Title: The predicted clinical workload associated with early post-term surveillance and inductions of labour in south Asian women in a non-tertiary hospital setting

Short running title: Impact of early post-term IOL in south Asian women

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Impact of early post-term IOL in south Asian women

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Abstract:

Background: Stillbirth increases steeply after 42 weeks gestation; hence induction of labour (IOL) is recommended after 41 weeks. Recent Victorian data demonstrates that the term stillbirth risk rises at an earlier gestation in south Asian mothers (SAM).

Aims: To determine the impact on a non-tertiary hospital in Melbourne, Australia, if post-dates IOL were recommended one week earlier at 40+3 for SAM; and to calculate the proportion of infants with birthweight <3rd centile that were undelivered by 40 weeks in SAM and non-SAM, as these cases are may represent undetected fetal growth restriction.

Materials and methods: Singleton births > 37 weeks during 2017-18 were extracted from the hospital Birthing Outcomes System. Obstetric and neonatal outcomes for pregnancies that birthed after spontaneous onset of labour or IOL were analysed according to gestation and country of birth.

Results: 5408 births were included, 24.9% were born to SAM (n=1345). SAM women had a higher rate of IOL > 37 weeks compared with non-SAM women (42.5% vs 35.0%, p< 0.001). If all SAM accepted an offer of IOL at 40+3, there would be an additional 80 term inductions over two years. There was no significant difference in babies <3rd centile undelivered by 40 weeks in SAM compared with non-SAM (29.6% vs 37.7%, p= 0.42).

Conclusions: Earlier IOL for post-term SAM would only modestly increase the demand on birthing services, due to pre-existing high rates of IOL. Our current practices appear to capture the majority at highest risk of stillbirth in our SAM population.

Introduction

Australia has a stillbirth rate of 6.7 per 1000 births1. These numbers have remained stagnant for the past twenty years. Many risk factors have been identified worldwide, including fetal growth restriction (FGR), advanced maternal age, maternal infections, smoking, obesity, prolonged pregnancy, and communicable diseases2-4. However, half of term stillbirth
remains unexplained. In recent years maternal country of birth has emerged as an independent risk factor for stillbirth in high-income countries, with similar magnitude as smoking, preeclampsia, obesity and advanced maternal age\textsuperscript{3, 5, 6}. South Asian mothers (SAM) are more likely to experience term stillbirth than women born in Australia or New Zealand, with an odds ratio of 1.5\textsuperscript{2}. This is pertinent as 7.8\% of women giving birth in Australia in 2017 were born in a south Asian country\textsuperscript{7}. While Safer Care Victoria acknowledge the research linking peripartum complications with ethnicity and country of birth, current recommendations advise against maternal country of birth as a stand-alone indication for induction of labour (IOL)\textsuperscript{8}.

The Safer Baby Bundle, led by the Stillbirth Centre of Research Excellence, identifies five key elements to reduce stillbirth after 28 weeks gestation. These include; Supporting women to stop smoking in pregnancy, improving detection and management of fetal growth restriction, raising awareness and improving care for women with decreased fetal movements, improving awareness of maternal safe going-to-sleep position in late pregnancy, and improving decision-making about the timing of birth for women with risk factors for stillbirth\textsuperscript{9}. These recommendations aim to prevent 20-30\% of stillbirths in Australia.

In Victoria, IOL for prolonged pregnancy is routinely recommended between 41+0 and 42+0 gestation due to the increased risk of stillbirth with gestation greater than 42 weeks\textsuperscript{10}. However, perinatal mortality has been observed to increase at an earlier gestation in SAM when compared to Caucasian women\textsuperscript{2, 11}. It has been suggested that SAM may benefit from earlier fetal surveillance and monitoring, as well as earlier post-term IOL, to reduce the incidence of term stillbirth.

Following recommendations for optimising timing of birth, we aimed to calculate the expected demand on birthing services at a non-tertiary hospital in Melbourne, Australia, if a policy of earlier IOL were initiated at 40+3 weeks gestation for SAM.
FGR is a known risk factor for term stillbirth\textsuperscript{2-4}, but antenatal detection is poor and FGR is frequently undiagnosed even when universal third trimester ultrasound is used\textsuperscript{12}. Babies with severe FGR (birthweight <3\textsuperscript{rd} centile) delivered at or after 40 weeks gestation are presumed to represent missed cases of FGR as elective delivery before 40 weeks is considered best practice for these infants. Rates of babies with severe FGR delivery at or after 40 weeks are collected in the Victorian perinatal services performance indicators report (PSPI)\textsuperscript{13}. Our secondary aims were to analyse the indications for IOL in SAM vs non-SAM, and to estimate the proportion of “missed” cases of severe FGR who gave birth by spontaneous onset of labour (SOL) or IOL from 40 weeks gestation.

**Materials and methods**

We undertook a retrospective study of singleton births at term (≥ 37 weeks gestation) at the Northern Hospital, a non-tertiary public hospital in Melbourne, Australia, between 1 January 2017 and 31 December 2018. The hospital has level five maternity and neonatal service capability, caring for low- and high-risk obstetric patients with planned births ≥32 completed weeks of gestation.

Routinely collected obstetric and perinatal data were extracted from the hospital electronic database, Birthing Outcome Systems (BOS). We limited our analysis to women presenting in spontaneous labour or for IOL between January 2017 to December 2018. Women who underwent elective caesarean section (CS) and IOL after prior CS were excluded. Elective CS was excluded from this population as it would not directly impact numbers of IOL, and therefore not relevant to the study. IOL after prior CS was excluded as this practice is rare at our health service, and decisions regarding IOL for these women differs between clinicians.

The primary outcome was to determine the impact on maternity services, measured as percentage increase in annual IOL and post-dates monitoring visits, if IOL were routinely recommended at 40+3 weeks, with one visit for post-dates monitoring at 40+0 weeks gestation for women of south Asian country of birth. South Asian countries, as defined by the Standard Australian Classification of Countries, included Bangladesh, Bhutan, India,
Maldives, Nepal, Pakistan and Sri Lanka\textsuperscript{14}. Secondary outcomes included indication for IOL, babies with birthweight < 3rd centile born at 40 or more weeks gestation, and neonatal outcomes.

Statistical analyses were performed using GraphPad Prism version 8 (GraphPad Software, La Jolla, CA) (Serial number: GPS-1584128-TJQO-87662). A Student’s t-test was used for continuous variable approximating a normal distribution, Mann-Whitney U tests for skewed data, and Fisher’s exact test or Chi-square test for categorical variables as appropriate. Data were expressed as a median and interquartile range (IQR) or as a percentage of total. Statistical significance was defined as a p value < 0.05.

Severe fetal growth restriction (FGR) was defined as birth weight less than the 3\textsuperscript{rd} centile, according to population-based birthweight centiles\textsuperscript{15}. These charts are recommended for use by the Perinatal Society of Australia and New Zealand (PSANZ)\textsuperscript{16} and are used by Safer Care Victoria in reporting the annual Victorian perinatal services performance indicators (PSPI)\textsuperscript{13}. We defined undiagnosed term FGR as the proportion of babies with birthweight < 3\textsuperscript{rd} centile born from 40 weeks gestation or more as a percentage of all babies with birthweight < 3\textsuperscript{rd} centile born from 37 weeks gestation. This differs from the definition used in the Victorian PSPI report, which uses all babies with birthweight < 3\textsuperscript{rd} centile from 32 weeks gestation as the denominator.

Ethics approval for this project was obtained from the Northern Health Low Risk Ethics Committee (project number ALR 49.2018). As this was a retrospective cohort study, individual patient consent was not required.

**Results**

A total of 7624 women had singleton births at or after 37 weeks gestation during the study period. Of these, 2211 (29.0\%) women underwent an elective CS, and 5 had IOL following...
CS. These women were excluded from this analysis. Our final cohort included 5408 births with SOL (63.1%) or IOL (36.9%), and included those that resulted in emergency CS (Figure 1). SAM constituted 24.9% of this population (n= 1345).

Table 1 presents the demographic characteristics of our population. SAM were significantly older, leaner and less likely to be multiparous than non-SAM. Rates of pre-existing hypertension and diabetes mellitus were similar between groups.

Projected increase in IOL and post-dates monitoring

Over the two year study period 422 SAM delivered at or after 40+0 weeks gestation; 251 had SOL, and 171 underwent IOL. Of those with SOL, 80 birthed after 40+3 weeks. If these women accepted an offer of IOL at 40+3, this would result in 80 additional IOL over two years, less than one per week. There were 94 SAM who had IOL after 40+3 who would require their IOL rescheduled to occur earlier should policy change.

Currently, all women receive routine post-dates monitoring in the hospital assessment centre at 41+0 weeks gestation. If policy changed, this would occur at 40+0 weeks for SAM. Our population had 422 SAM with SOL or IOL at or after 40+0 weeks. Of these women, 221 delivered between 40+1 and 40+6. If policy facilitated earlier monitoring for SAM, an additional 221 post-dates visits would occur over two years (2 per week). SAM who birthed at or after 41 weeks (n= 96) were excluded as they would already have post-dates monitoring booked.

Indications for IOL

SAM had significantly higher rates of term IOL when compared to other women (42.5% vs 35.0%, p <0.001). 87.1% of SAM, and 82.7% of non-SAM were already delivered by 40+3 weeks gestation (p < 0.001).
The most common reason for IOL for both groups was suspected fetal compromise, including; suspected intrauterine growth restriction, uteroplacental insufficiency, abnormal dopplers or cardiotocograph, or reduced fetal movements (Table 2). There were significantly more IOL for gestational diabetes mellitus (GDM) in SAM vs non-SAM (30.9% vs 20.1%, p < 0.001). IOL for hypertensive disorders was also significantly more common in the SAM population (10.1% vs 6.9%, p= 0.02). SAM had fewer IOL for large for gestational age fetus (0.4% vs 3.2%, p< 0.001), and for post-dates (8.6% vs 13.0%, p= 0.004).

Of women who had labour induced at term, SAM were more likely to experience early-term IOL at 37-38+6 weeks gestation than non-SAM (51.6% vs 43.3%, p= 0.001)(See supporting information for detailed week by week results). While the majority of these were due to PROM/prolonged latent phase of labour or suspected fetal compromise (n= 197, 67.0%), or GDM between 38-38+6 weeks gestation (n= 110, 37.3%), there were also numerous IOL for non-standard indications.

Of those women who underwent IOL, 25.2% of SAM (n=144), and 23.3% of non-SAM (n= 330) had more than one indication recorded (p= 0.39). Amongst our population, there were no SAM, and 6 non-SAM, who underwent IOL after 41+6 weeks gestation.

Neonatal outcomes and proportion of infants <3rd undelivered by 40 weeks

SAM in our study cohort (term singleton pregnancies, with SOL or IOL) delivered their babies at a significantly earlier gestation, 39.3 vs 39.6 weeks (p <0.001), at significantly lower median birthweight, 3230g vs 3410g (p <0.001)(Table 3). Babies born to SAM had a higher prevalence of birthweight <10th centile, than of babies born to non-SAM (14.7%, vs 9.1% respectively, p <0.001). There were also more babies born with a birthweight <3rd centile in the SAM population vs non-SAM (3.3% vs 1.7%, p< 0.001). For detailed week by week results, see supporting information.

During the two year study period, 29.6% of severe FGR babies of SAM were delivered > 40 weeks gestation (n= 13), compared to 37.7% in the non-SAM population (n= 26)(p= 0.42).
There were no significant differences in rate of admission to Special Care Nursery, or Apgar<7 at 5 minutes.

Discussion

Our maternity service cares for a relatively high number of women born in south Asia (24.9%) compared to the general Australian population (7.8%)\(^7\). We expected our health service to be strongly impacted by any proposed IOL recommendation based on south Asian country of birth. Surprisingly, we demonstrated only a small increase in IOL would be required, translating to less than one additional IOL per week. This is largely explained by the significantly higher rates of term IOL for SAM compared to the rest of the antenatal population (42.5% vs 35.0%, \(p <0.001\)). There were similar proportions of IOL for suspected fetal compromise for SAM and non-SAM, in our study population. Of women induced at term, the indication was more likely to be GDM and hypertensive disease of pregnancy for SAM than for other women. While others have raised concerns that IOL for minor risk factors may place undue burden on birthing services, it seems that IOL on the basis of ethnicity would not significantly increase workload at our health service\(^17\).

In addition to the maternal complications of preeclampsia and gestational diabetes, severe FGR (birth weight < 3\(^{rd}\) centile) was significantly more common in our SAM population, in keeping with the published literature (Table 3)\(^{18-20}\). Undetected FGR is one of the largest population attributable risks for stillbirth\(^4\), and the recognition of FGR has been identified by the Safer Baby Bundle as a key component of preventing stillbirth\(^9\). Detecting FGR is challenging given the poor sensitivity of symphysis-fundal height measurements and routine ultrasound\(^{21,22}\). Severe growth restriction undelivered by 40 weeks is a Victorian Perinatal Services Performance Indicator (PSPI) as reported by the Consultative Council on Obstetric and Paediatric Mortality and Morbidity\(^13\). Reassuringly, there were no more babies <3\(^{rd}\) centile undelivered after 40 weeks in our SAM population compared with non-SAM (29.6% vs 37.7%), though this did not meet statistical significance due to small numbers.
Impact of early post-term IOL in south Asian women

This might be due to the lower BMI of SAM (25 vs 27, p <0.001), as well as their higher term IOL rates overall, resulting in fewer SAM birthing after 40 weeks.

An incidental finding of our study was a leftward-shift of the gestation at birth curve in SAM, previously reported by others\textsuperscript{2,23}. SAM had fewer post-dates IOL, potentially as a result of this. Iatrogenic causes may contribute to the shorter gestation period, with more early-term (37-38 weeks gestation) IOL in this population. IOL at an earlier gestation is not without consequences. Compared to babies born at 39-41 weeks, those born during the early-term period have an increased risk of mortality and morbidity\textsuperscript{24, 25}. These infants require increased respiratory support and admission to neonatal units. Timing IOL should be considered carefully, with risks and benefits explored to reduce harm.

In addition to country of birth, our pregnant patients have other demographic factors that place them at increased risk of stillbirth, including low socioeconomic status\textsuperscript{3}. A previous study of this maternity service demonstrated that it cares for a relatively deprived population, with 28.2\% of pregnant women in the most disadvantaged socioeconomic group and only 1.2\% in the most advantaged, as classified by the Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD)\textsuperscript{26}. This study was underpowered to show a difference in rare perinatal outcomes such as term stillbirth between SAM and non-SAM. However, using severe FGR as a proxy for fetuses at highest stillbirth risk, most are delivered by 40 weeks gestation.

Another study limitation is that we did not attempt to define ethnicity, but simply used country of birth. Defining ethnicity is difficult given the variations in how our population understands ethnicity. A previous study of an Australian antenatal population demonstrated inaccuracies in self-reported ethnicity, with concepts of ethnicity varying between ethnic groups\textsuperscript{27}. Therefore, we use the objective measure of country of birth for this study. Whether the increase in stillbirth risk in SAM is mediated by the physical environment or genetic ancestry is not possible to determine in our study.

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Our study modelled the theoretical increases in demand on birthing services on retrospective data. We have not accounted for projected population growth or migration patterns. These trends would potentially change future demands on hospital resources. We also assumed that 100% of SAM would accept an offer of earlier post-term IOL. In practice, this number is not likely. As a retrospective study we could not investigate women’s perspectives regarding earlier IOL and how recommendations based on country of birth might be received. In any clinical recommendations about IOL, health care providers must acknowledge the importance of shared decision making and individual perspectives regarding labour and birth.

Our hospital experience underscores the need for individual health services to assess the impact of new research findings on their specific population, in the context of existing antenatal care practices and perinatal outcomes. Any future changes to our IOL indications that incorporates country of birth is unlikely to create major disruption to our health service.

This study has indicated only a modest increase in workload at our health service if IOL were routinely recommended at 40+3 for women born in south Asia due to pre-existing high rates of IOL. Individualised discussion regarding each woman’s risk factors for stillbirth is needed when planning for timing of delivery, as well as patient preferences for labour and birth.
Impact of early post-term IOL in south Asian women

Figure legend:

Figure 1: Flow Chart of Recruitment

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Table 1: Demographics

<table>
<thead>
<tr>
<th></th>
<th>SAM (n=1345)</th>
<th>Non-SAM (n=4063)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (IQR)</td>
<td>30.5 (28.1, 33.2)</td>
<td>29.4 (25.8, 33.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Primiparous (%)</td>
<td>711 (52.9%)</td>
<td>1817 (44.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median booking BMI* (IQR)</td>
<td>25 (23, 28)</td>
<td>27 (23, 32)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pre-existing medical condition (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Hypertension</td>
<td>8 (0.6%)</td>
<td>28 (0.7%)</td>
<td>0.85</td>
</tr>
<tr>
<td>- Diabetes mellitus</td>
<td>4 (0.3%)</td>
<td>11 (0.3%)</td>
<td>0.77</td>
</tr>
<tr>
<td>SACC region of birth† (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Australia</td>
<td>2247 (55.3%)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>- Middle East</td>
<td>830 (20.4%)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>- Mainland south-east Asia</td>
<td>177 (4.4%)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>- Other†</td>
<td>139 (3.4%)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>- New Zealand</td>
<td>129 (3.2%)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>- Maritime south-east Asia</td>
<td>104 (2.6%)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>- Polynesia</td>
<td>95 (2.3%)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>- Chinese Asia</td>
<td>90 (2.2%)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>- South Eastern Europe</td>
<td>85 (2.1%)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>- Southern and East Africa</td>
<td>80 (2.0%)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>- North Africa</td>
<td>46 (1.1%)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>- Central Asia</td>
<td>40 (1.0%)</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

SAM, south Asian mothers; IQR, interquartile range; BMI, body mass index; SACC, Standard Australian Classification of Countries.

† Other regions include; Central and West Africa; United Kingdom, Channel Islands and the Isle of Man; Western Europe; South America; Eastern Europe; Japan and the Koreas; Northern America; Southern Europe; Ireland; Not Stated; Central America; Micronesia; Melanesia; Northern Europe.

Table 2: Indications for Induction of Labour at term

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<table>
<thead>
<tr>
<th>Indication</th>
<th>SAM (n= 572)</th>
<th>Non-SAM (n= 1421)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROM/prolonged latent phase of labour</td>
<td>165 (28.9%)</td>
<td>413 (29.1%)</td>
<td>0.96</td>
</tr>
<tr>
<td>FGR/UPI/Abnormal dopplers or CTG/Reduced fetal movements</td>
<td>268 (46.9%)</td>
<td>620 (43.6%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Pre-existing</td>
<td>4 (0.7%)</td>
<td>11 (0.8%)</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>- GDM</td>
<td>177 (30.9%)</td>
<td>285 (20.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other maternal medical condition</td>
<td>31 (5.4%)</td>
<td>47 (3.3%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Hypertensive disorders</td>
<td>58 (10.1%)</td>
<td>98 (6.9%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Advanced maternal age (&gt; 40yo)</td>
<td>2 (0.4%)</td>
<td>21 (1.5%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Large for gestational age</td>
<td>2 (0.4%)</td>
<td>46 (3.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-dates</td>
<td>49 (8.6%)</td>
<td>185 (13.0%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Other</td>
<td>16 (2.8%)</td>
<td>64 (4.5%)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

SAM, south Asian mothers; IQR, interquartile range; PROM, prolonged rupture of membranes; FGR, fetal growth restriction; UPI, uteroplacental insufficiency; CTG, cardiotocograph; GDM, gestational diabetes mellitus. Hypertensive disorders includes; preeclampsia toxemia, gestational hypertension, chronic hypertension, superimposed preeclampsia toxemia.

Table 3: Neonatal outcomes

<table>
<thead>
<tr>
<th></th>
<th>SAM (n= 1345)</th>
<th>Non- SAM (n= 4063)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median gestational age, weeks (IQR)</td>
<td>39.3 (38.4, 40.0)</td>
<td>39.6 (38.6, 40.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median birthweight, grams (IQR)</td>
<td>3230 (2960, 3500)</td>
<td>3410 (3090, 3710)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Birthweight &lt;10th, n(%)</td>
<td>198 (14.7%)</td>
<td>369 (9.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>------------------------</td>
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<td>------------</td>
<td>--------</td>
</tr>
<tr>
<td>Birthweight &lt;3rd, n(%)</td>
<td>44 (3.3%)</td>
<td>69 (1.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Special care nursery admission, n(%)</td>
<td>55 (4.1%)</td>
<td>165 (4.1%)</td>
<td>0.94</td>
</tr>
<tr>
<td>Apgar score &lt;7 at 5 minutes, n(%)</td>
<td>22 (1.6%)</td>
<td>42 (1.0%)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

SAM, south Asian mothers; IQR, interquartile range.
Singleton births ≥ 37 weeks
n= 7624

Excluded:
- Elective caesarean section (n= 2211)
- Induction following caesarean section (n= 5)

Total births
n= 5408

South Asian women
n= 1345 (24.9%)

Induction of labour
n= 572 (42.5%)

Spontaneous onset of labour
n= 773 (57.5%)

Non-south Asian women
n= 4063 (75.1%)

Induction of labour
n= 1421 (35.0%)

Spontaneous onset of labour
n= 2642 (65.0%)
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Author/s:
Green, B; Howat, P; Hui, L

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