Fetal Growth and Adipose Fat Tissue Trajectories in Twin Pregnancies after Gastric Bypass Surgery

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Keywords

Bariatric surgery · Twin pregnancy · Fat tissue · Fetal growth restriction · Gestational diabetes

Abstract

Introduction: Previous studies demonstrated a continuous decline in fetal growth throughout singleton pregnancy after bariatric surgery. However, intrauterine growth in twin pregnancy is subjected to further underlying processes. This study was to investigate the longitudinal assessment of fetal biometry and abdominal fat thickness of twin pregnancies conceived after gastric bypass (GB) surgery and compare them to body mass index-matched (BMIM) and obese (OB) controls. **Materials and Methods:** We retrospectively assessed ultrasound data of 30 women with dichorionic-diamniotic twin pregnancy (11 women after GB surgery, 9 OB mothers with pregestational BMI ≥ 30 kg/m², and 10 BMIM and age-matched controls). We assessed fetal growth parameters including fetal subcutaneous adipose tissue thickness (FSCTT) as well as newborn biometry after delivery. Patient characteristics were obtained from the medical records. **Results:** The rise in FSCTT curves was markedly slower in the twin offspring of women with history of GB as compared to the offspring of OB mothers and offspring of BMIM controls.

Hence, FSCTT was significantly decreased in the GB offspring as compared to both control groups at 34 weeks of gestation. Also, growth curves of abdominal circumference were decreased in the offspring of GB patients as compared to OB mothers. Infants of mothers with history of GB showed significantly lower birth weight percentiles compared to newborns of OB mothers (27.2 vs. 48.8 pct, $p = 0.025$). There was no significant difference in inter-twin birth weight difference between the offspring of GB (median: 9.9%, interquartile ranges [IQR]: 6.5–20.0) versus OB (median: 14.6%, IQR: 8.2–21.6) and BMIM controls (median: 9.0%, IQR: 6.3–12.6, $p = 0.714$). **Conclusions:** In summary, intrauterine growth delay in twin pregnancies after GB is assumed to be a multifactorial event with altered metabolism as the most important factor. However, special attention must be paid to the particularity of twin pregnancies as they seem to be subject to other additional mechanism.

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Introduction

The number of obese (OB) women is growing and subsequently the number of women at reproductive age undergoing bariatric surgery has risen within the last de-

acades [1]. Recent studies showed that bariatric surgery has become to be the most effective treatment for morbid obesity [2]. Although the obesity-related risk could be reduced, women after bariatric surgery are still at higher risk for perinatal complications such as small for gestational age (SGA) infants, prematurity, and a tendency toward perinatal mortality [3]. It is believed that bariatric surgery has a positive influence on some maternal outcomes such as gestational diabetes (GDM) and hypertension and may affect fetal growth as well [4].

In this context, we demonstrated in previous studies a continuous decline in fetal growth throughout singleton pregnancy after bariatric surgery [5] and second a markedly decline of fetal subcutaneous adipose tissue thickness (FSCTT) of fetuses of mothers with a history of bariatric surgery [6]. Although the pathophysiological mechanisms remain unclear, it is believed that fetal growth restriction and low FSCTT are more likely caused by nutrient deficiency and by multifactorial genesis with altered metabolism as the most important factor, rather than by growth restriction due to placenta etiology or pre-eclampsia (PE) [7]. Those assumptions are supported by previous studies, which observed that low birth weight in newborns was more likely the result of reduction in fetal subcutaneous fat tissue rather than in lean mass [8]. Furthermore, it has been indicated that trajectories of ultrasound-derived FSCTT are very sensitive to maternal metabolic alterations during pregnancy like GDM [9] and closely related to established predictors of fetal nutrition status such as amniotic fluid, abdominal circumference, ponderal index, and triceps and subscapular skinfold thickness in newborns [10]. Therefore, longitudinal assessment of FSCTT may become an important role to identify nutritional fetal abnormalities [9].

However, a longitudinal observation of FSCTT in twin pregnancies of mothers with history of gastric bypass (GB) has not been assessed so far, although there has been a markedly increase in twin pregnancies worldwide including women with history of bariatric surgery [4, 11]. This is most likely due to continued fertility problems, despite weight loss after surgery and the use of assisted reproductive technology [4, 11]. But little is known about twin pregnancy outcome after bariatric surgery as twin pregnancies only contribute to a small number despite their increase and are therefore often excluded from clinical studies.

In general, twin pregnancies are at higher risk for fetal growth restriction as singletons [12]. Therefore, the question arises how much the factor of bariatric surgery affects a possible growth retardation of twins or whether other

factors also make a significant contribution. To clarify this question, the aim of this study was to assess fetal biometry and ultrasound-derived abdominal FSCTT of twin pregnancies conceived after GB surgery and compare them to body mass index-matched (BMIM) and OB controls.

Materials and Methods

Research Design

In this study, we retrospectively assessed data of 30 women with dichorionic-diamniotic twin pregnancy: 11 women after GB surgery (9 OB mothers with pregestational BMI ≥ 30 kg/m² and 10 BMIM and age-matched controls). All women received GB procedure. The majority of the patients were operated with Roux-en-Y procedure, whereas 1 woman was operated with Omega-loop technique. All women were treated at our pregnancy outpatient department between January 2007 and January 2018. Monochorionic twin pregnancies or mothers with pregestational diabetes were not included. Specialized ultrasound technicians performed all ultrasound examinations with commercially available real-time equipment using standard 3.75-MHz linear or sector transducers transabdominally (Power Vision and Aplio MX, Toshiba, Japan, and Voluson E8, GE Healthcare Company, Germany). Longitudinal assessment of ultrasound-derived FSCTT was performed retrospectively from the second trimester onward after recalibration of the image. For that purpose, the abdominal circumference level (AC) has been used for all measurements since it is a standardized cutting plane (according to ISUOG guidelines) [13], for unification and therefore having a continuity and equality within the measurements as reported in our previous study [6] with measure points of FSCTT (measured in millimeters [mm] between the outer and inner margin of the echogenic subcutaneous tissue after magnifying the area of interest) on (i) the anterior abdominal wall in front of the intrahepatic tract of the umbilical vein, (ii) on the left side next to the stomach, and (iii) on the exact opposite right side of the abdomen. Medical records were used to collect data on BMI before pregnancy or before bariatric surgery and time between operation and pregnancy. Results of the diagnostic 2 h-75 g oral glucose tolerance test including fasting and 60-min and 120-min post-load glucose levels were available in 7 GB, 9 OB, and 10 BMIM patients. In addition, pregnancy outcome and weight of the newborns were assessed.

Statistical Analysis

Continuous variables were summarized by mean $\pm$ standard deviation or median and interquartile ranges (IQRs) and compared by analysis of variance (followed by Fisher least significant difference tests) or rank-based inference. Categorical variables were summarized by counts and percentages and compared by Fisher's exact test. Linear mixed-effects models with random intercepts were used to account for correlated residuals, which occurred due to repeated measurements or twin pregnancies. A group by time interaction term was included into the linear mixed-effects models to evaluate differences between subgroups in fetal biometry as well as in time-dependent changes. Statistical analysis was performed with R (V4.0.2) and contributing packages, especially "nlme" and "ggplot2" [14]. A 2-sided p value ≤ 0.05 was considered statistically significant.

Table 1. Characteristics of the study sample

	GB (n = 11)	OB (n = 9)	Control (n = 10)	p value
Age, years	35.7±5.0	32.6±6.6	34.0±2.4	0.363
BMI, kg/m ² , before pregnancy	29.6±5.7	38.4±6.0*	30.3±6.6	0.006
Gravida	3.0 (2.0–6.5)	3.0 (2.0–5.0)	3.0 (2.0–3.8)	0.853
Para	3.0 (2.0–4.5)	2.0 (1.0–3.0)	2.0 (1.0–3.0)	0.381
PE/HELLP	0 (0.0)	1 (11.2)	3 (30.0)	0.128
IVF	2 (18.2)	3 (33.3)	2 (20.0)	0.752
C-section	8 (72.7)	9 (100)	9 (90.0)	0.350
Gestational age at delivery, weeks	36.4 (35.6–37.3)	37.0 (35.9–37.7)	36.9 (35.8–37.3)	0.794
OGTT-0 min, mg/dL	76.9±6.1	86.7±11.3	84.8±13.8	0.220
OGTT-60 min, mg/dL	183.9±32.6	151.4±28.8	156.3±39.5	0.160
OGTT-120 min, mg/dL	65.7±34.1	120.2±32.9*	135.0±38.0*	0.002
OGTT-120 min <70 mg/dL	5 (71.4)	0 (0.0)*	1 (10.0)*	0.003
Insulin use in pregnancy	2 (18.1)	4 (44.4)	3 (30.0)	0.477

Data are numbers of included subjects, means±standard deviation or medians (IQR) for continuous variables, as well as counts (%) for categorical variables. Women after GB compared to OB and BMIM controls.

Table 2. Growth differences of fetuses conceived after GB compared to OB and BMIM controls

	Measures	Mean difference	95% CI	p value
34 weeks of pregnancy: OB versus GB	Abdomen (percentile)	7.4	−8.2 to 23.1	0.337
	Head curve (percentile)	12.9	−3.8 to 29.7	0.125
	Head/abdomen	−0.01	−0.05 to 0.03	0.554
	BPD (percentile)	19.6	4.0–35.3	0.016
	Femur (percentile)	8.2	−17.5 to 33.8	0.519
	FSCTT, mm	3.1	0.12–0.18	<0.001
34 weeks of pregnancy: BMIM versus GB	Abdomen (percentile)	−0.5	−15.6 to 14.6	0.947
	Head curve (percentile)	0.5	−15.7 to 16.7	0.953
	Head/abdomen	−0.01	−0.05 to 0.02	0.473
	BPD (percentile)	8.1	−6.9 to 23.2	0.277
	Femur (percentile)	−2.1	−25.6 to 21.5	0.857
	FSCTT, mm	2.2	1.3–3.2	<0.001
Birth: OB versus GB	Weight (percentile)	21.6	2.9–40.2	0.025
	Length (percentile)	12.1	−8.6 to 32.8	0.232
	Head (percentile)	6.0	−10.5 to 22.5	0.460
Birth: BMIM versus GB	Weight (percentile)	−3.6	−21.7 to 14.5	0.684
	Length (percentile)	5.3	−14.1 to 24.7	0.589
	Head (percentile)	−3.8	−20.3 to 12.6	0.636

Mean differences represent growth deviations in GB patients compared to OB and BMIM controls. Percentile: see [32].

Ethical Approval

Ethical approval for this study was provided by the Ethics Committee of the Medical University Vienna (No.: 1319/2016). The study was performed according the Helsinki Declaration. Informed consent was not necessary due to the retrospective nature of the study.

Results

Characteristics of the study population are reported in Table 1. Women after GB surgery showed lower glucose levels at 120 min after oral glucose load as well as a high proportion of postprandial values below 70 mg/dL. The

Fig. 1. Trajectories of FSCCT, in twin pregnancies after GB and OB, or BMIM. Solid line represents a trend curve derived by locally weighted regression.

mean time between bariatric surgery and pregnancy was 5.2 ± 2.2 years (IQR: 4–7). The mean BMI before surgery was 46.5 ± 8.8 kg/m², and the average weight loss between surgery and index pregnancy was 47.8 ± 20.7 kg. The average weight gain during pregnancy in each group was GB versus OB versus BMIM: 11.4 ± 7.8 versus 17.6 ± 8.1 versus 13.1 ± 7.1 , $p = 0.285$. The main outcomes are reported in Table 2. At 34 weeks of gestation, the FSCCT was significantly lower in the GB offspring as compared to both control groups (GB vs. OB vs. BMIM: 3.2 vs. 5.3 vs. 5.5 mm), whereas differences in other fetal growth parameters were marginal. As visualized in Figure 1, the rise in FSCCT curves was markedly slower in the twin offspring of patients with history of GB as compared to the offspring of OB mothers (b: 1.29 mm, 95% CI 0.95–1.64, $p < 0.001$, whereas b is the difference in the mean increase between the groups per 8 weeks of gestation) and offspring of BMIM controls (b: 0.62, 95% CI 0.28–0.96, $p < 0.001$). This was accompanied by a significant group per time interaction in abdominal circumference, which increased by 81.7 mm (per 8 weeks of gestation) in infants of GB mothers and by 85.5 mm in infants of OB mothers (mean difference of the increase of OB vs. GB per 8 weeks of gestation: 3.78 mm, 95% CI 0.21–7.34, $p = 0.038$). No differences were observed when the offspring of GB patients was compared to BMIM mothers ($p = 0.663$). As a consequence, infants of GB mothers showed significantly lower birth weight percentiles compared to newborns of OB mothers (27.2 vs. 48.8 pct, resulting in a mean differ-

ence of 21.6, 95% CI 2.9–40.2, $p = 0.025$). There was no significant difference in inter-twin birth weight difference between the offspring of GB (median: 9.9%, IQR: 6.5–20.0) versus OB (median: 14.6%, IQR: 8.2–21.6) and BMIM controls (median: 9.0%, IQR: 6.3–12.6, $p = 0.714$). Placental weight and birth weight to placental weight ratio in these 3 groups of dichorionic twin pregnancies has been calculated and compared. Placental weight in kg for this cohort is as follows: GB versus OB versus BMIM: 0.9 ± 0.2 versus 1.0 ± 0.2 versus 0.9 ± 0.2 , $p = 0.366$. The BW/PW ratio was calculated by dividing the total birth weight (the sum of both twins' birth weight) by the placenta weight as it is described in a previous work by Souza et al. [15] for twin pregnancies. The results do not show a significant difference regarding BW/PW ratio; therefore, no substantial difference in placental mass as a possible index of reduced placental function could be observed: GB versus OB versus BMIM: 5.8 ± 1.7 versus 5.5 ± 1.5 versus 5.2 ± 0.7 , $p = 0.639$.

Discussion

To our knowledge, this is the first study aiming to assess the impact of maternal bariatric surgery on fetal development in twin pregnancies. As a main finding, we observed that fetuses conceived after maternal GB surgery showed significantly reduced ultrasound-derived FSCCT as compared to BMIM or OB controls. Further-

more, we observed a markedly slower rise in FSCTT growth curves from the beginning of the second trimester until delivery. Although a multifactorial genesis including nutritional deficiencies and altered metabolism after bariatric surgery may be the most suitable explanation, the exact pathophysiological mechanism remains elusive. There is a clear evidence that impaired maternal nutritional uptake occurs after GB. Especially after malabsorptive techniques, nutrient deficiencies are expected (including iron, calcium, and different vitamins) with consequences for the pregnancies in terms of fetal growth restriction [16]. Several former studies found that prenatally reduced abdominal adipose tissue thickness is associated with low birth weight and decreased skinfold thickness [17–20], as well as with impaired nutrition status of the newborns of mothers with history of bariatric surgery. Moreover, Tantanasis et al. [18] observed that the amount of fetal subcutaneous fat tissue is related to maternal diabetes, suggesting that altered fetal subcutaneous fat trajectories are a consequence of alterations in maternal glucose metabolism after bariatric surgery. Indeed, we observed lower glucose levels at 120 min after oral glucose load and a tendency toward hypoglycemia in GB mothers of dichorionic twins, comparable to previous observations in singleton pregnancies [21, 22]. However, the growth pattern of other fetal growth parameters in this study, such as the AC, showed only marginal differences. This is in contrast to previous observations but may be a consequence of the lower sample size in this very special study population [5, 6]. While a causal relationship between glycemic alterations and fetal development is obvious, we are convinced that the intrauterine growth restriction in twins in women with history of GB surgery is more complex and subject to other additional processes as it is for singletons.

In general, twin pregnancies are at higher risk for fetal growth restriction, preterm delivery, and perinatal morbidity and mortality in general [12]. Nevertheless, the recommended management for intrauterine growth restriction for twins does not differ from singletons with fetal growth restriction [23]. It should be noted that this is mainly true for dichorionic twin pregnancies, for which reason monochorionic twin pregnancies were excluded from this study. However, recent studies suggest that the cause of intrauterine growth restriction in singleton and dichorionic twin pregnancies is not similar [24, 25]. Therefore, the question arises whether different mechanisms intervene in fetal growth and whether the results in this study (especially regarding abdominal circumference) are not as extreme as in our previous study popula-

tion because this is counteracted more strongly. A recent study, conducted by Vanlieferinghen et al. [25], observed that twins were less severely SGA than singletons and that the interval from development of umbilical artery Doppler abnormalities to birth was significantly longer in growth-restricted twins than in growth-restricted singletons [25]. In general, the pathophysiological mechanism of fetal growth restriction in twins may be related to failed placentation and pathological blood flow distribution. However, it is assumed that close monitoring of twin pregnancies leads to earlier diagnosis of SGA in twins compared to singletons before severe growth restriction occurs since they are high-risk pregnancies per se. Vanlieferinghen et al. [25] stratified the population as moderate and severe SGA to minimize the effect of this bias and could confirm their findings for both groups. As a result, it is believed that fetal growth restriction does not appear to have the same prognostic significance for the course of pregnancy in singleton and twins and changes in the umbilical artery Doppler and cerebral artery Doppler should be used and interpreted differently for twins and singletons regarding monitoring and decision-making [25]. However, there has been just 1 recent study published by Rottenstreich et al. [4] regarding twin pregnancy outcomes following bariatric surgery: maternal complication such as GDM and hypertension was less frequent after surgery compared to controls (9.1% vs. 36.4% and 0% vs. 25%, respectively). Furthermore, noteworthy in this context, the amount of SGA twins was comparable between the 2 groups with a higher inter-twin birth weight discordance in the control group [4]. In this present study of twin pregnancies, no significant difference in inter-twin birth weight difference between the offspring of GB versus OB and BMIM controls could be observed. This can perhaps be explained by the fact that the massive weight loss after the operation reduces the risk of pregnancy-associated diseases such as PE and may counterbalance the negative effect of GB on fetal growth [4]. However, it does not explain why Rottenstreich et al. [4] had higher inter-twin birth weight discordance in the control group whereas we could not show a significant difference. However, a recent study by Xiao et al. [26] observed that an increase in inter-twin delivery weight discordance is a consequence of inadequate maternal weight gain during pregnancy. These results would support the hypothesis that fetal growth and FSCTT are more likely caused by multifactorial genesis with altered metabolism as the most important factor, rather than by growth restriction due to placenta etiology or PE.

Another report in favor of our assumption described intravenous nutrition for a twin pregnancy after jejunoileal bypass for 6 weeks after diagnosis of fetal growth restriction. The authors claimed that twins were born with appropriate fetal birth weight for their age of gestation [27]. In general, close monitoring of vitamin and micro-nutrient status (ideally every trimester) with adequate supplementation, if necessary, has been recommended as a clinical practice for pregnancies after bariatric surgery [28].

Nevertheless, even if twin pregnancies are subject to different physiological processes regarding fetal growth, such as pathological blood flow distribution and placentation, our results cannot fully explain the association between maternal history of GB surgery and significant reduced abdominal adipose tissue in twins on 1 side and the marginal differences in the AC in all 3 groups on the other side. The retrospective setting and the sample size of this very special study population can be seen as disadvantage in this study as some possible contributors are not available. However, we believe in an interplay in the sense of a multifactorial event with altered metabolism as the most important factor. But most probably just as important is the influence of placentation and blood flow distribution in twin pregnancies. The latter may not apply for singleton pregnancies after GB the same way as for twins. It is claimed that micronutrient deficiency after GB is more pronounced in twins compared to singletons [4]. Nevertheless, another assumption is the impact of weight loss after such an operation on the prevalence of hypertensive disorders and PE as the condition is a main cause of fetal growth restriction. Weight loss after GB may be a reason for the lower birth weight discordance between twin pregnancies after GB and the control group as lower prevalence of PE after GB may counterbalance the degree of fetal birth weight discordance [26, 29, 30]. This positive effect of a decrease of inter-twin birth weight discordance may be caused by less release of antiangiogenic and inflammatory factors through the placenta and subsequently a better cytotrophoblast migration and uterine spiral artery remodeling and therefore better placentation and blood flow distribution [31].

Conclusion

In summary, intrauterine growth delay in twin pregnancies after GB is assumed to be a multifactorial event with altered metabolism as the most important factor. However, special attention must be paid to the particular-

ity of twin pregnancies as they seem to be subject to the other additional mechanism. In this context, futures studies should incorporate nutrition status and life style habits as well as ultrasound and Doppler assessment as the course and severity of growth retardation is differently pronounced in twins compared to singletons. In general, more studies of twin pregnancies after bariatric surgery are warranted as current recommendation for pregnant women after GB surgery or bariatric surgery is based on studies that have mainly targeted singleton pregnancies.

Statement of Ethics

Ethical approval for this study was provided by the Ethics Committee of the Medical University Vienna (No.: 1319/2016). The study was performed according the Helsinki Declaration. Informed consent was not necessary due to the retrospective nature of the study.

Conflict of Interest Statement

Authors have nothing to disclose.

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Author Contributions

G. Y.-S. and C.S.G. and M.F. made substantial contribution to the conception and design of the work. T.S. and G.K. contributed to acquisition of data. D.E. and G.Y.-S. and C.S.G. contributed to analysis and interpretation of data for the work. G.Y.-S. and C.S.G. contributed to drafting the work. K.W. and W.H. contributed to revising it critically for important intellectual content. G.Y.-S. and C.S.G. and W.H. contributed to final approval of the version to be published.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

References

- Edison E, Whyte M, van Vlymen J, Jones S, Gatenby P, de Lusignan S, et al. Bariatric surgery in obese women of reproductive age improves conditions that underlie fertility and pregnancy outcomes: retrospective cohort study of UK National bariatric surgery registry (NBSR). *Obes Surg*. 2016;26(12):2837–42.
- Mingrone G, Panunzi S, De Gaetano A, Guidone C, Iaconelli A, Leccesi L, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. *N Engl J Med*. 2012 Apr;366(17):1577–85.
- Johansson K, Stephansson O, Neovius M. Outcomes of pregnancy after bariatric surgery. *N Engl J Med*. 2015 04;372(23):2267.
- Rottenstreich A, Levin G, Rottenstreich M, Ezra Y, Elazary R, Elchalal U. Twin pregnancy outcomes after metabolic and bariatric surgery. *Surg Obes Relat Dis*. 2019 May;15(5):759–65.
- Feichtinger M, Falcone V, Schoenleitner T, Stopp T, Husslein PW, Eppel W, et al. Intra-uterine fetal growth delay during late pregnancy after maternal gastric bypass surgery. *Ultraschall Med*. 2020 Feb;41(1):52–9.
- Yerlikaya-Schatten G, Feichtinger M, Stopp T, Huhn EA, Chalubinski K, Husslein P, et al. Trajectories of fetal adipose tissue thickness in pregnancies after gastric bypass surgery. *Obes Surg*. 2020;30(1):96–101.
- Hammeken LH, Betsagoo R, Jensen AN, Sørensen AN, Overgaard C. Nutrient deficiency and obstetrical outcomes in pregnant women following Roux-en-Y gastric bypass: a retrospective Danish cohort study with a matched comparison group. *Eur J Obstet Gynecol Reprod Biol*. 2017 Sep;216:56–60.
- Galan HL, Rigano S, Radaelli T, Cetin I, Bozzo M, Chyu J, et al. Reduction of subcutaneous mass, but not lean mass, in normal fetuses in Denver, Colorado. *Am J Obstet Gynecol*. 2001 Oct;185(4):839–44.
- Larciprete G, Valensise H, Vasapollo B, Novelli GP, Parretti E, Altomare F, et al. Fetal subcutaneous tissue thickness (SCTT) in healthy and gestational diabetic pregnancies. *Ultrasound Obstet Gynecol*. 2003 Dec;22(6):591–7.
- Skinner J, O'Donoghue K, Gardeil F, Greene R, Turner MJ. Is fetal abdominal subcutaneous fat comparable with established indices of growth restriction? *J Obstet Gynaecol*. 2001 Sep;21(5):439–42.
- Chauhan SP, Scardo JA, Hayes E, Abuhamad AZ, Berghella V. Twins: prevalence, problems, and preterm births. *Am J Obstet Gynecol*. 2010 Oct;203(4):305–15.
- Townsend R, Khalil A. Fetal growth restriction in twins. *Best Pract Res Clin Obstet Gynaecol*. 2018 May;49:79–88.
- Salomon LJ, Alfrevic Z, Berghella V, Bilardo C, Hernandez-Andrade E, Johnsen SL, et al. Practice guidelines for performance of the routine mid-trimester fetal ultrasound scan. *Ultrasound Obstet Gynecol*. 2011 Jan;37(1):116–26.
- R Core Team. *R: a language and environment for statistical computing*; 2020. Available from: <https://www.R-project.org/>.
- Souza M, Brizot M, Biancolin S, Schultz R, Carvalho M, Francisco R, et al. Placental weight and birth weight to placental weight ratio in monochorionic and dichorionic growth-restricted and non-growth-restricted twins. *Clinics*. 2017 May;72(5):265–71.
- Eppel D, Göbl CS. Pregnancy after bariatric surgery: a growing challenge in feto-maternal medicine. *Am J Clin Nutr*. 2020 Feb;111(2):250–1.
- Aksoy H, Aksoy U, Açmaz G, Tutuş S. The effect of impaired 50-gram oral glucose challenge test on fetal abdominal wall thickness. *Diabetes Metab Res Rev*. 2014 Oct;30(7):570–4.
- Tantanasis T, Daniilidis A, Giannoulis C, Tzafettas M, Dinas K, Loufopoulos A, et al. Sonographic assessment of fetal subcutaneous fat tissue thickness as an indicator of gestational diabetes. *Eur J Obstet Gynecol Reprod Biol*. 2010 Oct;152(2):157–62.
- Gardeil F, Greene R, Stuart B, Turner MJ. Subcutaneous fat in the fetal abdomen as a predictor of growth restriction. *Obstet Gynecol*. 1999 Aug;94(2):209–12.
- O'Connor C, Doolan A, O'Higgins A, Segurado R, Sheridan-Pereira M, Turner MJ, et al. Fetal subcutaneous tissue measurements in pregnancy as a predictor of neonatal total body composition. *Prenat Diagn*. 2014 Oct;34(10):952–5.
- Feichtinger M, Stopp T, Hofmann S, Springer S, Pils S, Kautzky-Willer A, et al. Altered glucose profiles and risk for hypoglycaemia during oral glucose tolerance testing in pregnancies after gastric bypass surgery. *Diabetologia*. 2017 Jan;60(1):153–7.
- Göbl CS, Bozkurt L, Tura A, Leutner M, Andrei L, Fahr L, et al. Assessment of glucose regulation in pregnancy after gastric bypass surgery. *Diabetologia*. 2017 Dec;60(12):2504–13.
- Khalil A, Rodgers M, Baschat A, Bhide A, Gratacos E, Hecher K, et al. ISUOG practice guidelines: role of ultrasound in twin pregnancy. *Ultrasound Obstet Gynecol*. 2016 Feb;47(2):247–63.
- Antonakopoulos N, Pateisky P, Liu B, Kalafat E, Thilaganathan B, Khalil A. Selective fetal growth restriction in dichorionic twin pregnancies: diagnosis, natural history, and perinatal outcome. *J Clin Med*. 2020 May;9(5):1404.
- Vanlieferinghen S, Anselem O, Le Ray C, Shen Y, Marcellin L, Goffinet F. Prognostic value of umbilical and cerebral doppler in fetal growth restriction: comparison of dichorionic twins and singletons. *PLoS One*. 2015 Apr;10(4):e0123067.
- Xiao Y, Shen M, Ma S, Tao X, Wen SW, Tan H. The association between weight gain during pregnancy and intertwin delivery weight discordance using 2011–2015 birth registration data from the USA. *Int J Gynaecol Obstet*. 2018 Jun;141(3):371–7.
- Karamatsu JT, Boyd AT, Cooke J, Vinnal PS, McMahon MJ. Intravenous nutrition during a twin pregnancy. *J Parenter Enter Nutr*. 1987 Oct;11(5):499–501.
- Stopp T, Falcone V, Feichtinger M, Göbl C. Fertility, pregnancy and lactation after bariatric surgery: a consensus statement from the OEGGG. *Geburtshilfe Frauenheilkd*. 2018 Dec;78(12):1207–11.
- Kent EM, Breathnach FM, Gillan JE, McAuliffe FM, Geary MP, Daly S, et al. Placental pathology, birthweight discordance, and growth restriction in twin pregnancy: results of the ESPRiT Study. *Am J Obstet Gynecol*. 2012 Sep;207(3):220.e1–5.
- Sparks TN, Nakagawa S, Gonzalez JM. Hypertension in dichorionic twin gestations: how is birthweight affected? *J Matern Fetal Neonatal Med*. 2017 Feb;30(4):380–5.
- Spradley FT, Palei AC, Granger JP. Increased risk for the development of preeclampsia in obese pregnancies: weighing in on the mechanisms. *Am J Physiol Regul Integr Comp Physiol*. 2015 Dec;309(11):R1326–43.
- Stirrup OT, Khalil A, D'Antonio F, Thilaganathan B. Fetal growth reference ranges in twin pregnancies: analysis of the Southwest Thames obstetric research collaborative (STORK) multiple pregnancy cohort. *Ultrasound Obstet Gynecol*. 2015;45:301–30.