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Maternal and fetal factors which affect fetometry: use of in vitro fertilization and birth register data

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ABSTRACT

Background: Fetometry dating of gestational age is the gold standard in most developed countries but may have some inborn errors. Dating pregnancies after in vitro fertilization can be used for the evaluation of fetometric studies and for studies of variables which may affect them.
Methods: We compared the actual gestational age of 9543 singleton and 869 twin pregnancies with estimates based on second-trimester fetometry. Mean gestational age, percentage of births classified as preterm, and skewness of the distribution of differences between actual and estimated gestational age were studied. Subanalyses were made of data on singletons for males and females, for infants born to overweight or obese women or to smoking women, for infants judged to be small or large for gestational age, and on twins.
Results: In the majority of cases, good agreement was found between actual and estimated gestational age but in singletons there was an excess of positive differences resulting in a moderate over-estimate of the rate of preterm births (8%), more marked for females (11%) than for males (6%) and increased for infants born to overweight (7%) or obese (16%) mothers. Singleton infants born small for gestational age also showed an excess of positive differences (3%). These differences were less marked for twins.
Conclusions: In most IVF pregnancies, routine fetometry correctly predicts gestational age but deviations exist which indicate that ultrasound underestimates the age of fetuses that will be born small for gestational age and when the woman is obese. The differences between actual age and estimates based on fetometry seem to be smaller than those between estimates based on last menstrual period and fetometry.

1. Background

The classical method of determining gestational age is from the last menstrual period (LMP). Uncertainty of LMP data (including digit preference – that is, women reporting LMP favour dates ending with 0 or 5 – and the possibility that early pregnancy bleeding has been mistaken for menstruation) sometimes makes this method uncertain. In most developed countries, gestational age is nowadays estimated from fetometry performed before gestational week 20. Studies have, however, pointed out some limitations of this method also [1–3]. The possibility of using data from assisted reproduction for the validation of gestational age assessment methods was recently discussed [4] and has been used by some studies of limited size [5–9]. A slightly shorter mean gestational age was found when estimated from fetometry than when based on the date of embryo transfer but the difference was only 0.9–2.1 days or 1.9–2.1 days in singletons [8,9]. Similar results were obtained in a study of 72 infertile women with known ovulation date, using crown-rump length estimates [10]. One study of early fetometry found a better agreement between estimated age and true age when based on biparietal diameter (BPD) than when based on crown-rump length (CRL) [11] but another found no marked difference [9].

We used a large number of infants born after in vitro fertilization (IVF) with known length of embryo culture, date of embryo transfer and date of delivery, and with information on gestational duration estimated by fetometry. The material was large enough to investigate the possible effect of some maternal and fetal variables on the validity of the fetometric determinations.

Abbreviations: BMI, body mass index; BPD, biparietal diameter; CRL, crown-rump length; ICSI, intracytoplasmic sperm injection; IVF, in vitro fertilization; LMP, last menstrual period; LGA, large for gestational age; MBR, Medical Birth Register; SEM, standard error of the mean; SGA, small for gestational age.

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2. Methods

Women undergoing IVF between 2002 and 2006 were identified from reports from all IVF clinics in Sweden. These include women who had standard IVF or ICSI and also transfer of fresh or frozen embryos. The information contained the identification number of the woman, the date of embryo transfer and the number of days of culture before transfer. Before 2002, no information on embryo transfer date or culture duration was registered. This file was linked with the Swedish Medical Birth Register (MBR) [12]. From the MBR record we took the expected date of delivery, calculated from second trimester fetometry (<20 weeks), and also the gestational age estimated from that date and expressed in days. Women with higher order multiples than twins were excluded ($n = 14$). No other exclusions were made.

Fetometry during pregnancy is done in Sweden using a combination of BPD and femur length [13]. In one hospital, dating was instead routinely based on CRL. This hospital contributed slightly less than 2% of all IVF cases. Comparisons of dating made with BPD or with CRL have shown only small differences [14,15].

Information was obtained from the MBR on parity, maternal smoking, and pre-pregnancy maternal weight and height from which body mass index (BMI) was calculated. Furthermore, date of birth, birth weight, infant sex, and number of infants born was used. Intrauterine growth deviations were analyzed based on sex- and parity-specific growth curves from the MBR [16] with gestational age based on IVF information. Small for gestational age (SGA) was defined as <2 standard deviations and large for gestational age (LGA) as >2 standard deviations from the mean weight for that gestational week.

In the MBR record for antenatal care, dates for LMP, expected date for delivery calculated from LMP, and expected date of delivery estimated from second trimester fetometry are given. The analysis was restricted to singleton and twin deliveries. Among a total of 14,135 such deliveries, information on the expected date of delivery from second trimester fetometry was given for 10,447 (74%). Absence of this information can mean that fetometry was not performed or the result was not recorded or that the expected date of delivery agreed closely with that calculated from LMP.

The exact gestational age was calculated as the number of days between delivery and embryo transfer plus the number of days in culture. In order to make this comparable with the length estimated from fetometry, two weeks were added in order to get a measure, which was comparable with the fetometric measure. In both cases a hypothetical time of conception 14 days after LMP was assumed, which may not be correct but the difference will be the same for both measurements.

We analyzed the difference between the length of gestation calculated from IVF information and that calculated from fetometry. A positive difference means that the fetometry underestimated and a negative difference that it overestimated the true gestational age. Cases with <-10 or >10 days difference were excluded from the analysis because the majority were likely due to registration errors, leaving 9543 singleton and 869 twin pregnancies for analysis (99.7%).

In order to measure skewness in a distribution, the skewness coefficient with its error was determined. A normal distribution has a skewness coefficient of 0. For calculations and production of distribution graphs we used the software Analyse-it for Excel, Analyse-it Software Ltd.

2.1. Ethics

The study was performed within the responsibilities of the National Board of Health and Welfare and therefore no ethical approval from outside ethical committees was needed.

3. Results

3.1. Singleton pregnancies

Table 1 shows that the mean gestational age is slightly higher when based on IVF data than when it is based on fetometry but the difference is small, averaging 0.87 days, and is higher for females than for males. About two thirds of the fetometry estimates differed by two days or less from the gestational age based on IVF information.

This difference between fetometry and IVF data is also apparent in the estimated rate of preterm births, which was lower when based on IVF data than on fetometry. The difference is small, about 8%, and larger for females than for males. This finding was valid only for gestational ages between 32 and 36 weeks, and no difference was found at gestational age <32 weeks.

For women with a BMI ≥ 30, the difference between the two methods is larger and for women with a BMI of 26–29.9 it is intermediate (Table 2). The difference is also larger among infants born of smoking women (Table 2). As few women with IVF smoke, the number of preterm births is low in this group and the rate of preterm births was similar when IVF information or fetometry were used.

Two groups of infants with intrauterine growth deviations were analyzed with gestational age based on IVF information (Table 3). The difference in mean gestational age was close to two days for SGA infants and only 0.6 days for LGA infants, but the distribution

Table 1
Mean estimated gestational age at birth of singleton infants and rates of preterm births. Based on IVF data and on second trimester ultrasound fetometry (FET), stratified by gender.

Variable studied	Method	All infants	Males	Females
Number of infants	–	9543	4956	4587
Mean gestational age, days	IVF	278.5	277.9	279.0
	FET	277.6	277.5	277.7
Mean IVF–FET difference ± SEM	–	0.87 ± 0.03	0.46 ± 0.04	1.32 ± 0.02
Number (%) of preterm births <37 weeks	IVF	597 (6.3)	334 (6.7)	263 (5.7)
	FET	645 (6.8)	343 (7.1)	293 (6.4)
Ratio FET/IVF of % preterm births <37 weeks	–	1.08	1.06	1.11
Number (%) of preterm births <32 weeks	IVF	115 (1.21)	64 (1.29)	51 (1.11)
	FET	115 (1.21)	62 (1.25)	53 (1.16)
Ratio FET/IVF of % preterm births <32 weeks	–	1.00	0.97	1.05
Number (%) of preterm births 32–36 weeks	IVF	482	270	212
	FET	530	291	239
Ratio FET/IVF of % preterm births 32–36 weeks	–	1.10	1.08	1.13
Skewness coefficient ± error	–	0.23 ± 0.03	0.12 ± 0.04	0.36 ± 0.04
t and P values for skewness coefficient	–	$t = 7.7$, $P < 0.001$	$t = 3.0$, $P = 0.004$	$t = 9.0$, $P < 0.001$