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Induction of Labor in Obese Women: Is there evidence of the best method? - A Systematic Review

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Dissertação de Candidatura ao grau de Mestre em Medicina submetida ao Instituto de Ciências Biomédicas de Abel Salazar, Universidade do Porto

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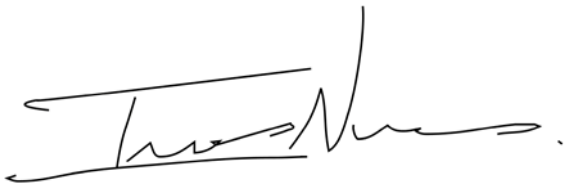
Assinatura do Estudante



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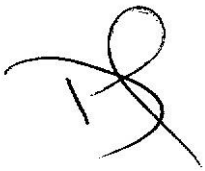

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Dedicatória

Aos meus pais, irmãos e restante família, por apoiarem sempre este sonho e todo o meu percurso académico até aqui.

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Resumo

Enquadramento: A crescente prevalência global da obesidade tem um impacto significativo nos desfechos obstétricos. A literatura indica que as mulheres obesas têm maior probabilidade de desenvolver complicações durante a gravidez. A obesidade está ainda associada a aumento da incidência de indução de trabalho de parto (ITP), a maior duração do trabalho de parto e a aumento da falha de ITP. Tal associa-se a maior prevalência de partos por cesariana. Atualmente, não se conhece qual o protocolo de ITP mais eficaz em mulheres obesas, que aumente a probabilidade de parto vaginal.

Objetivos: Resumir a literatura existente sobre ITP em mulheres obesas, e determinar qual o melhor método de indução do parto nesta população. Pretende-se contribuir com a elaboração de um protocolo ITP na mulher obesa, que vise melhorar as taxas de sucesso de ITP, reduzir os partos por cesariana, e melhorar os desfechos materno-fetais decorrentes.

Métodos: Abordagem sistemática com avaliação crítica por pares, conduzida de forma independente, para selecionar e analisar a literatura publicada na PubMed e Cochrane, usando palavras-chave relevantes e, finalmente, reunindo o consenso dos autores. A pesquisa incluiu estudos referentes à ITP em mulheres obesas, publicados em inglês ou português e com versão completa disponível. Relatos de casos, revisões não sistemáticas ou comentários, e artigos sem menção ao protocolo de ITP usado foram excluídos.

Resultados: Nove estudos de coorte, com um número total de 6956 mulheres, foram incluídos na revisão final: seis estudos retrospectivos, um prospectivo e duas subanálises de ensaios controlados randomizados. A obesidade está associada a aumento da duração do trabalho de parto, necessidade de utilização de doses mais elevadas de prostaglandinas e de uso de oxitocina em doses cumulativas. Associa-se a maior taxa de falência no atingimento da fase ativa do parto e a maior taxa de cesariana após ITP. A utilização por via vaginal do misoprostol parece ser mais eficaz do que a via oral e, de entre as prostaglandinas, o misoprostol revelou-se mais eficaz do que a dinoprostona. Comparando métodos de maturação cervical, os catéteres transcervicais são mais eficazes do que as prostaglandinas.

Conclusão: A obesidade associa-se a um aumento de risco de falha de indução do trabalho de parto. Métodos de maturação cervical mecânicos parecem ser superiores aos farmacológicos na maturação cervical e deverá haver ajuste da dose dos fármacos utilizados nos protocolos de indução de trabalho de parto nesta população. A evidência disponível não permite identificar qual o melhor protocolo de ITP na população de grávidas obesas.

Palavras-chave: *Obesity, Induction of labor, Pregnancy, Obese, Body mass index, Misoprostol, Cervical ripening, Oxytocin, Prostaglandins, Dinoprostone.*

Abstract

Background: The increasing prevalence of obesity worldwide has a huge impact on obstetric outcomes. Literature shows that obese women have higher odds of developing complications during pregnancy. They also have a higher risk of induction of labor (IOL), prolonged labor and failed IOL with secondary higher rates of cesarean section (CS). Currently, there is no evidence of the best IOL protocol, to use in this population, that increases the probability of vaginal delivery.

Objectives: Summarize the literature regarding IOL in obese women, and evaluate if there is evidence of the best IOL protocol for this population. The authors would like to define a labor induction protocol for obese women, aiming to improve the rates of successful IOL, reduce cesarean sections and ultimately to improve maternal and fetal outcomes.

Methods: A peer-reviewed systematic approach involving critical appraisal was conducted independently, collecting and examining published literature in PubMed and Cochrane databases using relevant keywords. Disagreement was solved by consensus of the 3 authors. Searches included studies about IOL in obese women, published in English or Portuguese languages available in full-text. Case reports, non-systematic reviews or comments, and articles not mentioning the IOL protocol were excluded.

Results: Nine cohort studies, including 6956 women in total were included in the final review: six retrospective, one prospective and two sub analysis of randomized controlled trials. Obese women were more likely to experience longer time to delivery, higher doses of prostaglandins and cumulative oxytocin, higher failure to achieve active labor and increasing c-section rates after IOL. Misoprostol delivered vaginally is apparently more efficient than orally. For cervical ripening, misoprostol was more effective than dinoprostone and transcervical catheters more effective than prostaglandins in general.

Conclusion: Obesity is associated with an increased risk of IOL failure. Cervical ripening with transcervical catheters is apparently more effective than using pharmacological methods. The dose of drugs used in IOL protocols should probably be adjusted in this population. The scientific evidence that is available does not allow the authors to define the best IOL protocol to implement in obese pregnant women.

Keywords: Obesity, Induction of labor, Pregnancy, Obese, Body mass index, Misoprostol, Cervical ripening, Oxytocin, Prostaglandins, Dinoprostone.

List of abbreviations

ACOG: American College of Obstetricians and Gynecologists
BMI: body mass index
CS: cesarean section/ c-section
GDM: gestational diabetes mellitus
GWG: gestational weight gain
IOL: induction of labor
IUPC: intrauterine pressure catheter
NRFS: nonreassuring fetal status
PO: per os
PV: per vaginal
RCT: randomized controlled trial
UC: uterine contraction
WHO: World Health Organization

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Introduction

Obesity, measured by body mass index (BMI), has emerged as one of the major public health challenges worldwide, becoming an epidemic in modern obstetrics, and being associated to a significant impact on obstetric and perinatal outcomes.[1-3] Women are getting pregnant at an older age and, subsequently, are presenting more regularly to clinicians with chronic medical conditions, that contributes to a higher risk of pregnancy complications.[4]

Although being a major risk factor for childbearing women, pre-pregnancy obesity is rarely documented in patient´s clinical records and, when available, BMI is documented at the first antenatal visit, what can slightly overestimate the mother's pre-pregnancy BMI.[5] In the European Perinatal Health Report the prevalence of maternal obesity varies from 8 to 26 %, and these women have higher rates of severe maternal morbidity and maternal death.[5]

Women with maternal obesity have increased odds of developing hypertensive disorders during pregnancy, gestational diabetes mellitus (GDM), preeclampsia, post term pregnancy, fetal macrosomia (birthweight>4500g), miscarriage and postpartum hemorrhage, when compared with women with a normal BMI.[6-8] These conditions are exacerbated by the high incidence of excessive gestational weight gain (GWG) and associated with an increased risk of induction of labor (IOL).[9]

According to the World Health Organization (WHO) obesity is subdivided into 3 classes: class I (BMI 30-34.9 kg/m²), class II (BMI 35-39.9 kg/m²) and class III (BMI≥40 kg/m²).[5] The need of induction of labor (IOL) increases, in a dose-dependent relation, by each unit of BMI class.[3,10-12] Obese pregnant women have higher prevalence of IOL failure, which causes higher rates of cesarean birth. Various studies also stated the proportional rate increase of cesarean section (CS) associated with increasing classes of BMI.[13-15]

In pregnancy complicated by obesity there is a prolongation of the time required to reach the active phase of cervical dilatation (6cm), known as latent phase.[16,17] This results in longer total duration and "abnormal" slower progress in labor, specially for obese women class III that require significantly longer time to achieve 6 cm than women with class I or II.[18] Beyond 6 cm of cervical dilatation there is no such difference - once obese women reach the active phase of labor, the vaginal birth ratio is equal to normal BMI women.[19,20] Redefinition of labor arrest using adjusted criteria in obese women is important to avoid over-diagnosis of labor dystocia before the active phase of labor and consequently unnecessary decision to perform CS due to arrest in the first stage.[16] The ACOG and the Society for Maternal-Fetal Medicine did not indicate an ideal length for the diagnosis of active phase protraction or labor arrest, but proposed that before achieving 6 cm of dilation neither diagnosis should be applied.[21] The higher odds of obstetric complications, the

longer labor and increased need of IOL are independent risk factors implicated in the increased rates of CS in this population.[8]

The high cesarean rates in obese pregnancies are also explained by the inhibitory influence of obesity on the uterine contractile efficacy.[20,22-24] Myometrial smooth muscle contraction is dependent on the rise of intracellular concentration of calcium.[25] Maternal obesity is associated with hypercholesterolemia and higher levels of leptin and apelin, all of them triggering the inhibition of calcium influx into uterine smooth muscle and reducing the uterine contractility. [23,26,27] The restriction of calcium signaling causes an antagonistic effect in response to oxytocin. **[23,26,28]** Additionally, fat deposition in maternal pelvis seems to cause obstruction to the birth canal, and along with fetal macrosomia, may contribute to labor dystocia.[20]

It is well-documented that laboring women with increased BMI are more likely to be admitted to the hospital with an earlier cervical dilatation and less favorable stage of labor[29] and, as a result, less likely to start spontaneous labor before 41 weeks of gestation.[18] They are nearly twice as likely as normal-weight women to have prolonged pregnancy (≥41 week's gestation), especially with BMI class II or III.[2,30] Therefore, the lower cervical dilatation at admission, the prolongation of the latent phase of labor, the elevated concentrations of cholesterol, leptin and apelin, the fat deposition in maternal pelvis and the fetal macrosomia represent various risk factors that contribute to induction failure in obese pregnant women. (Table I)

Induction of labor includes a process of cervical ripening with cervical softening and dilatation beginning, and an increase in the frequency of rhythmic synchronized uterine contractions, recreating the conditions of spontaneous onset of labor.[31] As obesity is associated with increased odds of failed IOL[32], this should be taken into account in the definition of the IOL protocol to be used. Efforts should be made to reduce the rates of induction failure and induction to delivery time.

However, in daily clinical practice, the route of administration and dose of the agents used for induction and augmentation of labor are not adjusted to maternal BMI. Observational studies have described elevated rates of CS after labor induction, especially if vaginal prostaglandins are used.[33,34] In fact, there is a lack of evidence regarding the most successful method(s) of IOL, timing and dosage and about the risk of CS following labor induction among obese women.[18,35]

The aim of this systematic review is to collect and analyze the actual evidence regarding induction of labor in obese women and to evaluate if there is evidence of the most effective method of IOL in this population.

Methods

An internal review protocol was developed to make the review process applicable for 2 independent researchers, using the PRISMA-P (Preferred reporting items for systematic review and meta-analysis protocols) recommendations.[36]

The target exposure consisted of pregnant obese women. The intervention under study was induction of labor. This includes several methods to start labor and achieve a vaginal delivery, including cervical ripening and the use of oxytocin. Original research studies, including observational studies and randomized controlled trials (RCTs), were considered for this review. Case reports, case series, review articles and commentaries were excluded.

First, an electronic database search was conducted in PubMed and Cochrane Library by using the following search terms: (obese OR obesity) AND [induction of labor OR (induction of labor AND (prostaglandins OR misoprostol OR dinoprostone OR cervical ripening OR oxytocin)) OR (induction of labor AND body mass index) OR (induction of labor AND pregnancy) OR (pregnancy AND (prostaglandins OR cervical ripening OR oxytocin))]. Second, the reference lists of relevant studies identified in the first step of the search strategy were screened for additional relevant publications. The search was performed due to April 2020.

All studies identified were screened for these inclusion criteria: 1) published in English or Portuguese; 2) with full-text available; 3) performed induction of labor with prostaglandins (misoprostol or dinoprostone), transcervical catheters, oxytocin, and combinations of these methods; 4) description of labor induction and delivery outcomes stratified by maternal BMI. No limit of publishing time was established. Studies using other methods for IOL, not described above, or studies without the method of IOL clearly described in the abstract, were excluded.

The initial search of the literature was made using the same criteria by 2 authors. The results of these 2 autonomously guided searches were combined (Figure 1). EndNote was used to remove duplicates. Titles and abstracts were pre-screened independently, using inclusion criteria, and then a second exclusion based on reading the full text was conducted; subsequently full-text articles of selected studies were accessed and saved. Any disagreement regarding study inclusion were resolved by all three authors through consensus.

Results

The initial searches involved a total of 447 articles (320 in PubMed, 127 in Cochrane). Seven additional studies were identified through reference lists. After removing the duplicates, a total of 197 articles remained. Screening of the titles and abstracts to determine those that met the aforementioned inclusion criteria ended up excluding 172 articles (seven of them with no full-text available[37-43]). The remaining 25 articles were accessed and analyzed for eligibility. A further exclusion of 16 articles was made for the following reasons: not centered on induction of labor, other scope (n=5); non-standard BMI classification (n=1); method of induction of labor and/or dosage not described (n=8); induced only nulliparous women (n=2). For the systematic synthesis remained 9 relevant studies.[8,44-51] An overview of the most important characteristics of the studies was made and can be consulted in Table II. The systematic review included 9 cohort studies with a total of 6956 women: six studies with a retrospective design,[44-47,49,50] one study with prospective data[51] and two studies were secondary analysis of RCTs.[8,48]

The main characteristics of the studies are described below. The results of the primary and secondary outcomes of the studies can be accessed in table III. Our review focused on the effect of maternal BMI, as well as the influence of different methods of IOL, when available, on the indications for induction, the failure to achieve active labor, the type of birth and indications to CS, the instrumental delivery rate, the time from induction to delivery, the time in active labor, the maternal and neonatal outcomes and the use of analgesia.

Body Mass Index determination time and categories

The timing of BMI determination varied among included studies (Table II), including prepregnancy,[46] prenatal enrolment in the first trimester[51] and at the time of hospital admission (the same as using time of delivery).[8,44-50] The study from Beckwith et al.[46] was the only research study that performed analysis of outcomes with the prepregnancy BMI and the delivery BMI, testing the hypothesis that a larger volume of pharmacologic distribution at the time of hospital admission may have a negative effect on the prostaglandin efficacy at equivalent dosing. Many studies used different BMI categories among themselves to compare the groups, but the majority used standard categories according to the WHO classification or the Institute of Medicine guidelines. In one study, the categorization of underweight and normal weight was wrongly described in the section of materials and methods, and in the analysis was applied the categorization as normal weight and overweight instead.[51] In three studies, investigators just included obese and non-obese women, with the limit of 30 kg/m² used to separate the two categories.[46,48,50] Soni et al.[44] and Suidan et al.[49] were the only investigators who just included obese women in their studies.

Induction of Labor Protocols

There was a large heterogeneity in the IOL protocols, including the definition of a successful or failed cervical ripening, the administration route, dosage, timing and combination of induction agent(s) used. The labor induction is described in detail in most of the studies (n = 8 of 9 studies); however, in the study by Suidan et al.,[49] the authors did not describe the protocol used in the section of methods. The description of onset of active labor was not defined in two studies,[44,45] and in the studies of O´Dwyer et al.[51] and of Lassiter et al.[47] the cervix was considered "favorable" without a formal assessment of the Bishop score or measurement of cervical length.

Indications for Induction of Labor

In the study of Pevzner et al. the indications for induction were statistically different among the BMI groups, mostly for hypertensive disorders of pregnancy, diabetes mellitus and suspected macrosomia, conditions that are frequently linked with obesity.[8] In the study by O´Dwyer et al., comparing among primigravidas, the obese group had significantly higher odds of IOL due to pre-eclampsia versus the normal BMI group (11.5% vs. 3.6%; p<0.0001). When comparing between multigravidas, the obese women had increased odds of induction for GDM versus the normal BMI women (3% vs. 0%; p=0.008).[51] Beckwith et al. found that indications for induction varied between the groups (p=0.001), having obese women higher rate of induction for pre-eclampsia and diabetes (30% vs. 23% for pre-eclampsia and 17% vs. 7.4% for diabetes), reduced rate for nonreassuring fetal status (NRFS) and postdates (4.6% vs. 12.3% for NRFS and 18.1% vs. 23.4% for postdates), compared to non-obese women.[46] In the studies of Roloff et al.[50] and Anabusi et al.[48] there was no significant difference in the indications among obese and non-obese women.

Use of prostaglandins or combination of prostaglandins

In the studies using prostaglandins for labor induction, when the dosage and method of administration were described, they differed in the case of misoprostol, from 25 to 100 mcg either vaginally,[8,46,47] or vaginally and orally.[44,49,50] The dosage of dinoprostone used was 10 mg as a sustained release vaginal insert.[8,49]

In a study assessing IOL with vaginal misoprostol, Lassiter et al. described higher mean doses of misoprostol required in women from BMI >40 and BMI 30-40 groups, compared to BMI<30 group (1.59, 2.05 and 2.32 doses for BMI group <30, BMI 30-40 and BMI>40, respectively; p<0.003).[47] In a study involving only obese women, comparing the vaginal route of misoprostol versus the oral route, Soni et al. observed significantly increased doses given in the group of oral misoprostol, compared to the vaginal group (7.4 vs. 2.9; p<0.0001).[44]

Transcervical catheters

From the included studies three described outcomes of IOL using transcervical ripening with Foley[46,48,50] or Cook catheters.[48] One study compared undergoing induction with medical (vaginal misoprostol) versus mechanical (Foley catheter) cervical ripening.[46] None of the selected studies analyzed the combination of prostaglandins with transcervical catheters.

The results of the studies are described in more depth below, according to the outcome analyzed, but in general, the process of mechanical cervical ripening was not affected by the maternal BMI. Except for the maternal satisfaction,[48] the other outcomes such as the failure to achieve active labor, the method of delivery and time to delivery were similar between obese and non-obese induced with transcervical catheters.

Oxytocin

Use of oxytocin for IOL was analyzed in five studies.[8,45,47,50,51] Pevzner et al. noticed greater oxytocin dose and duration of infusion in extremely obese and obese women, compared to normal BMI women (5.0 units and 8.5 hours for extremely obese vs. 3.5 units and 7.7 hours for obese vs. 2.6 units and 6.5 hours; $p<0.001$, $p=0.008$).[8] In the study by O´Dwyer et al., compared with normal BMI primigravidas, obese primigravidas had higher odds of induction requiring oxytocin agents (46.6% for obese vs. 28.5% for normal BMI; $p=0.007$) and comparing among multigravidas no difference was observed.[51] In 2015, Roloff et al. in a center with low rate of primary CS, evaluated the cumulative oxytocin dose needed to reach vaginal delivery according to the WHO class of BMI, performing IOL with oxytocin or misoprostol (oral or vaginal), or Foley catheter, or amniotomy, or a successive combination of these methods. Their results indicated that women who experienced IOL required increased oxytocin dose, with increasing class of BMI ($p<0.001$).[50] In 2016, Lassiter et al. described longer oxytocin duration in higher BMI groups, in comparison with non-obese women (7.17, 8.54 and 10.39 h of oxytocin, for BMI<30, BMI 30-40 and BMI>40, respectively; $p<0.023$).[47] In 2017, Maeder et al. study focused on oxytocin titration across BMI groups - obese women had increased total oxytocin dose compared to overweight women (7.50 units for obese and 5.92 units for overweight; $p=0.031$).[45] In all of these studies, investigators found a positive association between obesity and higher doses of oxytocin needed and also longer total duration of labor.

Failure to achieve active labor

Generally, the onset of active labor is the reference to establish a successful or failed labor induction. The failure to reach active labor was only directly evaluated in two studies,[8,46] and indirectly assessed by successful cervical ripening rate in another two studies.[48,49]

In the secondary analysis of Pevzner et al.,[8] significant fewer obese and extremely obese women reached active labor during the course of induction, compared with women of the BMI less than 30 group (BMI<30 - 96.4%; BMI 30-39.9 - 92.1%; BMI 40 or higher - 91.5%; p=0.004, p=0.009).

In 2015, Suidan et al. compared the efficacy of misoprostol (oral 50 or 100 mcg, or vaginal 25 mcg) and dinoprostone (vaginal 10 mcg) on IOL in obese patients, and found that misoprostol was associated with an increased successful cervical ripening rate compared with dinoprostone, even when comparing misoprostol PO and misoprostol PV separately to dinoprostone (77.7% for misoprostol PO vs. 66.7% for dinoprostone and 79.7% for misoprostol PV vs. 66.7% for dinoprostone; p=0.006, p=0.04).[49] When comparing misoprostol PO to misoprostol PV no differences were found in the efficacy rates (77.7% for misoprostol PO vs. 79.7% for misoprostol PV; p=0.73).[49]

In a study evaluating transcervical catheters when inducing labor in obese and non-obese women, Anabusi et al. showed no differences in the successful cervical ripening rate among the groups (94.9% for obese, 98% for non-obese; p=0.41).[48] Similarly, when comparing medical and mechanical ripening, a later study of Beckwith et al. did not observe significant differences in failure to achieve active labor, between obese and non-obese women induced with Foley catheter (19% for obese vs. 15% for non-obese; p=0.55).[46] When ripening the cervix with vaginal misoprostol (25 mcg), obese women were associated with increased failure to achieve active labor, compared to non-obese women (24% for obese vs. 15% for non-obese; p=0.01).[46]

Type of birth and indications to cesarean section

In the study by Pevzner et al., women of BMI 30-39.9 group and the BMI 40 or higher group were significantly more likely to require a CS, compared to women of BMI less than 30 group.[8] Similarly, Lassiter et al. found increased CS rate for BMI >40 group and BMI 30-40, compared to BMI<30 group, evaluating IOL with vaginal misoprostol (17.48%, 37.09% and 40% for BMI<30, BMI 30-40 and BMI>40, respectively; p<0.0006).[47] Also, Maeder et al. found increased CS rate with increasing BMI group and described significant predictors for performing a CS, including: overweight and obese BMI groups; absence of anxiety/depression diagnosis; nulliparity; fewer units per hour of oxytocin infusion; greater newborn birth weight; intrauterine pressure catheter (IUPC) monitoring and use of cervical ripening.[45] Roloff et al. was the only study showing no differences in the type of delivery between obese and non-obese women experiencing IOL.[50]

When comparing the efficacy of misoprostol and dinoprostone on IOL in obese patients, Suidan et al. found that misoprostol was associated with a lower CS rate compared with dinoprostone, even when comparing misoprostol PO and misoprostol PV individually to dinoprostone (39.5% for misoprostol PO, 37.5% for misoprostol PV and 51.3% for dinoprostone; p=0.008; p=0.04).[49] When

comparing misoprostol PO to misoprostol PV, they did not find differences in the rates.[49] Contrary to these findings, a recent study of Soni et al. showed that obese women had higher rates of vaginal birth within 12h (29% for vaginal vs. 9.9% for oral; p<0.0001) and 24h (59.2% for vaginal vs. 42.3% for oral; p<0.0001) of misoprostol administration, and lower CS rate following induction of labor in the vaginal misoprostol group, compared to the oral misoprostol group (24.5% for vaginal vs. 31.2% for oral¸ p=0.03).[44]

The study of Anabusi et al. that compared obese to non-obese women, experiencing mechanical ripening, observed no differences in the method of delivery.[48] In the study of Beckwith et al. when evaluating medical versus mechanical cervical ripening as part of IOL, obese women induced with vaginal misoprostol were linked to higher CS rate, as compared to women of BMI ≤30 kg/m², and this association was not seen in women induced with Foley catheter.[46]

In the studies that assessed the obstetric outcomes by parity, O´Dwyer et al. showed a significant higher emergency CS rate for obese primigravidas, compared to normal BMI primigravidas, in a population of women receiving vaginal prostaglandins (34.6% for obese vs 19.5% for normal BMI primigravidas; p=0.006).[51] Lassiter et al. described vaginal delivery more likely to happen in multigravida (76%), compared to primigravida women (61.6%), also in a population experiencing the vaginal route but specifically with misoprostol.[47]

The heterogeneity among the indications to undergo a CS[8,49,50] was considerable. Pevzner et al. found that in the higher BMI groups the rate of CS, because of failed IOL and failure to progress, was slightly increased, but only elective IOL established an independent relation with CS rates. In the study that women underwent IOL with different options of combinations of methods, Roloff et al. stated that indications to perform a CS were not affected by obesity. In the study of Suidan et al. in both misoprostol and dinoprostone groups, the most common indication for CS was failed cervical ripening.

Instrumental delivery

O´Dwyer found similarity in the rates of instrumental deliveries through all BMI groups in both primi and multigravidas (primigravidas: 14.9% for obese vs. 12.2% for normal BMI, p-value non-significant (NS); multigravidas: 4.1% for obese vs. 3.1% for normal BMI, p-value NS).[51] Roloff et al. also did not find differences in the operative vaginal delivery rates between obese and non-obese that were induced (4.9% vs. 2%; p=0.530).[50]

Time to delivery and time in active labor

Pevzner et al. showed that time to delivery was significantly longer in obese and extremely obese women, compared to women of BMI less than 30 group (4 hours slower in extremely obese

and 2 hours slower in obese women; p<0.001).[8] Accordingly, two posterior and retrospective studies found significantly longer time to delivery associated with increasing BMI class (17.72 h for BMI<30, 20.01 h for BMI 30-40 and 22.9 h for BMI>40 group, in the Lassiter study; 13.96 h for BMI<24.99, 16h for BMI between 25-29.99 and 18.30 h for BMI≥30, in the Maeder study).[45,47] Suidan et al.[49] did not find differences for this outcome between the misoprostol and dinoprostone groups and neither found Roloff et al.,[50] between obese and non-obese women after an IOL with individual or multiple sequential methods for IOL. In a subsequent study, Anabusi et al. found similarity in the median time from catheter insertion to delivery, when evaluating mechanical labor induction between obese and non-obese participants (16.57 h for obese and 16 h for non-obese; p=0.092).[48] Soni et al. found shorter time from IOL to delivery in the vaginal misoprostol group, compared to the oral misoprostol group (17.4 h for vaginal vs. 24.8 h for oral, p< .0001).[44]

The time in active labor was observed to be longer in obese (16 h) and extremely obese women (19.3 h) than women of BMI<30 (14.9 h; p=0.001) in the study by Pevzner et al.[8] In disagreement with these findings, the research of Roloff et al observed no significant differences in this labor outcome comparing obese and non-obese women undergoing IOL.[50]

Maternal and Neonatal outcomes

Suidan et al described a slightly increased fetal birth weight in the group of obese women using misoprostol, compared to dinoprostone group (3,325 vs 3,230 g, p=0.02).[49] Furthermore, Roloff et al showed that obese women who experienced IOL (with mixed protocols of cervical ripening methods) had neonates with a higher birth weight, compared to non-obese women (3,371 vs. 3,141 g, p=0.008).[50] Recently, from a research focused on comparing the outcomes of IOL with vaginal against oral misoprostol, maternal complications were similar in both groups.[44] However, significant differences in the neonatal outcomes of the oral misoprostol group included lower pH of the umbilical artery and increased neonatal jaundice rates (mean pH: 7.24 for vaginal misoprostol vs. 7.22 for oral misoprostol, p=0.004; neonatal jaundice: 0% for vaginal vs. 2% for oral, p=0.006).

Relating to mechanical cervical ripening, Anabusi et al observed a significant reduced maternal satisfaction with this method in obese women, even though they did not report more pain during catheter insertion nor did the obstetrician described more difficulties during the procedure (mean maternal satisfaction and pain perception (both range 1-10): 7.58 for non-obese vs. 5.95 for obese, p<0.01 and 3.57 for non-obese vs. 3.26 for obese, p=0.54; no technical difficulty for the obstetrician: 80.9% vs. 76.8%, p=0.55).[48]

The study of Maeder et al. documented a significant greater GWG for obese women (16.81 kg) compared to overweight (14.47 kg) and normal BMI women (12.13 kg; p=0.001).[45]

Use of Analgesia

In the studies that analyzed the use of analgesia there was a trend towards a greater use of analgesia in obese women. O´Dwyer et al. described significant difference in the use of epidural analgesia between BMI groups in primigravidas (48.6% for obese, 28.7% for overweight and 28.4% for normal BMI; p=0.002) and no difference in multigravidas.[51] In the study of Anabusi et al.[48] the analgesia, including epidural or pethidine or both, had higher use in the obese group but no statistical difference was found (90.8% of use for obese vs. 86.9% for non-obese; p=0.48).

Discussion

This systematic review revealed that the literature on induction of labor in obese pregnant women is limited to a small number of studies (n=9), 7 observational (a prospective cohort (n1), and six retrospective cohorts (n6)) and 2 sub analysis of RCTs. There are multiple choices for inducing labor in obese parturient women, but the best method, route, dosing, and timing continues to be actively debated. From the outcomes of IOL analyzed in this review, we can say that increased maternal BMI is linked to higher doses and increased longer need for induction agents. Longer time to delivery as maternal BMI increases was observed,[8,47] and longer time in active labor was also seen in obese and extremely obese women, compared to normal weight women.[8]

Although most of the studies used the time of measurement of BMI at the moment of hospital admission, Beckwith et al.[46] used prepregnancy BMI and delivery BMI, what allows the analysis of which BMI should be considered to best conclude about labor outcomes. They were able to demonstrate a significant association between BMI and unsuccessful IOL, in obese women at the time of hospital admission, compared to normal BMI women. These findings can probably be explained by the higher volume of body distribution at the time of delivery compared to prepregnancy BMI. The increased volume of distribution in obese women, compared to normal weight women, has a dilutional effect on both the cervical ripening agent and oxytocin, administered during labor induction.[8] This can explain the decreased response to agents and consequent need for higher doses and longer duration of IOL agent(s), contributing to the increased labor duration.[8,29] In the case of vaginal route, the technical difficulty to administer prostaglandin vaginally, in part, can help explaining the lower prostaglandin sensitivity associated with obesity.

Obese pregnant women have prolongation of the latent phase and slower labor progress.[17] It is known that cervical dilatation of 6 cm should be the threshold for the active phase of labor.[21] Only in two studies the start of active phase of labor was considered to be after 6 cm of cervical dilatation.[46,50]

In this review we find evidence that obese and extremely obese women are more likely to experience poor labor outcomes such as failure to achieve active labor and, consequently, higher rates of cesarean birth due to IOL failure. In a study using oxytocin as the induction agent, increased BMI, nulliparity, need for cervical ripening, lower infusion rate of oxytocin, IUPC monitoring and increased birth weight were found to be important predictors of CS.[45] O´Dwyer et al. also highlighted the importance of parity when considering IOL in obese women. For obese primigravida the odds of a CS in labor was higher – in this special population IOL is even more challenging.[51]

Comparing the efficacy of misoprostol and dinoprostone in obese women undergoing IOL, Suidan et al. found that misoprostol had an increased successful cervical ripening rate and a lower

CS rate, compared with dinoprostone. Even when comparing distinctly misoprostol PO and misoprostol PV to dinoprostone.[49]

The study of Anabusi et al., which only included 181 patients, showed that maternal obesity did not influence the success of mechanical cervical ripening or the time from induction to delivery.[48] The only significant outcome observed was reduced maternal satisfaction related to the insertion of transcervical catheter as part of the IOL process. The findings of Beckwith et al.[46] established that maternal obesity influences negatively vaginal misoprostol efficacy – with this method of cervical ripening, obese women are more likely to fail achieving active labor and to have a CS compared to non-obese women. With Foley catheter, no positive relation was observed between obesity and failure to achieve active labor.[46] Further, vaginal route of misoprostol seems to be more effective than the oral route, because it showed shorter time from induction to delivery, higher rates of vaginal birth within 12h and 24h, and lower CS rate.[44] In the other hand, the oral misoprostol group was associated to increased doses required and worse neonatal outcomes.[44] Thereby, vaginal misoprostol is more effective for medical cervical ripening than dinoprostone. Nevertheless, transcervical catheters are more effective than prostaglandins, and seem to be the best option in the obese population, in order to obtain a successful IOL and thus to achieve a vaginal delivery.

A limitation of this systematic review is that it relies mostly in cohort and retrospective studies. Cohort studies are known to have low internal validity, they are sensitive to bias and systematic errors, and consequently, are positioned in the middle of the levels of evidence. The limitations of retrospective studies include memory bias and inability to assess level of drugs in maternal blood. Besides, they use retrospective definition of active phase of labor, the doses effectively administered due to failure can be missing in the patient files and other drugs that can interact with the course of labor may be administered and not described, such as magnesium sulfate. The heterogeneity in the findings of our review makes it hard to generate and summarize the ideal method for IOL in obese women. This heterogeneity is reflected by the following aspects: 1) studies using different threshold values to define onset of labor; 2) studies including women with significant difference in parity and/or ethnicity; 3) studies including higher risk cohort populations, with medical indications to have the labor induced; 4) great variety of doses, timing and route of administration of the IOL methods used and 5) non-uniformized BMI categorization of classes.

Additional available background characteristics of the populations in the studies, such as prepregnancy BMI and GWG (commonly excessive in obese women), would be of value in testing the hypothesis of whether a greater weight gain during pregnancy could have an effect on BMI at admission, and so it would influence an increase on admission BMI class and thus impact on the IOL outcomes, or not. The studies that evaluate oxytocin use neither control for cervical ripening

methods nor establish a comparison between low and high dose protocols - this is a very important limitation. For obese women, the difficulty in adequately evaluate uterine contractions (UC) with the most commonly used method (tocodynamometer) is a limitative factor that should be taken into account when evaluating titration of oxytocin infusion. Alternative methods of evaluating UC such as IUPC or trans-abdominal electromyography would be of value to objectively evaluate uterine activity in response to different induction agents in future studies.

A major strength of this study is that all of the available evidence was collected in a systematic way. In addition, studies were strictly matched to inclusion and exclusion criteria and a differentiation between induction of labor and cervical ripening was made when selecting the studies, analyzing rigorously the available outcomes. This is a strength compared to the first and only, to our knowledge, published systematic review on this topic.[52]

Considering the significant association between obesity and the increased risks of IOL and CS, it is essential to give obese women the best chance to achieve a vaginal delivery. The risk of long-term maternal morbidity increases with increasing number of c-sections.[53] Along with increased complications related to cesarean deliveries in obese women, namely, increased surgical-site infection rates,[54] women who undergo a CS in their first pregnancy have an increased probability to have a cesarean section in the future. Therefore, clinicians should carefully balance the risks and benefits of IOL in obese women.

Conclusion

Obesity is associated with an increased risk of IOL failure and cesarean sections. Cervical ripening with transcervical catheters is apparently more effective than using pharmacological methods. The use of vaginal misoprostol is more effective than oral misoprostol or sustained release inserts of dinoprostone, and also related to lower neonatal risks when compared to oral misoprostol. The dose of drugs used in IOL should probably be adjusted in this population, but there is no evidence of the best protocol to be used either with cervical ripening agents or with oxytocin. Therefore, the available scientific evidence does not allow the authors to define the most effective IOL protocol to implement in obese pregnant women. Further research is needed in order to establish the most effective and safest IOL protocol and thus increase the chance of vaginal delivery in this obstetrical high-risk population.

Agenda for future research:

- Crucial need to have standardized protocols of labor induction, adjusted to maternal BMI class (class I, class II and class III)
- To study the impact of GWG in labor, maternal and neonatal outcomes
- To establish the optimal therapeutic dose of drugs used in IOL, establish the best cervical ripening agent or combination of methods to use in obese population, considering both efficacy and maternal and perinatal safety
- Control for cervical maturation methods in studies that evaluate the use of oxytocin
- In the use of oxytocin compare low to high dose protocols
- There is an urgent need to produce good quality evidence in this subject, ideally in well-designed prospective cohort studies and randomized controlled trials

Appendix

Table I - The risk and protective factors for failure of induction of labor, in obese women [18,23,26,27,32,55]

IOL failure	
Risk factors	**Protective factors**
Lower cervical dilatation at admission	Multiparity
Prolongation of the latent phase	Bishop´s score at admission ≥ 5
Higher levels of cholesterol, leptin and apelin	
Fat deposition in maternal pelvis	
Fetal macrosomia	
Nulliparity	
Without a prior successful vaginal delivery	

IOL - induction of labor.

Table II - Overview of the included studies

Study, Year	Sample size	Study design	Inclusion criteria	Time of BMI	BMI distribution (kg/m²)	Induction Method, Dosage and Timing	Induction of labor protocol	Definition of onset of active labor	Primary Outcomes	Secondary Outcomes
Pevzner et al. 2009	1273	Secondary analysis of a randomized controlled trial	≥18 y of age, singleton pregnancy, ≥36-week gestation, low parity (≤3 earlier births)	Hospital admission	<30 30-39.9 ≥40	Sustained-release vaginal inserts: Vaginal misoprostol 100 mcg Vaginal misoprostol 50 mcg Vaginal dinoprostone 10 mg (+ predelivery oxytocin)	Ripening protocol continued for 24 h or until onset of active labor (earlier removal if drug insert falling out of the vagina or maternal-fetal complications)	4 cm dilatation or ≥3 firm, rhythmic contractions lasting ≥ 45 sec within 10 min period with progressive cervical dilatation	Number of women who reached active labor during the course of induction	Total oxytocin for induction Delivery within 24 h Cesarean delivery rate
O´Dwyer et al. 2013	1927	Prospective cohort	>18 y of age, White European, singleton pregnancy in the first trimester, no gestational diabetes mellitus, able to give informed consent	After enrollment (in the first trimester)	<18.5 25-29.9 >29.9 (different in methods and table)	Vaginal prostaglandin, amniotomy and oxytocin	Ripening continued until favorable cervix Induction of labor with amniotomy and then oxytocin if normal fetal heart rate	Favorable cervix	Induction rate PGE2 induction rate	Total oxytocin for induction Emergency CS rate
Roloff et al. 2015	413	Retrospective cohort	Viable singleton pregnancy at term (37–42 weeks gestation) with cephalic presentation	Hospital admission	<30 ≥30	Oxytocin/ Vaginal or oral misoprostol 25-50 mcg/ Foley catheter/ amniotomy/ sequential combination of these methods	Cervical ripening agent administered every 4–6 h as needed at the discretion of physician Oxytocin following cervical ripening: minimum of 4h since misoprostol admin; if transcervical ripening, oxytocin started after catheter expulsion	6 cm	Cumulative oxytocin dose needed for vaginal birth	Neonatal outcomes
Suidan et al, 2015	564	Retrospective cohort	Cephalic singleton gestation at ≥24 weeks of gestation, Bishop score of ≤6, BMI of ≥ 30 kg/m²	Hospital admission	≥30	Vaginal misoprostol 25 mcg Oral misoprostol 50 or 100 mcg (every 4h) Vaginal dinoprostone 10 mg (every 12) (+ oxytocin when needed)	Not mentioned	>4 cm	Successful cervical ripening rate Cesarean delivery rate	Time to delivery Vaginal births within 12h and 24h Maternal complications rates Neonatal outcomes
Anabusi et al. 2016	181	Secondary analysis of 2 randomized controlled trials	Singleton, cephalic with vertex presentation, intact membranes, term (≥37-week gestation), with an unfavorable cervix (Bishop score ≤4), planning induction	Hospital admission	≤30 >30	Cook or Foley catheter (+ oxytocin and/or amniotomy) Vaginal prostaglandins (if first attempt was unsuccessful)	Catheter remained for up to 12 h (if not spontaneously expelled balloons were deflated and device removed) Ripening continued to Bishop score increase of ≥ 2 points or ≥3 cm cervical dilation	≥4 cm in the presence of regular uterine contractions	Time from device insertion to delivery	Successful cervical ripening Vaginal delivery rate Cesarean delivery rate Maternal and Neonatal outcomes

Study, Year	Sample size	Study design	Inclusion criteria	Time of BMI	BMI distribution (kg/m²)	Induction Method, Dosage and Timing	Induction of labor protocol	Definition of onset of active labor	Primary Outcomes	Secondary Outcomes
Lassiter et al. 2016	329	Retrospective cohort	All women undergoing induction of labor at the research site, gestational age ≥37-week, Bishop score <5	Hospital admission	<30 30-40 >40	Vaginal misoprostol 25 mcg every 4h Oxytocin 1 milliunit/min, increased by 1–2 milliunits/min every 30 min or amniotomy	Ripening continued until favorable cervix/ a total of 6 doses; then oxytocin was started 4h after the last misoprostol dose Amniotomy was performed at the discretion of the Obstetrician	Favorable cervix	Time from induction to delivery	Doses of misoprostol Duration of oxytocin Cesarean delivery rate
Beckwith et al. 2017	709	Retrospective cohort	Singleton, live birth, nonanomalous fetus, induced labor	Prepregnancy Hospital admission	≤30 >30	Vaginal misoprostol 25 mcg every 4h Foley catheter inflated to 30 mL, accompanied by oxytocin titration to effect	Maximum of 6 doses of misoprostol Ripening continued to Bishop score >5	6 cm	Failure to achieve active labor	Cesarean delivery rate Doses of misoprostol Protocol deviation rate
Maeder et al. 2017	280	Retrospective cohort	All women admitted for postdate induction, received intravenous oxytocin, singleton pregnancy, vertex position, documented weight and height at initiation of prenatal care and at labor admission	Hospital admission	< 24.99 25-29.99 ≥30	Oxytocin at 1–2 milliunits/min, increased every 15–30 min	Cervical ripening balloon to 3–4 cm Oxytocin per protocol 1–2 milliunits/min, may be increased every 15 to 30 min at the discretion of the nurse or obstetric provider; rate must be decreased if signs of fetal intolerance (e.g., fetal heart rate decelerations) or tachysystole	Not mentioned	Total oxytocin dose	Length of labor Method of birth
Soni et al. 2019	1280	Retrospective cohort	Obese women (≥30 kg/m²) with singleton live pregnancies in cephalic presentation undergoing induction of labor from 37 to 42 completed weeks, initial Bishop score of ≤7 and cervical dilatation <2 cm	Hospital admission	≥30: 30-34.9 and ≥35	Vaginal misoprostol 25 mcg every 4h Oral misoprostol 20 mcg every 2h for 3 doses followed by 40 mcg every 2h for 3 doses followed by 60 mcg every 2h for 3 doses	100 mcg tablets broken into 25 mcg doses, each tablet administered every 4h if the contraction frequency was less than 3 in 10 min; maximum dose given 200 mcg Given as a solution in a titrated dose, ensuring contraction frequency ≤5 in 10 min averaged over 30 min; maximum dose 500 mcg The fetal heart activity was monitored with CTG at least 20 min before and after each dose Amniotomy done when considered appropriate by the attending obstetrician	Not mentioned	Time from the start of induction to the attainment of 3 cm of cervical dilatation	Time to delivery Vaginal births within 12h and 24h Cesarean delivery rate

BMI - body mass index, CTG – cardiotocography

Table III – Results of the primary and secondary outcomes of the studies

IOL method	Study	Route, agent, dose, timing (when compared)	BMI classes (kg/m²)	Primary Outcomes	Results	Secondary Outcomes	Results
Prostaglandins	Pevzner et al. 2009	Vaginal misoprostol or Vaginal dinoprostone inserts + Oxytocin	<30 - reference 30-39.9 ≥40	Number of women who reached active labor during the course of induction	Significant fewer obese and extremely obese women **reached active labor** (p=0.004; p=0.009) BMI<30 - 96.4%; BMI 30-39.9 - 92.1%; BMI 40 or higher - 91.5%	Total oxytocin for induction Delivery within 24 h CS rate	Obese and extremely obese women were more likely to require **oxytocin for induction** (p=0.004; p<0.001): BMI<30 - 30.9%; BMI 30-39.9 - 39.4%; BMI 40 or higher - 48.3% Median **dose and duration of oxytocin** in the BMI<30 group (2.6 units and 6.5 hours) was significantly lower compared to women in either obese (3.5 units and 7.7 hours) or extremely obese (5.0 units and 8.5 hours) group Obese and extremely obese were less likely to **delivery within 24h** (p=0.025; p=0.002): BMI<30 - 54.6%; BMI 30-39.9 - 47.5%; BMI 40 or higher - 41.7% Obese and extremely obese were more likely to **require a CS** (p=0.002; p<0.001): BMI<30 - 21.3%; BMI 30-39.9 - 29.8%; BMI 40 or higher - 36.5%
	O´Dwyer et al. 2013	Vaginal prostaglandin + Oxytocin	<18.5 - reference 25-29.9 >29.9	Induction rate PGE2 induction rate	Obese primigravidas (52.7%) were more likely to have a **labor induction**, compared to normal BMI primigravidas (35.7%); p=0.01 Obese primigravidas (31.8%) were more likely to have a **PGE2 induction**, compared to normal BMI primigravidas (20%); p=0.02	Total oxytocin for induction Emergency CS rate	Obese primigravidas (46.6%) were more likely to **require oxytocin for induction**, compared to normal BMI primigravidas (28.5%); p=0.007 Significant **higher emergency CS rate** for obese primigravidas (p=0.006): 34.6% for obese vs 19.5% for normal BMI primigravidas
	Suidan et al. 2015	Oral misoprostol 50 or 100 mcg (every 4h) or Vaginal misoprostol 25 mcg (every 4h) **VS** Vaginal dinoprostone 10 mg (every 12h) - reference (+ Oxytocin when needed)	≥30	Successful cervical ripening rate CS rate	Obese women using misoprostol (either PO or PV) had a higher **successful cervical ripening rate**, than those using dinoprostone (77.7% for misoprostol PO, 79.7% for misoprostol PV, 66.7% for dinoprostone; p=0.006; p=0.04) Lower **CS rate** for women using misoprostol versus those using dinoprostone (39.5% for misoprostol PO, 37.5% for misoprostol PV, 51.3% for dinoprostone; p=0.008; p=0.04) No significant difference was observed when comparing misoprostol PO with PV groups	Time to delivery Vaginal births within 12h and 24h Maternal complications rates Neonatal outcomes	Without statistically significant differences in time to delivery, vaginal births and maternal complications rates The misoprostol group had only a slight increased **birth weight**, compared to dinoprostone group (3,325 vs. 3,230 g, p=0.02)

IOL method	Study	Route, agent, dose, timing (when compared)	BMI classes (kg/m²)	Primary Outcomes	Results	Secondary Outcomes	Results
	Lassiter et al. 2016	Vaginal misoprostol 25 mcg every 4h + Oxytocin 1 milliunit/min, increased by 1–2 milliunits/min every 30 min or amniotomy	<30 - reference 30-40 >40	Time from induction to delivery	Significantly higher **time to delivery** with increasing BMI group (17.72 h for BMI<30, 20.01 h for BMI 30-40 and 22.9 h for BMI>40 group; p<0.0008)	Doses of misoprostol Duration of oxytocin CS rate	Increased number of **doses of misoprostol** and longer **oxytocin duration** with increasing BMI group (1.59, 2.05 and 2.32 doses of misoprostol and 7.17, 8.54 and 10.39 h of oxytocin, for BMI<30, BMI 30-40 and BMI>40, respectively; p<0.003; p<0.023) Increased **CS rate** for BMI >40 group and BMI 30-40, compared to BMI<30 group (17.48%, 37.09% and 40% for BMI<30, BMI 30-40 and BMI>40, respectively; p<0.0006)
	Soni et al. 2019	Vaginal misoprostol 25 mcg every 4h **VS** Oral misoprostol 20 mcg every 2h for 3 doses followed by 40 mcg every 2h for 3 doses followed by 60 mcg every 2h for 3 doses	≥30: 30-34.9 and ≥35	Time from the start of induction to the attainment of 3 cm of cervical dilatation	Significantly shorter **time from induction to the attainment of 3 cm dilatation** in the vaginal group, comparing to the oral group (10.5 h for vaginal vs. 17.2 h for oral; p<0.0001) When groups were stratified by BMI an increasing BMI was associated with an increased duration of time to 3 cm (9.3 h for vaginal vs. 16.7 h for oral, in the BMI 30-34.9 group and 11.9 h for vaginal vs. 18.5 h for oral, in the BMI≥35 group; both p<0.0001)	Time to delivery Vaginal births within 12h and 24h CS rate	Shorter **time to delivery** (17.4 h for vaginal vs. 24.8 h for oral; p<0.0001), higher rates of **vaginal birth within 12h** (29% for vaginal vs. 9.9% for oral) and **within 24h** (59.2% for vaginal vs. 42.3% for oral; both p<0.0001), and lower **CS rate**(24.5% for vaginal vs. 31.2% for oral; p=0.03) in the vaginal group, compared to oral misoprostol group When groups were stratified by BMI an increasing BMI was associated with an increased duration of **time to delivery** (16.5 h for vaginal vs. 24.8 h for oral, in the BMI 30-34.9 group and 19.3 h for vaginal vs. 27.1 h for oral, in the BMI≥35 group; both p<0.0001)
Oxytocin	Roloff et al. 2015	Oxytocin/ Vaginal or oral misoprostol 25-50 mcg/ Foley catheter/ amniotomy/ successive combination of these methods	<30 - reference ≥30	Cumulative oxytocin dose needed for vaginal birth	Significantly increased **cumulative oxytocin dose** with increasing BMI, in women that experienced IOL (p<0.001)	Neonatal outcomes	Obese women who experienced IOL had neonates with a higher **birth weight**, compared to non-obese women (3,371 vs. 3,141 g, p=0.008)
	Maeder et al. 2017	Oxytocin at 1–2 milliunits/min, increased every 15–30 min	<24.99 - reference 25-29.99 ≥30	Total oxytocin dose	Obese women received more **total oxytocin dose** than overweight women (7.50 units for obese and 5.92 units for overweight; p=0.031)	Time from induction to delivery Method of birth	**Time to delivery** increased with increasing BMI group, with women who were normal weight having a mean time to delivery of 13.96 h compared to 16 h and 18.30 h for women who were overweight and obese, respectively (p=0.018) **CS rate** increased with increasing BMI group (4.8% for normal BMI, 33.6% for overweight and 42.4% for obese; p=0.001); For type of birth, significant **predictors for CS** were: overweight and obese BMI groups, greater newborn birth weight, nulliparity, absence of an anxiety/depression diagnosis, fewer units per hour of infusion, IUPC monitoring and use of cervical ripening

IOL method	Study	Route, agent, dose, timing (when compared)	BMI classes (kg/m²)	Primary Outcomes	Results	Secondary Outcomes	Results
Transcervical catheters	Anabusi et al. 2016	Cook or Foley catheter (+ oxytocin and/or amniotomy) if first attempt unsuccessful --> Vaginal prostaglandins	≤30 - reference >30	Time from device insertion to delivery	Without statistically significant difference	Successful cervical ripening rate Vaginal births rate CS rate Maternal outcomes Neonatal outcomes	Without statistically significant differences, except for **maternal satisfaction** that was significant lower in obese women (p<0.01)
Prostaglandins versus Transcervical catheters	Beckwith et al. 2017	Vaginal misoprostol 25 mcg every 4h **VS** Foley catheter inflated to 30 mL (+ oxytocin)	≤30 - reference >30	Failure to achieve active labor	In women induced with misoprostol: increased **failure to achieve active labor in** obese women versus non-obese women (24% for obese vs. 15% for non-obese; p=0.01) In women induced with Foley catheter: without significant difference in failure to achieve active labor between obese and non-obese women (19% for obese vs. 15% for non-obese; p=0.55)	CS rate Doses of misoprostol Protocol deviation rate (misoprostol to oxytocin/foley catheter)	In women induced with misoprostol: higher **CS rate** in obese women (35% for obese vs. 26% for non-obese; p=0.03); without differences in **misoprostol doses needed** (1 dose needed for both obese and non-obese to have a successful IOL; p=0.23) nor in **protocol deviation** rate (11% for both; p=0.50) In women induced with Foley catheter: without differences in CS rate (31% for obese vs. 29% for non-obese; p=0.69)

BMI - body mass index, IOL - induction of labor, IUPC - intrauterine pressure catheter

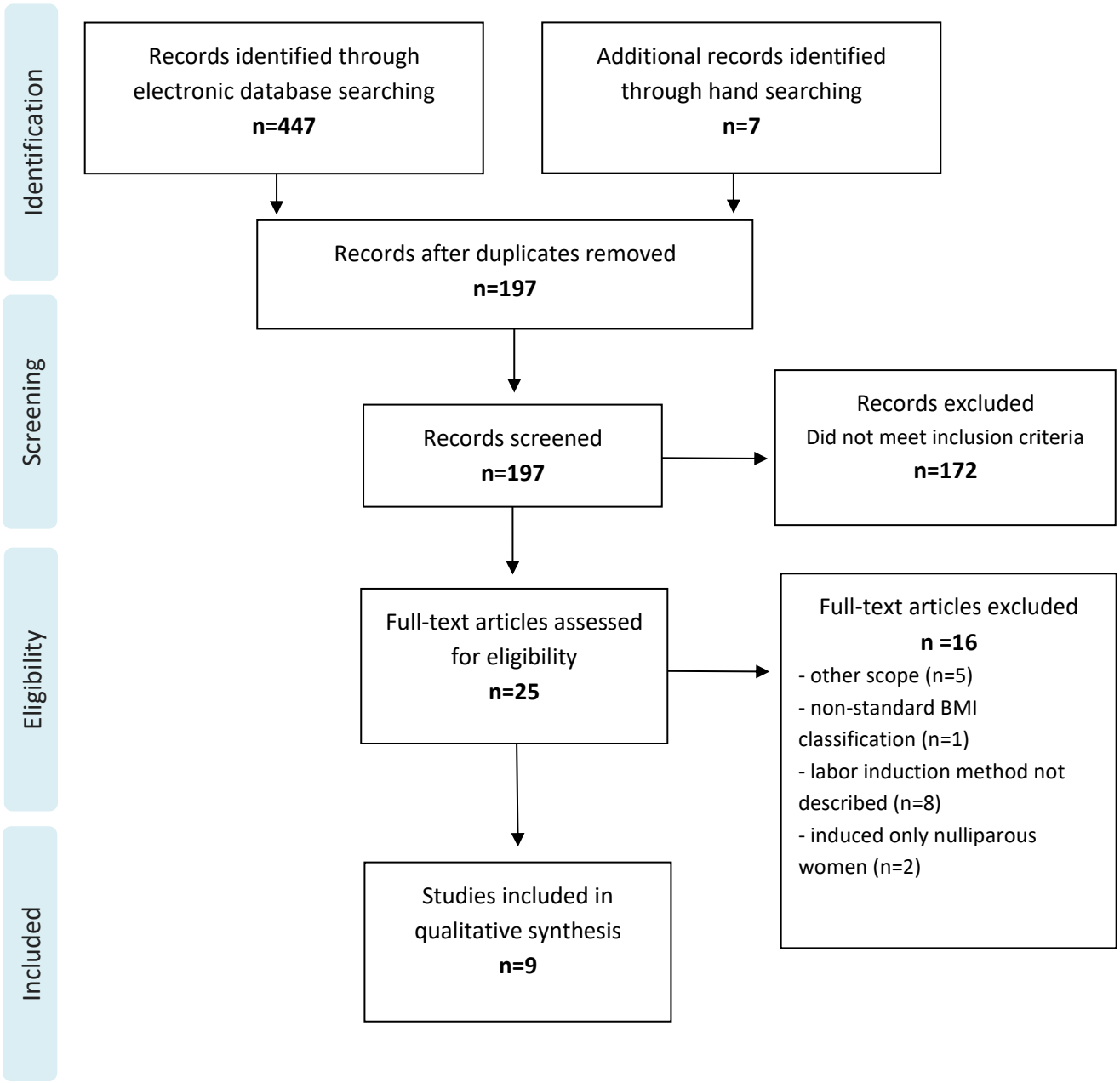

Figure 1 - Flow chart of the literature search

BMI - body mass index.

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