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Risk Factors for Late Preterm Births: A Case-Control Study

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Abstract

Aim: This study examines the influence of selected sociodemographic and pregnancy specific factors on the risk of Late Preterm Births (LPB) analyzing separately induced and spontaneous.

Methods: We conducted a case-control study of LPB observed in 5 Italian Centers. Cases are 305 women who delivered at 34, 35 and 36 weeks gestation. The controls were 269 women who gave birth at term (>37 weeks of gestation).

Results: Considering the total series, the risk of LPB was above unity in hypertensive women, but the OR was 6.70 (95% CI 3.25-13.82) in women with induced LPB and 0.90 (95% CI 0.35-2.32) in women with spontaneous LPB. Positive culture of vaginal smear was associated with an increased risk of LPB.

Conclusions: According to our results hypertension increases the risk of medically indicated LPB while a history of preterm birth or positive vaginal smear are associated with an increased risk of spontaneous and induces LPB.

Keywords: Hypertension; Preterm birth; Risk factor

Introduction

Neonatal mortality and morbidity, early and late as well, are significantly higher in preterm births (before 37 weeks of gestation) as compared with full term ones. The rates of adverse outcome are inversely proportional to gestational age at birth and this trend is also evident at 34-36 weeks [1].

Mortality rate among moderately preterm (32-33 weeks) is seven times and among late preterm (34-36 weeks) three times higher than that observed in term infants [2].

Neonatal morbidity is mainly represented by respiratory problems. For example, it has been shown that respiratory distress syndrome is higher at 34 weeks (9%) 35 weeks (4%) and 36 weeks (3%) when compared to 38 to 39 or 40 weeks (0.7, 0.2 and 0% respectively) [3]. Also other morbidities (intra ventricular hemorrhage, necrotizing enterocolitis, NICU admission and sepsis) are more frequently associated with late preterm birth when compared to infants born at term [4]. This observation is a matter of concern. On the other hand it has been observed that the increased rate of Late Preterm Births (LPB) can be associated with lower rates of stillbirths and neonatal death [5].

Epidemiological studies have suggested that sociodemographic and pregnancy specific factors may increase the risk of preterm birth. Obstetric history, diseases and procedures in pregnancy, as well as lifestyle habits, such as smoking, have been associated with the risk of preterm delivery [6]. Few studies however have considered separately early and late preterm deliveries. Moreover, about 32% of LPB are medically indicated [7]. The characteristics of these cases may differ from spontaneous LPB. It has also been shown that elective Cesarean Section is responsible of the increasing rate of early term births [8].

It has been suggested that in many cases it is possible to prevent LPB without negatively affect the clinical outcome [4,9].

In order to identify possible preventive measures a better knowledge of the risk factors is essential. Most of the published studies on LPB are retrospective s taking into consideration a limited number of risk factors [10,11].

This multicenter study, beside other clinical aspects, analyzes the role of selected sociodemographic and pregnancy specific factors on the risk of LPB with the opportunity of evaluating separately induced and spontaneous late preterm births.

Methods

We conducted a case-control from January 2010 to December 2011 on late preterm births. Cases were 305 womens who delivered at 34 to 36 weeks gestation identified in five second level Italian obstetric centers (Palermo, Napoli, Brescia, Treviso, Catania).

The controls were 269 women who gave birth at term (37 or more weeks of gestation) to healthy infants immediately after a case occurred at the same hospital. The researchers identified the cases and controls in the obstetric wards on randomly selected days; each woman who met the inclusion criteria was interviewed in the framework of clinical routine care and data were collected from clinical records. Information regarding the newborn was collected at the moment of discharge from clinical records.

Cases and controls mothers were identified in the same hospital within two days after delivery.

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No exclusion criteria were foresaw.

The mean number of LPB observed in these centers for year is about 100 cases. Since the data collection started in different periods in each centers in the five participating centers and in general lasted about 4 months, the centers included about the 95% of eligible cases observed in the data collection period.

Gestational age was confirmed by an ultrasound scan performed before the 20th week of gestation in all cases and controls.

Data have been collected regarding the following aspects:

1. sociodemographic and anamnestic data;

2. Current pregnancy; 3. mode of delivery; 4. newborn conditions and complications.

Gestational hypertension has been defined according to the ACOG criteria [12].

Gestational diabetes was defined according to the International Association of Diabetes and Pregnancy Study Groups Consensus Panel [13].

Data analysis

Odds ratios and corresponding 95% confidence interval of LPB were computed for the total series and separately for spontaneous and medically induced cases.

We used unconditional multiple logistic regression, with maximum likelihood fitting [14] including terms for age, parity, history of LPB, hypertension, culture for vaginal infection in pregnancy.

For 36 cases no control was identified the inclusion or exclusion from the analysis of these cases did not change substantially the OR estimates. Thus, analysis including all cases and controls interviewed are presented.

Results

Among the 305 cases, birth was medically indicated in 127 (41.6%). A maternal indication was present in 43 cases (33.8%) cases. Spontaneous premature rupture of membrane (PROM) occurred in 140 cases (45.9%) while 88 PROM have been observed among controls (32.7%). Of the 140 PROM among cases 46 (32.85%) underwent induction of labour. For the purpose of this study these cases have been considered as spontaneous LPB.

Among controls PROM occurred in 88 cases (32.7%) and in 35 of them labour has been induced (39.7%). The caesarean section rate was 49.8% (152/305) among cases and 43.1% (115/269) in controls. These high rates reflect the trends observed in Italy.

The prevalence of composite neonatal morbidity (intubation in delivery room, respiratory assistance, transient tachypnea, mechanical ventilation and respiratory distress syndrome or admission to Intensive Unit) was 25, 8% among cases and 2, 3% among controls. This frequency was inversely related to gestational age being 71.15% at 34, 28.07% at 35 and 20.87% at 36 gestational week (gw).

Tables 1 and 2 show the distribution of cases and controls according respectively to selected pre-pregnancy maternal characteristics and smoking habits in pregnancy, invasive diagnostic procedures in pregnancy, results of vaginal smear or urine culture in pregnancy and presence of hypertension or diabetes in pregnancy.

A history of preterm birth increased the risk of medically induced and spontaneous LPB.

Considering the total series, the risk of LPB was above unity in hypertensive women (3.11-95% CI 1.57-6.14 data not shown in table), but the OR was 6.70 (95% CI 3.25-13.82) in women with induced LPB and 0.90 (95% CI 0.35-2.32) in women with spontaneous LPB.

Positive culture of vaginal smear was associated with an increased risk of LPB.

Maternal age seems not to be associated with LPB except for the case of teenage mothers.

A total of 9 cases of maternal aged less than 20 years at delivery have been observed. 8 were LPB and 1 was a control. The number is small but anyway the calculated OR for LPB was 7.76 (95% CI 0.92-65.75). Of the pregnancy specific evaluated factors only hypertension and and positive vaginal culture appear to be associated with LPB. In this of pregnancies no significant association has been found between all the other evaluated factors and the risk of LPB.

Discussion

Before discussing our results some potential limitation of this study should be considered. Cases included in this series were identified in second level delivery centers, thus cannot be considered representative of all late preterm births. Among the strengths consider the fact that data were collected directly from mothers and in part from clinical records, but in a standardized and prospective way.

In the majority of the available studies risk factors for preterm births (<37 gw) are presented [6,15]. The main interest of this study is the fact that we have included only LPB, a population that may differ from the overall preterm births and we analysed separately the risk factors for medically indicated and spontaneous LPB.

Young and advanced maternal age have been associated with the risk of preterm delivery. For example, in the previous quoted retrospective study conducted in Texas maternal age <17 and >35 increased the risk [16]. Our results are consistent with this observation for the very young age also if the observed number of cases is limited.

In our study parity do not show any significant association with LPB. This finding is in agreement with the data reported by [7,17]. On the contrary Melamed reported a significant increased prevalence of nullipara among LPB [11].

In accord to the study of Reddy [17] in our material no association has been found between educational level and LPB.

Laughton et al. [7] found an association between the single status and spontaneous LPB and PROM. In our study the marital status condition does not seem to be associated with LPB.

Diabetes and hypertension are more common among overweight women [18]. As a consequence, it has been suggested that maternal weight is associated with the risk of preterm birth, but the data regarding the role of this association is less consistent [19]. We did not found any association between maternal weight and risk of spontaneous or medically indicated LPB.

In accord to other studies [7,17] a history of a previous preterm birth increases the risk of recurrent preterm birth. For instance, this association was observed in a case-control study conducted in Italy. In that study however the analysis included all preterm births, without distinguishing late preterm ones [20].

Maternal age (years)	Induced LPD		Spontaneous LPD		Term deliveries		Induced LPD vs Term deliveries		Spontaneous LPD vs Term deliveries	
	No.	(%)	No.	(%)	No.	(%)	OR	(95% CI)*	OR	(95% CI)*
≤ 30	41	32.3	41	23.0	82	30.5	1.00		1.00	
31-34	23	18.1	43	24.2	72	26.8	0.80	0.41-1.57	1.31	0.74-2.31
≥ 35	49	38.6	53	29.8	103	38.3	1.11	0.41-1.57	1.10	0.64-1.87
Missing	14	11.0	41	23.0	12	4.5				
Education(years)										
≤ 8	25	19.7	28	15.7	44	16.4	1.00		1.00	
9-13	38	29.9	42	23.6	85	31.6	0.79	0.39-1.61	0.80	0.41-1.54
≥ 14	23	18.1	20	11.2	50	18.6	0.88	0.39-2.01	0.84	0.39-1.84
Missing	41	32.3	88	49.4	90	33.5				
Marital status										
Never married	20	15.7	35	19.7	43	16.0	1.00		1.00	
Ever Married	93	73.2	110	61.8	207	77.0	0.88	0.45-1.70	0.62	0.36-1.07
Missing	14	11.0	33	18.5	19	7.1				
BMI										
≤ 24	29	22.8	44	24.7	76	28.3	1.00		1.00	
24.1-27.5	33	26.0	40	22.5	73	27.1	1.23	0.64-2.37	1.06	0.60-1.89
≥ 27.6	38	29.9	40	22.5	77	28.6	0.79	0.40-1.55	0.99	0.56-1.76
Missing	27	21.3	54	30.3	43	16.0				
Spontaneous abortion										
0	36	28.3	38	21.3	73	27.1	1.00		1.00	
1	70	55.1	104	58.4	138	51.3	0.82	0.47-1.44	1.09	0.65-1.83
≥ 2	21	16.5	36	20.2	58	21.6	0.49	0.24-1.04	1.06	0.57-1.98
Induced abortions										
0	109	85.8	162	91.0	237	88.1	1.00		1.00	
≥ 1	18	14.2	16	8.99	32	11.9	0.87	0.44-1.72	1.38	0.68-2.78
Parity										
0	82	64.6	101	56.7	141	52.4	1.00		1.00	
1	36	28.3	49	27.5	94	34.9	0.48	0.28-0.84	0.60	0.37-0.97
≥ 2	9	7.1	28	15.7	34	12.6	0.29	0.12-0.72	0.86	0.46-1.61
History of preterm birth										
No	109	85.8	158	88.8	250	92.9	1.00		1.00	
Yes	18	14.2	20	11.2	19	7.1	2.44	1.11-5.39	2.37	1.14-4.89
Smoking in pregnancy										
No	103	81.1	143	80.3	208	77.3	1.00		1.00	
Yes	12	9.4	23	12.9	40	14.9	0.57	0.26-1.24	0.73	0.39-1.36
Missing	12	9.4	12	6.7	21	7.8	0.86	0.37-2.03	0.91	0.41-2.02
N. Cigarettes/die										
≤ 4	4	36.4	10	50.0	18	48.6	1.00		1.00	
≥ 5	7	63.6	10	50.0	19	51.4	1.26	0.21-7.57	1.55	0.29-8.23

*multivariate estimates including terms for age, parity, history of LPB, hypertension, culture for vaginal infection in pregnancy

Tabel 1: Sociodemographic and anamnestic factors and risk of late preterm birth.

The association between induced and spontaneous abortions and risk of late preterm birth is still open to debate. For example in a review article published in 2002 out of 24 considered papers, 12 reported an increased risk of preterm birth among women reporting previous induced abortions [21]. In our experience no association has been found between previous spontaneous or induced abortions and LPB.

There are some suggestions that maternal smoking is associated with a moderate risk of preterm delivery [22,23]. The indications that the risk increase with the number of cigarettes smoked per day give some support to this association [24]. However, available data are controversial. The risk seems to be higher for delivery before the 33th week of gestation [25]. This suggestion is consistent with our results showing no association between smoking habits and risk of LPB.

In our study invasive diagnostic procedures was not associated with the risk of LPB. This finding is consistent with previous published data generally considering preterm birth all together [26].

Comorbidities, in particular hypertension and gestational diabetes have been associated with the risk of LPB. For example, in a retrospective cross-sectional analysis using routine delivery data from all births in San Antonio/Bexar County, Texas between 2000 and 2008 and including 259,576 births, variables associated with an increased risk of LPB were black race, age <17, age ≥ 35, gestational hypertension, eclampsia, chronic hypertension, and diabetes [16].

In our analysis hypertension increased the risk of medically indicated, but not of spontaneous LPB. This finding suggests that in some cases a cesarean section has been performed in hypertensive women without fetal indication as it has been observed in other study [8]. Also the presence of gestational diabetes increased risk of induced LPB, but the OR was not statistically significant.

In our study positive urine and/or vaginal culture was associated with the risk of induced and spontaneous LPB.

Amniocentesis	Induced LPD		Spontaneous LPD		Term deliveries		Induced LPD vs Term deliveries		Spontaneous LPD vs Term deliveries	
	No.	(%)	No.	(%)	No.	(%)	OR	(95% CI)§	OR	(95% CI)§
No	105	82.7	142	79.8	211	78.4	1.00		1.00	
Yes	22	17.3	36	20.2	58	21.6	0.84	0.44-1.61	1.19	0.69-2.04
Chorionic villus sampling										
No	121	95.3	167	93.8	255	94.8	1.00		1.00	
Yes	6	4.7	11	6.2	14	5.2	0.94	0.32-2.79	1.10	0.44-2.75
Hypertension*										
No	89	70.1	169	94.9	256	95.2	1.00		1.00	
Yes	38	29.9	9	5.1	13	4.8	6.70	3.25-13.82	0.90	0.35-2.32
Diabetes**										
No	112	88.2	166	93.3	246	91.4	1.00		1.00	
Yes	15	11.8	12	6.7	23	8.6	0.78	0.34-1.77	0.59	0.16-1.33
Vaginal culture										
Negative	43	35.5	61	36.3	175	66.5	1.00		1.00	
Positive	12	9.9	23	13.7	23	8.7	2.57	1.12-5.91	3.25	1.65-6.37
Not done	66	54.5	84	50.0	65	24.7	3.84	2.28-6.46	3.82	2.42-6.02
Urino culture										
Negative	44	34.6	43	24.2	94	34.9	1.00		1.00	
Positive	11	8.7	7	3.9	11	4.1	1.51	0.51-4.44	1.32	0.45-3.91
Not done	72	56.7	128	71.9	164	61.0	0.61	0.35-1.07	0.92	0.56-1.52

*chronic hypertension was diagnosed in 7 cases and 4 controls
**pre pregnancy diabetes was diagnosed in 6 cases and 2 controls
§multivariate estimates including terms for age, parity, history of LPB, hypertension, culture for vaginal infection in pregnancy

Table 2: Pregnancy specific factors and risk of late preterm birth.

Conclusion

LPB are associated with significantly increase of newborns morbidity and mortality, early and late as well as compared to full term births. About 59% of LPB are spontaneous and 41% are iatrogenic for maternal or fetal indications. In order to prevent LPB the identification of the risk factors is fundamental. Among sociodemographic and anamnestic factors potentially associated to LPB only a history of previous preterm birth has been identified.

Among pregnancy specific factors infections of the genitourinary tract are associated with spontaneous LPB while hypertension is associated with induced LPB. According to these results a prevention of some LPB is feasible. Attention should be given in pregnancy to the detection of genitourinary infection, especially in cases presenting a history of previous preterm birth in order to reduce or avoid PROM. In case of maternal hypertension iatrogenic deliveries should be considered only in case of evidence based indications.

Therefore a policy of prevention should focus the attention on screening and treatment of genitourinary infections and limitations of iatrogenic LPB to evidence based indications.

According to our results and in agreement with available studies the most important anamnestic risk factor for LPB is represented by a history of previous preterm birth. As far as pregnancy specific factors are concerned urinary and/or vaginal infections are risk factors possibly related to PROM. Also hypertension is significantly associated with induced LPB but not with spontaneous. A prevention of LPB seems to be feasible by a close survey and treatment of infections and by performing induced births only by evidence based indication.

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