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Risk factors for failed induction of labor among pregnant women with Class III obesity

Yohan Kerbage¹  | Marie V. Senat² | Elodie Drumez³ | Damien Subtil¹ |
Christophe Vayssiere^{4,5} | Philippe Deruelle¹

¹Department of Obstetrics, Jeanne de Flandre University Hospital (CHRU), Lille, France

²Gynecology-Obstetrics Service, Le Kremlin-Bicêtre Hospital, Public Hospital Assistance of Paris (APHP), Université Paris Sud, Orsay, France

³Department of Biostatistics, University of Lille, EA 2694 - Public Health: Epidemiology and Quality of Care, University Hospital of Lille (CHU), Lille, France

⁴Women's-Maternity-Couple Center, Gynecology-Obstetrics Department, Paule de Viguier Hospital, University Hospital of Toulouse, Toulouse, France

⁵UMR 1027 INSERM, Université Paul-Sabatier Toulouse III, Toulouse, France

Correspondence

Yohan Kerbage, Department of Obstetrics, Jeanne de Flandre Hospital, CHRU de Lille, Lille, France.

Email: yohan.kerbage@gmail.com

Abstract

Introduction: Our aim was to identify risk factors for failed induction in morbidly obese patients undergoing the induction of labor at term.

Material and methods: This was a retrospective multicenter study on a cohort of 235 patients with a body mass index greater than 40 kg/m² and giving birth to a singleton in cephalic presentation, who had an induction of labor from 38 weeks of amenorrhea. Scheduled cesareans and spontaneous vaginal deliveries were excluded. Maternal, peri-partum and neonatal characteristics were analyzed according to the delivery route.

Results: In all, 235 patients were included. Of these, 62.5% patients delivered vaginally and 37.5% by cesarean section. The frequency of nulliparity was greater in patients who had a cesarean section (56 [interquartile range, IQR, 38.1] vs 56 [IQR 63.6], $P < .001$). In multivariate analysis, nulliparity (odds ratio [OR] 2.81, 95% confidence interval [CI] 1.58-4.97), $P < .001$, low Bishop's score (OR .794, 95% CI .70-.90, $P < .001$) and weight gain (OR 1.04, 95% CI 1.01-1.08, $P = .033$) were independent risk factors for failed induction. Umbilical cord pH at birth lower than 7 (0 vs 7 [IQR 8.0], $P < .001$) and lower than 7.20 (36 [IQR 24.5] vs 35 [IQR 39.8], $P = .014$) as well as the Apgar at 1 minute (14 [IQR 9.5] vs 17 [IQR 19.3], $P = .032$) was significantly higher in infants born by cesarean section.

Conclusions: In this cohort, 63% of women with Class III obesity had successful inductions of labor; risk factors for failed induction include nulliparity and unfavorable Bishop score.

KEYWORDS

cesarean delivery, induction of labor, morbid obesity, obesity, pregnancy, vaginal delivery

1 | INTRODUCTION

Obesity and overweight are currently a public health problem in France. The World Health Organization has described obesity according to three increasing classes of severity as a function of body mass index (BMI), Class I (30-34.9 kg/m²), Class II (35-39.9 kg/m²)

and Class III (≥ 40 kg/m²). This description is correlated with the numbers and severity of complications observed in these populations. The specific and nonspecific complications of obesity are numerous. Cardiovascular complications are those responsible for the highest morbidity.¹ In obstetrics, obesity leads to the risk of complications (preeclampsia, gestational diabetes, pregnancy-induced

Abbreviations: BMI, body mass index; CI, confidence interval; IQR, interquartile range; OR, odds ratio.

hypertension and venous thromboembolic events).^{2,3} These complications are also correlated with the importance of obesity.^{4,5} This is why patients with increased obstetric risks more frequently have indications for induction of labor. This population also experience more frequent induction of labor due to the higher proportion of post term pregnancies.⁶ This population is also special because of the high frequency of labor failure and the need for higher doses of oxytocin.⁷⁻¹⁰ These problems are even more important in patients with morbid obesity. Currently, 1.5% of the French female population is Class III obese according to the OBEPI survey.¹¹ In an American sample, Wolf et al⁸ have shown in that 34% of these patients were induced and had an increased risk of induction failure. However, it is not clear whether these induction failures are exclusively attributable to patient obesity (and induced complications) or whether other factors such as initial cervical dilation or less expectative management in the obese patient. Attempted vaginal delivery is associated with a risk of emergency cesarean section in more difficult conditions, even though planned strategies have been implemented.¹² Transfer and installation for cesarean section are made more difficult when an emergency cesarean section is required. In addition, the time between incision and extraction is prolonged for obese women¹³ and the rate of surgical, infectious and hemorrhagic complications is higher.¹⁴ To our knowledge, there is no consensus on the management of morbidly obese patients.¹⁵ These observations led us to evaluate induction of labor specifically in the obese Class III population in order to identify factors that need to be taken into account when deciding the delivery route and the information that should be given to the patients on the expected outcome.

2 | MATERIAL AND METHODS

This is a retrospective multicenter study performed between 2009 and 2015 at three French centers that included all patients with a BMI ≥ 40 kg/m² at the beginning of the pregnancy, and who had an induction of labor from 38 weeks of amenorrhea. The three tertiary centers were the regional and university hospital of Lille, the university hospital Kremlin-Bicêtre and the university hospital of Toulouse. Exclusion criteria included the following: spontaneous labor pregnancies with <38 weeks of amenorrhea, history of multiple cesarean sections, scheduled cesarean section indications, misidentification and patients with unknown BMI. Multiple pregnancies, pregnancies with congenital malformations, chromosomal abnormalities and fetal deaths in utero were also excluded. The congenital malformations excluded were those detected in utero or at birth that required immediate neonatal intervention or prolongation of hospitalization, or those resulting in neonatal death. For patients with multiple pregnancies during the study period, only the first pregnancy was taken into account. The analysis ultimately involved 235 pregnancies. Weight and height at the beginning and at the end of pregnancy were collected. The BMI at the beginning of pregnancy was calculated using these data. Induction modalities were the cervical dilation balloon, prostaglandins Dinoprostone 1 and 2 mg, Dinoprostone 10 mg LP, Misoprostol 25 μ g), and oxytocin. Bishop's

Key message

Obese nulliparous women requiring induction of labor should be cautioned about the high risk of cesarean delivery.

score was used to evaluate the cervix. The choice of induction modality was left to the discretion of each practitioner, nevertheless, within the centers, the methods or the proportions used were not always the same. Patients with a favorable cervix were typically managed with oxytocin followed by amniotomy according to the protocols of each center. Induction modalities on an unfavorable cervix consisted of the administration of prostaglandin (Dinoprostone or Misoprostol) or the cervical dilation balloon. Misoprostol 25 μ g was used every 4 hours until regular contractions and cervical changes occurred. Successive induction modality means were used in some patients. Cesarean section indications were based on national and international recommendations. Obstetricians, residents and midwives carried out the labor. Comorbidities, conditions and complications of pregnancy, delivery and postpartum information were collected in a computerized medical file. From the medical history, we extracted age, parity, the existence of an essential hypertension, the presence of diabetes prior to pregnancy, smoking and history of uterus scarring. The following were used as indicators of complications of pregnancy: gestational weight gain, pregnancy-induced hypertension (PIH) (defined as the occurrence of hypertension beyond 20 weeks of amenorrhea), preeclampsia, the occurrence of preterm labor and the existence of gestational diabetes defined by the recommendations of the National College of French Obstetrician Gynecologists and the Francophone Society of Diabetes.¹⁶ With regard to delivery, data regarding gestational age, mode of delivery (spontaneous, instrumental or cesarean section), indication of labor induction, Bishop score, induction modalities and cesarean indication were collected. Postpartum complications identified were postpartum hemorrhage (≥ 500 mL within 24 hours postpartum), shoulder dystocia, infectious complications, thromboembolic complications, transfusion, wall abscess, postpartum fever or re-intervention. Collected data on neonatal outcomes concerned intrauterine growth retardation, macrosomia, birthweight, Apgar score at 1 and 5 minutes, umbilical cord pH, and intensive care unit transfer. These data were compared between patients who gave birth vaginally and those who had a cesarean section after the induction of labor.

Qualitative variables are expressed as frequency (percentage) and quantitative variables as mean \pm standard deviation (SD) or median (interquartile range [IQR]) in the case of a non-Gaussian distribution. Normality of distribution was checked graphically and using the Shapiro-Wilk test. Population characteristics were compared between the two delivery routes using the Chi-square test (or Fisher's exact test when expected cell frequency was <5) for qualitative variables, and Student's *t* test (or Mann-Whitney *U* test for a non-Gaussian distribution) for quantitative variables.

Variables associated with cesareans in bivariate analyses ($P < .20$) were included into a backward-stepwise multivariable logistic regression model using a removal criteria of .05. The same bivariate strategy analysis was used to compare population characteristics by delivery route in nulliparous women and to compare maternal and neonatal outcomes. Statistical testing was done at a two-tailed α level of .05. Data were analyzed using the SAS software package, release 9.4 (SAS Institute).

2.1 | Ethical approval

The study protocol was approved by the Ethics Committee for Research in Obstetrics and Gynecology (CEROG) of the French National College of Obstetrician Gynecologists (CNGOF) (CEROG OBS 2014-04-04, 3 July 2014). Informed consent was not necessary given the retrospective nature of the study. The data have been anonymized.

3 | RESULTS

During the study period, 644 patients with a BMI ≥ 40 kg/m² delivered a single fetus. Of these patients, 567 (88%) gave birth at a gestational term ≥ 38 weeks. Delivery occurred after spontaneous labor in 232 patients (41%), by cesarean section before labor in 100 patients (17.5%) and after induction of labor in 235 patients (41.5%) (Figure 1). These 235 were selected for analysis as part of our study. The mean BMI of our population was 44.0 kg/m² ± 4.0 . In all, 202 had a BMI between 40 and 50 kg/m² and 23 patients a BMI greater than or equal to 50 kg/m². The cesarean section rate was 37.5% ($n = 88$). Twenty-five percent of patients delivered after 41 weeks of amenorrhea. The more frequent induction of labor indications were post term pregnancies ($n = 49$), uncontrolled gestational diabetes ($n = 50$), premature rupture of membrane ($n = 34$) and diabetes ($n = 15$) (Table 1). Indications for cesarean section were non-reassuring fetal heart rate ($n = 50$), arrest in labor ($n = 16$), failed labor induction ($n = 14$) and cephalopelvic disproportion ($n = 8$). Twenty patients had a forceps-assisted delivery and 14 patients a vacuum-assisted delivery. Table 2 describes the characteristics of the population according to the route of delivery. There was no difference in age between patients with failed induction of labor and those who delivered vaginally (31.5 ± 5.4 vs 30.8 ± 6.1 , $P = .71$), but more nulliparous patients had failed induction of labor (56 [IQR 38.1] vs 56 [IQR 63.6], $P < .001$). Patients who had a cesarean section after induction had significantly less advanced cervical dilation (median Bishop score 4 [IQR 2-6] vs 2 [IQR, 1-4], $P < .001$). Gestational weight gain appeared to be a failure factor of vaginal delivery (5.8 ± 7.3 vs 8.3 ± 8.3 , $P = .022$). In contrast, BMI had no influence on the delivery route (43 [IQR 41-46] vs 43 [IQR 41-46], $P = .83$). History of cesarean section was not associated with a risk of induction failure (14 [IQR 9.5] vs 6 [IQR 6.8], $P = .47$). There was no significant difference in the mode

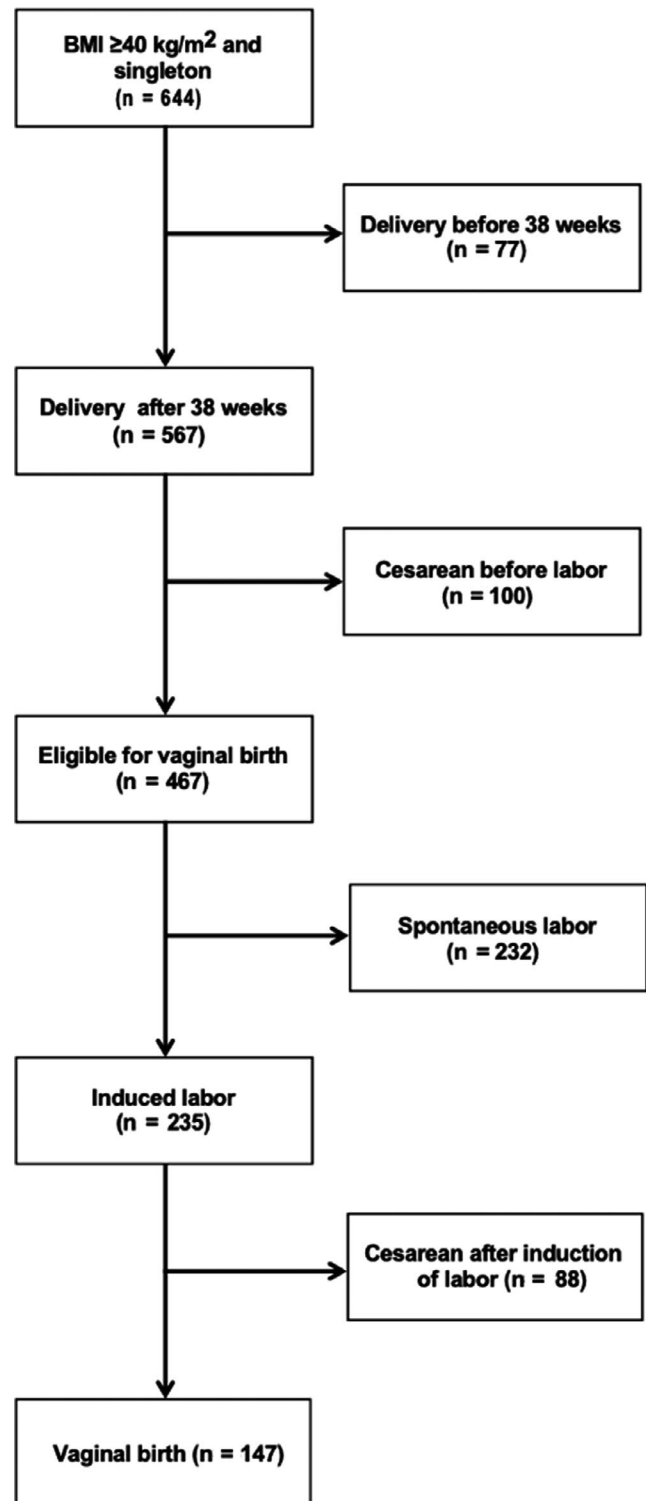


FIGURE 1 Flow chart

of induction used except for the use of oxytocin (50 [IQR 34.0] vs 19 [IQR 21.6], $P = .043$) in the univariate analysis. Success of induction of labor was also studied stratifying by week of gestation (Table 3). There was no evidence that a precise week of induction would improve its success for all the patients included but also specifically in nulliparous women. In the multivariate analysis, the independent risk factors for failed induction were nulliparity

TABLE 1 Indication for labor induction and cesarean

	n	%
Indication for induction of labor		
Abnormal fetal heart rate pattern	5	2
Decreased fetal movement	5	2
Type 1 or 2 diabetes	15	6
Uncontrolled gestational diabetes	50	21
Fetal growth restriction	7	3
Hypertension	10	4
Low amniotic fluid at term	13	5
Maternal request	6	2
Macrosomia	5	2
Preeclampsia	23	10
Premature rupture of membrane	34	14
Post term pregnancy	49	21
Obstetric cholestasis	5	2
Metrorrhagia	1	0.4
Others (isoimmunization, thrombopenia, metrorrhagia, maternal indication)	7	3
Indication for cesarean section		
Failed labor induction	14	16
Non-reassuring fetal heart rate	50	57
Arrest in labor	16	18
Cephalopelvic disproportion	8	9

(odds ratio [OR] 2.81, 95% confidence interval [CI] 1.58-4.97, $P < .001$), weight gain (OR 1.04, 95% CI 1.01-1.08, $P = .033$), and a low Bishop score (OR .79, 95% CI .70-.90, $P < .001$) at the time of induction (Table 4). Specific analysis of the nulliparous patients showed that in half of the patients, the induction of labor resulted in a cesarean section. The only risk factor for failed induction in this population was the initial Bishop score. With regard to neonatal morbidity, a level of umbilical cord pH at birth below 7 (0 vs 7 [IQR 8.0], $P < .001$) and below 7.20 (36 [IQR 24.5] vs 35 [IQR 39.8], $P = .014$) as well as Apgar score at 1 minute (14 [IQR 9.5] vs 17 [IQR 19.3]; $P = .032$) was significantly higher in neonates born by cesarean section (Table 5). There was no significant difference in maternal morbidity.

4 | DISCUSSION

Our study demonstrated in a multivariate analysis that weight gain, low Bishop score at induction and nulliparity were risk factors for failed induction of labor in Class III obese patients beyond 38 weeks of amenorrhea. This is the only study of a European population that has identified risk factors for failed induction of labor in a large multicenter cohort of Class III obese patients. The induction failure rate in our study was 37.5%. This rate is within the average of the various retrospective studies conducted in morbidly obese patients, with cesarean

TABLE 2 Characteristics of included patients, by mode of delivery

	Vaginal (n = 147)	Cesarean (n = 88)	P value
Characteristics			
Age, y	31.1 ± 5.4	30.8 ± 6.1	.71
Nulliparous	56 (38.1)	56 (63.6)	<.001
History of vaginal delivery	91 (61.9)	32 (36.4)	<.001
History of cesarean delivery	14 (9.5)	6 (6.8)	.47
Body mass index	43 (41-46)	43 (41-46)	.83
Medical comorbidities			
Hypertension	10 (6.8)	11 (12.5)	.14
Weight gain during pregnancy, kg	5.8 ± 7.3	8.2 ± 8.3	.022
Diabetes	7 (4.8)	8 (9.1)	.19
Current smoker	22 (15.0)	14 (15.9)	.85
Gestational hypertension	18 (12.2)	12 (13.6)	.76
Preeclampsia	12 (8.2)	11 (12.5)	.28
Fetal growth restriction	11 (7.5)	9 (10.2)	.47
Gestational diabetes	69 (46.9)	38 (43.2)	.58
Insulin therapy	54 (36.7)	25 (28.4)	.19
Bishop (median)	4 (2-6)	2 (1-4)	<.001
Induction of labor			
By oxytocin	50 (34.0)	19 (21.6)	.043
By vaginal prostaglandin	85 (57.8)	62 (70.4)	.053
By cervical ripening balloon	34 (23.1)	24 (27.3)	.48

Note: The data are presented in counts (percentage), mean ± standard deviation or median (IQR).

section rates ranging from 31.6% to 43%.^{8,17} Evidence of the influence of parity and low Bishop score as risk factors for failed induction was expected. These are induction failure factors classically found in the literature. However, the influence of weight gain is less well documented, specifically in an induced morbidly obese population. It is known that weight gain >12 kg is an overall risk factor for cesarean section regardless of BMI.¹⁸ In the obese patient, the Institute of Medicine (IOM) recommends a weight gain of between 5 and 9 kg.¹⁹ Nine kilograms was not identified as discriminatory in our study. The explanation for this difference could lie in the fact that these recommendations apply to obese patients regardless of class of obesity. This result shows the importance of prevention, especially dietary, when monitoring pregnancy to improve the perinatal outcome.

Univariate analysis demonstrated the superiority of an oxytocin induction. This is explained by the large proportion of multiparous patients in this group (60%). In the multivariate analysis, the absence of any induction method was identified as a success factor. Data from the literature, even if based on a low number of patients, corroborate this result.²⁰ There is some evidence that a cervical dilation

TABLE 3 Outcomes for induction of labor by week of induction (Chi-square test)

	Weeks of induction				P value ^a
	38 wk (n = 75)	39 wk (n = 60)	40 wk (n = 35)	41 wk (n = 65)	
Failed induction of labor n = 88	24 (32%)	28 (47%)	11 (31%)	25 (38%)	.29
Failed induction of labor in nulliparous n = 56	13 (54%)	19 (67%)	8 (72%)	16 (64%)	.28

^aP value based on a comparison between all groups.

balloon may be more effective than use of prostaglandin in the obese patient, but this requires prospective and specific verification in Class III obese patients.²¹

Two other induction failure factors were identified in the literature but were not significant in our population. First, the history of cesarean section appeared to be pejorative, most notably in the study by Borghesi et al.²² The small sample size (16 patients) with a history of cesarean section made it difficult to interpret the results in our study. In fact, it is likely that a large number of patients had a cesarean section before labor and that the small remaining number delivered spontaneously. This is in agreement with the latest French and international recommendations that retain the possibility of induction because of a low risk of uterine rupture, but with a high number of induction failures.²³⁻²⁵ The second factor that was not found to be significant in our study is BMI. Gunatilake et al¹⁷ identified this factor as a predictor of cesarean section. BMI is associated with an increased risk of failed induction of labor, which is the basis for this study. Our study appears underpowered to detect differences with progressing BMI among women with Class III obesity. Other teams have suggested that rather than BMI, other tools such as centrally distributed fat augmentation may be more relevant.²⁶ Therefore, some authors propose new tools that seem to have a better statistical association with the occurrence of a cesarean section, such as measurement of the waist circumference before 14 weeks of amenorrhea and the ultrasound measurement of the subcutaneous abdominal fat between 18 and 22 weeks of amenorrhea.^{26,27}

The rate of induction failure in our population is significantly higher than in patients with normal BMI. This is robust, regardless of other factors, which leads us to question the physiopathological

TABLE 4 Multivariate analyses of predictive factors of failed induction of labor

Factors	OR (95% CI)	P value
Nulliparity	2.81 (1.58-4.97)	<.001
Weight gain, kg ^a	1.04 (1.01-1.08)	.033
Bishop score	.79 (.70-.90)	<.001

Abbreviations: CI, confidence interval; OR, odds ratio.

^aWeight gain was identified as a risk factor of failed induction but no weight threshold was statistically identified.

^bLow Bishop score (<6) was identified as a predictive factor of failed induction of labor.

mechanisms involved in the failure of labor in the obese patient. One of the main theories explaining the increased rates of cesarean delivery in obese women is the difference in the contractile capacity of obese women compared with non-obese women. The myometrium of obese patients who did not have a spontaneous labor showed decreased contractile function compared with normal weight patients.²⁸ However, despite this decrease in myometrium contractility

TABLE 5 Maternal and neonatal outcomes by delivery route

Outcome	Vaginal delivery (n = 147)	Cesarean (n = 88)	P value
Maternal			
Instrumental delivery			
Vacuum	14	NA	NA
Forceps	20		
Postpartum hemorrhage (≥500 mL within 24 h postpartum)	15 (10.2)	10 (11.4)	.78
Transfusion	1 (0.7)	0	NA
Surgical reoperation	0	0	NA
Fever	2 (1.4)	1 (1.1)	NA
Thromboembolic event	0	2 (2.3)	NA
Surgical site infection	0	1 (1.1)	NA
Neonatal			
Birthweight, g	3540.9 ± 470.6	3589.9 ± 457.3	.44
Macrosomia	23 (15.7)	12 (13.6)	.56
Apgar score <7 at 1 min	14 (9.5)	17 (19.3)	.032
Apgar score <7 at 5 min	2 (1.4)	6 (6.8)	.055
pH <7	0	7 (8.0)	<.001
pH <7.2	36 (24.5)	35 (39.8)	.014
Shoulder dystocia	4 (2.7)	0	NA
Admission to NICU	8 (5.4)	11 (12.5)	.055

Note: The data are presented in counts (percentage), mean ± standard deviation or median (IQR).

Abbreviation: NA, non-applicable.

in obese patients, there does not appear to be a difference in the number of oxytocin receptors in the myometrium of obese patients compared with normal-weight patients.²⁹

Cholesterol and leptin are two substances whose levels are increased in obese patients. Their role in altering the contractility of the myometrium has been mentioned. Leptin, a hormone produced by adipose tissue and thus having an increased presence in obese women, has been shown to reduce the influx of calcium ions into the uterine smooth muscle.³⁰ It has also been shown that high levels of cholesterol, again found in the obese patient, inhibit calcium in the myometrium, leading to decreased contractility.³¹ The inhibition of calcium by leptin and cholesterol therefore plays an antagonistic role to oxytocin, the action of which is to induce myometrial contractions by releasing intracellular calcium.²⁹⁻³¹ The clinical manifestation of this antagonistic effect is an increase in the rate of cesarean sections, and also in the number of prolonged pregnancies, and the alteration in intensity and duration of labor in obese patients. This result is confirmed by a high rate of cesarean performed for arrest of labor (34%) in this group compared with the general population (16%). This rate refers to a study that evaluated the contribution of dystocia to the cesarean section rate in a tertiary center (labor induced or not).³²

The rationale for our study was to identify the risk factors for induction failure in view of the implications for maternal and neonatal morbidity observed in the literature. The data found in our sample are in line with the literature and show a pejorative outcome for women and their newborns in the case of cesarean section in the event of an induction failure. These data are corroborated by Subramaniam et al,¹⁴ who retrospectively compared patients who had a scheduled cesarean section and those who had a labor induction. In a population of 45% nulliparous women, 41% had a cesarean section. Nevertheless, the primary endpoint was a composite of maternal and neonatal morbidity, the outcome of which was insignificant, in part due to the morbidity induced by the high number of cesarean sections. Finally, we did not perform a cost study applied to the French health model. In the USA, Subramaniam et al³³ estimated that, in terms of cost, the induction policy compared with a systematic cesarean was more cost-effective when the vaginal delivery rate was greater than 57%. This applied in all cases except those with a history of cesarean section.

Recent data on the benefit of labor induction at 39 weeks³⁴ was not confirmed in our study. This could be explained by the particular profile of our population, as Grobman et al³⁴ included low-risk nulliparous women, but also by a lack of power.

Our study, however, has some limitations. It is primarily a retrospective study whose limits are well known. However, the inclusion of multiple centers in this study limits a number of these biases. The lack of recommendation and harmonization of practices on the care of the morbidly obese patient could have revealed heterogeneity between the centers. However, the analysis performed by center did not find any significant differences. The induction method may also be a limitation of our study, as it was left to the discretion of each practitioner in each center. However, as our study and the literature

show,³⁵ there does not seem to be any induction method that is more common than another in the obese patient. Finally, there may be a lack of statistical power to detect significant associations, particularly in subgroup analyses. Therefore, caution should be exercised when interpreting these results.

5 | CONCLUSION

In this cohort, 63% of women with Class III obesity have successful induction of labor; risk factors for failed induction include nulliparity and unfavorable Bishop's score. Our results also suggest that obese nulliparous women requiring induction of labor should be cautioned about the high risk of failed induction of labor. Nevertheless, it seems unreasonable to offer cesarean delivery systematically to all these patients in view of the induced morbidity, as well as on an economic level.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

ORCID

Yohan Kerbage  <https://orcid.org/0000-0002-5957-4768>

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