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MATERNAL-FETAL MEDICINE

Relation between induced labour indications and neonatal morbidity

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Abstract
Purpose To assess the main neonatal morbidity results in relation to induced labour indications.
Methods Historical groups from a total of 3,817 deliveries over a three year period (2009, 2010 and 2011) in "Mancha-Centro" Hospital (Alcázar de San Juan) formed the study group. All programmed and non-avoidable caesarean sections and pregnancies under 35 weeks were excluded. The main variable result was a neonatal morbidity variable made up of the Apgar score after 5 min, pH of umbilical artery <7.10 and the neonatal need for resuscitation type III–V. Multivariate analysis was used to control confounding variables.
Results The incidence of induced labour was 22.6 % (862). The highest indication was premature rupture of membranes for more than 12 h 22.8 % (190), poorly controlled diabetes 22.6 % (189) and oligoamnios 16.2 % (135). The rate of pH lower than 7.10 was 2.8 % (22), the rate of the Apgar score lower than 7 after 5 min was 0.2 % (2) and the neonatal need for resuscitation type III–IV was 5.7 % (48) for induced labour. The relation between induced labour and neonatal morbidity indicators were not statistically significant. 10.1 % (4) of induced labour for suspected intrauterine growth restriction and 8.6 % (10) of postterm pregnancies required neonatal resuscitation type III–IV.
Discussion No relation was found between induced labour and the neonatal morbidity indicators. The highest neonatal risk indicator is when a intrauterine growth restriction, hypertensión/preeclampsia or a postterm pregnancy is suspected.

Keywords Induced labour · Neonatal morbidity · Indications · Variability

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Introduction

Induced labour is one of the interventions with the greatest variability within Obstetrics, around 20 % of all births [1], although this figure varies between 5 % in some Latin American countries [2], and 30 or 40 % in countries like England and the United States, respectively [3–5].

What many centres and countries seem to have in common is the progressive increase in the use of induction [1, 6–8], justified by new medication for cervical ripening, professional fear of litigation [9, 10] pressure of patients and their awareness, professional convenience [7], as well as the further development of diagnosis methods.

The mothers and their foetuses who underwent induced labour, generally have diseases or have a high probability that their health would be affected if the pregnancy is allowed to progress naturally. The growing trend towards induced labour is performed regardless of potential neonatal complications. After the literature review, only a few studies deal with the differences between spontaneous and induced births in relation to infant's ability to adapt to life [2, 11, 12].

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Most publications providing information on neonatal morbidity compare policies focused on induction versus expectant attitude, especially with the management of post-term pregnancy obtaining a wide variety of results [13–19].

It can also be very interesting to determine which of the induction indications carry the highest risk for newborns. This could be useful for both the clinic and for the patient, to have more objective information on potential neonatal complications and, therefore, make a more informed decision about the birth.

The hypothesis of this study is based on the belief that inductions have a higher neonatal morbidity than spontaneous labour and, therefore, the aim of our study is to determine the relation between induced labour indications and neonatal morbidity.

Methods

Design and participants

The nature of the study is observational, analytical of retrospective groups. It was carried out in the Delivery Unit of the "Mancha-Centro" Hospital in Alcázar de San Juan. This is a Level II centre attending nearly 1,300 births a year.

The studied group is composed of all the groups of pregnant women who gave birth in "Mancha-Centro" Hospital from 2009 to 2011. All programmed and non-avoidable caesarean sections, twin births, pregnancies under 35 weeks and induced labour for antepartum stillbirth (only for estimating the risk of morbidity) were excluded from the study. This selection process is detailed in Fig. 1.

To estimate the sample size, we considered as the main event the pH of umbilical artery as being a critical objective and the best predictor of perinatal adverse outcomes [20, 21] and as a cutoff, values less than 7.10 [22]. Considering that the average number of births a year is 1,300 and that around 3 % may have pH values of below 7.10, we would have nearly 39 newborns a year.

To build a multivariate model, ten events are required (pH under 7.10) to add to each variable. Assuming a maximum of ten variables in the initial model, we would need 3 years data.

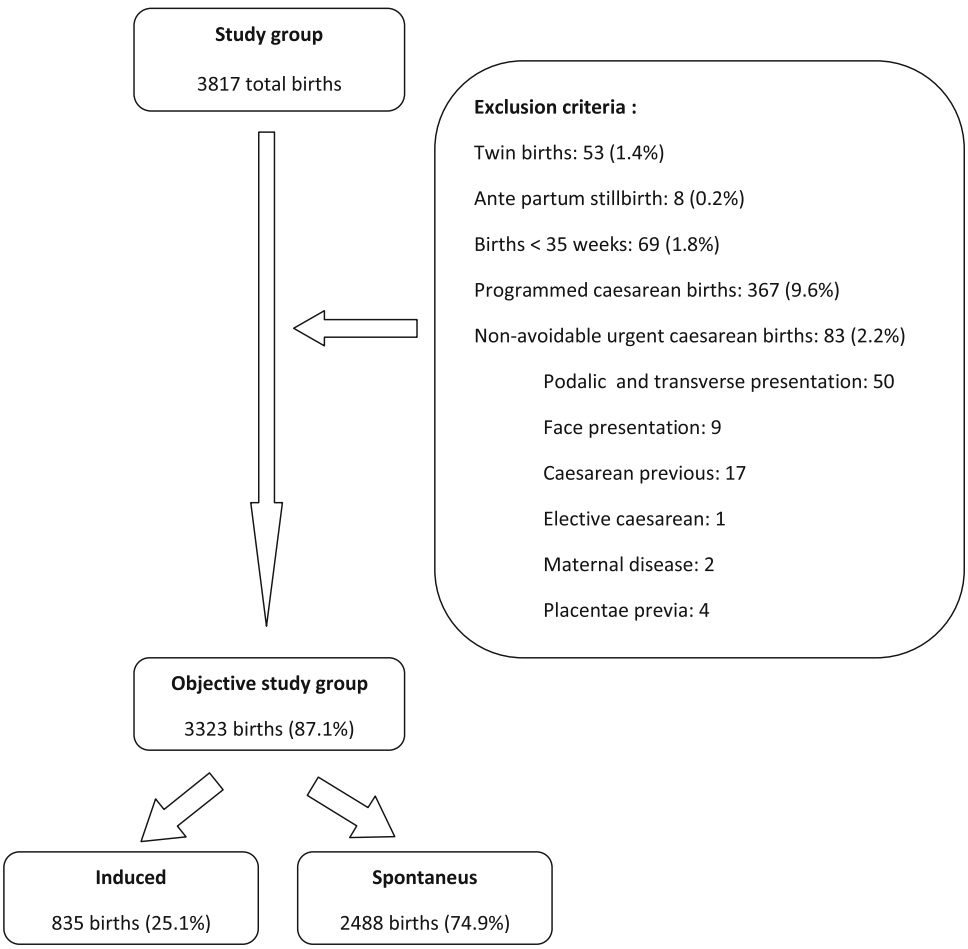

Fig. 1 Selection process and exclusion criteria

Information sources

To collect the data, we have used the medical records of the patients participating in the study.

We collected the following variables:

Main outcome variables: Apgar Test score after 5 min, pH of umbilical artery, degree of neonatal resuscitation and composite morbidity (created on the basis of the other three variables).

Main independent variables: the onset of labour (spontaneous or induced) and labour induced indications on current labour.

The control variables were: maternal age, gestational age, previous caesarean section, type of pregnancy, use of epidural analgesia, parity, type of delivery, and birth weight.

Statistical analysis

First of all, a descriptive statistic analysis was performed using absolute and relative frequencies for qualitative variables and arithmetic means and standard deviation for quantitative ones.

Then, bivariate analysis was performed on the obstetric history, development and outcome of current labour and neonatal morbidity with the onset of labour (spontaneous/induced), using the Chi-square test for qualitative variables or exact tests when there is infringement of the application of the conditions.

To define the risk of neonatal morbidity by induced labour, multivariate analysis was performed using binary logistic regression. The aim of the model was to determine the clear effect of induced labour controlling potential confounding factors. Explanatory variables involved were selected on the basis of Greenland and Maldonado (associations $P < 0.2$). We estimated odds ratio (OR) with confidence intervals of 95 %, using as a reference category the most physiological or normal option. The software PASW Version 19.0 was used for the statistical analysis (SPSS, Inc., Chicago, IL, USA).

Ethical and legal considerations

The approval of the Committee of Ethical Clinical Research of the Centre was requested, ensuring during all the process the confidentiality of medical records and the information in them.

Results

The studied group consisted of a total of 3,817 pregnant women. The global induction rate stood at 22.6 % (862). Excluding all programmed and non-avoidable caesarean sections, twin births, antepartum stillbirth and births <35 weeks the induction rate stood at 25.1 % (835). Selection process and exclusion criteria are detailed in Fig. 1.

As for the main maternal and obstetric characteristics and their relation to the onset of labour (spontaneous/induced) and potentially confounding factors influencing neonatal morbidity, we observed a statistically significant association with maternal age, gestational age, parity, use of regional analgesia, birth weight and type of delivery. No relation was found with previous caesarean section and type of gestation. Obstetric characteristics are detailed in Table 1.

We also studied the relationship between the onset of labour and neonatal morbidity and found no statistically significant differences between spontaneous and induced deliveries on values <7.10 in the pH of umbilical artery (2.4 % (53) vs 2.8 % (22), $P = 0.471$) or Apgar scores <7

Table 1 Factors associated with induced labour may be presented as potentially confounding

Variables	Onset of labour		
	Spontaneous ($n = 2{,}488$) n (%)	Induced ($n = 835$) n (%)	P value
Maternal age			0.030
<20 years	75 (3.0)	25 (3.0)	
20–35 years	1,926 (77.7)	613 (73.5)	
>35 years	477 (19.3)	196 (23.5)	
Gestational age			<0.001
35−36 + 9	79 (3.2)	63 (7.5)	
37–41	2,104 (84.6)	592 (70.9)	
>41	305 (12.2)	180 (21.6)	
Parity			<0.001
Nulliparous	1,225 (50.2)	545 (65.6)	
Multiparous	1,213 (49.8)	286 (34.4)	
Previous caesarean			0.336
No	2,297 (94.2)	790 (95.1)	
Yes	142 (5.8)	41 (4.9)	
Regional analgesia			<0.001
No	418 (17.0)	47 (5.7)	
Yes	2,042 (83.0)	773 (94.3)	
Birthweight (grams)			<0.001
<2,500 grams	66 (2.7)	76 (9.1)	
2,500–4,000 grams	2,284 (92.1)	728 (87.2)	
≥4,000 grams	130 (5.2)	31 (3.7)	
Type of delivery			<0.001
Eutocic	2,059 (82.8)	528 (63.2)	
Instrumental	156 (6.2)	63 (7.6)	
Emergency caesarean section	273 (11.0)	244 (29.2)	

at 5 min (0.4 % (9) vs 0.2 % (2), $P = 0.591$), both in the univariate analysis and adjusting for confounding factors. According to the degree of neonatal resuscitation, statistical association was observed in the univariate analysis with induced labour (3.0 % (73) vs 5.7 % (48), $P < 0.001$), but not the adjusted model (OR 1.26; CI 0.84–1.90). The same situation was observed with the created composite morbidity variable, where the statistical association reflects univariate analysis (4.5 % (112) vs 7.7 % (64), $P < 0.001$), but not the adjusted model (OR 1.27; CI 0.90–1.80). Data on neonatal morbidity and delivery onset are shown in Table 2.

Finally we determined the frequency of different reasons for induction, finding that premature rupture of membranes (PROM), followed by poor controlled diabetes, oligohydramnios and postterm pregnancy are the top four reasons for induction, together totalling 75 % of total indications. Also we related the type of indication with neonatal morbidity indicators, when the pH of umbilical artery was below 7.10 the indication showed an increased risk due to hypertension/preeclampsia (HTN) with 4.8 % (2), followed by PROM with 4.0 % (7) and postterm pregnancy with 3.7 % (4). For Apgar scores below 7 after 5 min, only two cases were reported, one of them in postterm pregnancy and one in suspected IUGR. For newborns who required at least a degree of resuscitation type III, suspected IUCR with 10.8 % (4), followed by the meconium amniotic fluid with 9.1 % (5), hypertensión/preeclampsia with 8.7 % (4) and postterm pregnancy with 8.6 % (10) were the four main indications. For postterm pregnancy composite morbidity presented the worst results with 11.2 % (13), followed by hypertensión/preeclampsia with 10.9 % (5) and suspected IUGR with 10.4 % (4). We found no statistically significant differences between the different indications of induction and neonatal morbidity and the four indicators used. The indication data types and their relation to neonatal morbidity are detailed in Table 3.

Discussion

The incidence of induced labour in our study stands at 22.6 %, which is among the Latin American countries [2] with figures ranging between 5 and 20 % and more developed countries like Australia with 29.1 % [1], England [3] with 32.3 % and the United States with over 40 % [5, 23]. In the Spanish context we only found one study providing figures of induction incidence with a rate of 21.3 % [24]. This variability is related to the rate of inductions and elective caesarean sections, with fewer inductions in areas with a more liberal use of elective caesarean indications. In this respect the indication of caesarean sections and/or elective inductions is a rare event in our centre with 0.5 %.

In the literature, the assessment of neonatal morbidity was performed according to gestational age, certain indications and various morbidity criteria: ICU admissions, Apgar scores and pH of umbilical artery with different cut off points, etc. This makes it really difficult to establish comparisons.

Table 2 Main indicators of neonatal morbidity and its relationship with induced labour

Variables	Onset of labour			
	Spontaneous ($n = 2,448$) n (%)	Induced ($n = 835$) n (%)	Or	Or Aj[a]
pH of Umbilical artery				
≥7.10 (Ref)	2,192 (97.6)	756 (97.2)	1.00	1.00
<7.10	53 (2.4)	22 (2.8)	1.20 (0.73–1.99)	1.09 (0.68–1.87)
Missing	203	57		
Apgar after 5 min				
≥7 (Ref)	2,470 (99.6)	833 (99.8)	1.00	1.00
<7	9 (0.4)	2 (0.2)	0.66 (0.14–3.06)	0.34 (0.07–1.69)
Missing	9	0		
Degree of neonatal resuscitation				
Not required + type I. II (Ref)	2,401 (97.0)	787 (94.3)	1.00	1.00
Type III–IV	73 (3.0)	48 (5.7)	2.01 (1.38–2.91)	1.26 (0.84–1.90)
Missing	14	0		
Composite morbidity				
No (Ref)	2,376 (95.5)	771 (92.3)	1.00	1.00
Yes	112 (4.5)	64 (7.7)	1.76 (1.28–2.42)	1.27 (0.90–1.80)
Missing	0	0		

Ref Reference Category

[a] Odds ratio with binary logistic regression adjusted for maternal age, infant weight, gestational age, type of delivery, parity and epidural analgesia use

Table 3 Indications of induction and its relation with pH of umbilical artery <7.10, Apgar scores <7, neonatal resuscitation type III–IV and composite morbidity

Induction indications	Total frequency *n* (%)	pH < 7.10 *n* (%)	Apgar 5 < 7 *n* (%)	Resuscitation type III–IV *n* (%)	Composite morbidity *n* (%)
Premature rupture of membranes >12 h	190 (22.8)	7 (4.0)	0 (0.0)	10 (5.3)	17 (8.9)
Poor controlled diabetes	189 (22.6)	4 (2.3)	0 (0.0)	5 (2.6)	7 (3.7)
Oligoamnios	135 (16.2)	2 (1.6)	0 (0.0)	6 (4.4)	8 (5.9)
Postterm pregnancy	116 (13.9)	4 (3.7)	1 (0.9)	10 (8.6)	13 (11.2)
Meconium amniotic fluid	55 (6.6)	1 (1.9)	0 (0.0)	5 (9.1)	5 (9.1)
HTN/preeclampsia	46 (5.5)	2 (4.8)	0 (0.0)	4 (8.7)	5 (10.9)
Suspected IUGR	37 (4.4)	1 (3.2)	1 (2.7)	4 (10.8)	4 (10.4)
Pathological monitor	15 (1.8)	0 (0.0)	0 (0.0)	1 (6.7)	1 (6.7)
Foetal interest/bad obstetric history	13 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hydramnios	12 (1.4)	0 (0.0)	0 (0.0)	2 (16.7)	2 (16.7)
Cholestasis	9 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Metrorrhagia	5 (0.6)	1 (20.0)	0 (0.0)	0 (0.0)	1 (20.0)
Maternal disease	4 (0.5)	1 (33.3)	0 (0.0)	0 (0.0)	1 (33.3)
Elective	4 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unstable presentation	3 (0.4)	0 (0.0)	0 (0.0)	1 (33.3)	1 (33.3)
Maternal stroke	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Antepartum fever	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	57	0	0	0
P value[a]		0.667	0.197	0.263	0.386
Total induction indications	835 (100)	22 (2.8)	2 (0.2)	48 (5.7)	64 (7.7)

To establish a ranking in morbidity according to the indication we have only evaluated those induction indications with a minimum of 30 cases

NC not calculated

[a] *P* value estimated by Monte Carlo exact test bilaterally

Regarding the influence of induced labour on the adverse neonatal outcomes, there is no association between induction and low Apgar scores after 5 min, pH of umbilical artery values <7.10, greater need for neonatal resuscitation and composite morbidity after making adjustments for confounding factors. Ironically, increased morbidity is not found, in spite of having potentially dangerous conditions when labour is induced. This lack of relation may be justified either by reaching a balance in the clinical management of these patients and their newborns or as a result of an over- induction rate. To clearly identify the real reason, it would be necessary to do clinical trials for every induction indication.

Glantz et al. [25] globally comparing spontaneous versus induced births, have found no relation between higher rates of induction and increased neonatal morbidity, in contrast to Guerra et al. [2] and Janakiraman et al. [12], who both reported an increased risk of low Apgar scores when induced. A drawback of these two studies is that neither of them introduces a control for confounding factors by means of multivariate analysis, making it impossible to separate the effect of induced labour from other variables that may also affect neonatal morbidity.

The most frequent indications we have observed for induction are: premature rupture of membranes (PROM) for more than 12 h with 22.8 %, poor controlled diabetes with 22.6 %, oligohydramnios with 16.2 % and postterm pregnancy with 13.9 %. These results show discrepancies with those found in two large studies: Mealing et al. [1] carried out in Australia on 196,827 inductions, where the main reason for induction was postterm pregnancy with 33.4 %, followed by HTN with 13.0 % and PROM with 11 %. The other study, conducted by Guerra et al. [2] in eight Latin American countries with a sample of 11,077 inductions, concluded that the first induction indication was elective induction with 28.9 %, followed by PROM with 25.3 % and postterm pregnancy with 8.8 %. In Spain, although only two studies have been found, PROM with 45 % [24] and postterm pregnancy with 54.6 % [26] are reported as the main indications for induction. Possible reasons to justify these differences are the different guidelines introduced in each centre and/or country, the different use of elective procedures or the increasing importance of private medicine and legal pressure on professionals.

When it comes to the indications which show the worst results of neonatal morbidity, we could consider, in our study, that postterm pregnancy, HTN and suspected IUGR are the indications with the worst neonatal results. In this sense we have not found in the reviewed literature any other studies dealing with this issue specifically. On the other hand, considering that the neonatal morbidity

obtained is low (expressed in Apgar scores after 5 min), a high percentage of low pH and a high degree of resuscitation have been observed, which seem to show the correct handling of neonatal resuscitation for induced labour and spontaneous labour. Nevertheless, the physical presence of a neonatologist in the delivery room when there is a suspected IUGR, HTN and postterm pregnancy would be justified, owing to the greater need for resuscitation type III–IV required in 10.8, 8.7 and 8.6 % of the cases of these indications, respectively.

As a drawback to our study, we found a significant number of missing pH values. Although in most cases these values belong to successful deliveries, where late umbilical cord clamping was permitted and it was not possible to obtain the sample. Besides, technical problems in the extraction and/or analysis of the blood sample could be another source of missing values. On the other hand, as a strong point, we can ignore the lack of other similar studies in Spain, providing a starting point for further investigation and research into standards which allow the use of induced labour to be compared and audited through its major obstetric results.

Conclusion

The global induction rate is around 22.6 % of all births, the main induction indications being PROM followed by poorly controlled diabetes. There is no relation found between induction and indicators of neonatal morbidity, especially when controlling confounding factors. The indications with the worst results are suspected postterm pregnancy, HTN and IUGR.

Nowadays in our hospital, induced labour is presented as a safe practice for newborns. While some guidelines should be reviewed, especially those related to controlling gestational diabetes. As well as assessing the physical presence of a neonatologist in the delivery room when the induction indication is associated with an increased neonatal risk.

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Conflict of interest The authors have no conflicts of interest to disclose.

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