Ultrasound Obstet. Gynecol. 5 (1995) 20–25

The implementation of first-trimester scanning at 10–13 weeks' gestation and the measurement of fetal nuchal translucency thickness in two maternity units

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Key words: FETAL KARYOTYPING, NUCHAL TRANSLUCENCY THICKNESS, ULTRASONOGRAPHY

ABSTRACT

The aim of this prospective screening study was to evaluate the implementation of an additional ultrasound examination, incorporating the measurement of fetal nuchal translucency thickness, at 10–13 weeks' gestation in two maternity units providing routine antenatal care. During the 1 year prior to the introduction of the first-trimester scan, the major indication for fetal karyotyping was maternal age ≥ 35 years and only two out of the total of 11 cases of trisomy 21 were identified. In the first 5 months of the study, 70% of the women delivering in these hospitals attended for measurement of fetal nuchal translucency thickness and the measurement was obtained in all cases. This was achieved without an increase in the number of sonographers or ultrasound machines. The incidence of fetal nuchal translucency thickness ≥ 2.5 mm was 3.6% (63 of 1763), and this group included three of the four fetuses with trisomy 21. The findings of this study demonstrate the feasibility of introducing scanning at 10–13 weeks' gestation and the measurement of fetal nuchal translucency thickness in routine maternity units. The sensitivity and specificity of this method of screening are at present being evaluated in a large multicenter study.

INTRODUCTION

Increased fetal nuchal translucency thickness during the first trimester of pregnancy is associated with increased risk for chromosomal abnormalities. A prospective study of 827 women with singleton pregnancies, undergoing fetal karyotyping at 10–13 weeks' gestation, reported that, in 80% of fetuses with trisomies 21, 18 and 13 and in 4.1% of chromosomally normal fetuses, the nuchal translucency was ≥ 2.5 mm (or ≥ 3.0 when using machines that give measurements to the nearest 1 mm)[1]. A study of an expanded series of 1273 women showed that it was possible to derive estimates of risks for fetal trisomies on the basis of maternal age and fetal nuchal translucency thickness; nuchal translucency < 2.5 mm was associated with a 4.5-fold reduction, whereas nuchal translucency ≥ 2.5 mm was associated with 12-fold increase in maternal age-related risk[2]. In a subsequent study of 560 fetuses with nuchal translucency ≥ 2.5 mm, it was possible to derive risks for trisomies with increasing nuchal translucency thickness; translucencies of 3 mm, 4 mm, 5 mm and ≥ 5.5 mm were associated with 4-fold, 21-fold, 26-fold and 41-fold increase in maternal age-related risks[3,4].

These data suggest that measurement of fetal nuchal translucency thickness at 10–13 weeks' gestation may provide an effective method of screening for fetal trisomies. However, this method of screening needs to be evaluated in large multicenter studies. The aim of the present study is to examine the implementation of this method in two maternity units providing routine antenatal care.

PATIENTS AND METHODS

St. Peter's Hospital in Chertsey and Frimley Park Hospital in Camberley are general hospitals within the National Health System, 40 km and 58 km from London, respectively, serving the local populations. The combined annual number of deliveries in the two maternity units is approximately 6000.

The policy of these hospitals is to offer amniocentesis for fetal karyotyping free of charge to women with a

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Received 5–9–94
Revised 14–11–94
Accepted 25–11–94

family history of chromosomal abnormalities and to those aged ≥ 35 years. In addition, amniocentesis is carried out if women under the age of 35 years request it because of a screen-positive result from maternal serum biochemistry testing; the latter is not offered by these hospitals but women wishing to have it done do so privately. Amniotic fluid is analyzed at the Regional Cytogenetics Laboratory (St. George's Hospital Medical School, London). The policy on ultrasound scanning is to offer an examination to all women at 18–20 weeks' gestation and the scans are performed by sonographers; when there is a suspicion of fetal abnormality, the patients are referred to the Harris Birthright Research Centre for Fetal Medicine.

In August 1993, an additional ultrasound examination at 10–13 weeks' gestation was offered to all women for assessment of fetal viability and measurement of crown–rump length. In addition, the nuchal translucency thickness was measured and, if this was ≥ 2.5 mm, the parents were counselled concerning the increased risk for fetal trisomies and were offered the option of fetal karyotyping by chorion villus sampling at the Harris Birthright Research Centre. The introduction of this policy was preceded by practical training of the sonographers to measure nuchal translucency thickness and a series of seminars explaining the policy to obstetricians, radiologists, pediatricians, general practitioners, midwives and sonographers. Letters were sent to all local general practitioners requesting that they refer the women at the appropriate gestation. The women were given leaflets explaining the possible significance of nuchal translucency thickness and were given the option of whether they wanted this measured or not.

At the ultrasound examination, a sagittal section of the fetus is obtained for measurement of crown–rump length. The maximum thickness of the subcutaneous translucency between the skin and the soft tissue overlying the cervical spine is measured, taking care to distinguish between fetal skin and amnion. The ultrasound examinations are performed transabdominally using 5-MHz or 3.5-MHz curvilinear transducers and, if visualization is inadequate, then transvaginal sonography (5-MHz transducer) is carried out. All ultrasound findings of the viable pregnancies are entered into a computer database at the time of the examination.

Both hospitals have a central computer system for recording demographic and medical details of all patients at the time of booking and details on pregnancy outcome after delivery (Patient Administration System). All babies with any abnormalities or dysmorphic features are examined by a pediatrician and karyotyping is performed in the Regional Cytogenetics Laboratory. The indications for amniocentesis and results of cytogenetic analysis are recorded in the computer system at the Regional Cytogenetics Laboratory. For patients referred to the Harris Birthright Centre, the ultrasound findings and results of the various investigations are recorded in a fetal database.

For the 1-year period before August 1993, the appropriate computer searches were made to determine:

(1) The number of deliveries and the maternal age distribution of the populations;

(2) The number, indications and results of amniocenteses; and

(3) The number of deliveries of Down's syndrome babies.

Computer searches were also made to determine the above during the first 5 months (1st August–31st December 1993) of the introduction of the first-trimester scan. In addition, the uptake of the scan, the distribution of nuchal translucency thickness, and the results of chorion villus sampling, for those with increased nuchal translucency thickness, were determined.

RESULTS

Screening before the introduction of first-trimester scanning

During the 1-year period prior to the introduction of the first-trimester scan, the total number of deliveries in the two hospitals was 5705. The maternal age was ≥ 35 years in 15.5% (884 of 5705) of the women and the uptake of amniocentesis in this group was 21.8% (193 of 884). Amniocentesis was performed in an additional 53 cases for other indications (Table 1).

There were 11 cases of trisomy 21, and two (18.2%) of these were detected by amniocentesis. In two of the nine cases of trisomy 21 that were missed, the maternal age was ≥ 35 years. Therefore, had the uptake of amniocentesis in the eligible group been 100%, the detection rate of trisomy 21 would have been 36.4% (four of 11 cases) for an invasive testing rate of 15.5%. Six of the nine cases from the group that did not have amniocentesis resulted in livebirths and three in terminations of pregnancy. The three terminations were for trisomy 21 diagnosed by cordocentesis after the detection of fetal abnormalities by ultrasound examination.

Successful implementation of first-trimester scan

In the ultrasound departments of the two hospitals, there are a total of eight part-time ultrasonographers using four ultrasound machines. Successful implementation of the first-trimester scan was achieved without the need for increasing the staff or equipment.

During the study period (1st August–31st December 1993), the total number of women that had a first-trimester scan which demonstrated a viable singleton (n = 1774) or multiple pregnancy (n = 45) was 1819, with a total of 1864 fetuses; the cases with anembryonic pregnancies or missed abortions were not recorded.

During the same period, the total number of women referred to the two hospitals for antenatal care was 2586. These data are not computerized and only the total number of cases is recorded; not all patients referred for antenatal care actually attended antenatal clinics or delivered in these hospitals. Therefore, successful uptake

Table 1 Data from the two hospitals during the 1-year period prior to the introduction of the first-trimester scan. The maternal age was ≥ 35 years in 15.4% (884 of 5705) of the women and the uptake of amniocentesis in this group was 21.8% (193 of 884). There were 11 cases of trisomy 21 and two of these were diagnosed by amniocentesis

	St. Peter's	*Frimley Park*	*Total*
Deliveries	3072	2633	5705
Maternal age ≥ 35 years	519	365	884
Amniocentesis	169	77	246
Maternal age ≥ 35 years	126	67	193
Family history of chromosomal defect	6	6	12
Biochemical screen positive	37	4	41
Trisomy 21 detected	1	1	2
Trisomy 21 missed	3	6	9
Maternal age ≥ 35 years	1	1	2*
Maternal age < 35 years	2	5	7†

*This includes one livebirth and one termination. The latter was diagnosed by cordocentesis after the detection of a ventricular septal defect at a 20-week ultrasound scan; †this includes five livebirths and two terminations. The latter were diagnosed by cordocentesis after the detection of fetal abnormalities by ultrasound examination; in one case, tetralogy of Fallot was detected at the routine 20-week ultrasound scan and in the second case duodenal atresia was detected at an ultrasound scan for polyhydramnios at 30 weeks' gestation

of the first-trimester scan was at least 70% (1819 of 2586 cases).

The estimated date of delivery of the women recruited to the study was between 2nd February and 8th July 1994. During this period, the total number of deliveries in the two hospitals was 2514. On the basis of this number, successful uptake of the first-trimester scan was 74% (1864 of 2514 deliveries). The mean maternal age of women having a first-trimester scan was 29.6 years (range 15–45 years), which was not significantly different from the mean maternal age (29.9 years) of the women who did not have a scan ($z = 1.68$, $p = 0.09$).

The individual records of the 510 women that delivered in the two hospitals in June 1994 were examined to determine the possible reasons for the failure of complete uptake of first-trimester scanning. In 22.2% (113 of 510) of cases the women were referred for antenatal care after 13 weeks' gestation, 3.5% (18 women) booked for antenatal care at less than 10 weeks and were not scanned at the appropriate gestation, and 4.7% (24 women) had their antenatal care in other hospitals and were referred to Frimley Park or St. Peter's hospitals for delivery. First-trimester scanning at 10–13 weeks was performed in 355 of the women, which represents 69.6% of deliveries; only two of these women requested not to be informed of the nuchal translucency thickness.

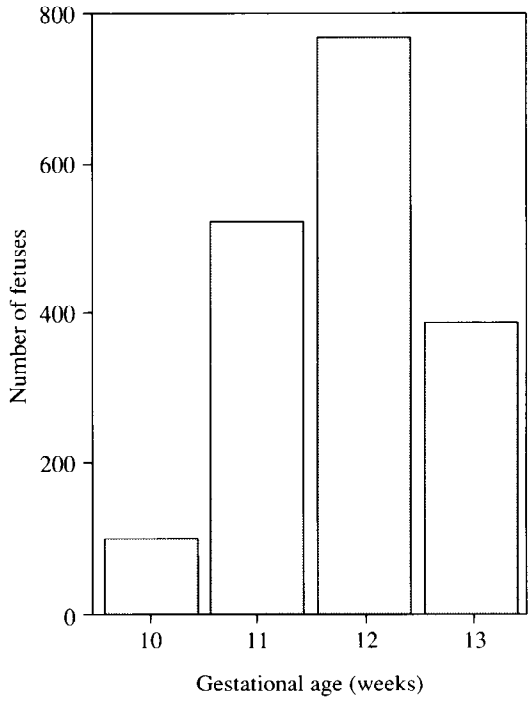

Figure 1 The gestational age distribution of the 1763 fetuses that had a first-trimester scan at 10–13 weeks. The median gestational age was 12 weeks

Ultrasound findings

In 94.6% (1763 of the 1864) of fetuses that had first-trimester scanning, the crown–rump length was equivalent to 10–13 weeks' gestation; the gestation was < 10 weeks in 4.7% (88 cases), and > 13 weeks in 0.7% (13 cases). The 1763 fetuses used in this study included 1673 from singleton and 90 from twin pregnancies. The fetal crown–rump length and nuchal translucency thickness were successfully measured in all cases. The median gestational age at the ultrasound examination was 12 weeks (Figure 1).

The distribution of nuchal translucency thickness is shown in Table 2. The incidence of nuchal translucency ≥ 2.5 mm was 3.6% (63 of 1763 fetuses) and this incidence increased with gestational age (Figure 2). In 62 of the 63 fetuses with increased nuchal translucency thickness, the pregnancies were singleton and one was a twin pregnancy. In the twin pregnancy, which was monochorionic and monoamniotic, the nuchal translucency thicknesses of the two fetuses were 2 mm and 6 mm, respectively; no fetal karyotyping was performed but the pregnancy resulted in intrauterine death of both

Table 2 Distribution of nuchal translucency thickness, showing the data from the individual hospitals and the combined results. Karyotyping was performed in 49 of the 63 fetuses with translucency ≥ 2.5 mm and this group contained three of the four cases of trisomy 21. In addition, amniocentesis was performed in 55 pregnancies where the nuchal translucency was < 2.5 mm

Nuchal translucency (mm)	*St. Peter's*	*Frimley Park*	*Total*	*Karyotyping*	*Trisomy 21*
0.0–0.4	12 (1.0%)	—	12 (0.7%)	—	
0.5–1.4	544 (49.5%)	262 (39.5%)	806 (45.7%)	25	
1.5–2.4	507 (46.1%)	375 (56.5%)	882 (50.0%)	30	1
2.5–3.4	30 (2.7%)	18 (2.7%)	48 (2.7%)	36	1
3.5–4.4	5 (0.5%)	3 (0.5%)	8 (0.5%)	7	
4.5–5.4	—	2 (0.3%)	2 (0.1%)	2	
≥ 5.5	2 (0.2%)	3 (0.5%)	5 (0.3%)	4	2

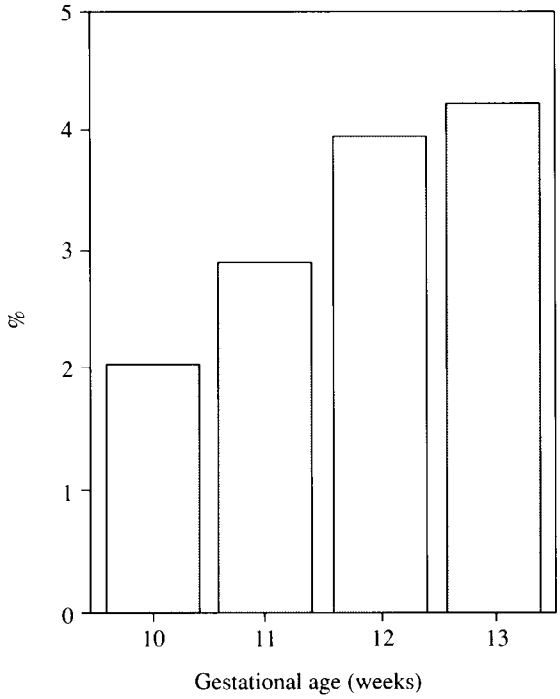

Figure 2 The incidence of fetal nuchal translucency thickness ≥ 2.5 mm was 3.6% (63 of 1763 fetuses) and this increased with gestational age

fetuses at 20 weeks' gestation with sonographic evidence of twin–twin transfusion syndrome.

Fetal karyotyping

In 15.3% (263 of 1718 pregnancies) of the women who had a scan at 10–13 weeks' gestation, the maternal age was at least 35 years. The mean maternal age of this population was higher than that of all deliveries in England and Wales (Figure 3)[5].

In 49 of the 62 singleton pregnancies with increased nuchal translucency thickness, the parents elected to have chorion villus sampling (Table 3); the karyotype was normal in 45 cases and abnormal in four (three cases of trisomy 21 and one case of Turner syndrome). In one case of trisomy 21, the parents decided to continue with the pregnancy and a trisomic infant was delivered at term; in the other three cases with chromosomal abnormalities, the pregnancies were terminated. All 13 pregnancies that did not have karyotyping resulted in the delivery of phenotypically normal babies.

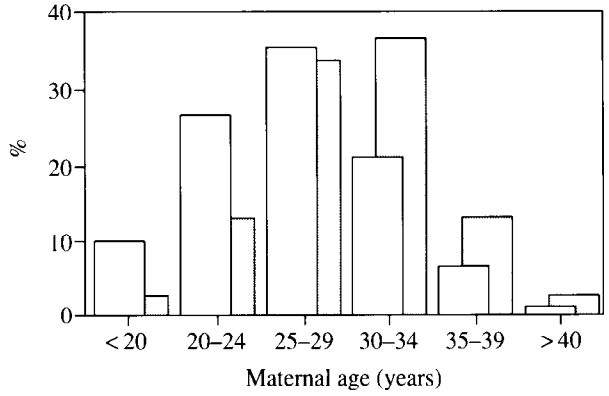

Figure 3 The maternal age distribution of the women at St. Peter's Hospital and Frimley Park Hospital that had a first-trimester scan (shaded columns) compared to that of all deliveries in England and Wales (data from reference 5)

Karyotyping was also performed, by second-trimester amniocentesis, in 55 of the 1700 fetuses with nuchal translucency < 2.5 mm and the main indication for amniocentesis was maternal age ≥ 35 years (Table 3). There was one case of trisomy 21 in a 42-year-old woman with fetal nuchal translucency of 2.2 mm. The karyotype in the other 54 cases was normal. Amniocentesis was also performed in 24 women that did not have a first-trimester scan and the karyotype was normal in 23 and abnormal in one (partial trisomy 15).

The total rate of fetal karyotyping was 5.1% (128 of 2514 deliveries) compared to 4.3% (246 of 5705) for the preceding year.

Pregnancy outcome

In the group of 1718 pregnancies (1763 fetuses) that had a first-trimester scan at 10–13 weeks' gestation, there were 12 terminations of pregnancy. These included:

(1) Four cases of fetal chromosomal abnormalities (three diagnosed by chorion villus sampling because of increased nuchal translucency thickness and one by amniocentesis);

(2) Three cases of fetal abnormalities diagnosed at the 18–20-week scan (bilateral renal agenesis, thanatophoric dwarfism and neural tube defect); and

(3) Five cases for psychosocial reasons.

Table 3 Data from the two hospitals during the first 5 months after the introduction of an ultrasound scan at 10–13 weeks' gestation. During this period, 2586 women booked in these hospitals. Amniocentesis for advanced maternal age was offered to 15.7% (405 of 2586) of the women and the uptake was 19.5% (79 of 405). There were four cases of trisomy 21, one following amniocentesis for advanced maternal age and three were diagnosed by the chorion villus sampling following the detection of increased fetal nuchal translucency thickness. The numbers in the brackets refer to women that had a first-trimester scan prior to amniocentesis

	St. Peter's	*Frimley Park*	*Total*
Patients referred for antenatal care	1348	1238	2586
Deliveries	1371	1143	2514
Maternal age ≥ 35 years	223	182	405
Ultrasound scans at 10–13 weeks	1100	663	1763
Nuchal translucency thickness ≥ 2.5 mm	37	26	63
Chorion villus sampling	27	22	49
Trisomy 21 detected	1	2	3
Amniocentesis	51 (38)	28 (17)	79 (55)
Maternal age ≥ 35 years	34 (26)	23 (13)	57 (39)
Family history of chromosomal defect	1 (1)	5 (4)	6 (5)
Biochemical screen positive	16 (11)	—	16 (11)
Trisomy 21 detected	1	—	1

There were ten cases of spontaneous abortion at 13–23 weeks' gestation. Three pregnancies resulted in intrauterine deaths; there were two unexplained deaths in singleton pregnancies at 24 and 37 weeks, respectively and two fetal deaths in the twin pregnancy with twin–twin transfusion syndrome. There were 1734 livebirths and all babies were phenotypically normal; in three cases the babies died in the neonatal period (one after premature delivery at 25 weeks and two after emergency delivery at 38 and 40 weeks due to a major placental abruption).

DISCUSSION

This prospective screening study demonstrates the successful implementation of first-trimester ultrasound scanning in two maternity units providing routine antenatal care. During the first 5 months of the introduction of the new policy, approximately 70% of women delivering in these hospitals attended at 10–13 weeks' gestation for measurement of fetal nuchal translucency thickness and this measurement was obtained in all cases. Uptake of the first-trimester scan will inevitably increase with more widespread awareness of the need for referral before 14 weeks.

These two hospitals are representative of the majority of maternity units in Britain, where ultrasound examinations are performed routinely at 18–20 weeks by well-trained sonographers. The first-trimester scan was successfully introduced with minimal additional training and without the need to increase the numbers of staff or equipment. All sonographers performing fetal scans should be capable of measuring reliably the crown–rump length and obtaining a proper sagittal view of the fetal spine. For such sonographers, it is easy to acquire, within a few hours, the skill to measure nuchal translucency thickness.

The maternal age distribution of the women delivering in these hospitals is shifted to the right of the distribution of all deliveries in England and Wales[5]. Thus, approximately 15% of our women, compared to 8% of those in England and Wales, were at least 35 years old. During the 1 year prior to the introduction of the first-trimester scan, the major indication for fetal karyotyping was maternal age, accounting for about 80% of the cases. If all women aged ≥ 35 years had an amniocentesis, the detection rate of trisomy 21 would have been only 36% for an invasive testing rate of 15%. However, only one in five of the eligible group actually accepted the offer for invasive testing and only two of the total of 11 cases of trisomy 21 were identified.

The incidence of nuchal translucency ≥ 2.5 mm was 3.6% and this group included three of the four fetuses with trisomy 21. These findings are consistent with those of a previous study of 1273 women with singleton pregnancies undergoing first-trimester fetal karyotyping because of advanced maternal age, parental anxiety or family history of a chromosomal abnormality; nuchal translucency ≥ 2.5 mm was found in 4.5% of the chromosomally normal fetuses and in 84% of those with trisomy 21[2]. The policy of introducing the first-trimester scan and offering chorion villus sampling to those with nuchal translucency ≥ 2.5 mm, while at the same time maintaining the previous policy of offering amniocentesis for maternal age ≥ 35 years, was not associated with a significant increase in the overall rate of invasive testing from 4.3% to 5.1%. Many women aged ≥ 35 years were reassured by the decreased risk for trisomies associated with nuchal translucency < 2.5 mm and decided against invasive testing.

This study has demonstrated that the incidence of nuchal translucency ≥ 2.5 mm increases with gestational age. A continuing study will establish a reference range with gestation for nuchal translucency thickness. This will allow calculation of the risk for trisomies on the basis of the deviation of a given translucency thickness from the normal mean at that gestation rather than from an absolute measurement.

The findings of the present study demonstrate the feasibility of introducing ultrasound scanning at 10–13 weeks' gestation and measurement of fetal nuchal translucency thickness in routine maternity units. Recent studies have shown that the risk for fetal trisomies at 10–13 weeks' gestation can be derived by combining data from fetal nuchal translucency thickness, maternal age and maternal serum free β-human chorionic gonadotropin and pregnancy-associated placental protein-A[6,7]. The sensitivity and specificity of this new approach in screening for chromosomal abnormalities can now be established by major prospective studies involving several maternity units.

ACKNOWLEDGEMENTS

We are grateful to the sonographers Sandra Hudson, Ann Ing, Jeanette O'Neill, Janet Fowler, Pat Manton, Pat Wilson and Hariksha Lapham from St. Peter's Hospital and Frimley Park Hospital. We also wish to thank Karen Marks, Elaine Gane, Jean Sherwood and the antenatal clinic staff for their assistance in collecting the data for amniocentesis and outcome of pregnancy.

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