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Moderate to late preterm intrauterine growth restriction; a retrospective, observational study of the indications for delivery and outcomes in an Australian perinatal centre.

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## **Abstract**

## **Background**

The management of preterm intrauterine growth restriction is limited to fetal surveillance and timely delivery. Despite the existence of evidence-based guidelines uncertainty regarding the optimal timing of delivery is common, and management remains individualised for each patient.

## **Aims**

To provide recent Australian data on the indications for delivery of moderate to late preterm growth restricted infants and the outcomes of these deliveries.

## **Materials & Methods**

Retrospective study of singleton live births delivered between 32 and 37 weeks gestation over a 3-year period (2012 - 2014) at a Melbourne Metropolitan Hospital. 'Small for gestational age' (birthweight <10<sup>th</sup> centile for gestation) identified intrauterine growth restricted infants. Indications for iatrogenic delivery were broadly categorised into maternal, fetal or pregnancy related. Obstetric and neonatal outcome variables were compared to other preterm infants using logistic regression.

## **Results**

Of the 146 (18.6%) small for gestational age infants born during the study period 103 were iatrogenic deliveries, most commonly due to fetal indications (53.4%). Small for gestational age infants had higher odds of hypoglycaemia (OR = 1.88, 95% CI:1.24 – 2.85, p = 0.003) and jaundice (1.52, 1.02 – 2.26, p = 0.037) than their appropriately grown counterparts, however there was no increase in the risk of serious morbidity or mortality.

## **Conclusions**

In this cohort, iatrogenic preterm delivery of small for gestational age infants between 32 to 37 weeks gestation was most commonly due to fetal indications and did not increase the risk of serious, short term neonatal outcomes compared to their appropriately grown counterparts.

## **Introduction**

Intrauterine growth restriction (IUGR), defined as failure of the fetus to achieve its growth potential in utero, is a major cause of stillbirth and adverse neonatal outcomes. Obstetric management is limited to ultrasound surveillance for evidence of fetal compromise and delivery. Diagnosis of IUGR at preterm gestations is a common clinical dilemma for the

obstetrician as there remains considerable uncertainty about the optimal timing for delivery. The risks of fetal hypoxia and demise<sup>1</sup>, must be weighed against the significant neonatal and long term morbidity associated with iatrogenic preterm birth<sup>2,3</sup>.

Although the detection and diagnosis of IUGR is contentious in itself, it is most commonly suspected when a fetus is small for gestational age (SGA, ie. Ultrasound estimated fetal weight <10<sup>th</sup> centile for gestation). Inevitably this definition captures a proportion of healthy, constitutionally small infants and conversely can exclude IUGR infants that may have inappropriate interval growth but are not small. Despite this, SGA remains an important surrogate for IUGR as it identifies a group of infants that are at high risk of adverse outcomes, including potential long-term health decrements for the mother and child<sup>4</sup>.

The Growth Restriction Intervention Trial (GRIT), concluded that overall obstetricians were choosing the right time, despite clinical uncertainty, to deliver comprised preterm infants in order to minimise mortality and long term morbidity<sup>5-7</sup>. However, there are no recent Australian data regarding the outcomes of moderate to late preterm IUGR that can be used to confidently counsel women and inform decision-making.

This study focused on a cohort of moderate to late preterm infants (born at 32 to 37 weeks gestation) in a Metropolitan Hospital in Melbourne. We aimed to determine the indications for iatrogenic preterm delivery of SGA infants and compare their obstetric and short term neonatal outcomes to other infants delivered preterm. We hypothesised that iatrogenic preterm delivery of SGA infants would result in obstetric and short term neonatal outcomes that were similar compared to other infants delivered preterm.

## **Methods**

### **Study population**

This retrospective study included all singleton births, delivered between 32+0 and 36+6 weeks gestation over a 3-year period (January 2012 – December 2014) at Sunshine Hospital in Melbourne's Western suburbs. Gestational age was calculated from the first day of the last menstrual period but modified to an ultrasound based estimated birth date if a first trimester ultrasound at 7 to <9 weeks or 9 to <16 weeks derived a discrepancy in estimated birth date greater than 5 or 7 days respectively<sup>8</sup>. We excluded all multiple births, stillbirths and infants

with major congenital or chromosomal anomalies. Ethics approval for this study was obtained from Western Health Office for Research (QA2015.14).

#### Data sources

Demographic information as well as data regarding obstetric and neonatal outcomes was obtained from the Birthing Outcome System (BOS) and supplemented by individual record review. Where neonates were transferred to another centre postnatally, discharge summaries were obtained from the referral hospitals.

Maternal characteristics included: age (years), parity, country of birth, body mass index (BMI; kg/m<sup>2</sup>) and smoking during pregnancy. Neonatal characteristics included: gestation at birth, antenatal suspicion of IUGR (estimated fetal weight <10<sup>th</sup> centile for gestational age or inappropriate interval growth on serial ultrasound scans) and birth weight.

#### Definition of small for gestation age, onset of delivery and indications for delivery

SGA was defined as birth weight less than the 10<sup>th</sup> percentile for gestational age and sex using Australian population based centile charts<sup>9</sup> and women were managed according to the Royal College of Obstetricians and Gynaecologist's guidelines<sup>10</sup> during the study period.

Preterm birth was classified as either iatrogenic delivery (induction of labour or caesarean section, prior to the onset of labour) or spontaneous delivery (spontaneous onset of labour, followed by vaginal delivery or caesarean section). Indications for iatrogenic preterm delivery were broadly categorised into pregnancy, maternal or fetal triggers defined as follows: pregnancy triggers for iatrogenic preterm delivery were: preterm pre-labour rupture of membranes (PPROM, +/- chorioamnionitis, prolonged PPRM, PPRM in the setting of previous caesarean section or malpresentation), antepartum haemorrhage (APH) or praevia without APH (vasa praevia, placenta praevia with suspected concealed abruption); maternal triggers for iatrogenic preterm delivery were: hypertensive disease (pre-eclampsia; eclampsia; haemolysis, elevated liver enzymes and low platelets syndrome; essential hypertension), diabetes (gestational diabetes, type I diabetes mellitus, type II diabetes mellitus) or another medical condition, and fetal triggers for iatrogenic preterm delivery were: non reassuring cardiotocograph, oligohydramnios, abnormal Dopplers or SGA alone (<1 - 3<sup>rd</sup> centile at >36 weeks gestation).

#### Definition of outcome variables

The primary outcome of interest was whether the pregnancy resulted in an iatrogenic preterm delivery.

We considered the following secondary outcomes, obstetric outcomes: administration of antenatal corticosteroids within 10 days of delivery and caesarean section rates; neonatal

outcomes: common morbidities (i.e. respiratory distress, jaundice requiring phototherapy, sepsis requiring antibiotics and hypoglycaemia requiring treatment with IV dextrose and/or IM glucagon), serious morbidity/mortality in addition to Apgar score at 5 minutes, resuscitation, requirement of transfer to a tertiary hospital and neonatal length of stay (LOS).

#### Statistical analysis

Secondary obstetric and neonatal outcomes were compared between the SGA and non-SGA cohort using univariable and multivariable logistic regression. For the multivariable model we adjusted for gestational age (categorised as less than 35 weeks gestation and greater than or equal to 35 weeks gestation) where clinically significant. Results of logistic regression are represented as odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was accepted at the 0.05 level. All data were analysed using Stata version 13.1<sup>11</sup>.

## Results

### Study participants

A total of 15,431 births occurred at Sunshine Hospital between January 2012 and December 2014. After relevant exclusions, we identified a cohort of 784 singleton births delivering between 32+0 and 36+6 weeks gestation (Figure 1).

Of these, 146 (18.6%) infants were SGA based on Australian population based centiles<sup>9</sup>. The demographic data are presented overall and by SGA status in Table 1. Average maternal age was similar between the two groups. The SGA cohort had a larger proportion of nulliparity, lower proportion of women who were overweight or obese, a higher proportion of mothers born in India and lower proportion of mothers born in Australia or New Zealand compared to the non-SGA cohort.

### Primary outcomes

Of 784 moderate to late preterm births, 363 (46.3%) were a result of iatrogenic delivery. Of the 146 SGA infants, 103 (70.5%) underwent iatrogenic preterm delivery and of the 638 non-SGA infants, 260 (40.8%) underwent iatrogenic preterm delivery. The indication for iatrogenic preterm delivery and mode of delivery are represented in Table 2.

Iatrogenic preterm delivery of the 103 SGA infants was most commonly attributed to fetal indications of which the most frequent triggers were abnormal fetal Dopplers or non-reassuring cardiotocograph (Table 2). In contrast to the SGA infants, non-SGA infants were most commonly delivered iatrogenically due to pregnancy related conditions, the most

frequent trigger being PPRM (Table 2). Maternal hypertensive disease was a common indication for iatrogenic delivery in both cohorts.

#### Secondary outcomes

Neonatal, obstetric and maternal outcomes of SGA and non-SGA infants are described in Table 1.

#### Small for gestational age; iatrogenic compared to spontaneous delivery

Within the SGA cohort, infants that underwent iatrogenic delivery had a higher antenatal clinical suspicion of IUGR and subsequently higher proportion of infants with birth weights <5<sup>th</sup> centile for gestational age compared to those that spontaneously delivered.

Iatrogenically delivered SGA infants had higher rates of hypoglycaemia and jaundice, longer total LOS and increased requirement of transfer to a tertiary hospital compared to spontaneously delivered SGA infants.

#### Small for gestational age compared to appropriate for gestational age

Neonatal sex and gestational age at delivery were similar between the two groups and SGA infants weighed less at birth (Table 1). The SGA group had a slightly higher proportion of infants with an Apgar scores less than 7 at 5 minutes. There were no neonatal deaths in the cohort and extremely low rates of severe neonatal morbidities and requirement for extensive resuscitation overall (Table 1, Table 4 – Online supplementary).

The four most common neonatal morbidities seen in this preterm cohort were jaundice (278 (35.5%)), suspected sepsis (266 (34.1%)), hypoglycaemia (184 (23.5%)) and respiratory distress (151 (19.3%)). SGA infants had increased odds of hypoglycaemia and jaundice compared to non-SGA infants after adjusting for gestational age (Table 3). SGA infants had decreased odds of respiratory distress and neonatal sepsis compared to non-SGA infants (Table 3). Of all preterm births, SGA infants were less likely to require neonatal transfer to a tertiary hospital (3 (2.1%) vs 32 (5.0%)), however we did observe longer median LOS (12; 4 – 21 days vs 5; 3 – 14 days) in SGA compared to non-SGA infants (Table 1).

Obstetric outcomes are shown in Table 1. SGA infants were more likely to be exposed to antenatal corticosteroids if delivered prior to 34 weeks gestation than the non SGA group (13 (100%) vs 58 (75.3%)). Mothers of SGA infants had an increased odds of corticosteroid administration within 10 days prior to delivery after adjusting for gestational age compared to mothers of non-SGA infants (OR = 1.69 ;1.07 – 2.67; p = 0.023) and higher rates of caesarean section (OR = 1.54; 1.07 – 2.21; p = 0.021) (Table 3).

## Discussion

We confirmed that a significant proportion of SGA infants underwent iatrogenic preterm delivery, however, the common, short term neonatal and obstetric outcomes for preterm SGA infants were similar to non-SGA infants delivered preterm.

The inherent difficulty in detecting and diagnosing IUGR through routine antenatal care combined with the enormity of consequences in clinical decision-making make randomised controlled studies in this field particularly challenging. The GRIT study provided reassurance that current obstetric management of preterm IUGR in the UK and Europe is optimising perinatal outcomes<sup>5-7</sup>. This is the first Australian study to report on the indications for delivery and outcomes in moderate to late preterm IUGR, providing the necessary local benchmark data that arguably corroborates the GRIT study findings. The definition of IUGR is often subject to debate and consequently inconsistent in the research conducted. In this preterm cohort SGA can be considered a justifiable proxy for IUGR as a recent national population based study has suggested that at preterm gestations SGA is likely to comprise a significant proportion of truly growth restricted fetuses<sup>12</sup>.

There are limitations to this study inherent to the retrospective study design; the determination of gestational age, birthweight measurements and record keeping of other important clinical information such as indications for delivery and maternal outcomes could not be rigorously adjudicated. We recognise that the indication for delivery is often multifactorial and subjective, and attempted to reduce this documentation bias by retrospective review of individual medical records. Whilst the short term markers of neonatal welfare in this study were reassuring, we did not include follow up of neonatal outcomes beyond the birth admission therefore we cannot comment on the medium to long term consequences of prematurity and IUGR, infant neurodevelopmental outcomes and lifetime cardiovascular risk for the mother which is believed to be increased. We also acknowledge that a proportion of the 18 stillbirths excluded in this study may have been SGA infants, and without examination of these data it is not known whether this reflects the challenges of diagnosing IUGR through routine antenatal care or failures to intervene despite detection and surveillance. On balance, we considered the exclusion of stillbirths necessary given the heterogeneity of the group and low numbers overall.

A further major limitation of this study was the small number of participants, which limited statistical analysis to binary variables. Likewise, due to the small sample size, this study was underpowered to compare the effect of iatrogenic delivery compared to spontaneous delivery independent of gestational age within the SGA and non-SGA infant cohorts. Nevertheless, this retrospective cohort represents a substantial cohort in which to investigate the common obstetric and neonatal outcomes, which we have examined.

This study found that 60 of the 150 SGA infants (41.1%) were suspected of having IUGR prior to birth, which demonstrates a notably increased sensitivity of diagnosis compared to a multicenter study, which reported that only a quarter of SGA births were detected prenatally as IUGR<sup>13</sup>. An emphasis on antenatal detection and monitoring of IUGR is critical, as it has been shown to reduce perinatal mortality<sup>14</sup>. The sensitivity of diagnosing IUGR is consistent with our finding that 55 SGA infants underwent iatrogenic delivery based on fetal indication. The specificity of IUGR diagnosis in this study was 98.3%, which is considerably higher than a previous study, which found up to one third of prenatally diagnosed IUGR were not born SGA<sup>15</sup>.

There is conflicting evidence in the field of preterm IUGR research regarding mortality rates as well as the rates of the full spectrum of common and severe neonatal morbidities. Other regional and multicentre studies, which define IUGR similarly as birthweight <10<sup>th</sup> centile, are consistent with this study in demonstrating that there is no increased risk of respiratory distress in growth restricted preterm infants<sup>16-18</sup>. Few retrospective cohort studies have reported rates of hypoglycaemia requiring treatment; one small cohort study reported significantly increased frequency of hypoglycaemia (blood glucose <40mg/dL) in SGA infants<sup>19</sup>, which is concordant with this study. However, the same cohort study<sup>19</sup> also found similar levels of hyperbilirubinaemia between SGA and non-SGA infants, which contrasts with the results of this study.

It has been demonstrated that hypoglycaemia in late preterm infants is due to deficient gluconeogenesis, hepatic glycogenolysis and lipolysis<sup>20</sup> therefore the significantly increased rates of hypoglycaemia requiring treatment amongst the SGA infants is likely to be attributed to the decreased fat stores in growth restricted infants. The lower rate of respiratory distress in the SGA cohort is consistent with previously described activation of the fetal adrenal stress response in the growth restricted fetus which enhances lung maturity<sup>21</sup>. A possible

explanation for the increased rates of sepsis requiring antibiotics in the non-SGA cohort is that a much larger number of iatrogenic preterm deliveries were preceded by PPRM compared to the SGA cohort (41.8 % vs 17.0%). PPRM is associated with chorioamnionitis and subsequent neonatal infection. Likewise, spontaneous preterm labour (which was more prevalent in the non-SGA group) is known to be associated with an increased rate of clinical and subclinical chorioamnionitis<sup>22</sup>.

The current study included only pregnancies that were delivered after 32 weeks gestation. This reflects the current status of Sunshine Hospital with nursery facilities to provide care for neonates born after 32 weeks gestation. An important corollary is that infants who are likely to require iatrogenic delivery prior to 32 weeks are more likely to be transferred in utero to a tertiary hospital prior to delivery. This has important implications for the generalisability of this study since the findings regarding the neonatal outcomes are only applicable to this moderate to late preterm cohort (after 32 weeks gestation). Sunshine Hospital is recognised as a busy, non-tertiary referral centre with high levels of obesity, diabetes, and cultural and socioeconomic diversity in the population. The results of this study could be considered reflective of similar hospitals in Australia. Prospective studies are required to validate these data.

## **Conclusions**

There are many reasons for preterm delivery of SGA infants, most commonly due to fetal indication but also pregnancy complications and maternal hypertensive disease. Infants that are SGA and delivered preterm between 32 and 37 weeks may be at increased risk of hypoglycaemia and neonatal jaundice requiring treatment, but appear to be at lower risk of respiratory distress and sepsis compared to non-SGA preterm infants within this same gestation range. Importantly, we confirmed that serious adverse short term neonatal outcomes for SGA infants delivered iatrogenically preterm between 32 and 37 weeks were similar to non-SGA infants delivered at this gestation. These data are crucial to support obstetricians in their clinical decision making and counselling for women in whom a preterm delivery for IUGR may be required.

## **List of abbreviations**

APH – antepartum haemorrhage

GA – gestational age  
GRIT – Growth Restriction Intervention Trial  
IQR – interquartile range  
IUGR – intrauterine growth restriction  
IVH – intraventricular haemorrhage  
OR – odds ratio  
PPH – post partum haemorrhage  
PPROM – preterm, pre-labour rupture of membranes  
SGA – small for gestational age

### Table/Figure Legends

#### Table 1.

Continuous variables are summarised with mean [standard deviation] or median {interquartile range} and categorical variables with number (%).

\*Birthweight <10<sup>th</sup> percentile by sex and gestational age. \*\* Birthweight ≥10<sup>th</sup> percentile by sex and gestational age.

<sup>A</sup> ‘Not stated’ for 49 SGA and 10 non-SGA.

<sup>B</sup> n =735 in total cohort, n = 138 in SGA, n = 597 in Non-SGA.

<sup>C</sup> SGA [n = 144 total; n = 43 spontaneous, n = 101 iatrogenic]. Non-SGA [n = 635 total; n = 295 spontaneous, n = 258 iatrogenic].

<sup>D</sup> Requiring intubation +/- adrenaline.

<sup>E</sup> Requiring continuous positive airway pressure, intubation, assisted ventilation.

<sup>F</sup> intravenous dextrose and/or glucagon.

<sup>G</sup> SGA [n = 144 total; n = 43 spontaneous, n =101 iatrogenic]. Non-SGA [n = 635 total; n = 377 spontaneous, n = 258 iatrogenic].

<sup>H</sup> SGA [n = 13 total; n = 2 spontaneous, n = 11 iatrogenic]. Non-SGA [n = 77 total; n = 56 spontaneous, n = 31 iatrogenic].

SGA, small for gestational age. NZ, New Zealand. BMI, body mass index (kg/m<sup>2</sup>). IUGR, intrauterine growth restriction.

IVH, intraventricular haemorrhage. PVL, periventricular leukomacia. LOS, length of stay.

#### Table 2.

Categorical variables are summarised with number (%).

\* Birthweight <10<sup>th</sup> percentile by sex and gestational age.

\*\* Birthweight ≥10<sup>th</sup> percentile by sex and gestational age.

<sup>A</sup> Vasa praevia, praevia with suspected concealed abruption.

<sup>B</sup> Including concurrent chorioamnionitis, prolonged PPROM, PPROM + previous caesar or malpresentation.

<sup>C</sup> Essential hypertension, pregnancy induced hypertension, pre-eclampsia, haemolysis elevated liver enzymes and low platelet levels syndrome, eclampsia.

<sup>D</sup> Type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes.

<sup>E</sup> polyhydramnios (n = 2), at risk of neonatal thrombocytopenia (n = 2)

<sup>F</sup> Social circumstances (n = 1)

<sup>G</sup>Social circumstances (n = 2), acute fatty liver of pregnancy (n = 1)

SGA, small for gestational age. APH, antepartum haemorrhage. PPRM, preterm pre-labour rupture of membranes. CTG, cardiotocograph

### Table 3.

\* Birthweight <10<sup>th</sup> percentile by sex and gestational age.

\*\* Birthweight ≥10<sup>th</sup> percentile by sex and gestational age.

<sup>A</sup> Multivariable model includes gestational age (categorised as <35 weeks and ≥35 weeks gestation), for all neonatal outcomes and antenatal corticosteroids administered < 10 days before delivery.

<sup>B</sup> requiring continuous positive airway pressure, intubation, assisted ventilation.

<sup>C</sup> treated with intravenous dextrose or glucagon.

SGA, small for gestational age. CI, confidence interval. LOS, length of stay.

### Figure 1.

\* Birthweight <10<sup>th</sup> percentile by sex and gestational age.

\*\* Birthweight ≥10<sup>th</sup> percentile by sex and gestational age

SGA, small for gestational age. GA, gestational age.

### Table 4. (Online supplementary)

Categorical variables are summarised with number (%).

\* Birthweight <10<sup>th</sup> percentile by sex and gestational age.

\*\* Birthweight ≥10<sup>th</sup> percentile by sex and gestational age.

SGA, small for gestational age.

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Table 1. Population characteristics and study outcomes.

Maternal demographics	SGA group* n = 146	Non-SGA group** n = 638				
Maternal age, years	30.4 [6.0]	30.2 [5.7]				
Nulliparous	81 (55.5)	266 (41.7)				
Country of birth <sup>A</sup>						
Australia or NZ	61 (41.8)	305 (47.8)				
Asia, excluding India	33 (22.6)	125 (19.6)				
Africa	8 (5.5)	44 (6.9)				
India	23 (15.8)	61 (9.6)				
Other	11 (7.5)	64 (10.0)				
BMI >25 kg/m <sup>2B</sup>	52 (37.7)	263 (44.1)				
Smoking during pregnancy	33 (22.6)	114 (17.9)				
Neonatal demographics and outcomes	SGA spontaneous delivery n = 43	SGA iatrogenic delivery n = 103	Non-SGA spontaneous delivery n = 378	Non-SGA iatrogenic delivery n = 260		
Male sex	74 (50.7)	24 (55.8)	50 (48.5)	333 (52.2)	194 (51.3)	139 (53.4)
Gestational age at delivery, weeks.days	36 {35.1 – 36.4}	36.1 {35.2 – 36.5}	36 {34.6 – 36.5}	35.6 {35 – 36.3}	35.6 {34.6 – 36.3}	36 {35 – 36.3}
Antenatal suspected IUGR	60 (41.1)	3 (7.0)	57 (55.3)	11 (1.7)	0 (0.0)	11 (4.2)
Birthweight, grams	2004 {1740 – 2252}	2172 {1942 – 2346}	1950 {1690 – 2180}	2650 {2400 – 2930}	2680 {2430 – 2920}	2620 {2358 – 2933}
< 1 <sup>st</sup> centile	11 (7.5)	1 (2.3)	10 (9.7)			
1 <sup>st</sup> to < 3 <sup>rd</sup> centile	40 (27.4)	4 (9.3)	36 (35.0)			
Apgar score < 7 at 5 mins <sup>C</sup>	7 (4.9)	3 (7.0)	4 (3.9)	17 (2.7)	5 (1.3)	12 (4.7)
Extensive resuscitation <sup>D</sup>	3 (2.1)	0 (0.0)	3 (2.9)	8 (1.2)	3 (0.8)	5 (1.9)
Neonatal death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neonatal morbidity						
Respiratory distress <sup>E</sup>	19 (13.0)	4 (9.3)	15 (14.6)	132 (20.7)	67 (17.7)	65 (25.0)
Jaundice + phototherapy	61 (41.8)	14 (32.6)	47 (45.6)	217 (34.0)	128 (33.9)	89 (34.2)
Suspected sepsis + antibiotics	40 (27.4)	13 (30.2)	27 (26.2)	227 (35.6)	138 (36.5)	89 (34.2)
Hypoglycaemia + treatment <sup>F</sup>	47 (32.2)	8 (18.6)	39 (37.9)	137 (21.5)	68 (18.0)	69 (26.5)
Transfer to tertiary hospital	3 (2.1)	0 (0.0)	3 (2.9)	32 (5.0)	15 (4.0)	17 (6.5)
Total LOS, days <sup>G</sup>	12 {4 – 21}	8 {4 – 19}	13 {4 – 22}	5 {3 – 14}	4 {3 – 14}	5 {3 – 14}
Obstetric outcomes						
Corticosteroids < 10 days before delivery	45 (30.8)	4 (9.3)	41 (39.8)	152 (23.8)	60 (15.9)	92 (35.4)
and < 34 weeks gestational age <sup>H</sup>	13 (100.0)	2 (100.0)	11 (100.0)	58 (75.3)	30 (53.6)	28 (90.3)
Caesarean, pre-labour + during labour	66 (45.2)	8 (18.6)	58 (56.3)	223 (35.0)	83 (22.0)	140 (53.8)

Continuous variables are summarised with mean [standard deviation] or median {interquartile range} and categorical variables with number (%).

\*Birthweight <10<sup>th</sup> percentile by sex and gestational age. \*\* Birthweight ≥10<sup>th</sup> percentile by sex and gestational age.

<sup>A</sup> ‘Not stated’ for 49 SGA and 10 non-SGA.

<sup>B</sup> n =735 in total cohort, n = 138 in SGA, n = 597 in Non-SGA.

<sup>C</sup> SGA [n = 144 total; n = 43 spontaneous, n = 101 iatrogenic]. Non-SGA [n = 635 total; n = 295 spontaneous, n = 258 iatrogenic].

<sup>D</sup> Requiring intubation +/- adrenaline.

<sup>E</sup> Requiring continuous positive airway pressure, intubation, assisted ventilation.

<sup>F</sup> intravenous dextrose and/or glucagon.

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<sup>G</sup> SGA [n = 144 total; n = 43 spontaneous, n = 101 iatrogenic]. Non-SGA [n = 635 total; n = 377 spontaneous, n = 258 iatrogenic].

<sup>H</sup> SGA [n = 13 total; n = 2 spontaneous, n = 11 iatrogenic]. Non-SGA [n = 77 total; n = 56 spontaneous, n = 31 iatrogenic].

SGA, small for gestational age. NZ, New Zealand. BMI, body mass index ( $\text{kg}/\text{m}^2$ ). IUGR, intrauterine growth restriction. IVH, intraventricular haemorrhage. PVL, periventricular leukomacia. LOS, length of stay.

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Table 2. Indication for iatrogenic preterm delivery and mode.

	Total cohort – iatrogenic deliveries n = 363	SGA* - iatrogenic deliveries n = 103	Non-SGA** - iatrogenic deliveries n = 260
Method of iatrogenic preterm delivery			
Induction of labour	212 (58.4)	64 (62.1)	148 (56.9)
Caesarean, no labour	151 (41.6)	39 (37.9)	112 (43.1)
Indication for iatrogenic preterm delivery			
Pregnancy	172 (47.4)	24 (23.3)	148 (56.9)
APH	37 (10.2)	5 (4.9)	32 (12.3)
Praevia without APH <sup>A</sup>	5 (1.4)	1 (1.0)	4 (1.5)
PPROM <sup>B</sup>	130 (35.8)	18 (17.5)	112 (43.1)
Maternal	84 (23.3)	23 (22.3)	61 (23.5)
Hypertensive disease <sup>C</sup>	65 (17.9)	22 (21.4)	43 (16.5)
Diabetes <sup>D</sup>	7 (1.9)	1 (1.0)	6 (2.3)
Medical condition	12 (3.3)	0 (0.0)	12 (4.6)
Fetal	103 (28.4)	55 (53.4)	48 (18.4)
Non-reassuring CTG	43 (11.8)	16 (15.5)	27 (10.4)
Oligohydramnios	17 (4.7)	9 (8.7)	8 (3.1)
Abnormal Dopplers	30 (8.3)	23 (22.3)	7 (2.7)
SGA	9 (2.5)	7 (6.8)	2 (0.7)
Fetal other <sup>E</sup>	4 (1.1)	0 (0.0)	4 (1.5)
Other	4 (1.1)	1 <sup>F</sup> (1.0)	3 <sup>G</sup> (1.2)

Categorical variables are summarised with number (%).

\* Birthweight <10<sup>th</sup> percentile by sex and gestational age.

\*\* Birthweight ≥10<sup>th</sup> percentile by sex and gestational age.

<sup>A</sup> Vasa praevia, praevia with suspected concealed abruption.

<sup>B</sup> Including concurrent chorioamnionitis, prolonged PPROM, PPROM + previous caesar or malpresentation.

<sup>C</sup> Essential hypertension, pregnancy induced hypertension, pre-eclampsia, haemolysis elevated liver enzymes and low platelet levels syndrome, eclampsia.

<sup>D</sup> Type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes.

<sup>E</sup> polyhydramnios (n = 2), at risk of neonatal thrombocytopenia (n = 2)

<sup>F</sup> Social circumstances (n = 1)

<sup>G</sup> Social circumstances (n = 2), acute fatty liver of pregnancy (n = 1)

SGA, small for gestational age. APH, antepartum haemorrhage. PPROM, preterm pre-labour rupture of membranes. CTG, cardiotocograph

Table 3. Logistic regression model for the association of neonatal and obstetric outcomes comparing SGA group\* to the non-SGA group\*\*.

	Univariable model		Multivariable model <sup>A</sup>	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
<b>Neonatal outcomes</b>				
No respiratory distress <sup>B</sup>	Ref	-	Ref	-
Respiratory distress	0.57 [0.34 – 0.96]	0.036	0.56 [0.33 – 0.95]	0.033
No jaundice + phototherapy	Ref	-	Ref	-
Jaundice + phototherapy	1.39 [0.96 – 2.01]	0.077	1.52 [1.01 – 2.28]	0.043
No sepsis + antibiotics	Ref	-	Ref	-
Suspected sepsis + antibiotics	0.68 [0.46 – 1.02]	0.061	0.64 [0.41 – 0.99]	0.045
No hypoglycaemia + treatment <sup>C</sup>	Ref	-	Ref	-
Hypoglycaemia + treatment	1.74 [1.17 – 2.58]	0.006	1.87 [1.23 – 2.84]	0.003
<b>Obstetric outcomes</b>				
No antenatal corticosteroids <10 days before delivery	Ref	-	Ref	-
Antenatal corticosteroids <10 days before delivery	1.42 [0.96 – 2.12]	0.080	1.69 [1.07 – 2.67]	0.023
No caesarean, pre-labour + during labour	Ref	-	-	-
Caesarean, pre-labour + during labour	1.54 [1.07 – 2.21]	0.021	-	-

\* Birthweight <10<sup>th</sup> percentile by sex and gestational age.

\*\* Birthweight ≥10<sup>th</sup> percentile by sex and gestational age.

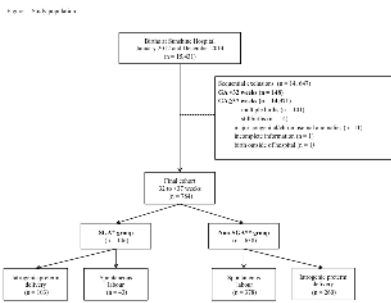
<sup>A</sup> Multivariable model includes gestational age (categorised as <35 weeks and ≥35 weeks gestation) for all neonatal outcomes and antenatal corticosteroids administered < 10 days before delivery.

<sup>B</sup> requiring continuous positive airway pressure, intubation, assisted ventilation.

<sup>C</sup> treated with intravenous dextrose or glucagon.

SGA, small for gestational age. CI, confidence interval. LOS, length of stay.

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