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Original Article

Are there risk factors for false-positive malformation diagnoses on obstetric ultrasound? A nested case-control study

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ABSTRACT

Introduction. – In a population-based study, we found an overall false-positive rate of 8.8% for the second and third trimester ultrasounds. Although numerous studies have been performed to examine factors which lead to false negatives, the same is not true for the factors associated with false positives. The principal objective of this study was to look for risk factors for false-positive diagnoses of fetal malformations on obstetric ultrasound scans.
Material and methods. – In this nested case-control study, the case infants were those whose mother had a false-positive antenatal ultrasound diagnosis of a malformation during the second or third trimester (ultrasound false-positives) and who were live – or stillborn in Auvergne in 2006–2010. The control group comprised all children who were ultrasound true-negatives in 2005 and 2007. The study included 46 cases and 184 controls, matched according to the level of the maternity unit in which they were born.
Results. – Most false-positive diagnoses were minor malformations. The mean term at this false-positive diagnosis was 27.7 ± 5.4 weeks; in 46.8% of cases, the diagnosis was made during the second-trimester ultrasound. A single malformation was suspected in 95.7% of the cases. In 97.9% of cases, only one anatomical system was affected. In all, 49 malformations were identified among the 46 cases and their distribution differed according to anatomical system. The only risk factor identified was a body mass index (BMI) < 25 (*ORa* = 1.7; 95%CI: 1.2–2.4).
Discussion. – A maternal BMI < 25 was the only risk factor identified for a false-positive ultrasound diagnosis of a fetal malformation.

Introduction

The rate of true-positive ultrasound diagnoses of congenital malformations has been estimated at 58% [1] to 68% [2] in general population studies. This rate varies according to anatomical system (heart, lungs, etc.) [2]. The false-positive rate, all body systems combined, has been estimated at 0.5 to 33.0% in the general population [3,4]. In a population-based study covering a 4-year period (2006–2009), we found an overall false-positive rate of 8.8% for the second and third trimester ultrasounds and a true-positive rate of 83.3% [5].

Although numerous studies have been performed to examine factors that might influence the quality of the ultrasound image and lead to the failure to visualize malformations (false negatives) [6–10], the same is not true for the factors associated with false positives. Maternal factors (obesity, history of abdominal surgery and parity) have been found to be associated with difficulty in detecting malformations, especially of the central nervous system and the heart [6,7]. Other factors, such as abnormal quantities of amniotic fluid and fetal position, were associated with poor ultrasound conditions [8]. The sensitivity of ultrasound also increases with gestational age; visualization is optimal starting

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at 18 weeks for the minor markers of aneuploidy and at 20 weeks for cardiac morphology [9]. Finally, the ultrasonographer's experience and equipment quality also influence the quality of fetal imaging [10].

The principal objective of our study was to determine the predictive factors that might result in false-positive antenatal ultrasound diagnoses of malformations on fetal scans, a topic that to the best of our knowledge has not been assessed.

Material and methods

The region of Auvergne has 10 maternity units, including one Level III unit, six level II and three level I facilities, all coordinated by a perinatal network. The region also has a multidisciplinary antenatal diagnosis center (CPDP) and a registry for surveillance of congenital malformations (CEMC-Auvergne), located in the Level III unit.

The CPDP's purpose is to promote access to all types of prenatal diagnosis. All the fetal ultrasound abnormalities identified in Auvergne are presented to the CPDP for an opinion during the weekly staff meeting, conducted with remote participation and teleradiology.

The CEMC-Auvergne registry is a regional, population-based, malformation-monitoring registry currently covering some 13,500 annual births. Terminations of pregnancy are included, regardless of term. Stillbirths are registered at a gestational age of 22 weeks$^{+0\ day}$ or later. Live born infants with malformations are identified up to the age of 1 year through voluntary reporting from the hospitals in the region and searches of the medical records of the maternity and pediatric units in the area. Regardless of the child's vital status, confirmation of the malformation is obtained after birth, by any means (including pathology examination of fetus or child, in case of death), before it is included in the CEMC-Auvergne database.

In accordance with national guidelines [11], women in France with low-risk pregnancies undergo three ultrasound examinations (one between 11 weeks$^{+0\ d}$ and 13 weeks$^{+6\ d}$, one between 20$^{+0\ d}$ and 24$^{+0\ d}$ weeks and one between 30$^{+0\ d}$ and 35 weeks$^{+0\ d}$). The women in our study all had subsequent clinical and ultrasound follow-up in Auvergne.

Our sample comprised women who gave birth in 2006 through 2010 in Auvergne, after 22 weeks ($\geq$ 22 weeks$^{+0\ d}$, or with a birth weight $\geq$ 500 g if term was uncertain), regardless of pregnancy outcome. The cases in our study were those whose mother had a false prenatal diagnosis of malformation (ultrasound false-positive diagnosis) after the second or third trimester ultrasound scans. All these women underwent follow-up (second-look) ultrasounds by CPDP sonographers and their files were examined at a multidisciplinary CPDP meeting, as explained in an earlier report [5]. The same CPDP sonographers served as experts throughout the study period. Ventriculomegaly (unilateral or bilateral) was considered present if the ultrasound-measured width of the lateral ventricles $\geq$ 10 mm opposite the internal parieto-occipital sulcus. Pyelectasis was defined by the anteroposterior diameter of the renal pelvis: $>$ 5 mm between 20–29 weeks and $>$ 7 mm between 30–40 weeks, over several examinations. An abnormal quantity of amniotic fluid was defined as either oligoamnios [amniotic fluid index $<$ 5 cm] or polyhydramnios [amniotic fluid index $>$ 15 cm] [12]. Intrauterine fetal growth restriction (IUGR) was defined as a birth weight $<$ 3rd percentile for gestational age [13] according to the biometric curves compiled by Association des utilisateurs de dossiers informatisés en pédiatrie, obstétrique et gynécologie, association of users of computerized files in pediatrics, obstetrics and gynecology (AUDIPOG) [14].

The control group comprised women who gave birth at $\geq$ 22 weeks$^{+0\ d}$ (or a fetus weighing $\geq$ 500 g if term was uncertain) to one or more children with no malformation identified before or at birth (true negatives with prenatal second or third trimester ultrasound), born in Auvergne during 2005 or during 2007. These children were live born or stillborn; the control group included no terminations of pregnancy.

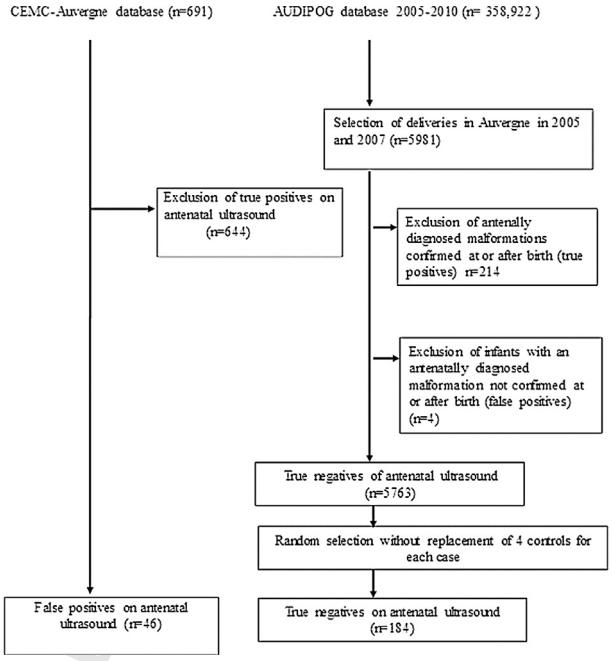

Fig. 1. Flow chart for selection of cases and controls.

The cases in this nested case-control study were prospectively identified during CPDP staff meetings. The establishment of this database was described in detail earlier [5].

Fig. 1 summarizes the constitution of the case and control groups. To constitute the control group (ultrasound true negatives), we used the national AUDIPOG perinatal database [14], which contains records from maternity units that participate voluntarily in it and has been described in earlier publications [15]. All the maternity units in Auvergne have participated regularly in the Audipog database, although not necessarily each year. For the study period, we selected the years during which all the maternity units in Auvergne participated for at least one month: 2005 and 2007 (n = 5981). This database was crossed with both the case database and the registry database to exclude both duplicates and those children with a real malformation identified during the prenatal examination (true positives). The Audipog database is anonymized, but the following variables were used to link files:

- mother's date of birth;
- child's date of birth;
- maternity ward of birth;
- child's birth weight;
- sex.

Controls were randomly selected without replacement in the study database. All the cases were presented to the CPDP and thus had identical antenatal management, regardless of the level of the maternity unit of birth. Cases and controls were then matched (1 case per 4 controls) for maternity unit level (I, II, and III), to ensure that the delivery and postnatal management would be comparable for case and control women. Finally, our analysis included 46 false-positive cases and 184 controls from among the 5981 births with antenatal care in Auvergne included in the Audipog database.

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