus atresia, polysplenia, horseshoe kidney, bilateral hydronephrosis, hydroureter
16	Cleft palate, polydactyly	Bilateral pes equino varus, absent ears, VSD
17	Cleft palate, polydactyly	Absent ears
3. *Urogenital*		
18	Bilateral renal agnesis	Anal atresia, pulmonary hypoplasia
19	Bilateral renal agnesis	Low-sitting ears, deformities of the 1st and 2nd metatarsals bilaterally
20	Renal dysplasia	VSD, pulmonary artery stenosis
21	Renal hypoplasia	Deformities of lower limbs
22	Absent urinary bladder	Anal atresia, fused lower limbs
23	Bilateral renal agnesis	Gastroschisis, pulmonary hypoplasia
24	Renal dysplasia	VSD, esophageal atresia
4. *Miscellaneous*		
25	Hydrops fetalis, cystic hygroma	Deformity left upper limb
26	Hydrops fetalis, cystic hygroma	Horseshoe kidney
27	Hydrops fetalis, cystic hygroma	VSD, hypoplastic aorta
28	Hydrops fetalis, cystic hygroma	Hypoplastic aorta, horseshoe kidney
29	Omphalocele	Dandy-Walker cyst

mean gestational age at termination was 18 weeks, and in accordance with our findings (7).

In Great Britain abortion is granted at any gestation when "there is a substantial risk that if the child were born it would suffer from such mental or physical abnormalities as to be seriously handicapped" (8). Termination by choice is legal up to 24 weeks. In 1994, there were 1796 late terminations of pregnancy in England and Wales, yielding a ratio of 2.7 per 1000 live births (9,10). Only 94 (5.2%) of these were at a gestational age of 25 weeks or above; the ratio for second-trimester terminations was only 1.2 per 10 000 live births. In comparison, only two cases in the present study were older than 24 weeks at the time of termination.

The trend toward higher numbers of terminations may in part reflect advances in antenatal diagnostics, both ultrasound and chorion biopsy/amniocentesis techniques, enabling accurate diagnoses as early as 10 gestational weeks, which is well within the limits of legal terminations. Thus, the rates toward the end of the period may be even higher, since some women may have undergone termination on medical indication before 12 weeks, and therefore are not registered as late terminations. The higher rates may also be due to more experienced examiners and changed thresholds for undertaking prenatal diagnostics among the population, a theory also postulated by others (11).

The numbers of induced terminations are often registered in national statistics, but reports on

specific indications for these are rare (10). In a questionnaire study from the northern part of the Netherlands, the authors found that terminations after 24 weeks (late second/third trimester) were practiced on a substantial scale. During the 5-year study period, 103 fetuses were terminated in 14 hospitals, 21% due to anencephaly and another 21% due to severe chromosomal aberrations (12). In the 97 fetuses where complete clinical and autopsy information was submitted, 77 had abnormalities, which were associated with increased antenatal and perinatal mortality. Nineteen had severe abnormalities that would have required the use of life-supporting procedures after birth. In a recent Swedish multicenter study including 328 fetuses, 35% were terminated due to cerebrospinal defects, 13% due to renal defects, 13% due to chromosomal abberations,13% due to complex abnormalities/defined syndromes, 7% due to musculoskeletal abnormalities, 4% due to cardiac abnormalities, and 4% due to gastrointestinal malformations such as gastroschisis and omphalocele (11). Neither these nor figures from similar studies differ substantially from those reported by us (11–13). Similar to the Swedish study, the number of terminations due to cardiac abnormalities in our study was low (only 2.7%). It is reasonable to believe that the true figure is higher, since several of these abnormalities are classified as either complex general abnormalities/syndromes or chromosomal aberrations (11, 14).

In the actual study period, 32 fetuses with proven trisomy 21 were aborted. Critical voices argue that termination of fetuses with disorders that (may be) are compatible with life, such as minor myelomeningocele, trisomy 21, or achondroplasia, may reflect a eugenic policy. Opinions on how severe a condition should be to grant a second- or third-trimester termination differ greatly between health professionals and also within the general population (1). Two French studies (15,16) showed that 78% of obstetricians would be prepared to terminate a pregnancy in trisomy 21, while a Belgian study found that only 38% of the general public found mental retardation an acceptable reason (17). Another study suggested that the public would consider terminations for conditions that might be regarded fairly minor, such as neural tube defects, even when the extent of the defect was described as entailing "minor physical defects that would allow the child to lead a relatively normal life" (18).

In accordance with others, we found that antenatal ultrasound had a high accuracy for major abnormalities leading to termination, with a correct diagnosis of the main anomaly in 99% of the terminated cases when compared to postmortem examinations (11, 14, 19–22). Additional autopsy findings were demonstrated in a fifth of the 151 fetuses, of which limb abnormalities such as a missing digit or contractures were the most common. Although polydactyly can be seen as early as 8–9 weeks (23), it may be difficult to ascertain in oligohydramnios or maternal obesity. A small VSD also proved difficult to assess. Again, difficult insonation may play a role. Improvements in ultrasound technology since closure of the study on January 1, 2002, may have reduced these problems to some extent. Thirteen cases were terminated due to features suggestive of severe skeletal abnormalities, of which nine had suspected skeletal dysplasia. In four of these cases, the specific ultrasound diagnosis was confirmed radiographically, namely in two cases of osteogenesis imperfecta type II, one case of thanatophoric dysplasia, and one case of chondroectodermal dysplasia. Currently, antenatal care practices, including ultrasound, detect more than 80–90% of all fetuses with lethal or severe dysplasias; however, a specific diagnosis can only be given in around 50–60% of these cases on prenatal ultrasound (23). Potential pitfalls include misdating of pregnancies, early gestational age, and intrauterine growth restriction (23). On the other hand, the reported proportion of false positives is low.

In only one case (0.7%) were no pathological findings seen on postmortem examination. This fetus was terminated because of possible damage due to maternal epilepsy medication. In the abovementioned Swedish study, all fetuses but one had evident abnormalities, and as such there was a good correlation between antenatal ultrasound and autopsy findings. However, in six cases, the decision to terminate was based on suboptimal prognostic and diagnostic evidence. Although 7.3% of the terminations were due to musculoskeletal disorders, no information was given on radiological confirmation of the diagnosis.

In conclusion, antenatal ultrasound screening is an accurate tool in the diagnosis of major fetal abnormalities when in experienced hands. Although the annual rates of terminations due to antenatal diagnostics tended to increase during the 14-year study period, the rates are still low. A multidisciplinary team, including dedicated obstetricians, pathologists, geneticists, and radiologists, has been in place for at least two decades in our institution, and is crucial for correct management in cases where fetal pathology is suspected.

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