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Prospective risk of stillbirth according to fetal size at term

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Abstract

Objectives: Fetal growth and size are associated with stillbirth risk. We wanted to investigate the week by week predictive value of fetal size at term on the prospective risk of stillbirth.

Methods: Anonymised database from the UK GAP program, with 2,094,702 term (≥ 37 weeks) deliveries including 4,670 stillbirths. Prospective stillbirth risk was defined as fetal death in the current week divided by total undelivered pregnancies. The data were analysed in five centile bands for stillbirth risk and risk ratios (RR) for 38, 39, 40 and 41+ weeks, using appropriate for gestational age (AGA) at 37 weeks as reference.

Results: Baseline stillbirth risk at 37 weeks was 0.29 per 1,000 and rose to 1.39 at 41+ weeks, with RR increasing to 4.8. In the 3<10 centile band risk rose from 0.72 to 2.43 over the same period, with RR increasing from 2.5 to 8.4. In the <3 centile group, the stillbirth risk rose from 1.62 to 6.16 (RR 5.6 to 21.2). In the 97>90 centile band, risk increased from 0.40 to 1.50 (RR 1.4 to 5.2) and for >97 centiles, it rose from 0.80 to 2.13 (RR 2.8–7.3).

Conclusions: Prospective risk of fetal death at term is related to fetal size. The information provided, together with other considerations and results of investigations where available, will help clinicians to determine the advice to give to mothers about the best timing for delivery, balancing the baby's risk of compromise with iatrogenic sequelae of early delivery.

Keywords: fetal growth; large for gestational age; small for gestational age; stillbirth.

Introduction

Fetal size is a major determinant of the risk of stillbirth [1, 2], and one of the key considerations for clinicians regarding advice to mothers on the best time to deliver. Royal College of Obstetricians and Gynaecologists guidelines [3] recommend delivery by 37 weeks if a fetus is small for gestational age (SGA, <10th centile), based largely on findings of the DIGITAT [4] trial. However early term delivery has been associated with risk of delayed effects including an increase in infants with special educational needs [5].

Therefore current versions of the NHS England saving babies lives care bundle [6] and the care pathway of the Growth Assessment Protocol (GAP) [7, 8] recommend a distinction between fetuses with estimated fetal weight below the third centile, which are more likely to have fetal growth restriction and should be delivered by 37 weeks, and those between the third and tenth centile, where delivery can be delayed until 39 weeks if Doppler investigations are normal [9]. At the other end of the size spectrum, fetuses that are large for gestational age (LGA, >90th centile) have an increased risk of shoulder dystocia and other birth injuries [10, 11] but guidelines for management are likely to follow completion of the 'Big Baby Trial' [12] expected in 2023.

To help clinicians with informed advice to expectant mothers on timing of birth, we wanted to investigate the predictive value of different fetal size bands on prospective risk of stillbirth at each week at term.

Materials and methods

Data origin

We used an anonymised database from the UK national GAP programme from 2015 to 2021. Data were collected prospectively during routine care which included the use of customised growth charts [13, 14] whereby the centile is calculated after adjustment for a set of physiological coefficients including maternal height, early pregnancy weight, parity and ethnic origin [13]. Gestational age of stillbirths was adjusted by deducting two days from the date of delivery as the approximate average death-to-delivery interval [15]. Birthweight centiles were grouped into completed weeks gestation (e.g. 40 weeks included 40+0 to 40+6 days).

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Calculation of prospective stillbirth risk

To obtain the prospective risk [16] we calculated the risk of fetal deaths in a given week as the proportion of the total ongoing pregnancies in that week; e.g.

$$\text{Prospective risk at 38 weeks} = \frac{\text{stillbirths in week 38}}{\text{total births from week 38 onwards}}$$

The risk calculation was stratified into five customised centile bands: <3, 3<10 and 10–90, 97>90 and >97. Risk ratios were calculated using the 10–90 centile band at 37 weeks as reference.

Statistical software

Analyses were carried out using Excel (2016; Microsoft, Redmond, WA) and Stata (version 15.1; StataCorp, College Station, TX).

Table 1: Descriptives (n=2,094,702 deliveries ≥37.0 weeks).

	n	%	Mean	SD	Median	IQR
Maternal height, cm			164.3	6.6	164.0	9.0
Maternal weight, kg			71.7	17.0	68.0	20.0
Body mass index, kg/m ²			26.5	5.9	25.3	7.3
<18.5	56,778	2.7				
18.5<25	948,834	45.3				
25<30	598,920	28.6				
30<35	294,728	14.1				
≥35	195,442	9.3				
Parity						
0	880,919	42.1				
1	734,032	35.0				
2	297,249	14.2				
≥3	182,502	8.7				
Ethnic groups						
British European	1,431,873	68.4				
Irish	45,997	2.2				
East European	136,633	6.5				
Other European	51,191	2.4				
South Asian	185,692	8.9				
South East Asian	17,467	0.8				
Far East Asian	14,406	0.7				
Middle Eastern & North African	26,859	1.3				
Sub-Saharan African	65,472	3.1				
Caribbean	14,870	0.7				
Mixed	20,367	1.0				
Other	83,875	4.0				
Gestation at delivery, d			277.9	8.6	278.0	12.0
Sex						
Male	1,063,849	50.8				
Female	1,030,130	49.2				
Unknown	723	0.0				
Birthweight, g			3,424.1	482.8	3,425.0	650.0
LGA >97	111,283	5.3				
LGA 97>90	59,678	2.8				
SGA 3<10	144,814	6.9				
SGA <3	65,307	3.1				
Stillbirth	4,670	2.2	/1,000			

SD, standard deviation; IQR, interquartile range; SGA, small for gestational age; LGA, large for gestational age.

Ethics

Ethics committee approval was not required as all data were recorded as part of routine care, and were fully anonymized before being released for analysis.

Results

The study cohort consisted of 2,094,702 term deliveries (≥37 weeks) and included 4,670 stillbirths (rate 2.2/1,000). Table 1 displays the characteristics of this population. The incidence of underweight (<18.5 BMI) pregnancies was 2.7% and 23.4% were classified as obese (BMI>30). The

largest ethnic group was British European (68.4%) followed by South Asian (8.9%) and East European (6.5%). The SGA rate was 10.0% and LGA rate was 8.2%.

Table 2 displays the prospective stillbirth risk and risk ratios from 37 to 41 completed weeks by centile band. The baseline stillbirth risk (10–90 centile at 37 weeks; per 1,000) was 0.29 and rose to 1.39 at 41+ weeks. In comparison, stillbirth risk in the 3<10 centile band rose from 0.72 to 2.43, and in fetuses <3 centile from 1.62 to 6.16. The table also shows the risk ratios in reference to a 10–90 centile fetus at 37 weeks: for example, a fetus <3rd centile at 37 weeks has a 5.6 fold higher risk of stillbirth, which progressively increases to 21.2 fold at 41+ weeks. Stillbirth risk and risk ratios for LGA >97 centile babies showed a less accelerated increase with gestational age, while in the 97>90 centile band they rose at a similar rate to the 10–90 centile control. These findings are illustrated in Figure 1A and 1B.

Discussion

This is to our knowledge the first study of prospective risk of stillbirth by fetal size as assessed by customised centiles, the standard used in most pregnancies in the UK national health service. We found that SGA and LGA fetuses have an increasing risk of fetal death after 37 weeks which increases

further with advancing gestation and is highest for babies below the third centile.

Our findings are consistent with previous studies of large databases. Muglu and colleagues' systematic review showed a steady increase in prospective stillbirth risk with advancing gestational age [17]. Pilliod et al. [18] stratified their cohort by uncustomised fetal size and also found the highest risk in fetuses that were <3rd centile.

A strength of our study is its large size with over two million term pregnancies, which allowed us to divide the cohort into different gestational age and centile bands. Pregnancies were routinely dated by scan, and size was assessed by customised centiles, which improves the distinction between pathologic growth restriction and the constitutionally small fetuses.

A potential limitation of our study was the use of birthweight rather than fetal weight to determine the size centile of the fetus. However ultrasound scans are less precise than birthweight due to systematic and random error [19]. Furthermore, assessment of fetal weight is not done routinely at term, and selecting only the cases where it had been performed is likely to reduce generalisability of our findings. Detection of SGA or LGA at scan may have influenced the timing of delivery, and it could be speculated that at the LGA end of the distribution, the observed drop in stillbirth rate at 39 weeks in the >97 centile group (Figure 1B) may have been due to elective deliveries to

Table 2: Prospective stillbirth risk and risk ratios by size and gestational age at term (n=2,094,702).

Centile band		Current week of gestation				
		37	38	39	40	41+
>97	Ongoing pregnancies, n	59,678	52,177	38,626	16,914	6,101
	Stillbirths, n	48	48	27	25	13
	Stillbirth risk ^a	0.80	0.92	0.70	1.48	2.13
	Risk ratio ^b	2.8	3.2	2.4	5.1	7.3
97>90	Ongoing pregnancies, n	111,283	102,344	81,564	42,536	15,979
	Stillbirths, n	45	67	62	46	24
	Stillbirth risk ^a	0.40	0.65	0.76	1.08	1.50
	Risk ratio ^b	1.4	2.3	2.6	3.7	5.2
10–90	Ongoing pregnancies, n	1,686,620	1,557,739	1,297,207	790,705	317,996
	Stillbirths, n	490	733	904	790	441
	Stillbirth risk ^a	0.29	0.47	0.70	1.00	1.39
	Risk ratio ^b	1.0	1.6	2.4	3.4	4.8
3<10	Ongoing pregnancies, n	144,814	118,018	86,574	42,516	27,992
	Stillbirths, n	104	93	134	98	68
	Stillbirth risk ^a	0.72	0.79	1.55	2.31	2.43
	Risk ratio ^b	2.5	2.7	5.3	7.9	8.4
<3	Ongoing pregnancies, n	65,307	46,884	33,416	19,764	8,114
	Stillbirths, n	106	97	85	72	50
	Stillbirth risk ^a	1.62	2.07	2.54	3.64	6.16
	Risk ratio ^b	5.6	7.1	8.8	12.5	21.2

^aper 1,000 births; ^breference for risk ratio: stillbirth risk for 10–90th centile fetus at 37 weeks.

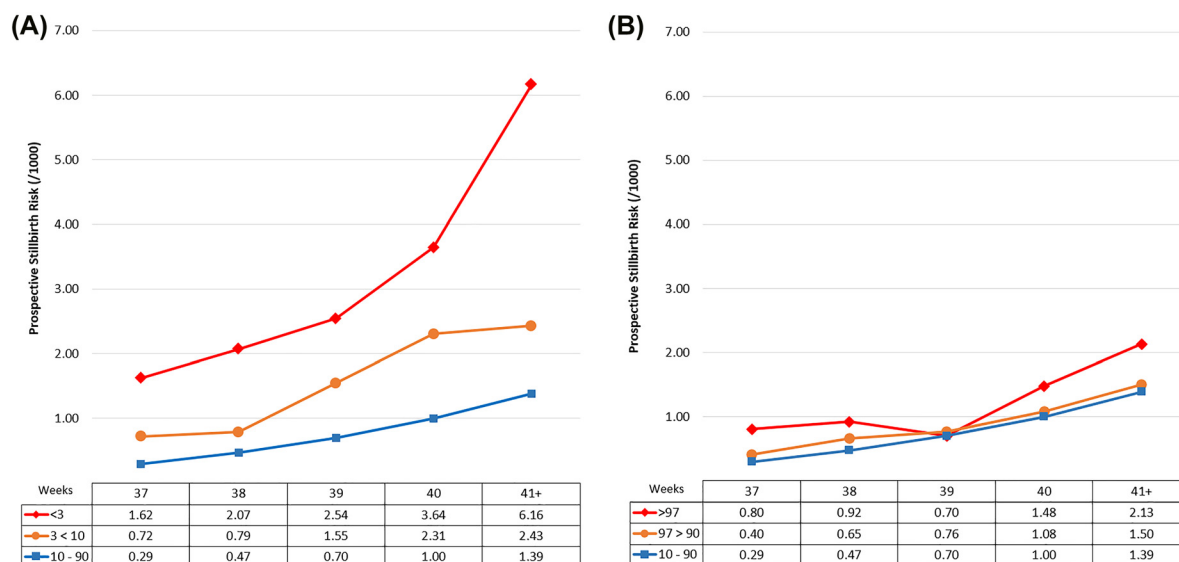


Figure 1: Prospective risk of stillbirth.

Appropriate for gestational age (AGA, 10–90 centile) is compared with (A) small for gestational age (SGA; <3 and 3<10) and (B) large for gestational age (LGA; >97 and 97>90) centile bands.

avoid birth complications such as shoulder dystocia. We did not have information on co-morbidities and ultrasound and Doppler investigations in this large cohort, and most growth scans in our population are carried out before 37 weeks. However these are additional factors which need to be taken into consideration when deciding on the optimal time for delivery.

Our study provides real world, routinely collected data of customised birthweight centiles as proxy for fetal growth in term pregnancies. The findings support the concept that, while there is a gradual increase in stillbirth risk for all pregnancies at term, small and large babies have a sharper, weekly increase in risk which is steepest when fetal size is <3rd centile.

These findings may assist clinicians in their advice to mothers on timing of delivery. The advice will need to balance the antenatal risk of a potentially compromised baby continuing in an unfavourable intrauterine environment, against increasing evidence that ‘early term’ delivery presents neurodevelopmental risk for the infant [5]. Currently, such developmental studies relate infant risk to gestational age at delivery alone, but it is hoped they will also be able to stratify risk according to subcategories of fetal size representing slow and accelerated growth.

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Author contributions: All authors participated in conceptualising the problem, analysis of data and write up of the manuscript. They accept responsibility for its content and approved its submission.

Competing interests: OH and JG work for the Perinatal Institute, a not-for-profit social enterprise that provides free tools to calculate customised centiles which are used in this study.

Informed consent: Not applicable.

Ethical approval: Not applicable – all data were fully anonymised.

Data availability: The datasets analysed during the current study are available on reasonable request, but restrictions may apply as the data were collected under license from National Health Service Trusts.

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