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## Is intrauterine growth retardation with normal umbilical artery blood flow a benign condition?

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### Abstract

**Objective**—To determine whether intrauterine growth retardation associated with normal umbilical artery blood flow is a benign condition.

**Design**—A prospective comparative study of growth retarded fetuses with normal and abnormal umbilical artery blood flow.

**Setting**—The fetal assessment clinic of a large maternity hospital in Ireland.

**Patients**—179 Women with singleton pregnancies in which the fetal abdominal circumference, measured by ultrasonography, was below the fifth centile for gestation.

**Main outcome measures**—Perinatal deaths, fetal distress requiring caesarean section, preterm delivery, cerebral irritation.

**Results**—Of 124 fetuses with normal flow, all physically normal fetuses survived but one baby had cerebral irritation; there were six preterm deliveries and four caesarean sections for fetal distress. Among 55 women with physically normal fetuses with abnormal flow there were two midtrimester abortions, three perinatal deaths, and one case of cerebral irritation; there were 23 preterm deliveries and six caesarean sections for fetal distress in labour.

**Conclusions**—Intrauterine growth retardation associated with normal umbilical blood flow is a different entity from that associated with abnormal flow, normal flow being largely benign and abnormal flow carrying a serious risk of adverse outcome.

### Introduction

Intrauterine growth retardation is an important cause of perinatal death. In the Republic of Ireland the death rate in late pregnancy of normal fetuses weighing between 2000 and 2499 g was 37.2 and 39.7 per 1000 in 1986 and 1987 respectively.<sup>1</sup> Babies of this birth weight accounted for only 2.7% of total births but for 27.6% of the deaths of normal fetuses in late pregnancy. No reliable method exists to establish whether a fetus is small because of placental insufficiency or because of genetic and racial factors, when it is small but appropriately nourished; in both cases it is classified as being growth retarded. Consequently, women with small but healthy fetuses may be admitted to hospital unnecessarily and have unneeded intervention, including caesarean section.

Intrauterine growth retardation associated with normal umbilical artery blood flow has been suggested to be a largely benign condition.<sup>2</sup> A recent report suggested that Doppler studies of the umbilical artery can identify a group of growth retarded babies at increased risk of intrapartum hypoxia.<sup>3</sup> Cordocentesis has shown a significant negative correlation between the severity of fetal hypoxia and the mean velocity of blood in the fetal aorta.<sup>4</sup> In addition, although no correlation has been found between the size of the fetus and hypoxia

or acidosis, absence of end diastolic blood flow seemed to be a good marker of asphyxia in growth retarded fetuses.

We tested the hypothesis that intrauterine growth retardation associated with normal patterns of umbilical artery blood flow is largely benign.

### Patients and methods

All high risk patients referred to the fetal assessment clinic at this hospital from September 1988 to May 1989 were entered into the study. Each woman had fetal biometry, and the biophysical profile of the fetus was scored.<sup>5</sup> Suspected intrauterine growth retardation was the commonest indication for referral to the clinic. Growth retardation was diagnosed if the fetal abdominal circumference, measured by ultrasonography, was below the fifth centile for gestation.<sup>7</sup> All women underwent velocity waveform analysis of the umbilical artery by continuous wave Doppler ultrasound at each visit to the clinic. The equipment consisted of a real time ultrasound scanner (General Electric RT 3600) and a spectrum analyser (Doptek 9012) which has a high pass filter of 150 Hz. Informed consent was obtained from each patient, and ethical approval was granted by the hospital.

Results of the Doppler investigation were withheld from the doctors managing the cases. We calculated the peak systolic to end diastolic ratio for each fetus and identified three blood flow patterns: in type 1 the ratio was  $\leq 2$  SD above the mean for gestational age<sup>8</sup>; in type 2 the ratio was  $> 2$  SD above the mean; and in type 3 end diastolic blood flow was absent or reversed.

Birthweight centiles for gestation were based on standards for Irish neonates<sup>9</sup> and were not applied to babies born before 34 weeks' gestation as no reliable data were available. A perinatal death was defined as a stillborn fetus weighing  $\geq 500$  g or the death within seven days of birth of a neonate who weighed  $\geq 500$  g at birth. Cerebral irritation was defined as convulsions, abnormal reflexes, or abnormal tone in the first seven days after birth.<sup>10</sup>

We calculated relative risks and 95% confidence intervals according to the method of Morris and Gardner.<sup>11</sup>  $\chi^2$  Tests, with correction for continuity, were performed for discrete variables.

### Results

At the final assessment 179 fetuses had an abdominal circumference below the fifth centile. Of these, 124 had normal umbilical artery velocity waveforms. Forty four fetuses had type 2 flow and 11 had type 3. Table 1 shows the outcome of pregnancy according to the type of umbilical artery blood flow. In the group with type 3 flow there were two midtrimester abortions: one fetus was born alive but weighed less than 500 g and could not be resuscitated. Of the 166 babies born after 34

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TABLE I—Outcome of pregnancy according to pattern of fetal blood flow. Figures are numbers (percentages)

	Type 1— systolic:diastolic ratio $\leq$ 2 SD above mean for gestation (n=124)	Type 2— systolic:diastolic ratio $>$ 2 SD above mean for gestation (n=44)	Type 3— no end diastolic blood flow (n=11)	Total (n=179)
Midtrimester abortions			2 (18)***†	2 (1)
Stillbirths:				
Total		3 (7)	2 (18)***	5 (3)
Congenital anomaly		2 (5)		2 (1)
Neonatal deaths:				
Total	4 (3)	1 (2)		5 (3)
Congenital anomaly	4 (3)	1 (2)		5 (3)
Major congenital anomaly	5 (4)	5 (11)		10 (6)
Cerebral irritation	1 (1)	1 (2)		2 (1)
Baby born before 37 weeks' gestation	6 (5)	14 (32)***	9 (82)***	29 (16)
Baby born before 34 weeks' gestation	2 (2)	3 (7)	8 (73)***	13 (7)
Baby admitted directly to neonatal intensive care unit‡	25 (20)	22 (56)***	6 (75)***	53 (31)
Induction of labour‡	65 (52)	16 (41)	1 (13)	82 (48)
Elective caesarean section‡	19 (15)	15 (38)	7 (88)*	41 (24)
Emergency caesarean section for fetal distress in labour‡	4 (3)	5 (13)*	1 (13)*	10 (6)

\* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$  Compared with group with type 1 flow.

†One fetus was born alive.

‡Percentages are of live births.

TABLE II—Incidence (per 1000 fetuses) of adverse outcome with normal and abnormal umbilical artery blood flow

Outcome	Normal flow (n=124)	Abnormal flow (n=55)	Relative risk (95% confidence interval)
Midtrimester abortion		36.4	
Perinatal death	32.3	109.1	3.4 (1.0 to 11.5)
Midtrimester abortion and perinatal death	32.3	145.5	4.5 (1.4 to 14.3)
Perinatal death (corrected for major congenital anomalies)		54.5	
Cerebral irritation	8.1	18.2	2.3 (0.1 to 36.1)
Preterm delivery	48	418.0	12.2 (5.2 to 28.4)
Emergency caesarean section for fetal distress (excluding stillbirths and elective caesarean sections)	38	222	7.2 (2.2 to 23.8)

weeks' gestation, 63 of the 122 with normal flow and 33 of the 44 with abnormal flow had a birth weight below the fifth centile ( $p < 0.05$ ).

Table II gives the relative risks of each outcome for abnormal flow (types 2 and 3) compared with normal flow (type 1).

### Discussion

Only one unfavourable outcome, cerebral irritation in a baby with a symmetric growth pattern, occurred among the 119 physically normal fetuses with retarded growth and normal umbilical artery waveforms. In the group with normal blood flow only one normal baby was delivered before 34 weeks' gestation and the incidence of fetal distress requiring emergency caesarean section (38 per 1000 births) was fairly low. On the other hand, intrauterine growth retardation accompanied by abnormal waveforms was associated with high perinatal mortality (both uncorrected (109.1 per 1000 fetuses) and corrected (54.5 per 1000) for congenital abnormalities) and a high rate of midtrimester abortion (36.4 per 1000). Abnormal flow also conferred a relative risk of seven for fetal distress requiring caesarean section and of 12 for preterm delivery. The increased incidence of adverse outcome was not confined to fetuses with no end diastolic blood flow, being found also in those with high peak systolic to end diastolic ratios (type 2 flow).

Data from the metropolitan Atlanta congenital defects programme showed that the risk of a major defect being diagnosed in the first year of life increases from 3.3% for infants who did not have intrauterine growth retardation to 8.0% for infants who do.<sup>12</sup> Fetuses with major abnormalities have an increased incidence of abnormal umbilical artery velocity waveforms.<sup>13</sup> We found an increased incidence of major congenital malformation in fetuses with intrauterine growth retardation whether the patterns of blood flow were normal (4%) or abnormal (9%), and this contributed to perinatal mortality in both groups.

When abnormal flow is defined as the absence of end diastolic flow Doppler analysis has a high specificity (95%) when used as a secondary diagnostic test for growth retardation suspected after routine fetometry.<sup>14</sup> The broader definition of abnormal flow that we used seemed to improve the sensitivity for detecting fetal compromise; several fetuses that were compromised had type 2 flow. In addition, the positive predictive value of the fetal abdominal circumference for a birth weight below the fifth centile for gestation is increased from 52% to 75% when umbilical artery blood flow is abnormal.

To our knowledge we are the first to show that intrauterine growth retardation associated with normal umbilical artery velocity waveforms is largely benign in physically normal fetuses. Intervention rates, however, were high whether fetuses had normal or abnormal flow, and this indicates the seriousness with which intrauterine growth retardation is regarded by obstetricians. We cannot determine how these high intervention rates contributed to the favourable results in the group with normal blood flow, but more conservative management could probably be safely implemented in this group; further studies are required to determine this.

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