Royal College of Obstetricians & Gynaecologists

Induction of Labour at Term in Older Mothers

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1. Background and introduction

The average age of childbirth is rising markedly across Western countries.[1] In the United Kingdom (UK) the proportion of maternities in women aged 35 years or over has increased from 8% (approximately 180 000 maternities) in 1985–87 to 20% (almost 460 000 maternities) in 2006–8 and in women aged 40 years and older has trebled in this time from 1.2% (almost 27 000 maternities) to 3.6% (approximately 82 000 maternities).[2]

There is a continuum of risk for both mother and baby with rising maternal age with numerous studies reporting multiple adverse fetal and maternal outcomes associated with advanced maternal age. Obstetric complications including placental abruption,[3] placenta praevia, malpresentation, low birthweight,[4–7] preterm[8] and post–term delivery[9] and postpartum haemorrhage,[10] are higher in older mothers. As fertility declines with age, there is a greater use of assisted reproductive technologies (ARTs) and the possibility of multiple pregnancy increases. This may independently adversely affect the risks reported.[11] Preexisting maternal medical conditions including hypertension, obesity and diabetes increase with advancing maternal age as do pregnancy–related maternal complications such as pre–eclampsia and gestational diabetes.[12] These medical co–morbidities can all influence fetal health and are likely to compound the effect of age on the risk of pregnancy in an older mother. However, after controlling for these co–morbidities, advanced maternal age is still found to be independently associated with an increase in antenatal and intrapartum stillbirth.[3,13] It is also associated with an increase in neonatal mortality.[14]

Epidemiological studies show that women aged 40 years or older have a similar stillbirth risk at 39 weeks of gestation to 25–29 year olds at 41 weeks of gestation.[15,16] On this basis, it will be questioned whether offering induction of labour earlier in older mothers is justifiable. The effects on emergency caesarean section rates need to be considered as well as ascertaining whether any reduction in antepartum stillbirth rates would be counteracted by an increase in intrapartum and neonatal deaths.

2. Risk of stillbirth in older mothers

Unexplained stillbirths increase with advancing maternal age and with increasing gestational age in both nulliparous and multiparous women.[17–20] The overall stillbirth rate by maternal age in the UK is shown in Table 1.[14]

When assessing risks of stillbirth at term, it is important to calculate stillbirth risk as a proportion of the ongoing pregnancies at a particular gestation. The perinatal mortality rate at a given gestational age is an inaccurate measure of antepartum stillbirth because the population at risk from continuing the pregnancy comprises all ongoing pregnancies rather than just the babies born that week. So although the perinatal mortality rate is lowest at 41 weeks of gestation, the gestational age associated with the lowest cumulative risk of perinatal death is 38 weeks of gestation.[21] Reddy et al.[15] studied over 5 million pregnant women in the United States of America (USA) in a retrospective population-based analysis looking specifically at women with singleton pregnancies excluding congenital anomalies. Table 2 shows the risks of stillbirth in their population of women with and without medical disease, by maternal age and late gestational age. Including women with medical diseases stillbirth rates increased the by 8–14%. At 41 weeks of gestation the risk of stillbirth is 0.75 in 1000 women under the age of 35 years old, and 2.5 in 1000 women aged ≥40 years old. The effect of maternal age persisted despite accounting for medical disease, parity, race and ethnicity.[15]

Afrocaribbean women have been shown to have rates of stillbirth over 2–fold higher (1.8%) in nearly all maternal age groups compared to women of Caucasian and Asian ethnicity (0.47% and 0.63% respectively), even when adjusted for parity and medical co–morbidities.[15,16]

Women that are nulliparous have a higher rate of stillbirth compared with multiparous women in all maternal age groups.[15,16,20] Women that are considered nulliparous, are aged ≥ 40 years old and at term

Table 1. Rate and absolute risk of stillbirth and neonatal death by maternal age in the UK[14]

Maternal age (years)	Stillbirths[a]		Neonatal deaths[a]	
	Rate (95% CI)[b]	Absolute risk (95% CI)	Rate (95% CI)[c]	Absolute risk (95% CI)
25–29	4.6 (4.3, 4.9)	1/ 217 (1/204, 1/233)	2.9 (2.7, 3.2)	1/345 (1/312, 1/370)
30–34	4.7 (4.4, 5.0)	1/213 (1/200, 1/227)	2.6 (2.4, 2.8)	1/385 (1/357, 1/417)
35–39	5.5 (5.1, 5.9)	1/182 (1/169, 1/196)	2.9 (2.6, 3.2)	1/345 (1/312, 1/385)
≥40	7.6 (6.6, 8.7)	1/132 (1/115, 1/152)	3.8 (3.1, 4.6)	1/263 (1/217, 1/323)

[a] Second and subsequent deaths from pregnancies with multiple losses are excluded
[b] Rates per 1000 maternities
[c] Rates per 1000 live births

also have an increased rate of intrapartum stillbirth due to intrapartum anoxia with an adjusted odds ratio (aOR) of 5.34 (95% CI 2.34–12.2) compared to younger women as shown in a large Scottish retrospective cohort study.[13]

Table 2. Absolute risk of stillbirth in women of advanced maternal age between 37–41 weeks of gestation in the USA.[15]

Maternal age	Absolute risk of stillbirth at different gestational ages excluding congenital abnormalities (absolute stillbirth risk with additional exclusion of medical diseases)		
	37–38 weeks of gestation	39–40 weeks of gestation	41 weeks of gestation
<35 years	1 in 1639 (1 in 1887)	1 in 1020 (1 in 1149)	1 in 1333 (1 in 1449)
35–39 years	1 in 1220 (1 in 1493)	1 in 735 (1 in 806)	1 in 775 (1 in 952)
≥40 years	1 in 893 (1 in 1064)	1 in 503 (1 in 667)	1 in 403 (1 in 463)

3. Aetiology of stillbirth in older mothers

The mechanism for the excess risk of stillbirth in women of advanced maternal age after exclusion of congenital abnormalities is unknown. There are data showing that fetal growth restriction (FGR) increases with maternal age. In a case–controlled study in the US which defined FGR as growth < 10th percentile for gestational age, women aged 35–39 years had an aOR of 1.4 for FGR (95% CI 1.1–1.8), which increased to 3.2 (95% CI 1.9–5.4) in women who were ≥ 40 years.[22]

However, the rates of FGR in the stillborn babies of older mothers is not greater than in younger mothers.[23,24] A retrospective cohort study found similar rates of FGR in the stillborn babies of women aged ≥ 35 years and women aged ≤ 35 years old.[23] No association between other clinical markers of utero–placental insufficiency and older mothers was found. On the other hand, a population–based study found less growth restriction in the stillborn babies of mothers aged ≥ 35 years.[24] This suggests that utero–placental insufficiency may not be the full explanation for the increase in stillbirths in the 3rd trimester in women that are older.

There is no evidence to support routine assessment of fetal growth or umbilical artery and uterine artery Doppler in older mothers to identify those who definitively have FGR.[25]

4. Intrapartum complications

Scientific and clinical data suggest that ageing impairs myometrial function, with several large population studies reporting increased rates of caesarean section for dystocia and instrumental delivery in older mothers who have gone through both spontaneous and induced labour.[5,6,12,26–29]

Studies have shown the association between maternal age and instrumental delivery, intrapartum caesarean section and duration of labour to be linear in women that are nulliparous.[28,29] In a large Scottish study of both spontaneous and induced labouring women, the adjusted OR for a 5 year increase in age was 1.49 (95% CI 1.48–1.50) for the risk of an instrumental delivery and 1.49 (95% CI 1.48–1.51) for the risk of intrapartum caesarean section.[28] A Dublin group found the incidence of prolonged labour (>12 hours) and surgical intervention because of dystocia approximately one third higher in spontaneously labouring nulliparous women aged ≥35 years compared to younger women.[29] This group employed a strict 'active management of labour' policy which may have removed any bias resulting from obstetricians intervening earlier in older women. The need for oxytocin augmentation of labour also increased with age until 30–34 years. Others have found women ≥35 years of age require oxytocin at higher doses and for a longer duration in order to achieve a successful vaginal delivery.[30]

There are no data available on failed instrumental delivery rates in older women.

5. Neonatal Mortality

Neonatal mortality varies with maternal age, being higher than the general maternity population in younger (<25 years old) and older (≥40 years old) mothers. In the UK, women ≥40 years old were 1.3 (1.1–1.6) times more likely to have a neonatal death compared to women aged 25–29 years old (Table 1).[14]

6. Will induction of labour at term improve outcome?

Induction of labour in older mothers is widely practiced as an intervention perceived to reduce the risk of late stillbirth.[6,27] A recent survey showed that 37% of obstetricians offer induction of labour at term to women aged 40–44 years of age and 55% to those ≥45 years old.[31] Elective caesarean sections in older women are also rising[5,6,26,27] and studies suggest there is a lower threshold among patients and providers to perform a caesarean section in older women.[5,6] The National Institute for Health and Clinical Excellence (NICE) recommends that the risks and benefits of caesarean section compared with vaginal birth should be fully discussed with women requesting a caesarean section, taking into account their circumstances, concerns, priorities and plans for future pregnancies.[32] It is difficult to determine the degree to which anxiety regarding maternal age, the use of ART and medical co–morbidities influence the obstetrician and woman to decide on a caesarean section, but a significant concern to them is prevention of neonatal harm. Planned caesarean sections result in increased neonatal intensive care admissions compared to vaginal deliveries (RR 2.20, 95% CI 1.4–3.18)[32] and those performed before 39 weeks of gestation risk an increase in neonatal adverse respiratory outcomes.[33] Emergency caesarean sections have higher risks of maternal and neonatal complications. However, vaginal birth remains more likely than an emergency caesarean section following induction of labour in women who are older and nulliparous. One USA study has shown vaginal delivery rates of 67% in women aged 40–44 years.[27] A Swedish study (1996–2006)showed vaginal birth rates of 77% in women aged ≥35 years.[9] In a more recent study from Australia, the caesarean section rate in women who are nulliparous aged 40–44 years old, who laboured was 40.6% (normal vaginal delivery rate of 34.4%; instrumental vaginal delivery rate of 24.9%; induced rate of 40%).[6] Induction of labour in women of all ages in unselected pregnancies ≥41 weeks of gestation, results in lower rates of caesarean section than serial antenatal monitoring, with similar rates of perinatal morbidity and mortality.[34] A Cochrane review has found that induction at 41 weeks of gestation results in improved perinatal outcomes without increasing the caesarean section rate.[35] These data have lead to a NICE recommendation in the UK that women over 41 weeks of gestation should have labour induced for the prevention of stillbirth due to post maturity.[36]

There is increasing evidence that induction of labour from 37 weeks of gestation also improves perinatal outcomes without increasing rates of caesarean section.[37–39] This goes against the commonly held belief that induction of labour leads to an increase in caesarean section rates. Studies alluding to the latter have compared elective induction of labour (without medical indication) with spontaneous

labour. However, it would be more robust and clinically relevant to compare elective induction of labour versus expectant management where spontaneous labour may occur or intervention at a future gestation will be required.

A recent systematic review of studies using this methodology found only three randomised controlled trials (RCT) which considered women induced < 41 weeks of gestation.[37] They failed to find a statistically significant increase in risk of caesarean section (OR 1.73, 95% CI 0.67–4.5). The value of these studies is limited by their small sample size. The hypertension and pre–eclampsia trial (HYPITAT) was a RCT which was published following this systematic review and reported that for women with gestational hypertension and mild pre–eclampsia ≥ 37 weeks of gestation, induction of labour did not lead to a higher caesarean section rate compared to expectant management.[38] None examined the influence of maternal age.

The results of these RCTs are supported by a recent large Scottish retrospective population–based study that compared women of all ages undergoing elective induction of labour without medical indication at weekly gestations from 37–41 weeks of gestation versus women managed expectantly.[39] They found elective induction of labour to be associated with a reduction in perinatal mortality with an aOR of 0.15 (95% CI 0.03–0.68) at 37 weeks of gestation increasing to 0.31 (95% CI 0.19–0.49) at 41 weeks of gestation, without an increase in assisted vaginal deliveries or caesarean sections. Surgical delivery was actually reduced in women electively induced at 40 weeks of gestation with an aOR of 0.85 (95% CI 0.82–0.89) for assisted vaginal deliveries and an aOR of 0.82 (95% CI 0.79–0.88) for caesarean sections. They did however find an increase in neonatal admissions to the special care facilities.[39]

There remains a paucity of data specifically addressing the maternal and neonatal outcomes of older women induced at term compared to those expectantly managed. Interestingly, such data from women of all ages shows favourable outcomes for the induction of labour at term. Applying the maternal and gestational age-specific stillbirth risks from Table 2 to UK data from 2009–10 suggests that if all women aged ≥ 40 years old, with a singleton pregnancy, were induced at 39 weeks of gestation instead of 41 weeks of gestation, 17 stillbirths could be prevented. This equates to inducing an extra 9350 women, or 550 women to prevent one stillbirth. Inducing at 40 weeks of gestation, instead of 41, would prevent 7 stillbirths and require an extra 4750 women to be induced.[40]

7. Opinion

The incidence of stillbirth at term in women is low. It is higher in women of advanced maternal age. This at 39–40 weeks of gestation equates to 2 in 1000 for women ≥ 40 years of age compared to 1 in 1000 for women < 35 years old.[15] Women ≥ 40 years of age having a similar stillbirth risk at 39 weeks of gestation to women in their mid 20s at 41 weeks of gestation, at which stage the consensus is that induction of labour should be offered to prevent late stillbirth.[15,16,36]

There is therefore an argument for offering induction of labour at 39–40 weeks of gestation to women ≥ 40 years of age. The available evidence suggests this practice would reduce late antenatal stillbirths and maternal risks of an ongoing pregnancy such as pre–eclampsia. The argument is stronger where there are concurrent medical co–morbidities, nulliparity, or Afrocaribbean ethnicity; all are known to have higher stillbirth rates. However, at present there are insufficient data available on the effect such a policy would have on surgical deliveries and perinatal mortality specifically in older mothers. It is possible that any beneficial effect from prevention of late antepartum stillbirth is reversed by an increase in intrapartum stillbirths and neonatal deaths, although data on women of all ages shows an improvement in perinatal outcome. There is growing evidence that such a policy would not increase the number of operative vaginal deliveries or emergency caesarean sections. Such issues should be discussed with women who are older and pregnant.

It may be expected that women who are older, and potentially nulliparous, will request elective caesarean section as a form of elective delivery rather than induction of labour. A discussion of risks and benefits of induction of labour versus elective caesarean section is appropriate in these circumstances.

Further research is urgently required to define the effect of induction of labour in women of advanced maternal age. The authors are aware that a National Institute for Health Research(NIHR) funded multicentre RCT comparing induction of labour at 39 weeks of gestation with expectant management in nulliparous women aged over 35 years of age is currently recruiting.[41] It will specifically investigate intrapartum complications and perinatal morbidity and mortality and recruitment is recommended.

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