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Fetal heart rate in chromosomally abnormal fetuses

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ABSTRACT

Objectives *To determine the effects of chromosomal defects on fetal heart rate at 10–14 weeks of gestation.*

Methods *Fetal heart rate at 10–14 weeks of gestation in 1061 chromosomally abnormal fetuses was compared to that from 25 000 normal pregnancies. The chromosomally abnormal group included 554 cases of trisomy 21, 219 cases of trisomy 18, 95 of trisomy 13, 50 of triploidy, 115 of Turner syndrome and 28 of sex chromosome abnormalities other than Turner syndrome.*

Results *In the normal group, fetal heart rate decreased from a mean value of 170 beats per minute (bpm) at 35 mm of crown–rump length to 155 bpm at 84 mm crown–rump length. In trisomy 21, trisomy 13 and Turner syndrome fetal heart rate was significantly higher, in trisomy 18 and triploidy the heart rate was lower and in other sex chromosome defects it was not significantly different from normal. Fetal heart rate was above the 95th centile of the normal range in 10%, 67% and 52% of fetuses with trisomy 21, trisomy 13 and Turner syndrome, respectively. The fetal heart rate was below the 5th centile in 30% of fetuses with triploidy and 19% of those with trisomy 18.*

Conclusions *Trisomy 21, trisomy 13 and Turner syndrome are associated with fetal tachycardia, whereas in trisomy 18 and triploidy there is fetal bradycardia. Inclusion of fetal heart rate in a first-trimester screening program for trisomy 21 by a combination of maternal age and fetal nuchal translucency thickness is unlikely to provide useful improvement in sensitivity.*

INTRODUCTION

In normal pregnancy, the fetal heart rate increases from about 110 beats per minute (bpm) at 5 weeks of gestation to 170 bpm at 9 weeks and then gradually decreases to 150 bpm by 14 weeks[1–4]. The early increase in heart rate coincides with the morphological development of the heart, and the subsequent decrease may be the result of functional maturation of the parasympathetic system[2,4,5].

Studies of heart rate in chromosomally abnormal fetuses have reported conflicting results. In a longitudinal study of one trisomy 21 fetus at 6–9 weeks of gestation, the heart rate was consistently below the 3rd centile of the normal range[6]. In another cross-sectional study of five affected fetuses at 7–13 weeks, the heart rate was always within the normal range[7]. A study of 17 trisomy 21 fetuses at 10–13 weeks reported that in 23.5% of cases, the heart rate was either above the 97th centile or below the 2.5th centile[8]. In another study of 85 trisomy 21 fetuses at 10–14 weeks, the heart rate was above the 95th centile in 21% of cases[1]. This study also examined fetuses with other chromosomal defects and reported that in the 34 cases with trisomy 18 and the eight cases with triploidy, fetal heart rate was decreased, whereas in 16 cases of trisomy 13 and 19 with Turner syndrome heart rate was increased[1].

This study of 554 trisomy 21 pregnancies and 507 with other chromosomal abnormalities diagnosed at 10–14 weeks of gestation examines further the relation between fetal heart rate and chromosomal defects.

METHODS

In our center screening for trisomy 21 is carried out by a combination of maternal age and fetal nuchal translucency thickness at 10–14 weeks of gestation[9,10]. During the ultrasound examination for measurement of fetal crown–rump length and nuchal translucency thickness the fetal heart rate is also recorded by the simultaneous use of Doppler and real-time B-mode imaging to obtain recordings of 6–10 cardiac cycles; the interval is measured with electronic callipers and the fetal heart rate is calculated using the software of the ultrasound machine. All ultrasound findings are recorded in a computer database during the scan and the results of fetal karyotype or pregnancy outcome are entered into the same database as soon as these become available.

A search of the database was carried out to identify all

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Table 1 Difference in mean fetal heart rate from the normal mean for crown–rump length in each of the chromosomal defects

Karyotype	n	*Mean difference (SD)*	*95% confidence interval*	*t*	P
Trisomy 21	554	0.17 (1.19)	0.07 to 0.27	3.43	0.0006
Trisomy 18	219	− 0.48 (1.79)	− 0.72 to − 0.25	− 4.00	< 0.0001
Trisomy 13	95	2.21 (1.55)	1.90 to 2.53	13.92	< 0.0001
Triploidy	50	− 0.82 (1.72)	− 1.31 to − 0.33	− 3.38	0.0014
Turner	115	1.71 (1.45)	1.44 to 1.98	12.62	< 0.0001
Other sex chromosome	28	− 0.30 (1.00)	− 0.69 to 0.09	− 1.58	0.126

singleton pregnancies with chromosomal abnormalities and 25 000 consecutive pregnancies resulting in the delivery of healthy and phenotypically normal babies.

Statistical analysis

A normal reference range (mean, 5th and 95th centiles) for fetal heart rate with crown–rump length was derived by regression analysis of the data from the 25 000 normal pregnancies. Each fetal heart rate value was then expressed as the number of standard deviations by which it differed from the appropriate normal mean for the corresponding crown–rump length (delta value). The distribution of fetal heart rate expressed in delta values was shown to be normally distributed using the Kolmogorov–Smirnov test. One sample *t*-test was then used to examine if there was a significant difference in the mean delta value in each subgroup of the chromosomal abnormalities when compared to the normal control group.

RESULTS

In the normal group of 25 000 pregnancies there was a significant association between fetal heart rate and crown–rump length (CRL) (fetal heart rate = 181.409–0.324 × CRL (mm), SD = 6.6 bpm, R = − 0.44, $P < 0.0001$; Figure 1). There were 1061 chromosomally abnormal pregnancies, including 554 cases of trisomy 21, 219 cases of trisomy 18, 95 of trisomy 13, 50 of triploidy, 115 of Turner syndrome and 28 of sex chromosome abnormalities other than Turner syndrome. In cases of trisomy 21, trisomy 13 and Turner syndrome fetal heart rate was significantly higher, in trisomy 18 and triploidy the heart rate was lower and in other sex chromosome defects it was not significantly different from normal (Tables 1 and 2, Figures 2, 3 and 4). There was no significant association between the deviation from normal in fetal nuchal translucency and fetal heart rate in trisomy 18 ($r = 0.02$), trisomy 13 ($r = -0.09$), Turner syndrome ($r = -0.05$), other sex chromosome aneuploidies ($r = 0.30$) and triploidy ($r = 0.22$), but there was a correlation in trisomy 21 ($r = 0.21$, $P < 0001$).

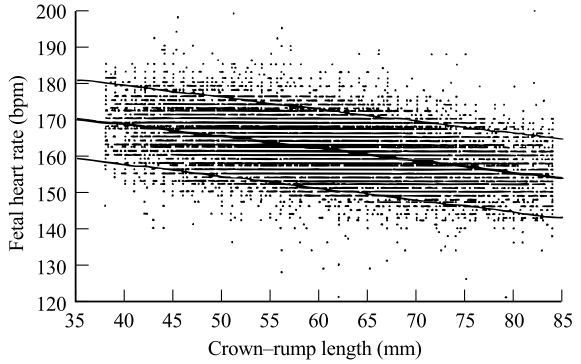

Figure 1 Fetal heart rate in the control group. The median, 5th and 95th centiles are also shown.

DISCUSSION

The decrease in fetal heart rate observed between 10 and 14 weeks of gestation is compatible with the results of previous studies[1,7]. Similarly, the increase in fetal heart rate in trisomy 21 was reported previously[1] but in the present much larger study this increase was very small and only about 10% of the values were above the 95th centile. Therefore, inclusion of fetal heart rate in a first-trimester screening program for trisomy 21 by a combination of maternal age and fetal nuchal translucency thickness is unlikely to provide useful improvement in sensitivity. In contrast to trisomy 21, the fetal heart rate was above the 95th centile in 67% of fetuses with trisomy 13 and 52% of those with Turner syndrome. Trisomy 18 and triploidy were associated with a relative bradycardia.

Possible explanations for differences in heart rate between the various chromosomal abnormalities include differences in the types of associated cardiac defects or varying degrees of developmental delay. The commonest defects observed in trisomy 21 fetuses are atrioventricular or ventricular septal defects and relative narrowing of the aortic isthmus. In trisomy 13, there are atrioventricular

Table 2 Number of cases with fetal heart rate below the 5th centile, above the median or above the 95th centile of the normal range for crown–rump length in each of the chromosomal defects

Karyotype	n	*< 5th centile*	*> median*	*> 95th centile*
Trisomy 21	554	5.2% (29)	54.0% (299)	9.7% (54)
Trisomy 18	219	18.7% (41)	39.7 (87)	4.6% (10)
Trisomy 13	95	2.1% (2)	94.7% (90)	67.4% (64)
Triploidy	50	30.0% (15)	26.0% (13)	4.0% (2)
Turner	115	1.7% (2)	89.6% (103)	52.2% (60)
Other sex chromosome	28	7.1% (2)	35.7% (10)	0% (0)

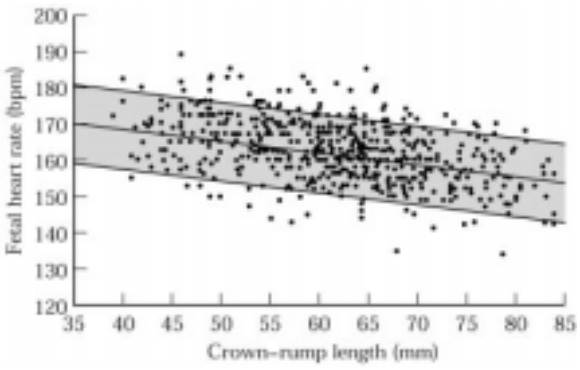

Figure 2 Fetal heart rate in cases of trisomy 21 plotted on the normal range for crown–rump length (shaded area defined by 5th and 95th centiles).

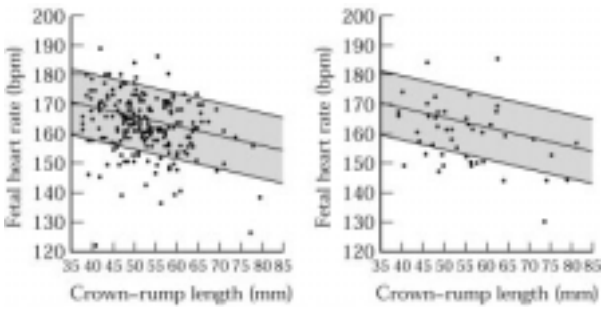

Figure 4 Fetal heart rate in cases of trisomy 18 (left) and triploidy cases (right) plotted on the normal range for crown–rump length (shaded area defined by 5th and 95th centiles).

or ventricular septal defects, valvular abnormalities and either narrowing of the isthmus or truncus arteriosus. Turner syndrome is associated with severe narrowing of the aortic arch. In both trisomy 13 and Turner syndrome, narrowing of the isthmus is accompanied by narrowing of the ascending aorta[11]. In trisomy 18 there are ventricular septal defects and/or polyvalvular abnormalities. It is of interest that tachycardia characterizes those chromosomal abnormalities in which there is narrowing of the outflow tract from the left ventricle and this tachycardia may well be mediated by the action of baroreceptors in the aortic arch. In fetal life, the heart normally performs near the peak of the Frank–Starling curve of ventricular function[12] and therefore tachycardia may represent a compensatory mechanism to increase cardiac output in the phase of left heart obstruction[13].

Triploidy and trisomy 18 are associated with severe early onset intrauterine growth restriction[14–19] and the bradycardia observed in some of these cases may represent a preterminal event.

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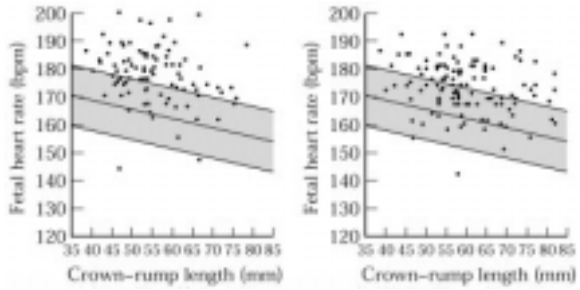

Figure 3 Fetal heart rate in cases of trisomy 13 (left) and Turner syndrome (right) plotted on the normal range for crown–rump length (shaded area defined by 5th and 95th centiles).

REFERENCES

1 Hyett JA, Noble PL, Snijders RJ, Montenegro N, Nicolaides KH. Fetal heart rate in trisomy 21 and other chromosomal abnormalities at 10–14 weeks of gestation. *Ultrasound Obstet Gynecol* 1996; 7: 239–44
2 Robinson HP, Shaw-Dunn J. Fetal heart rates as determined by sonar in early pregnancy. *J Obstet Gynaecol Br Commonw* 1973; 90: 805–9
3 Rempen A. Diagnosis of viability in early pregnancy with vaginal sonography. *J Ultrasound Med* 1990; 9: 711–6
4 Wisser J, Dirschedl P. Embryonic heart rate in dated human embryos. *Early Hum Dev* 1994; 37: 107–15
5 Wladimiroff JW, Seelen JC. Fetal heart action in early pregnancy. Development of fetal vagal function. *Eur J Obstet Gynecol* 1972; 2: 55–63
6 Schats R, Jansen CAM, Wladimiroff JW. Abnormal embryonic heart rate pattern in early pregnancy associated with Down's syndrome. *Hum Reprod* 1990; 5: 877–9
7 Van Lith JMM, Visser GHA, Mantingh A, Beekhuis JR. Fetal heart rate in early pregnancy and chromosomal disorders. *Br J Obstet Gynaecol* 1992; 99: 741–4
8 Martinez JM, Echevarria M, Borrell A, Puerto B, Ojuel J, Fortuny A. Fetal heart rate and nuchal translucency in detecting chromosomal abnormalities other than Down syndrome. *Obstet Gynecol* 1998; 92: 68–71
9 Nicolaides KH, Azar G, Byrne D, Mansur C, Marks K. Fetal nuchal translucency: ultrasound screening for chromosomal defects in first trimester of pregnancy. *Br Med J*, 1992; 304: 867–9
10 Snijders RJM, Noble P, Sebire N, Souka A, Nicolaides KH. UK multicentre project on assessment of risk of trisomy 21 by maternal age and fetal nuchal translucency thickness at 10–14 weeks of gestation. *Lancet* 1998; 351: 343–6
11 Hyett JA, Moscoso G, Nicolaides KH. Abnormalites of the heart and great arteries in first trimester chromosomally abnormal fetuses. *Am J Med Genet* 1997; 69: 207–16
12 Teitel D, Rudolph AM. Perinatal oxygen delivery and cardiac function. *Adv Paediatr* 1985; 32: 321–47
13 Rudolph AM, Heymann MA. Cardiac output in the fetal lamb: the effects of spontaneous and induced changes of heart rate on right and left ventricular output. *Am J Obstet Gynecol* 1976; 124: 183–92
14 Lynch L, Berkowitz RL. First trimester growth delay in trisomy 18. *Am J Perinatol* 1989; 6: 237–9
15 Kuhn P, Brizot ML, Pandya PP, Snijders RJ, Nicolaides KH. Crown-rump length in chromosomally abnormal fetuses at 10–13 weeks gestation. *Am J Obstet Gynecol* 1995; 172: 32–5
16 Bahado-Singh RO, Lynch L, Deren O, Morotti R, Copel JA,

Mahoney MJ, Williams J. First-trimester growth restriction and fetal aneuploidy: the effect of type of aneuploidy and gestational age. *Am J Obstet Gynecol* 1997; 176: 976–80

17 Jauniaux E, Brown R, Snijders RJ, Noble P, Nicolaides KH. Early prenatal diagnosis of triploidy. *Am J Obstet Gynecol* 1997; 176: 550–4

18 Schemmer G, Wapner RJ, Johnson A, Schemmer M, Norton HJ, Anderson WE. First-trimester growth patterns of aneuploid fetuses. *Prenat Diagn* 1997; 17: 155–9

19 Sherrod C, Sebire NJ, Soares W, Snijders RJ, Nicolaides KH. Prenatal diagnosis of trisomy 18 at the 10–14-week ultrasound scan. *Ultrasound Obstet Gynecol* 1997; 10: 387–90