

Prolonged pregnancy: evaluating gestation-specific risks of fetal and infant mortality

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Objective To evaluate gestation-specific risks of stillbirth, neonatal and post-neonatal mortality.

Design Retrospective analysis of 171,527 notified births (1989–1991) and subsequent infant survival at one year, from community child health records.

Setting Notifications from maternity units in the North East Thames Region, London.

Main outcome measures The incidence of births, stillbirths, neonatal and post-neonatal deaths at each gestation after 28 completed weeks. Mortality rates per 1000 total or live births and per 1000 ongoing pregnancies at each gestation were calculated.

Results The rates of stillbirth at term (2.3 per 1000 total births) and post-term (1.9 per 1000 total births) were similar. When calculated per 1000 ongoing pregnancies, the rate of stillbirth increased six-fold from 0.35 per 1000 ongoing pregnancies at 37 weeks to 2.12 per 1000 ongoing pregnancies at 43 weeks of gestation. Neonatal and post-neonatal mortality rates fell significantly with advancing gestation, from 151.4 and 31.7 per 1000 live births at 28 weeks, to reach a nadir at 41 weeks of gestation (0.7 and 1.3 per 1000 live births, respectively), increasing thereafter in prolonged gestation to 1.6 and 2.1 per 1000 live births at 43 weeks of gestation. When calculated per 1000 ongoing pregnancies, the overall risk of pregnancy loss (stillbirth + infant mortality) increased eight-fold from 0.7 per 1000 ongoing pregnancies at 37 weeks to 5.8 per 1000 ongoing pregnancies at 43 weeks of gestation.

Conclusion The risks of prolonged gestation on pregnancy are better reflected by calculating fetal and infant losses per 1000 ongoing pregnancies. There is a significant increase in the risk of stillbirth, neonatal and post-neonatal mortality in prolonged pregnancy. This study provides accurate data on gestation-specific risks of pregnancy loss, enabling pregnant women and their carers to judge the appropriateness of obstetric intervention.

INTRODUCTION

Prolonged pregnancy poses a number of risks to the fetus including meconium aspiration, birth injury and hypoxia. However, the concern that most occupies the minds of mothers and medical attendants, is the risk of fetal loss. Gestation-specific stillbirth rates expressed per 1000 total births at each week of gestation, is often incorrectly interpreted as equating to risk of stillbirth. As only women who are still pregnant are at risk of stillbirth, it would be more appropriate to calculate the risk of stillbirth as a proportion of the ongoing pregnancies at a particular gestation¹. By contrast, it is appropriate to use the number of live births as the denominator for neonatal mortality, as a neonate is at risk of dying only after it is liveborn. Most major studies on gestation-specific perinatal mortality were carried out before modern advances in the accuracy of determining gestational

age¹⁻⁵. Additionally, late neonatal and post-neonatal deaths are excluded from most analyses of obstetric outcome, even though preterm and post-term delivery has been associated with an increased risk of infant loss for up to two years⁶.

The aim of this study was to evaluate the rates of stillbirth and infant mortality per 1000 total or live births and ongoing pregnancies at each given gestation. The former allows direct comparison with other published studies, while the latter is a better reflection of mortality risk faced by the fetus and infant at each week of gestation. For this purpose we examined a large regional database of birth notifications linked to stillbirth and infant death registration.

METHODS

Data source

Details of each registerable birth in and to residents of the North East Thames Region, from 18 Hospitals were

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Table 1. The number of deliveries, ongoing pregnancies, cumulative percentage born, stillbirths (SB), neonatal (NN) and post-neonatal (PNN) deaths and mortality rates per 1000 total or live births at each week of gestation. Values are given as *n* and rate (95% CI) unless otherwise indicated. GAD = gestation at delivery.

GAD (weeks)	No. deliveries	Ongoing pregnancies*	Cumulative % born*	Deaths			Mortality rate		
				SB	NN	PNN	SB	NN	PNN
Missing data	745			4	5	14			
< 20 or > 46	249			2	3	1			
20-27	732			7	292	41			
28	317	169,801	0.2	33	43	9	104.1 (70.5-138.0)	151.4 (98.0-173.0)	31.7 (13.1-53.2)
29	298	169,484	0.2	30	23	8	100.7 (66.5-135.0)	85.8 (49.5-114.0)	29.9 (11.7-52.2)
30	457	169,186	0.3	56	25	7	122.5 (92.5-153.0)	62.3 (35.7-79.7)	17.5 (6.2-31.3)
31	530	168,729	0.3	43	17	6	81.1 (59.4-108.0)	34.9 (18.7-50.8)	12.3 (4.2-24.5)
32	809	168,199	0.5	59	23	11	72.9 (56.0-93.1)	30.7 (18.1-42.3)	14.7 (6.8-24.2)
33	914	167,390	0.6	40	22	9	43.8 (31.4-59.1)	25.2 (15.2-36.2)	10.3 (4.5-18.6)
34	1616	166,476	1.0	63	19	9	39.0 (30.1-49.6)	12.2 (7.1-18.2)	5.8 (2.5-10.6)
35	2254	164,860	1.4	54	13	14	24.0 (18.0-31.2)	5.9 (3.1-9.8)	6.4 (3.4-10.4)
36	4435	162,603	2.7	73	33	28	16.5 (12.7-20.2)	7.6 (4.9-10.0)	6.4 (4.0-8.6)
37	8990	158,171	5.7	56	22	31	6.2 (4.6-7.9)	2.5 (1.4-3.5)	3.5 (2.2-4.7)
38	22,021	149,181	14.8	83	44	60	3.8 (3.0-4.6)	2.0 (1.4-2.6)	2.7 (2.0-3.4)
39	33,332	127,160	26.2	72	41	65	2.2 (1.7-2.7)	1.2 (0.9-1.6)	2.0 (1.5-2.4)
40	54,512	93,828	58.1	81	65	82	1.5 (1.2-1.8)	1.2 (0.9-1.5)	1.5 (1.2-1.8)
41	28,988	39,316	73.7	50	21	37	1.7 (1.3-2.2)	0.7 (0.4-1.0)	1.3 (0.8-1.7)
42	8445	10,328	81.8	16	15	19	1.9 (1.0-2.8)	1.8 (0.9-2.7)	2.3 (1.2-3.3)
≥ 43	1883	1883	100.0	4	3	4	2.1 (0.5-5.4)	1.6 (0.3-4.7)	2.1 (0.5-5.4)

*Calculated for births from 28 to ≥ 43 weeks of gestation only

notified to the computerised Regional Interactive Child Health System⁷. Details included gestation at birth, which was defined as the working gestation at the time of birth, whether based on maternal history or ultrasound data. All the hospitals at the time of data collection offered routine mid-trimester anomaly screening, except for one consultant unit. Early dating scans were only available selectively. These data sets were used to derive the numbers of ongoing pregnancies and births at each gestational age. Multiple pregnancies were included in terms of the number (i.e. twins count as two pregnancies and two births). Records of death registration were linked to birth notification records in 96% of cases of infant death by one year of age. Details on entry, linkage, aggregation, validation and verification of the data are published elsewhere⁷. Agreement for release of data was obtained from each of the Data Custodians of the Child Health Data. Data are held on a password protected mainframe computer, which does not include names or addresses, and as far as possible all identifiers are obscured.

Definition of terms

Preterm deliveries are defined as those occurring before 37 weeks (259 days), while post-term deliveries are those occurring at 42 weeks (294 days) gestation or later. Term births are those born at 37 to 41 completed weeks of gestation. The very small number of birth notifications with gestations recorded as less than 20 weeks

or more than 45 completed weeks were excluded from the analysis (*n* = 249, Table 1).

Calculation of the rates of fetal and infant mortality at each week of gestation

Stillbirth, neonatal, post-neonatal and infant mortality rates at each gestational age were calculated as a proportion of births, and expressed per 1000 total or live births at that gestation. In addition, mortality rates were calculated as a proportion of the ongoing pregnancies at the onset of each week of gestation by subtracting the number of deliveries that had already occurred at earlier gestations. The overall rate of pregnancy loss at a particular gestation per 1000 ongoing pregnancies can be calculated from the sum of the rates of stillbirth and infant death at that gestation.

RESULTS

Information relating to 171,527 births to residents of the North East Thames in 1989-1991 was available for analysis. Only 1% of births were missing or out of the range of acceptable gestations. The number of deliveries, stillbirths, neonatal and post-neonatal deaths losses and mortality rates per 1000 total or live births at each gestation are shown in the Table 1 and Fig. 1. The rate of stillbirth, neonatal and post-neonatal death per 1000 ongoing pregnancies at each gestation are shown in Table 2 and Fig. 1. When mortality from stillbirth is

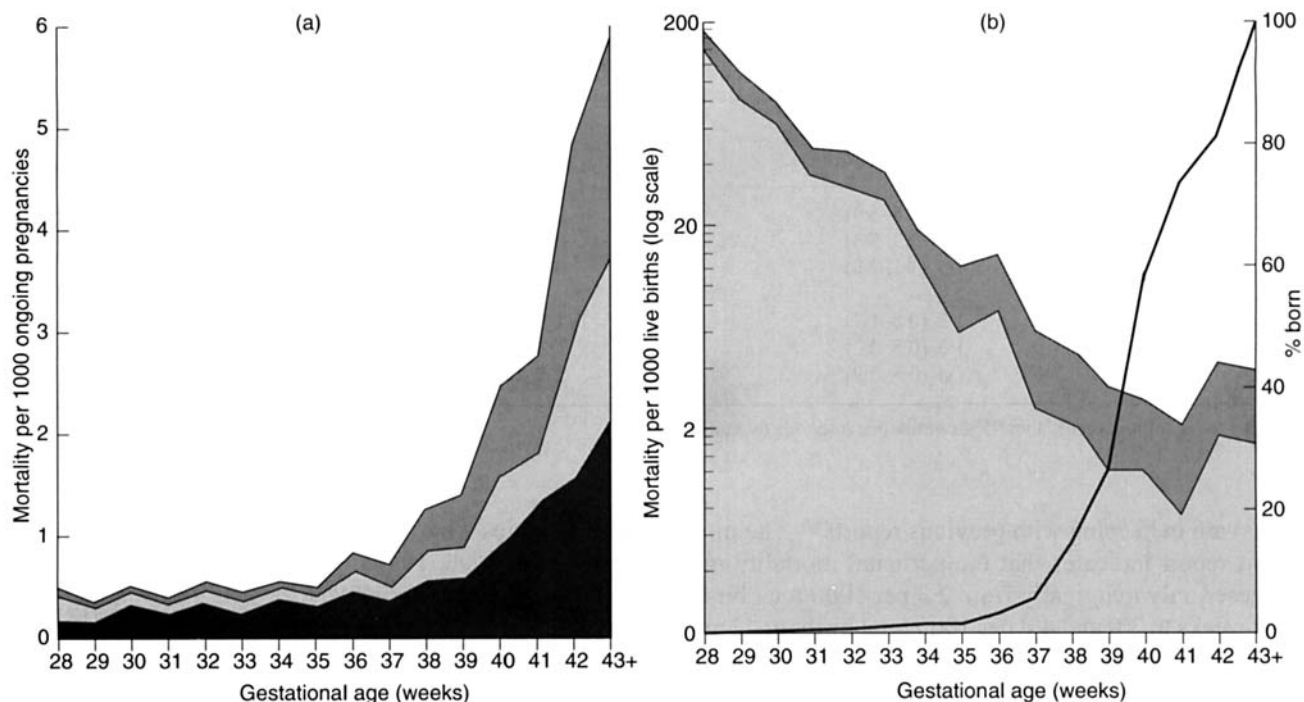


Fig. 1. (a) The summed mortality at each gestation for the rate of stillbirth (■), neonatal death (▒) and post-neonatal death (□) expressed (a) per 1000 ongoing pregnancies, and (b) per 1000 live births. The likelihood of delivery (—; cumulative percentage born) at each gestation is also shown in (b).

Table 2. The stillbirth, infant (neonatal + post-neonatal) death and total pregnancy loss rates per 1000 ongoing pregnancies (%OP) at each week of gestation. Values are given as rate (95% CI). Key as for Table 1.

GAD (weeks)	Stillbirth rate (%OP)	NN & PNN mortality rate (%OP)	Total pregnancy loss rate (%OP)
28	0.19 (0.13–0.26)	0.31 (0.22–0.39)	0.5
29	0.18 (0.11–0.24)	0.18 (0.12–0.25)	0.4
30	0.33 (0.24–0.42)	0.19 (0.12–0.26)	0.5
31	0.25 (0.18–0.33)	0.14 (0.08–0.19)	0.4
32	0.35 (0.26–0.44)	0.20 (0.13–0.27)	0.6
33	0.24 (0.16–0.31)	0.19 (0.12–0.25)	0.4
34	0.38 (0.29–0.47)	0.17 (0.11–0.23)	0.6
35	0.33 (0.24–0.42)	0.16 (0.10–0.23)	0.5
36	0.45 (0.35–0.55)	0.38 (0.28–0.47)	0.8
37	0.35 (0.26–0.44)	0.34 (0.25–0.43)	0.7
38	0.56 (0.44–0.68)	0.70 (0.56–0.83)	1.3
39	0.57 (0.44–0.70)	0.83 (0.68–0.99)	1.4
40	0.86 (0.68–1.05)	1.57 (1.31–1.82)	2.4
41	1.27 (0.92–1.62)	1.48 (1.10–1.85)	2.8
42	1.55 (0.79–2.31)	3.29 (2.19–4.40)	4.8
≥ 43	2.12 (0.55–5.43)	3.71 (1.53–7.63)	5.8

calculated per 1000 total births at each gestation, a non-significant increase in mortality is seen in post-term pregnancies (Table 3). In contrast, stillbirth mortality calculated per 1000 ongoing pregnancies increase significantly with advancing gestation (Table 3).

DISCUSSION

Incidence of post-term pregnancy

In the population studied, the overall incidence of post-term pregnancy was 6.2%, which is in accordance with the estimates from previous reports on prolonged pregnancy (4% to 14%)^{1-6,8,9}. It is likely that the true prevalence of post-term pregnancy in this population has been altered by policies for monitoring and induction of labour in prolonged pregnancy. These protocols may vary between units in this region, with the majority routinely offering induction of labour at 42 weeks of gestation. The overall effect of induction would be to reduce the post-term pregnancy rate, and hence lead to underestimation of gestation-related pregnancy losses. Conversely, uncertainty with estimation of gestational age may well have inflated the number of post-term pregnancies and the number of fetal and postnatal losses¹⁰. However, fewer than 1% of pregnancies are unbooked, and 10% were booked after 20 weeks when clinical and ultrasound estimation of gestational age are less accurate. Since all units used ultrasound to date the pregnancy when there was uncertainty with dates or a large discrepancy between menstrual and ultrasound dates, this effect is likely to be small.

Stillbirth rate and risk of stillbirth

The stillbirth rates in the present study, both at term (2.3 per 1000 total births) and post-term (1.9 per 1000 total

Table 3. The stillbirth rate expressed as both per 1000 total births (%TB) and per 1000 ongoing pregnancies (%OP) with the relative risk (RR) and 95% confidence intervals (95% CI). Relative risk has been calculated from 40 weeks for stillbirth rate per 1000 total births and from 37 and 40 weeks for stillbirth rate per 1000 ongoing pregnancies. Values are given as rates and RR (95% CI). Key as for Table 1.

GAD (completed weeks)	Stillbirth rate		Stillbirth rate		Stillbirth rate	
	(%TB)	RR at 40 weeks	(%OP)	RR at 40 weeks	(%OP)	RR at 37 weeks
37	6.2	4.2 (2.8–5.9)	0.4	0.4 (0.3–0.6)	0.4	—
38	3.8	2.5 (1.9–3.4)	0.6	0.7 (0.5–0.9)	0.6	1.4 (1.1–2.2)
39	2.2	1.5 (1.1–2.0)	0.6	0.7 (0.5–0.9)	0.6	1.6 (1.1–2.3)
40	1.5	—	0.9	—	0.9	2.4 (1.7–3.4)
41	1.7	1.2 (0.8–1.7)	1.3	1.5 (1.1–2.1)	1.3	3.6 (2.5–5.2)
42	1.9	1.3 (0.8–2.2)	1.6	1.8 (1.1–3.1)	1.6	4.3 (2.5–7.6)
≥43	2.1	1.4 (0.5–3.9)*	2.1	2.5 (0.9–6.7)*	2.1	6.0 (2.2–16.5)*

*Unable to calculate exact Fisher 95% confidence intervals due to sample size.

births) are in keeping with previous reports^{8,9}. The most recent report indicates that the perinatal mortality rate increases only marginally from 2.3 per 1000 total births at 40 weeks to 3.0 and 4.0 per 1000 total births at 42 and 43 weeks, respectively⁸. Indeed, a smaller study at the National Maternity Hospital Dublin demonstrated that total stillbirth rates were not significantly different in term (3.8 per 1000 total births) and post-term births (4.9 per 1000 total births)⁹. These data on stillbirth rates are often used as the basis for the conservative management of prolonged pregnancy, based on the findings that the 'risk' of stillbirth is unchanged or increases only marginally post-term^{1–5,8,9}. However, when ongoing pregnancies are used as the denominator in the current study, a completely different picture emerges. As shown in Fig. 1, the rate of stillbirth increases progressively with advancing gestation from 0.35 per 1000 ongoing pregnancies at 37 weeks to 2.12 per 1000 ongoing pregnancies at 43 weeks of gestation. The relative risk of stillbirth per 1000 total births does not increase significantly from the nadir at 40 weeks (Table 3; confidence intervals include 1). In contrast, the relative risk of stillbirth per 1000 ongoing pregnancies increases significantly with advancing gestation whether calculated from either 37 or 40 weeks (Table 3; confidence intervals do not include 1). This occurs in spite of increased surveillance in those pregnancies which extend beyond 41 weeks and widespread policies for induction of labour in prolonged gestation. Despite these procedures, which serve to reduce the risks of post-term pregnancy^{11–13}, it is apparent that the risk of stillbirth still increases six-fold from 37 to 43 weeks of gestation.

The working gestational age is determined during pregnancy, and is unlikely to be biased by subsequent mortality. For stillbirth, the gestation reported is that at birth which is a proxy for gestation at death only if there is a short interval between the two events. It is also important to note that the data include cases of congenital abnormalities and multiple pregnancies. Congenital

abnormalities were said to account for 30% of post-term losses in the late 1970s¹⁴, but this was mainly due to cranial neural tube defects, which have now been largely eliminated by biochemical screening, ultrasound diagnosis and termination in early pregnancy¹⁵. Multiple pregnancies have a significant effect on gestation-specific mortality in preterm deliveries, but rarely extend into the post-term period.

Neonatal and infant mortality rate and risk of infant mortality

This study demonstrates that the neonatal and post-neonatal mortality rates per 1000 live births fall significantly with advancing gestation to reach a nadir at 41 weeks of gestation, increasing slightly thereafter. However, the combined risk of delivery and subsequent infant death per 1000 ongoing pregnancies is found to be low before 37 weeks and increases 11-fold from 0.34 per 1000 ongoing pregnancies at 37 weeks to 3.72 per 1000 ongoing pregnancies at 43 weeks of gestation. Although before 37 weeks the rates of mortality per 1000 live births are high, rates per 1000 ongoing pregnancies are low because preterm delivery is an infrequent event.

The reason for the observed increased risk of neonatal and post-neonatal mortality in prolonged pregnancy is unclear. One explanation is that prolonged pregnancies may well be compromised before delivery, as suggested by the finding that the risk of both stillbirth and infant mortality increase with prolonged gestation. Indeed, the total risk of a pregnancy loss (stillbirth + infant mortality) in our study group increases from 2.4 per 1000 ongoing pregnancies at 40 weeks to 5.8 per 1000 ongoing pregnancies at 43 weeks of gestation. This finding is further supported by previous observations that childhood mortality is increased for up to two years after delivery in post-term pregnancies⁶. Further studies to take into account the effects of parity, multiple pregnancy, congenital abnormality, meconium aspiration

and uteroplacental insufficiency will enable more detailed analysis of the aetiology of fetal and infant losses in prolonged pregnancy.

CONCLUSIONS

The data clearly demonstrate that the risk of stillbirth and infant mortality increase significantly in prolonged pregnancy when expressed per 1000 ongoing pregnancies. If the association of mortality with prolonged pregnancy is confirmed, decisions regarding the expectant *versus* interventional management of prolonged pregnancy would depend on balancing the effects and acceptability of induction of labour¹¹⁻¹³, against the effectiveness of increased fetal surveillance in preventing fetal and infant loss¹⁶⁻¹⁹. Although, birthweight-specific rates of mortality may be calculated from national data, gestation-specific rates cannot be calculated as this information is not routinely collected in national birth registration data. Gestation-specific indices are more useful in clinical practice, as gestation is known prior to birth, whereas birthweight is at best poorly estimated. The value of collecting gestation at delivery in the same way as birthweight for national birth registration is evident from the data of this study.

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