ORIGINAL RESEARCH

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The Impact of the Gestational Week on Perinatal Outcome in Newborns with Moderate Small for Gestational Age: A Retrospective Study

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ABSTRACT Objective: Our study wants to assess the outcome of moderate small for gestational age (SGA) infants at term with reference to the week they find themselves in at birth in uncomplicated pregnancies. **Material and Methods:** The database is made of women delivering in Switzerland from 2005 through 2017 selecting uncomplicated singleton pregnancies in cephalic presentation, with birthweight between the 5th and 10th percentiles, and a gestational age at delivery between 37 0/7 and 41 6/7 weeks. We considered poor perinatal outcomes as either umbilical cord arterial pH<7.15, 5'Apgar score <7, admission to the neonatal intensive care unit, and/or perinatal mortality. Statistical analyses were performed using contingency tests and Spearman rank correlation adopting a $p<0.05$ as significant. **Results:** Out of the 429,863 available deliveries, we identifyied 1,796 cases matching our criteria. The final sample includes 1,327 (73.9%) vaginal deliveries and 473 (26.1%) caesarean sections (CS) and it is worth mentioning that the rate of secondary CS (r=0.828; p=0.03) and vaginal deliveries (r=0.965; p=0.01) increased with advancing gestation. In addition, 306 (19.3%) patients had induced labours. This is particularly concentrated between 40 and 41 weeks of gestation (r=0.967; p=0.002); among them, 80% delivered vaginally and 20% with a secondary CS. The percentage of adverse outcome was 16.9%, 11.3%, 8.6%, 18.8%, and 21.7% for gestational week 37, 38, 39, 41 and 42, respectively, whereas only 3 cases (0.17%) of intrauterine death occurred. **Conclusion:** Moderate SGA infants are best delivered between 39 0/7 and 40 0/7 weeks of gestation.

Keywords: Small for gestational age; adverse perinatal outcome; vaginal delivery; moderate intrauterine growth restriction

Small for gestational age (SGA) fetuses are commonly defined as newborns with a birth weight lower than the 10th percentile for their gestational age.[1] The incidence of SGA in developed countries is about 10%. One third of them are fetuses with true intrauterine growth restriction (IUGR) characterized by increased perinatal and neonatal morbidity.[1-6]

Moderate SGA fetuses are constitutionally small, with a birthweight between 5th and 10th percentile, no doppler abnomalies and usually associated with a favorable neonatal outcome; this differs from fetuses with IUGR who are unable to achieve their genetically determined potential size mainly due to pathological conditions including abnormal placentation, chronic maternal diseases, substance abuses, infections or placental insufficiency.[3,4]

The challenge is to exclude the subset of pregnancies not affected by pathological growth restriction in order to avoid intervention that would increase maternal/fetal morbidity and mortality.[7,8] The distinction between SGA and IUGR can only be perfomed by serial fetal monitoring of growth and

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well-being until delivery. In fact, a large proportion of SGA can evolve during pregnancies into a milder form of late-onset IUGR, which increase the risk of adverse perinatal outcomes, abnormal neonatal neurobehavioral performance as well as unsatisfactory neurodevelopment in childhood and cardiovascular risk in adult life.[9-11] However, regardless of the monitoring used, infants born SGA at term with uneventful pregnancy drag an intrinsic greater risk of mortality and morbidity in the neonatal period and beyond.[12]

In the last decade, most studies regarding SGA were performed to find the appropriate monitoring system to detect the development in IUGR as early as possible in order to reduce neonatale morbidity/mortality.[9-11] However, time of delivery in uneventful pregnancies is still widely debated expecially in moderate SGA at term.

The purpose of our study was to evaluate the perinatal and neonatal outcomes of moderate SGA infants at term in relation to the week at delivery in physiological pregnancies.

MATERIAL AND METHODS

We analyzed a database reporting details of deliveries collected prospectively by a Swiss obstretric study group (Arbeitsgemeinschaft Schweizerischer Frauenkliniken, Amlikon, Switzerland) over a 12-year period (January 2005-December 2017), merging data from more than 100 obstetric hospitals of different sizes and structure.

The quality of the records was controlled in a twofold way: the first control was implemented at the time of discharge by a senior obstetrician with the purpose of ensuring the completeness of the information. Secondly, the data center quality control group verified the data enter to check for its plausibility. SGA was defined as a newborn whose birth weight was less than the 10th centile for gestational age. Eligible women were healthy and presented during pregnancy a SGA characterized by normal umbilical artery Doppler. Gestational age was defined according to ultrasound measurements early in the second trimester or by gestational age estimated from information of the last menstrual period.[3] All data excluding maternal age and weight as well as birth weight, pH, Apgar were collected as categorical variables. Inclusion criteria were uncomplicated singleton pregnancy in cephalic presentation, with a birthweight ≥5th and <10th percentile (moderate SGA), gestational age at delivery between 37 0/7-42 0/7 weeks of gestation. The sample does not include pregnancies complicated by hypertensive pregnancy disorders, abnormal Doppler findings, abnormal placental findings and metabolic problems such as pregestational or gestational diabetes. Moreover, we excluded also cases with structural or chromosomal anomalies.

The study has 2 main inferences. The primary outcome was the success rate at term of vaginal birth in SGA in relation to the week of gestation. The secondary outcome was the incidence of adverse neonatal outcome defined as, 5' Apgar score <7, and/or umbilical artery pH<7.15 and/or transfer to the neonatal intensive care unit (NICU) and/or perinatal/neonatal death by week of gestation.

Ethical approval for the current study was obtained by the local institutional review board (Ethics Committee of the Canton of Bern, Switzerland, 2019-02007, approved on April 7, 2020). The study was carried out in accordance with the Helsinki Declaration principes and informed consent was not necessary due to the retrospective nature of the study.

STATISTICAL ANALYSIS

Statistical analysis was performed with GraphPad Prism version 8 for Mac, (GraphPad Software, San Diego CA). Continuous variables were compared using the student t-test or Mann-Whitney U test. Proportions were analyzed with chi-square or Fisher's exact test, where appropriate. Correlations were searched by using the Spearman rank test. The study adopts a p value <0.05 as statistically significant.

RESULTS

Starting from an initial population of 429,863 deliveries, 25,175 newborns were SGA (5.8%) and 1,796/25,175 (7.1%) met the inclusion criteria and were used for further analyses.

The clinical features of the analyzed sample are summarized in Table 1, that shows how the prevalence of SGA did not change during the period under examination. Similarly, no difference was found comparing the modes of each delivery that occurred at 37, 38, 39, 40, 41 week of gestation for 56 (3.1%), 314 (17.6%), 506 (28.2%), 567 (31.5%), 353 (19.6%) women respectively. Moreover, no significant differences in body mass index and maternal smoking were found among the gestational weeks described above.

Overall, 1,327/1,796 (73.9%) of the women included in this research delivered vaginally, 209/1,796 (11.6%) underwent an elective caesarean section (CS) while 260/1,796 (14.5%) an emergency CS. The vaginal delivery rate increased steadily from 37 weeks onwards with a maximum at 40 weeks of gestation. Thereafter a decline was noted while the CS rate increased significantly (Figure 1).

The rate of emergency CS increased significantly (r=0.828; p=0.03) until the 41st week of gestation. Similarly, the vaginal delivery rates increased with advancing gestation (r=0.965; p=0.01) but only up to 40-week of gestation and decreased afterwards. Induction of labour occurred in 306 (19.3%) patients and increased especially between 40 and 41 weeks of gestation (r=0.967; p=0.002). Among them, 80% delivered vaginally, while the remaining 20% via an emergency CS. The percentage of adverse outcome was 16.9%, 11.3%, 8.6%, 18.8%, and 21.7% for gestational week 37, 38, 39, 40 and 41, respectively. The fetal death rate was 3/1,796 (0.17%). One fetus died <39 0/7 and 2>40 0/7 (week of gestation) Table 1.

DISCUSSION

SGA infants at term with a birthweight ≥5th and <10th percentile find the best conditions for delivering between 39 0/7 and 40 0/7 weeks of gestation. Moreover, we were able to observe that 3 quarters of the moderate SGA delivered vaginally and if protracted beyond term a significant higher incidence of induction of labor and emergency CS occurred.

Moderate SGA infants are constitutionally small and usually are characterized by growing regulary throughout pregnancy. Nevertheless, several studies have confirmed that low birth weight is an important risk factor for poor perinatal and childhood outcomes.[9,12,13] Low Apgar score, neonatal death, hypoglycemia, hypothermia, academic, and mental disordes are the main findings that can occur in newborn with a birth weight <2,500 g.[14-16] In our study, we selected moderate SGA at term between ≥5th and <10th. The reason of this restricted range was to avoid potential bias, as below the 3rd percentile the number of unrecongnized fetal growth restriction due to placental insufficiency is higher and may include a potential variable that increases the additionally risk for adverse fetal outcome. However, the percentage of adverse neonatal outcome characterized by pH<7.15

TABLE 1: Clinical characteristics and outcomes of the study population according to gestational week.

Idiopathic SGA (n=1,796)	Week of gestation					
	37th (n=56)	38th (n=314)	39th (n=506)	40th (n=567)	41th (n=353)	p value
Age (mean±SD-years)	31.08±2.6	30.97±1.7	30.59±1	30.84±0.9	30.8±1.3	NS
BMI (mean±SD)	24.68±1.6	25.29±1.3	25.9±0.7	25.59±0.7	26.43±0.7	NS
Vaginal birth-n (%)	32 (51.1)	171 (54.4)	392 (77.4)	460 (81.2)*	275 (77.9)	0.01
Caesarean section-n (%)	15 (26.7)	42 (13.3)	49 (9.6)	84 (12.8)	71 (20.1)	0.03
Maternal death-n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NS
Apgar score at 5 minute<7-n (%)	5 (7.9)	7 (2.4)	10 (1.9)	17 (3.1)	17 (4.8)	0.007
pH<7.15-n (%)	3 (4.3)	26 (8.3)	51 (6.5)	82 (15)	55 (16.2)	0.006
Neonatal death-n (%)	1 (1.2)	0 (0)	0 (0)	0 (0)	2 (0.7)	NS
Sex (male)-n (%)	29 (51.7)	84 (26.7)	145 (28.6)	194 (34.2)	109 (30.8)	0.0006
NICU-n (%)	2 (3.5)	2 (0.6)	1 (0.2)	4 (0.7)	0 (0)	NS

Values are given in mean±SD or numbers as appropriate; SGA: Small for gestational age; SD: Standard deviation; BMI: Body mass index; NICU: Neonatal intensive care unit; NS: Not significant. *Indicates a statistically significant difference (p<0.05) from the reference value.

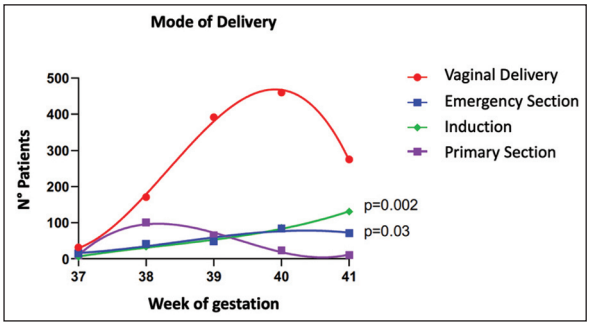

FIGURE 1: Mode of delivery/induction in patients with SGA according to the gestational week. SGA: Small for gestational age.

and/or Apgar at 5'<7 and/or admission to NICU was significantly higher at 37 weeks of gestation, a result attributable to the reduced birthweight (<2,500 g), earlier gestational age and a higher rate of elective CS. This consideration is consistent in previous literature findings. For example, Doctor et al. compared moderate SGA with infants appropriate for gestational age (AGA) until 40 0/7 week of gestation and the only difference was the development of neonatal hypothermia probably linked to different incidence of IUGR in the SGA groups and the association with a variety of obstetrical risk factors. The authors concluded that these neonatal morbidities were related to growth failure rather than being its cause.[17] Furthermore, Chauhan et al. compared SGA at term with AGA. An increased incidence of hypoxic neonatal morbidity in the SGA group was found in particular in the SGA group with a birthweight <2,500 g. In addition, the overall incidence of CS was similar to our findings even if the number of emergency CS was not reported. Moreover, stillbirths as well as the neonatal outcome for each gestational week of pregnancy were not analyzed.[12]

In SGA, fetuses' time of delivery is still under debate, in particular in the moderate one in which, at the exception of the birth weight, the obstetrical monitoring still remains uneventful. Until now, no adequately randomized studies have been performed to determine the optimal time of delivery in SGA after the 34th week of gestation. These regards not only the time of delivery but also the management of these pregnancies.[3] The Royal College Society of Obstetricians and Gynaecologists, in fact, recommends in patients with SGA after the 32 weeks of gestation and uneventful sonographic monitoring induction of labor at 37 weeks of gestation.[18] This contrast with the German (Deutsche Gesellschaft für Gynäkologie und Geburtshilfe) and American (Society for Maternal-Fetal Medicine) equivalent body which advises to deliver a week later for fetuses with similar characteristics.[19-22]

Our data shows that the incidence of adverse outcome decreases from 37 weeks to 40 weeks significantly, while a higher rate of emergency CS observed afterwards. At 40 weeks, the birth weight is >2,500 g and may play a marginal role in neonatal outcome. However, a clinically not detectable insufficiency of the uteroplacental blood supply could explain our results. Parra-Saavedra et al. analyzed placental pathological findings in SGA births delivered after 34 weeks with normal umbilical artery Doppler.[22] The authors found histological abnormalities in 78.2% of the cases, secondary to maternal underperfusion of the placenta.[23] Subsequent studies confirmed the close relation between placenta abnormalities and the insurgence of SGA.[24,25] This result could explain our increased incidence of emergency section, a percentage that remains lower than the one reported in the literature (14.5% vs. 23%).

A multicenter study is in preparation investigating exactly this group of small fetuses diagnosed in late gestation with the aim to find parameters, e.g. cerebral hemodynamics, which could be of value in selecting those with increased risk for adverse outcome to better tailor its management (Trial of Randomized Umbilical and Fetal Flow in Europe 2).

According to the week of gestation, no significant difference between the different mode of deliveries was observed even if, consistent with our expectations, a significant increase of vaginal delivery occurred within 40th week of gestation (Figure 1).

The limitation of our study is the retrospective design. Moreover we based our data on the actual birthweight which, naturally, during pregnancy is not exactly the same and could lead to a different clinical management. In addition, it is uncertain how many of these women had the suspect of SGA during pregnancy. On the other hand, we selected a homogenous group of moderate SGA excluding typical obstetrical risk factors to avoid potential bias which could influence our data analyses.

CONCLUSION

In conclusion, the overall success rate of vaginal birth in moderate SGA at term with a birthweight among ≥5th and <10th percentile within the 40th week of gestation is 73.9% and decreases afterwards in favor of emergency CS. Gestational age seems to have an important clinical impact on neonatal outcome. A better outcome has been found if women fulfilling our inclusion criteria gave birth between 39 0/7 and 40 0/7 weeks of gestation.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

All co-authors contributed substantially to the work and every author listed on the manuscript has seen and approved the submission of this version and takes full responsibility for the manuscript. BD and RL conceived the idea, developed the content and led the preparation of the article including writing and editing. FV helped with the writing and editing of the article. AMS and TR collected the data and helped with the editing of the article. FV made the statistical analysis. BD and RL provided expert knowledge and guidance on the article.

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