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Fetal Spina Bifida Repair in Obese Mothers: Is Maternal and Fetal Safety Compromised?

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Keywords
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Abstract

Introduction: The Management of Myelomeningocele Study (MOMS) eligibility criteria preclude in utero surgery for fetal spina bifida (fSB) when the maternal body mass index (BMI) is ≥35 kg/m^2. Some centers still respect this criterion, while others, like ours, do not. This study aimed to assess whether maternal and fetal safety is compromised with higher maternal BMIs. ***Methods:*** Data of 192 patients with open fSB repair at our center were retrospectively analyzed. According to their BMI, patients were divided into three groups: group 1 (BMI <30 kg/m^2), group 2 (BMI 30–35 kg/m^2), and group 3 (BMI >35 kg/m^2). Subgroup analysis was performed to assess differences in maternal and fetal outcomes. Additionally, complications were divided into grades 1 to 5 according to their severity and outcome consequences and compared among groups. ***Results:*** Out of 192 patients, 146 (76.0%) had a BMI <30 kg/m^2, 28 (14.6%) had a BMI 30–35 kg/m^2, and 18 (9.4%) had a BMI >35 kg/m^2. Significant differences occurring more often in either group 2 or 3 compared to group 1 were maternal wound seroma (50% or 56% vs. 32%, $p = 0.04$), amniotic fluid leakage (14% or 6% vs. 2%, $p = 0.01$) as well as vaginal bleeding (11% or 35% vs. 9%, $p = 0.01$). On the contrary, duration of tocolysis with atosiban was shorter in patients with BMI >30 kg/m^2 (4 or 5 vs. 6 days, $p = 0.01$). When comparing severity of maternal or fetal complications, grade 1 intervention-related complications occurred significantly more often in group 3 compared to group 1 or 2 (78% vs. 45% or 57%, $p = 0.02$). Gestational age at delivery was around 36 weeks in all groups without significant differences. ***Conclusion:*** This investigation did not identify clinically relevant maternal and/or fetal outcome problems related to BMIs >35 kg/m^2. Additional studies are however needed to confirm our results.

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Introduction

Spina bifida aperta (SB) is the most common neural tube defect and affects around 1:3,000 births [1, 2]. Different factors influence the occurrence of fetal spina bifida (fSB), such as genetic factors, geographical location, ethnic background, folate intake, maternal anticonvulsant therapy, as well as maternal disease like diabetes mellitus or, of particular note for this article, obesity [1, 3–8]. A meta-analysis by Stothard et al. [8] showed that the odds for a pregnancy affected by fSB were twice as high in obese mothers compared to mothers with recommended BMI. Considering that, obesity has globally nearly tripled since 1975, reaching a rate of 15% in women in general, but up to 40% in women of childbearing age in the USA, the correlation of obesity and SB reaches public health relevance [9, 10].

Prenatal SB repair became a treatment option in selected cases since data of the Management of Myelomeningocele Study (MOMS) showed better outcomes of prenatal compared to postnatal SB repair [11]. To date, many centers offering this treatment follow the eligibility criteria set as standard by the MOMS. Therefore, patients with a body mass index (BMI) ≥ 35 kg/m^2 are basically precluded from prenatal surgery programs due to safety issues [11, 12]. In 2018, when analyzing current practice and eligibility criteria, Sacco et al. [12] reported that only one out of 44 centers allowed patients with BMI up to 45 kg/m^2 to undergo fSB repair. Complications generally known to occur more frequently in obese compared to normal-weight mothers are surgical and postoperative problems, such as maternal hematoma, seroma or surgical-site infection, as well as hypertension, gestational diabetes mellitus (GDM), preeclampsia, and thromboembolic events [13–17]. Furthermore, fetuses of obese mothers are not only at increased risk for SB but also for other congenital anomalies as well as preterm birth (PTB), instrumental delivery, cesarean delivery, and being (too) large for gestational age (GA) at delivery [8, 17, 18].

Despite these complications, Hilton et al. [19] recently questioned the maternal BMI cutoff for fSB repair and therefore extended the BMI inclusion criterion to <40 kg/m^2 at their center. When subsequently analyzing outcomes of 11 patients with BMI 35–40 kg/m^2, they did not observe any adverse maternal outcome. However, regarding fetal outcomes, mean GA at delivery was lower compared to the MOMS trial (32 vs. 34 weeks) and the perinatal death rate as well as the shunt rate at 1 year of life was higher (9 vs. 3 and 45 vs. 40%) (no statistics given) [19].

Based on carefully individualized eligibility evaluation, our center has increasingly offered fSB repair outside the classical MOMS criteria over the last several years, especially since obesity is a risk factor for SB. A very recent publication of our group is summarizing our initial experience with a number of criteria violations including, but not limited to, BMI [20]. The present study aimed at investigating in detail the cohort of women undergoing maternal-fetal surgery with a BMI >35 kg/m^2 and to compare maternal and fetal outcomes with those of patients operated with a BMI ≤35 kg/m^2.

Materials and Methods

At the Zurich Center for Fetal Diagnosis and Therapy, inclusion and exclusion criteria for fSB repair were, over time, considerably modified from the MOMS criteria and published previously [20–22]. Concerning this study, the most important difference was that a BMI ≥35 kg/m^2 is not an exclusion criterion at our center. Notably, no upper limit of BMI has been defined. Particular risks associated with obesity were looked at in detail. To minimize risks, treatment of preexisting disease was optimized, and special attention was given to peri- and postoperative monitoring and therapy. Data of all women operated for open fSB were prospectively collected in our registry using Research Electronic Data Capture (REDCap) [23]. Details regarding the surgical technique as well as peri- and postoperative management were published earlier [21, 24, 25].

For this retrospective single-center cohort study, we analyzed data of 194 patients having had open fSB repair between 2010 and 2022. Two women were excluded due to missing informed consent. The remaining 192 women were divided into three groups according to their BMI at the time of fetal surgery (BMI <30 kg/m^2 = group 1, BMI 30–35 kg/m^2 = group 2, BMI >35 kg/m^2 = group 3) to assess outcomes and potential differences. The following parameters were analyzed and compared between the groups: maternal age at surgery, parity, BMI before pregnancy and at the time of surgery, either parent with a family history of SB, prior uterine surgery or prior abortion (<16 gestational weeks [GW]), country of residence, fetal findings such as type (myelomeningocele, myeloschisis) and anatomic level of lesion, ventricle size, as well as placenta location. Regarding peri- and postoperative characteristics, we analyzed GA at surgery, cervical length, hysterotomy location, total surgery duration, duration of hysterotomy and duration of fetal surgery, length of hospital stay, type and duration of postoperative tocolysis, amniotic fluid index (AFI) 48 h (h) after surgery and before cesarean delivery, as well as the hysterotomy tissue quality at delivery. Further outcomes and complications were divided into intervention-related and non-intervention-related issues. In addition, complications were classified according to the Zurich classification system into severity grades 1 to 5 based on the required therapy or outcome of the complication (Table 1, 2), as described by Vonzun et al. [26].

Statistical analysis was performed using IBM SPSS Statistics (version 29, IBM, USA). The Shapiro-Wilk test was used to test for normal distribution. Demographic data as well as pregnancy outcomes within the groups were analyzed with descriptive statistics. Groups were compared using an ANOVA test, Kruskal-Wallis test,

Table 1. Classification system of maternal complications

Grade 1	Minor complications not requiring any pharmacological treatment or surgical intervention (with the exception of analgesic, antipyretic, and antiemetic drugs)
Grade 2	Complications requiring pharmacological treatment
Grade 3	Complications requiring surgical intervention
Grade 4	Life-threatening complications requiring intensive care/intensive care unit management
Grade 5	Death

Table 2. Classification system of fetal complications

Grade 1	Minor complications including late PTB (34+0 – 36+6 GW)
Grade 2	Moderate complications including moderate PTB (32+0 – 33+6 GW)
Grade 3	Severe complications including very PTB (28+0 – 31+6 GW)
Grade 4	Life-threatening complications including severe PTB (<28+0 GW)
Grade 5	Death

PTB, preterm birth; GW, gestational weeks.

Pearson's χ^2 test, or Fisher's exact test as appropriate. Quantitative data are presented as mean with standard deviation or median with interquartile range. Categorical variables are given as percentages. A p value <0.05 was considered statistically significant.

The study was carried out in compliance with the Declaration of Helsinki and in accordance with the approval of the local Ethics Commission, Zurich (KEK-ZH, Nr. 2021-01101). All women included in the study gave their written informed consent.

Results

Out of the total cohort of 192 women, 146 (76.0%) had a BMI <30 kg/m^2 (group 1), 28 (14.6%) a BMI 30–35 kg/m^2 (group 2), and 18 (9.4%) a BMI >35 kg/m^2 (group 3) at the time of fetal surgery. Six (30%) women in group 3 had a BMI >40 kg/m^2. Baseline characteristics of the different groups are shown in Table 3. The only other significant difference beside BMI was the country of residence. Group 1 consisted of significantly more Swiss residents than group 3 (p = 0.02).

When analyzing peri- and postoperative characteristics shown in Table 4, GA at surgery was around 25 GW in all groups. Total surgery duration was shorter in group 1 compared to group 2 or 3 (135 [120–155] min vs. 144 ± 20 min or 149 ± 25 min, p = 0.09), and postoperative length of hospital stay was longer in group 1 compared to group 2 or 3 (18 [15–30] days vs. 17 [14–29] days or 15 [12–30] days, p = 0.39); however, these differences were statistically not significant. Type of postoperative tocolysis did not significantly differ among the groups; however, duration of intravenous atosiban tocolysis differed significantly. It was longer in group 1 compared to group 2 or 3 (6 [4–10] days vs. 4 [3–7] days or 5 [4–8] days, p = 0.01). The AFI, measured 48 h postoperatively and before cesarean delivery, did not significantly differ among the groups. The highest rate of intact hysterotomy sites at delivery was seen in group 3 (32% in group 1 vs. 23% in group 2 or 58% in group 3, p = 0.09). Group 2 had the highest, however, nonsignificant rate of thinned hysterotomy sites (62% in group 1 vs. 65% in group 2 or 42% in group 3, p = 0.38) as well as partially dehiscent hysterotomy sites (5% in group 1 vs. 12% in group 2 or 0% in group 3, p = 0.46). Table 5 shows complications and outcomes. Regarding intervention-related complications, group 1 had the lowest rate of maternal wound seroma when compared to group 2 or 3 (32% vs. 50% or 56%, p = 0.04), whereas no significant difference was found regarding maternal hematoma or wound infection. Amniotic fluid leakage (AFL) occurred significantly less frequently in group 1 compared to group 2 or 3 (2% vs. 14% or 6%, p = 0.01). No significant differences were found regarding the chorionic membrane separation, premature rupture of membranes, or amniotic infection syndrome rate. Vaginal bleeding was least frequent in group 1 compared to group 2 or 3 (9% vs. 11% or 35%, p = 0.01). No significant difference existed regarding other intervention-related complications such as unclear abdominal pain, ileus, maternal pulmonary edema, pulmonary embolism, or unplanned prenatal readmission. No maternal death occurred in any of the groups.

Table 3. Baseline findings

	Group 1 (BMI <30)	Group 2 (BMI 30–35)	Group 3 (BMI >35)	*p* value
Patients, *N* (%)	146 (76.0)	28 (14.6)	18 (9.4)	
Maternal age at surgery, years	32.8 (28.7–35.8)	32.4 (±5.0)	31.4 (±3.9)	0.68
Primiparous at surgery, *N* (%)	70 (47.9)	14 (50.0)	8 (44.4)	0.94
BMI before pregnancy, kg/m^2	23.0 (±2.9)	29.4 (±3.0)	37.2 (±4.4)	<**0.001**
BMI at surgery, kg/m^2	24.8 (±2.7)	32.3 (31.1–33.9)	37.4 (36.2–41.5)	<**0.001**
History of spina bifida[1], *N* (%)	10 (6.8)	1 (3.6)	1 (5.6)	1.00
History of uterine surgery, *N* (%)	27 (18.5)	8 (28.6)	5 (27.8)	0.40
Prior abortion (<16 GW), *N* (%)	47 (32.2)	9 (32.1)	8 (44.4)	0.63
Country of residence, *N* (%)				**0.04**
Switzerland	34 (23.3)	4 (14.3)	0 (0.0)	**0.04**
Neighboring country[2]	93 (63.7)	23 (82.1)	15 (83.3)	0.05
Non-neighboring country	19 (13.0)	1 (3.6)	3 (16.7)	0.32
Findings in the fetus				
Type of lesion, *N* (%)				0.74
Myelomeningocele	93 (63.7)	19 (67.9)	14 (77.8)	0.46
Myeloschisis	46 (31.5)	8 (28.6)	3 (16.7)	0.45
Other	7 (4.8)	1 (3.6)	1 (5.6)	1.00
Anatomic level of lesion, *N* (%)	*N* = 145	*N* = 27	*N* = 17	0.10
T12 or higher	7 (4.9)	1 (3.7)	3 (17.6)	0.12
L1–L2	23 (15.8)	8 (29.6)	3 (17.6)	0.20
L3–L4	84 (57.6)	16 (59.2)	10 (58.8)	1.00
L5–S1	31 (21.2)	2 (7.4)	1 (5.9)	0.12
Ventricle size, mm, *N* (%)	*N* = 113	*N* = 18	*N* = 17	0.62
≤ 10 mm	38 (33.6)	9 (50.0)	6 (35.3)	0.41
> 10 mm	60 (53.1)	6 (33.3)	8 (47.1)	0.29
> 15 mm	15 (13.3)	3 (16.7)	3 (17.6)	0.78
Location of placenta, *N* (%)				0.31
Anterior	75 (51.4)	16 (57.1)	11 (61.1)	0.64
Posterior	66 (45.2)	11 (39.3)	5 (27.8)	0.35
Low lying	4 (2.7)	0 (0.0)	1 (5.6)	0.50
Placenta previa	1 (0.7)	0 (0.0)	1 (5.6)	0.20

N (%), mean±SD or median with IQR. SD, standard deviation; IQR, interquartile range; BMI, body mass index; GW, gestational weeks. [1]Either parent with a family history of neural tube defect. [2]Austria, France, Germany, Italy.

When analyzing non-intervention-related complications (Table 5) among the groups, the rate of GDM, cholestasis of pregnancy, and gestational hypertension was nonsignificantly higher in group 3. Rates in group 1 vs. group 2 or 3 were the following: GDM: 17% vs. 14% or 35%, $p = 0.14$; cholestasis of pregnancy: 4% vs. 7% or 12%, $p = 0.20$; gestational hypertension: 0% vs. 0% or 6%, $p = 0.09$. On the contrary, urinary tract infections were more frequent in group 1 compared to group 2 or 3 (10% vs. 4% or 0%, $p = 0.34$), without being significant. Preeclampsia was slightly less frequent in group 1 compared to group 2, though not significant, whereas no cases were reported in group 3 (3% vs. 4% or 0%, $p = 1.0$).

Regarding fetal outcomes, shown in Table 5, GA at delivery was almost identical among all groups (36.6 [34.7–37.0] weeks in group 1 vs. 36.5 [35.3–37.0] weeks in group 2 or 36.4 [33.9–37.0] weeks in group 3, $p = 0.92$). The same applies to gestational weight (2,690 [2,220–2,910] g in group 1 vs. 2,647 ± 322 g in group 2 or 2,838 [2,368–2,935] g in group 3, $p = 0.67$). There was one fetal death each in groups 1 and 3. The fetal death in group 1 occurred 6 h after cesarean delivery at 37.4 GW due to respiratory failure after persistent anhydramnios that occurred 3 days after fetal surgery at 23.4 GW. However, since the parents declined an autopsy, the reasons for anhydramnios remain unclear. AFL, as one possible cause, was seen neither on ultrasound nor on magnetic resonance imaging (MRI), repetitively performed after fetal surgery. The preoperative MRI however showed small kidneys with little bladder filling, and the postoperative MRIs showed no kidneys. Tenably, ceftriaxone-induced renal injury with consequent pulmonary hypoplasia may have caused respiratory failure. The fetal death in group 3 occurred at 25.9 GW,

Table 4. Peri- and postoperative findings

	Group 1 (BMI <30)	Group 2 (BMI 30–35)	Group 3 (BMI >35)	*p* value
Patients, *N* (%)	146 (76.0)	28 (14.6)	18 (9.4)	
GA at surgery, weeks	25.1 (24.5–25.6)	25.1 (±0.7)	25.1 (±0.5)	0.86
Cervical length before surgery, mm	40.6 (37.0–45.3)[1]	44.5 (±6.5)[7]	42.5 (±5.5)[10]	0.08
Uterine hysterotomy location, *N* (%)				0.33
Anterior	67 (45.9)	14 (50)	5 (27.8)	0.28
Posterior	74 (50.7)	12 (42.9)	12 (66.7)	0.28
Fundal	5 (3.4)	2 (7.1)	1 (5.6)	0.34
Total surgery duration, min	135 (120–155)	144 (±20)	149 (±25)	0.09
Total hysterotomy duration, min	88 (75–99)[2]	91 (±17)[8]	88 (87–111)[10]	0.32
Total fetal surgery duration, min	43 (34–52)[3]	44 (±13)[8]	48 (±20)[10]	0.83
LOS, days	18 (15–30)	17 (14–29)	15 (12–30)	0.39
Postoperative use of tocolytics, *N* (%)	145 (99.3)	28 (100.0)	18 (100)	1.00
Type of postoperative tocolysis, *N* (%)				
Atosiban	132 (90.4)	24 (85.7)	17 (94.4)	0.69
Gynipral	112 (76.7)	18 (64.3)	11 (61.1)	0.19
Nifedipine	138 (94.5)	28 (100.0)	16 (88.9)	0.16
Indomethacin	17 (11.6)	0 (0.0)	3 (16.7)	0.07
Duration of tocolysis, days				
Atosiban	6 (4–10)	4 (3–7)	5 (4–8)	**0.01**
Gynipral	13 (7–25)	11 (±9)	12 (±8)	0.22
Nifedipine	62 (45–75)	67 (61–74)	65 (±16)	0.44
Normal AFI, *N* (%)				
4 h postoperative	139 (95.2)[4]	27 (96.4)	18 (100.0)	1.00
Before caesarean delivery	99 (68.3)[5]	16 (57.1)	13 (81.3)[11]	0.27
Hysterotomy site at delivery, *N* (%)				0.35
Intact	41 (31.5)[6]	6 (23.1)[9]	7 (58.3)[12]	0.09
Thin	80 (61.5)[6]	17 (65.4)[9]	5 (41.7)[12]	0.38
Focal or area of dehiscence	7 (5.4)[6]	3 (11.5)[9]	0 (0.0)[12]	0.46
Complete dehiscence	2 (1.5)[6]	0 (0.0)[9]	0 (0.0)[12]	1.00

N (%), mean±SD or median with IQR. SD, standard deviation; IQR, interquartile range; GA, gestational age; LOS, length of hospital stay; AFI, amniotic fluid index. [1]*N* = 130, [2]*N* = 140, [3]*N* = 142; missing data of other patients. [4]*N* = 145, 1 patient already delivered. [5]*N* = 145, [6]*N* = 130, [7]*N* = 23, [8]*N* = 27, [9]*N* = 26, [10]*N* = 17, [11]*N* = 13, [12]*N* = 12; missing data of other patients.

4 days after fetal surgery complicated by an unusually high fetal blood loss of 5–6 mL (very large lesion [5 × 3 × 2 cm], difficult anatomical conditions 180 min-long operation). Fetal blood transfusion was considered but not performed since criteria were not met. Autopsy revealed a fetal liver rupture with significant hematoma probably caused by a massive hepatic stress hematopoiesis. Additional findings (complex gut malrotation, partial corpus callosum agenesis, and discrete signs of facial dysmorphism, as well as four-finger furrow) made an underlying genetic disorder also possible. Finally, when classifying complications into severity grades 1 to 5 according the Zurich classification system and comparing them among the groups, grade 1 intervention-related complications occurred significantly more often in group 3 (45% in group 1 vs. 57% in group 2 or 78% in group 3, $p = 0.02$ (Table 6).

Discussion

This study shows that a maternal BMI higher than the MOMS-prescribed BMI of <35 kg/m^2 does not negatively influence maternal and/or fetal outcomes in open fSB repair. Even though some outcome differences were noted, these had no relevance regarding clinical outcomes. Nevertheless, the following aspects deserve a more detailed consideration.

Interestingly, the obese groups comprised significantly more patients from abroad, especially Germany. This might be explained in two ways: first, some centers in Germany and France preclude patients with BMI >35 kg/m^2 from fetal surgery [27, 28]. This may cause more referrals to our center. Second, according to the European Obesity Report 2022 by the WHO [29], obesity rates in females are generally lower in

Table 5. Complications and outcomes

	Group 1 (BMI <30)	Group 2 (BMI 30–35)	Group 3 (BMI >35)	*p* value
Patients, *N* (%)	146 (76.0)	28 (14.6)	18 (9.4)	
Intervention-related complications				
Maternal wound seroma, *N* (%)	46 (31.7)[1]	14 (50.0)	10 (55.6)	**0.04**
Maternal hematoma, *N* (%)	7 (4.8)	1 (3.6)	0 (0.0)	1.00
Maternal wound infection, *N* (%)	2 (1.4)	0 (0.0)	1 (5.6)	0.31
Placental hematoma, *N* (%)	1 (0.7)	0 (0.0)	0 (0.0)	1.00
CMS, *N* (%)	19 (13.2)[2]	3 (10.7)	1 (5.6)	0.86
AFL, *N* (%)	3 (2.1)[1]	4 (14.3)	1 (5.9)[6]	**0.01**
PROM, *N* (%)	43 (30.1)[3]	8 (28.6)	5 (27.8)	1.00
AIS, *N* (%)	13 (9.2)[4]	2 (7.4)[5]	2 (11.8)[6]	0.82
Vaginal bleeding, *N* (%)	13 (9.0)[1]	3 (10.7)	6 (35.3)[6]	**0.01**
Placental abruption, *N* (%)	9 (6.2)[1]	1 (3.6)	2 (11.8)[6]	0.58
Uterine rupture, *N* (%)	1 (0.7)[1]	0 (0.0)	0 (0.0)[6]	1.00
Unclear abdominal pain, *N* (%)	15 (10.4)[2]	5 (17.9)	3 (16.7)	0.40
Ileus, *N* (%)	4 (2.7)	1 (3.6)	0 (0.0)	0.75
Maternal pulmonary edema, *N* (%)	2 (1.4)[1]	0 (0.0)	0 (0.0)[6]	1.00
Pulmonary embolism, *N* (%)	1 (0.7)[1]	2 (7.1)	0 (0.0)	0.08
Maternal death, *N* (%)	0 (0.0)	0 (0.0)	0 (0.0)	
Unplanned prenatal readmission, *N* (%)	50 (35.5)[4]	8 (28.6)	7 (41.2)[6]	0.70
Non-intervention-related complications				
Urinary tract infection, *N* (%)	15 (10.4)[2]	1 (3.6)	0 (0.0)[6]	0.34
GDM, *N* (%)	25 (17.4)[2]	4 (14.3)	6 (35.3)[6]	0.14
Cholestasis of pregnancy, *N* (%)	6 (4.2)[3]	2 (7.1)	2 (11.8)[6]	0.20
Gestational hypertension, *N* (%)	0 (0.0)[1]	0 (0.0)	1 (6.3)[7]	0.09
Preeclampsia, *N* (%)	4 (2.8)[2]	1 (3.6)	0 (0.0)	1.0
Fetal outcomes				
GA at delivery, weeks	36.6 (34.7–37.0)	36.5 (35.3–37.0)	36.4 (33.9–37.0)	0.92
GA weight at delivery, g	2,690 (2,220–2,910)[3]	2,647 (±322)[5]	2838 (2368–2935)[7]	0.67
Fetal or neonatal death after surgery, *N* (%)	1 (0.7)	0 (0.0)	1 (5.6)	0.20

N (%), mean±SD or median with IQR. SD, standard deviation; IQR; interquartile range; CMS, chorionic membrane separation; AFL, amniotic fluid leakage; PROM, premature rupture of membranes; AIS, amnion infection syndrome; GDM, gestational diabetes mellitus; GA, gestational age. [1]*N* = 145, [2]*N* = 144, [3]*N* = 143, [4]*N* = 141, [5]*N* = 27, [6]*N* = 17, [7]*N* = 16; missing data of other patients.

Switzerland compared to neighboring countries, where most referrals come from.

Obstetric complications known to occur more frequently in obese patients are GDM, hypertensive disorders, preeclampsia, and thromboembolic events, as well as wound complications [13–18]. As expected, our study results showed that all of these complications were indeed more frequent in either group 2 or 3 compared to group 1 however without reaching statistical significance. Only the frequency of maternal wound seroma occurred significantly more often in women with BMI >35 kg/m^2 (p = 0.04). Nevertheless, since no interventions were needed (grade 1), this complication did not influence clinical outcomes. Furthermore, our cohort only showed a tendency toward higher rates of maternal wound infections in group 3 (6%), without being significant.

Among all groups, mean GA at birth was around 36 GW and premature birth rates <32 GW were low (8.3% in group 1, 3.6% in group 2, and 11.2% in group 3) without significant differences. According to the Zurich classification system, no significant differences in GA were seen among the groups. These results contrast with the results of Hilton et al. [19], who reported an earlier mean GA of 32 GW when analyzing 11 patients with BMI >35 kg/m^2. Furthermore, our results stand in contrast with multiple other studies reporting an increased risk for both spontaneous and medically indicated PTB in obese women [30, 31]. Among other factors, the increased production of adipokines by adipose tissue causes increased systemic inflammation and promotes cervical ripening, weakening of membranes, and myometrial contractions [30]. When analyzing factors potentially preventing a higher PTB rate, one can state that all our patients, independent from BMI, received tocolytics from the day of fetal surgery until cesarean delivery. According to our postoperative protocol published previously, patients first received intravenous tocolysis with atosiban, a selective oxytocin receptor antagonist, followed by oral

Table 6. Complications according to the Zurich classification system described by Vonzun et al. [26]

	Group 1 (BMI <30)	Group 2 (BMI 30–35)	Group 3 (BMI >35)	*p* value
Patients, *N* (%)	146 (76.0)	28 (14.6)	18 (9.4)	
Intervention-related complications, *N* (%)				0.71
Grade 1	65 (44.5)	16 (57.1)	14 (77.8)	**0.02**
Grade 2	62 (42.5)	11 (39.3)	8 (44.4)	0.94
Grade 3	42 (28.8)	12 (42.9)	8 (44.4)	0.17
Grade 4	4 (2.7)	2 (7.1)	0 (0.0)	0.30
Non-intervention-related complications, *N* (%)				0.78
Grade 1	21 (14.4)	3 (10.7)	3 (16.7)	0.82
Grade 2	27 (18.5)	3 (10.7)	6 (33.3)	0.12
Grade 3	3 (2.1)	1 (3.6)	0 (0.0)	0.67
Grade 4	1 (0.7)	0 (0.0)	0 (0.0)	1.00
Fetal complications, *N* (%)				0.62
Grade 1	53 (36.3)	12 (42.9)	8 (44.4)	0.69
Grade 2	19 (13.0)	3 (10.7)	1 (5.6)	0.86
Grade 3	9 (6.2)	1 (3.6)	1 (5.6)	1.00
Grade 4	3 (2.1)	0 (0.0)	1 (5.6)	0.41
Grade 5	1 (0.7)	0 (0.0)	1 (5.6)	0.20

tocolysis with nifedipine, a calcium-channel blocker, usually 48 h after fetal surgery, in the absence of contractions [21]. Hexoprenaline, a beta-mimetic agent, served as emergency medication to abolish contractions. Our results showed a shorter duration of tocolysis with atosiban in women with BMI ≥30 kg/m^2 and consequently longer tocolysis with nifedipine. The interpretation of these results remains difficult since apart from one study showing no association between BMI and nifedipine serum levels, little data exist regarding the effect of tocolysis dosage according to BMI [32]. A possible reason for the shorter intravenous tocolysis and therewith faster change to oral tocolysis in groups 2 and 3 might have been the increased difficulty of contraction monitoring by tocodynamometry with rising BMI that however did not affect GA at delivery and therewith fetal outcomes [33].

Our results furthermore showed that the hysterotomy scar integrity was highest in group 3 (58% vs. 32% in group 1 or 23% in group 2). Therefore, BMI is not a risk factor for scar dehiscence. Group 2 had the lowest rate of intact scars. Along goes the observation that AFL was significantly more frequent in group 2 (14% vs. 2% in group 1 or 6% in group 3). Seaman et al. [34] previously described that AFL, decreasing AFI, and uterine contractions are clinical signs for hysterotomy dehiscence.

A complication that occurred significantly more often in patients with BMI >35 kg/m^2 was vaginal bleeding. Reasons known to increase the risk of vaginal bleeding in pregnancy occurring more frequently in group 3 compared to group 1, though not significant, were placenta previa (6% vs. 1%), low lying placenta (6% vs. 3%), prior uterine surgery (28% vs. 19%), and placental abruption (12% vs. 6%) [35]. However, the bleeding intensity was less than menstrual flow in all cases. In four out of the 6 cases, the slight bleeding was due to preterm contractions that could not be stopped and ended in cesarean delivery. In the other two cases, once, a light bleeding occurred due to a placenta previa but stopped in the following course, whereas it lead to delivery in the other case, where it occurred due to placental abruption. When analyzing complication severity with the Zurich classification system, grade 1 intervention-related complications occurred significantly more often in group 3 (78% vs. 45% in group 1 or 57% in group 2). However, since grade 1 complications do not require any interventions, this finding has no clinical relevance.

Strength and Weaknesses

The single-center study design resulting in a smaller sample size, especially for women with BMI >35 kg/m^2, as well as the retrospective study design could be regarded as limitations. However, this design also enabled good comparability since patients were all treated according to the same protocol. Furthermore, we did not statistically analyze the following factors that might have played an important role in obtaining favorable results: rigorous treatment of preexisting disease, very careful peri- and postoperative monitoring, early mobilization, as well as weight-adapted antithrombotic prophylaxis.

Nevertheless, our study results showed that obese patients and their fetuses did not suffer significantly more often from clinically relevant complications, which we also emphasized when classifying complications according to the Zurich classifications system into severity grades 1 to 5 [26]. In regard of high-grade complications requiring interventions, intensive care unit observation, or leading to maternal or fetal death, no significant differences could be observed between the three BMI groups. We can therefore state that although complications after fSB repair do occur, the safety of obese patients and their fetuses around fSB repair was warranted.

Conclusion

This study did not show any clinically relevant maternal and/or fetal outcome differences among women with BMI >35 kg/m^2. Nevertheless, additional studies are needed to confirm our results, in order to equally provide fetuses of these women with best possible medical care. Given the increased risk of fSB in obese mothers and the rising obesity rates in women of childbearing age, confirming the study results will distinctly influence the management of obese patients.

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Statement of Ethics

The study was carried out in compliance with the Declaration of Helsinki and in accordance with the approval of the local Ethics Commission, Zurich (KEK-ZH, Nr. 2021-01101). All women included in this study gave their written informed consent.

Conflict of Interest Statement

None of the authors has any conflict of interest to declare.

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Author Contributions

N.O.-K., J.Z., L.V., L.R., F.K., N.S., L.M., M.M., and U.M. designed the study outline. N.S. and J.Z. performed data collection and data quality control. J.Z. conducted the data analyses and wrote the manuscript. All the authors mentioned above participated in the drafting and/or revising of the manuscript and contributed to its intellectual content. All the mentioned authors approved the final version of the manuscript prior to publication.

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from J.Z. upon reasonable request. Further inquiries can be directed to the corresponding author.

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