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ORIGINAL ARTICLE

Moderate to late preterm intrauterine growth restriction: A restrospective, observational study of the indications for delivery and outcomes in an Australian perinatal centre

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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 and methods: Retrospective study of singleton live births delivered between 32 + 0 and 36 + 6 weeks gestation over a three-year period (2012–2014) at a Melbourne Metropolitan Hospital. 'Small for gestational age' (birthweight < 10th 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 (adjusted odds ratio = 1.87, 95% CI: 1.23–2.84, $P = 0.003$) and jaundice (1.52, 1.01–2.28, $P = 0.043$) 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 + 0 and 36 + 6 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.

KEYWORDS

fetal growth restriction, premature birth, premature infant, small for gestational age infant, perinatal death

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[1] must be weighed against the significant neonatal and long-term morbidity associated with iatrogenic preterm birth.[2,3]

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 < 10th 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.[4]

The Growth Restriction Intervention Trial (GRIT), concluded that overall obstetricians were choosing the right time, despite clinical uncertainty, to deliver compromised preterm infants in order to minimise mortality and long-term morbidity.[5–7] 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 less than 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.

MATERIALS AND METHODS

Study population

This retrospective study included all singleton births, delivered between 32 + 0 and 36 + 6 weeks gestation over a three-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 seven to less than nine weeks or nine to less than 16 weeks derived a discrepancy in estimated birth date greater than five or seven days, respectively.[8] 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^2) and smoking during pregnancy. Neonatal characteristics included: gestation at birth, antenatal suspicion of IUGR (estimated fetal weight <10th centile for gestational age or inappropriate interval growth on serial ultrasound scans) and birth weight.

Definition of SGA, onset of delivery and indications for delivery

SGA was defined as birth weight less than the 10th percentile for gestational age and sex using Australian population-based centile charts[9] and women were managed according to the Royal College of Obstetricians and Gynaecologist's guidelines[10] 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 PPROM, PPROM 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. Fetal triggers for iatrogenic preterm delivery were: non-reassuring cardiotocograph, oligohydramnios, abnormal Dopplers or SGA alone (<1–3rd 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 (ie respiratory distress, jaundice requiring phototherapy, sepsis requiring antibiotics and hypoglycaemia requiring treatment with intravenous dextrose and/or intramuscular glucagon), serious morbidity/mortality in addition to Apgar score at five 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.[11]

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 (Fig. 1).

Of these, 146 (18.6%) infants were SGA based on Australian population-based centiles.[9] 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 PPROM (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 less that the fifth

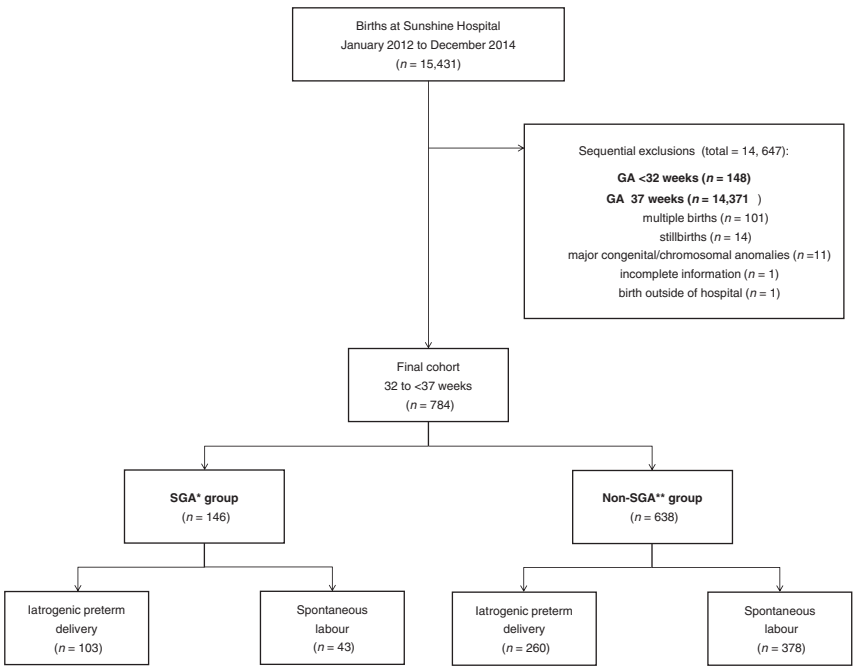

FIGURE 1 Study population. *Birthweight <10th percentile by sex and gestational age. **Birthweight ≥10th percentile by sex and gestational age. GA, gestational age; SGA, small for gestational age.

TABLE 1 Population characteristics and study outcomes

Maternal demographics	**SGA group[a], *n* = 146**			**Non-SGA group[b], *n* = 638**		
Maternal age, years	30.4 [6.0]			30.2 [5.7]		
Nulliparous	81 (55.5)			266 (41.7)		
Country of birth[c]						
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^2[d]	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, g	2004 {1740–2252}	2172 {1942–2346}	1950 {1690–2180}	2650 {2400–2930}	2680 {2430–2920}	2620 {2358–2933}
<First centile	11 (7.5)	1 (2.3)	10 (9.7)			
First to <Third centile	40 (27.4)	4 (9.3)	36 (35.0)			
Apgar score <7 at five minutes[e]	7 (4.9)	3 (7.0)	4 (3.9)	17 (2.7)	5 (1.3)	12 (4.7)
Extensive resuscitation[f]	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[g]	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)

(Continues)

TABLE 1 (Continued)

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
Hypoglycaemia + treatment[h]	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[i]	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[j]	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)

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

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

[a]Birthweight <10th percentile by sex and gestational age.

[b]Birthweight ≥10th percentile by sex and gestational age.

[c]'Not stated' for 49 SGA and 10 non-SGA.

[d]*n* = 735 in total cohort, *n* = 138 in SGA, *n* = 597 in Non-SGA.

[e]SGA [*n* = 144 total; *n* = 43 spontaneous, *n* = 101 iatrogenic]. Non-SGA [*n* = 635 total; *n* = 295 spontaneous, *n* = 258 iatrogenic].

[f]Requiring intubation ± adrenaline.

[g]Requiring continuous positive airway pressure, intubation, assisted ventilation.

[h]Intravenous dextrose and/or glucagon.

[i]SGA [*n* = 144 total; *n* = 43 spontaneous, *n* = 101 iatrogenic]. Non-SGA [*n* = 635 total; *n* = 377 spontaneous, *n* = 258 iatrogenic].

[j]SGA [*n* = 13 total; *n* = 2 spontaneous, *n* = 11 iatrogenic]. Non-SGA [*n* = 77 total; *n* = 56 spontaneous, *n* = 31 iatrogenic].

TABLE 2 Indication for iatrogenic preterm delivery and mode

	Total cohort –iatrogenic deliveries, *n* = 363	SGA[a] – iatrogenic deliveries, *n* = 103	Non-SGA[b] – 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[c]	5 (1.4)	1 (1.0)	4 (1.5)
PPROM[d]	130 (35.8)	18 (17.5)	112 (43.1)
Maternal	84 (23.3)	23 (22.3)	61 (23.5)
Hypertensive disease[e]	65 (17.9)	22 (21.4)	43 (16.5)
Diabetes[f]	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[g]	4 (1.1)	0 (0.0)	4 (1.5)
Other	4 (1.1)	1[h] (1.0)	3[i] (1.2)

APH, antepartum haemorrhage; CTG, cardiotocograph; PPROM, preterm pre-labour rupture of membranes; SGA, small for gestational age.
Categorical variables are summarised with number (%).
[a]Birthweight <10th percentile by sex and gestational age.
[b]Birthweight ≥10th percentile by sex and gestational age.
[c]Vasa praevia, praevia with suspected concealed abruption.
[d]Including concurrent chorioamnionitis, prolonged PPROM, PPROM + previous caesar or malpresentation.
[e]Essential hypertension, pregnancy induced hypertension, pre-eclampsia, haemolysis elevated liver enzymes and low platelet levels syndrome, eclampsia.
[f]Type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes.
[g]Polyhydramnios (*n* = 2), at risk of neonatal thrombocytopenia (*n* = 2).
[h]Social circumstances (*n* = 1).
[i]Social circumstances (*n* = 2), acute fatty liver of pregnancy (*n* = 1).

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.

SGA 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 score less than seven at five 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 and Table S1).

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).

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§	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Neonatal outcomes				
No respiratory distress¶	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††	Ref	–	Ref	–
Hypoglycaemia + treatment	1.74 [1.17–2.58]	0.006	1.87 [1.23–2.84]	0.003
Obstetric outcomes				
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	–	–

CI, confidence interval; LOS, length of stay; SGA, small for gestational age.
†Birthweight <10th percentile by sex and gestational age.
‡Birthweight ≥10th percentile by sex and gestational age.
§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.
¶Requiring continuous positive airway pressure, intubation, assisted ventilation.
††Treated with intravenous dextrose or glucagon.

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.[5–7] 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.[12]

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. While 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 multicentre study, which reported that only a quarter of SGA births were detected prenatally as IUGR.[13] An emphasis on antenatal detection and monitoring of IUGR is critical, as it has been shown to reduce perinatal mortality.[14] 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.[15]

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 <10th centile, are consistent with this study in demonstrating that there is no increased risk of respiratory distress in growth-restricted preterm infants.[16–18] Few retrospective cohort studies have reported rates of hypoglycaemia requiring treatment; one small cohort study reported significantly increased frequency of hypoglycaemia (blood glucose <40 mg/dL) in SGA infants,[19] which is concordant with this study. However, the same cohort study[19] 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;[20] therefore, the significantly increased rates of hypoglycaemia requiring treatment among 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.[21] 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 PPROM compared to the SGA cohort (41.8% vs 17.0%). PPROM 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.[22]

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 fetal indications but also pregnancy complications and maternal hypertensive disease. Infants that are SGA and delivered preterm between 32 + 0 and 36 + 6 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 + 0 and 36 + 6 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.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

Table S1. Neonatal outcomes; severe neonatal morbidities.