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ORIGINAL ARTICLE



Medically indicated late preterm delivery and its impact on perinatal morbidity and mortality: a retrospective population-based cohort study

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ABSTRACT

Objective: In the last few decades, attention has been focused on morbidity and mortality associated with late preterm delivery (34–36 + 6/7 weeks), accounting for 60–70% of all preterm births. This study is aimed to determine (1) the prevalence of late preterm deliveries (spontaneous and medically indicated) in our population; and (2) the rate of neonatal morbidity and mortality as well as maternal complications associated with the different phenotypes of late preterm deliveries.

Study design: This retrospective population-based cohort study, included 96,176 women who had 257,182 deliveries, occurred between 1988 and 2011, allocated into three groups: term ($n = 242,286$), spontaneous ($n = 10,063$), and medically indicated ($n = 4833$) late preterm deliveries.

Results: (1) Medically indicated late preterm deliveries were associated with increased maternal morbidity, as well as neonatal morbidity and mortality, in comparison with other study groups ($p < .01$ for all comparisons); (2) medically indicated late preterm delivery was an independent risk factor for composite neonatal morbidity (low Apgar score at 5', seizures, asphyxia, acidosis) after adjustment for confounding factors (maternal age and ethnicity and neonatal gender) and stratification according to gestational age at delivery; and (3) the proportion of medically indicated late preterm deliveries affected the neonatal mortality rate. Below 35% of all late preterm deliveries, indicated late preterm birth were associated with a reduction in neonatal mortality; however, above this threshold medically indicated late preterm deliveries were associated with an increased risk for neonatal death.

Conclusions: (1) Medically indicated late preterm deliveries were independently associated with adverse composite neonatal outcome; and (2) to benefit in term of neonatal outcome from the tool of medically indicated late preterm birth, their proportion should be kept below 35% of all late preterm deliveries, while exceeding this threshold increases the risk of neonatal mortality.

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Introduction

Preterm delivery, is responsible for 70% of all neonatal mortality, 36% of infant deaths, and an approximately 25–50% of long-term neurological impairment in children [1–3]. The reported rate of preterm delivery in the USA has reduced in the last few years from 12–13% to around 10% in 2014 [4]. In Europe as well as other developed countries it ranges between 5 and 9% [5,6], and recent studies suggest a rate of up to 18% in some African nations [7]. Preterm delivery can be further classified according to gestational age in which it

occurred, and whether it was the result of spontaneous onset of parturition or medically indicated due to maternal and/or fetal indications. The principal factor affecting neonatal outcomes in case of preterm delivery is gestational age at delivery. The earliest it occurs, the more severe are the sequelae of prematurity [8].

In the last few decades, attention has been focused on morbidity and mortality associated with late preterm deliveries which occur between 34 weeks to 36 + 6/7 weeks [9] and account for 60–70% of all preterm births [10].

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Supplemental data for this article can be accessed [here](#)

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From 1991 to 2006, the rate of late preterm delivery has shown an increase especially due to medically indicated late preterm delivery which doubled from 8.2% to 17.3% in the USA [11]. Since 2006, overall and late preterm delivery rates have each declined by 5% and the rate for late preterm delivery comprised 8.5% of all deliveries in 2010 [11]. This trend has been described in Europe [7,12,13] as well showing the same increase related to medically indicated preterm deliveries.

Recent evidence suggests that late preterm deliveries are associated with a significant neonatal morbidity including hypoglycemia and hypothermia in the first 12 hours after birth [14,15], reduced neonatal growth [16], jaundice [17], respiratory distress [18], compared with term deliveries. In addition, late preterm delivery is associated with about 8-fold increased risk for perinatal death and 5.5-fold increased risk for neonatal death [5,19].

Among the different studies that reported the morbidity associated with late preterm delivery [20–24], only few differentiated between spontaneous and medically indicated preterm deliveries and their definitions of medically indicated and spontaneous preterm delivery as well as maternal and neonatal outcomes were inconsistent. Therefore, the aim of our large population-based cohort study was (1) to determine the prevalence of late preterm deliveries (spontaneous and medically indicated) across time as well as (2) defining the rate of maternal and neonatal morbidity and mortality associated with its different phenotypes.

Materials and methods

This population-based study was performed at Soroka University Medical Center, a tertiary teaching hospital. Although designed including data only from our Institution, our study can be defined as population-based since Soroka University Medical Center is the only tertiary center covering the entire area of the Negev (southern Israel) that occupies 60% of the land of Israel, and provides services to the entire population of the region (14.4% of Israel's population) [25].

The Department of Obstetrics and Gynecology at our medical center has a computerized database of all the deliveries; the information is captured from the patient's medical records and coded according to the international classification of Diseases-9 (ICD-9), and then introduced into the database by trained secretaries. Our database is constantly tested and validated by the Department of Epidemiology at the Ben-Gurion University of the Negev (Be'er Sheva, Israel).

The study population composed of women with singleton pregnancies who delivered ≥ 34 weeks of gestation at our medical center. Women with fetuses who had chromosomal abnormalities or structural anomalies and preterm deliveries prior to 34 weeks were excluded from the study (1242 deliveries).

Our study is a retrospective cohort study, and since the information was obtained from a database, the institutional review board of the Soroka University Medical Center approved the study without the need for obtaining informed consent from the patients. Records/information were anonymized and deidentified prior to analysis.

Maternal outcomes

Maternal outcomes included anemia, blood transfusion, chorioamnionitis, wound infection, antibiotic care, fever, placental abruption, postpartum hemorrhage.

Neonatal outcomes

Newborns were classified by their birthweight, as (1) small for gestational age (SGA) – birthweight < the 10th percentile; (2) adequate for gestational age (AGA) – birthweight from 10th to 90th percentile; and (3) large for gestational age (LGA) – birthweight > 90th percentile according to regional growth curves [26]. Pathologic Apgar score was defined as <5 at 1 min and <7 at 5 min. Neonatal acidosis was defined as cord blood pH <7.0, and/or evidence of birth asphyxia [27]. Short-term neonatal complications included: respiratory distress syndrome, sepsis, jaundice, fever, hypoglycemia, tachypnea, convulsions, polycythemia, antibiotic care, anemia, blood transfusion, cardiogenic shock, necrotizing enterocolitis (NEC), and intraventricular hemorrhage (IVH). Bronchopulmonary dysplasia (BPD), and retinopathy of prematurity (ROP) were considered as long term complications. Perinatal mortality was defined as antepartum death (APD), intrapartum death occurring during the process of delivery (IPD), and post-partum death (PPD) which was defined as any neonatal death that occurred in the first 28 days after delivery.

Clinical definitions

See [Supplementary file](#).

Statistical analysis

The statistical analysis was performed using SAS 9.4 package (SAS Institute, Cary, NA) and R software

version 3.1. Primary univariate analysis was performed by comparison among the three groups regarding neonatal and maternal outcomes using Chi Pearson's Chi-square test. Continuous variables were analyzed by Student's *t*-test or ANOVA. Continuous variables without normal distribution were analyzed with non-parametric Mann–Whitney U test or Kruskal–Wallis. Statistical significance was achieved for *p* values <.05.

For multivariate analysis generalized estimating equation (GEE) model was used to analyze the association between neonatal complications and mode of delivery (spontaneous or medically indicated), among preterm deliveries. Since some women appear a number of times in the database (due to a multiple number of deliveries), we used GEE models in which every woman constitutes a cluster in the model. Due to the interaction between mode of delivery and gestational age at delivery, the analysis was stratified according to gestational age. Variables were included in the logistic regression models if they were found to be significant in the univariate analysis and were meaningful for the clinical management of these patients. To analyze a possible nonlinear association between the rate of neonatal mortality and the proportion of medically indicated late preterm delivery, we constructed a quasi-Poisson regression model (generalized additive models, GAM), using a smoothed function (penalized spline function [28]) of the proportion of medically indicated late preterm delivery.

Results

The study cohort composed of 96,176 women who met the inclusion criteria and had 257,182 births between the years 1988 and 2011. They were allocated to the three study groups: (1) term delivery group (*n* = 242,286 deliveries); (2) spontaneous late preterm delivery (*n* = 10,063 deliveries); and (3) medically indicated late preterm delivery (*n* = 4833 deliveries) (Figure 1).

Prevalence of late preterm delivery during the study period (1988–2011)

In the observation interval, the rate of late preterm delivery was 5.79%, of them 32.4% were medically indicated late preterm deliveries (Figure 2). The rate of late preterm delivery rose mostly from 1990 reaching a peak value of more than 7% in 1996. From that point, the prevalence of late preterm delivery did not follow a specific pattern but held a steady annual rate between 5% and 6.5%. Of interest, from 2007 to 2011, there was a progressive reduction in the prevalence of

late preterm delivery (Supplementary Figure 1). The rate of spontaneous late preterm deliveries during study period varied between 56% and 75% while that of medically indicated late preterm deliveries varied from 25% to 44%. The annual change in the rate of spontaneous and medically indicated late preterm deliveries is presented in Figure 3(a,b).

In addition, when related to gestational age at the time of induction, the proportion of medically indicated late preterm delivery out of all late preterm delivery decreased from 34 weeks (35.9%) to 36 weeks (31.6%) of gestation (Figure 4).

Demographic data

Women in the spontaneous late preterm delivery group had higher rate of Bedouin ethnicity, a history of prior preterm delivery, and SGA neonates (*p* < .01, for all comparisons); while those in the medically indicated late preterm delivery group had higher frequency of infertility treatments, history of preeclampsia, and placental abruption (*p* < .01 for all comparisons), than those in the other study groups (Table 1).

Maternal and neonatal outcomes

Medically indicated late preterm deliveries were associated with increased maternal morbidity during gestation (Table 2) and higher rate of maternal intrapartum and postpartum complications (Table 3) than the other study groups.

Neonates delivered by late preterm birth had a significantly higher rate of complications compared to those delivered at term (Tables 4 and 5).

Of interest, severe neonatal complications, including neonatal mortality, neonatal complications of prematurity, and neonatal infectious morbidity were not significantly different between the spontaneous and medically indicated late preterm deliveries groups (Supplementary Table 1(a–c)).

In light of the increase in perinatal morbidity in the medically indicated late preterm delivery group, we constructed a GEE model among the preterm groups, which used a composite neonatal morbidity score as the dependent factor (Table 6). Medically indicated late preterm delivery was an independent risk factor for composite neonatal morbidity after adjustment for confounding factors (maternal age, ethnicity, and fetal gender) and stratified according to gestational age at delivery (34 weeks odds ratio (OR) 1.52, 95% confidence interval (CI) 0.97–2.37; 35 weeks OR 1.55, 95%

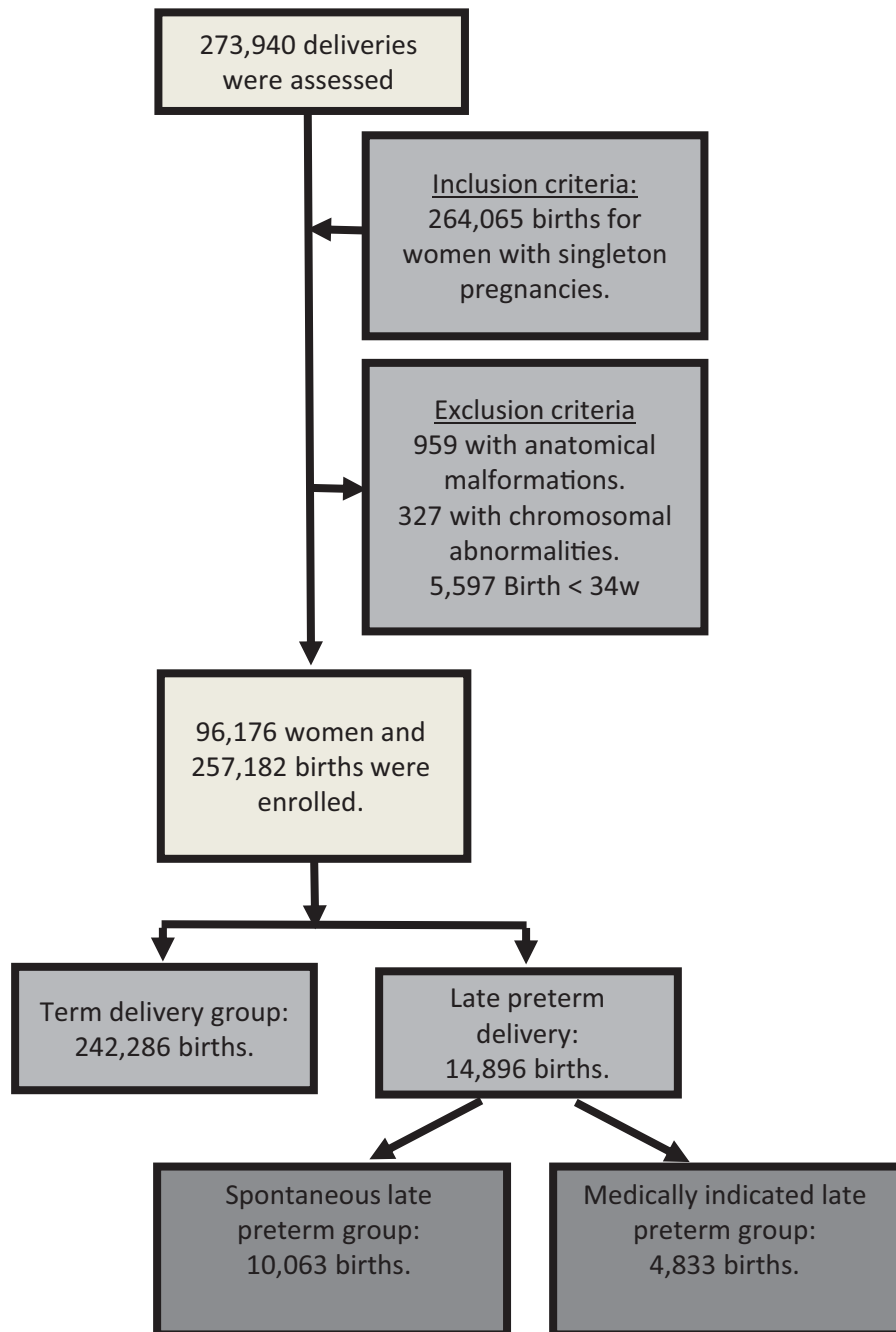


Figure 1. Study design.

CI 1.01–2.37; 36 weeks OR 2.16, 95% CI 1.53–2.30) (Table 6).

We defined another variable termed “neonatal distress” which included respiratory distress, transient tachypnea of the newborn, IVH and NEC. However, this model could not be used to determine the association between this variable and medically indicated late preterm delivery since we did not have enough cases to build a multivariate model (Supplementary Table 2).

The rate of neonatal death differed between term and late preterm delivery groups (0.2% versus 1.1%,

respectively, $p < .01$). No statistical significance was found when the same parameter was compared between medically indicated late preterm delivery and spontaneous late preterm delivery, as described in Supplementary Figure 2.

In addition, no differences were evidenced after stratifying data according to gestational age at delivery. Since there was a correlation between the rates of late preterm delivery and neonatal death ($R = 0.59$, $p = .004$) we further studied the relationship between these two parameters and constructed a GAM quasi-Poisson regression model. A penalized spline function

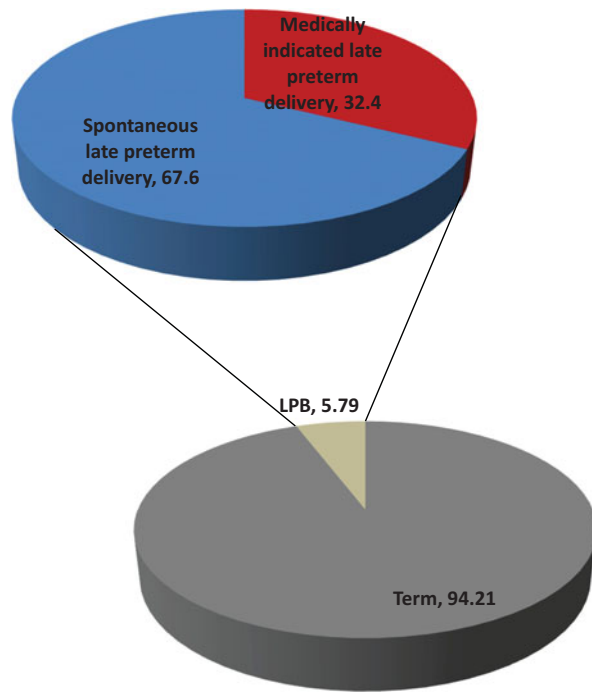


Figure 2. The prevalence of late preterm delivery during the research period – spontaneous and induced.

was used to explore a possible nonlinear association between the rate of medically indicated late preterm delivery and neonatal mortality. However, as shown in Figure 5, there was an association between these two parameters; an increase in the rate of medically indicated late preterm delivery sustained a decrease in neonatal mortality up to a rate of 35% of medically indicated late preterm delivery of all late preterm delivery. However, beyond this point, any further increase in the proportion of medically indicated late preterm delivery led to an increased neonatal mortality.

Discussion

Principal findings of the study

(1) Medically indicated late preterm delivery is associated with an increased maternal morbidity, as well as neonatal morbidity and mortality; (2) throughout the study period, we see an increase in the proportion of medically indicated late preterm delivery until 2005 and a decrease thereafter, representing the changes

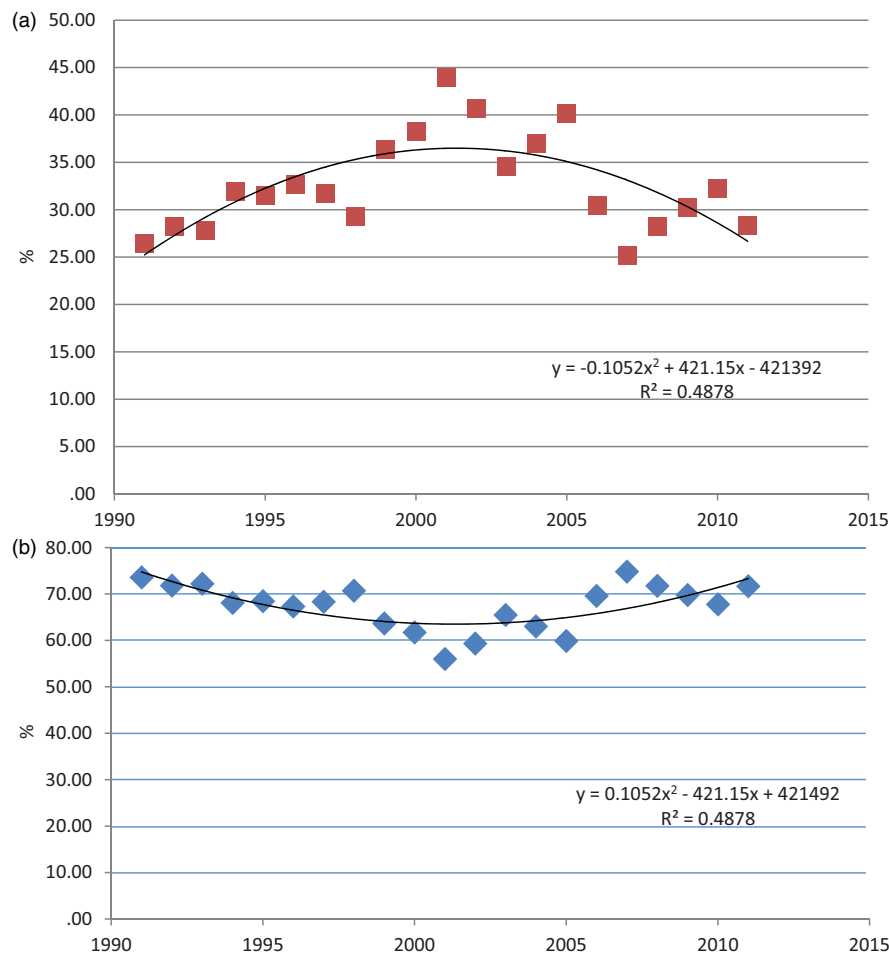


Figure 3. (a) The rate of spontaneous late preterm deliveries out of all late preterm deliveries during the study period. (b) The rate of indicated late preterm deliveries out of all late preterm deliveries during the study period.

through time of the approach toward medically indicated late preterm delivery; (3) medically indicated late preterm delivery is an independent risk factor for composite neonatal morbidity, after adjustment for confounding factors and stratification according to gestational age at delivery; and (4) of interest, the rate of neonatal mortality is affected by the proportion of medically indicated late preterm deliveries. If the

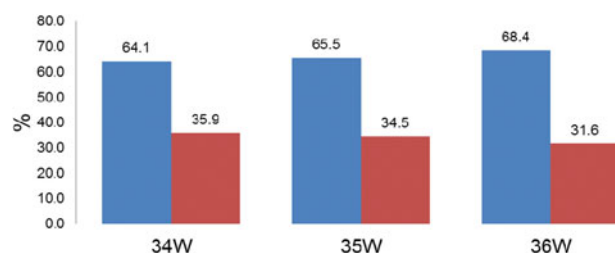


Figure 4. The rate of preterm delivery related to gestational age at the time of induction versus spontaneous preterm delivery.

proportion of medically indicated late preterm delivery exceeds 35% of all late preterm deliveries, it results in an increased neonatal mortality.

Why to induce late preterm delivery

Induction of labor is a tool used by physicians in order to prevent or treat pregnancy complications that may put the mother or her fetus at risk. Indeed, the most common indications for medically indicated late preterm delivery are preeclampsia, intrauterine growth restriction, and non-reassuring fetal heart rate [29]. Indeed, in our study, the rates of maternal and neonatal morbidity are higher in medically indicated late preterm versus spontaneous late preterm delivery, suggesting that in many of the cases, medical intervention was needed (Tables 2–5). However, evidence in the literature suggests that, due to the concept of the relatively low morbidity, especially between 35

Table 1. Demographic features.

| Variable | Term (N = 242,286 deliveries) | Spontaneous (N = 10,063 deliveries) | Medically indicated (N = 4,833 Deliveries) | p value |
|--------------------------------------|----------------------------------|--|---|---------|
| Maternal age at delivery | 28.56 ± 5.79 | 28.46 ± 6.27 | 28.78 ± 6.27 | .775 |
| Gravidity | 3 (1;20) | 3 (1;20) | 3 (1;18) | <.01 |
| Parity | 3 (1;17) | 3 (1;17) | 2 (1;17) | <.01 |
| Hospitalization, days | 2 (0;78) | 3 (0;75) | 6 (0;73) | <.01 |
| Bedouin origin | 51.6 | 58.2 | 44.1 | <.01 |
| History of preterm deliveries | 11.1 | 26.8 | 21 | <.01 |
| History of small for gestational age | 9 | 13 | 10.1 | <.01 |
| Infertility treatment | 1.7 | 2.5 | 4.3 | <.01 |
| History of preeclampsia | 2.3 | 2.7 | 5.7 | <.01 |
| History of placental abruption | 0.3 | 0.5 | 0.6 | <.01 |

Data are presented as percentage, mean ± standard deviation, median (range).

Table 2. Maternal pregnancy complications.

| Variable | Term (N = 242,286 deliveries) | Spontaneous (N = 10,063 deliveries) | Medically indicated (N = 4833 deliveries) | p value |
|-------------------------------|----------------------------------|--|--|---------|
| Placental abruption | 0.3 | 0.9 | 6.1 | <.01 |
| Placenta previa | 0.2 | 0.1 | 6.5 | <.01 |
| Abnormal presentation | 3.4 | 9.5 | 8.3 | <.01 |
| Gestational diabetes mellitus | 4.4 | 4.7 | 7.0 | <.01 |
| Diabetes mellitus | 1.0 | 2.3 | 3.2 | <.01 |
| Oligohydramnios | 2.1 | 2.3 | 7 | <.01 |
| Polyhydramnios | 3.4 | 4.4 | 4.9 | <.01 |
| Chorioamnionitis | 0.4 | 1.6 | 3 | <.01 |

Data are presented as percentage.

Table 3. Maternal intrapartum and postpartum complications.

| Variable | Term (N = 242,286 deliveries) | Spontaneous (N = 10,063 deliveries) | Medically indicated (N = 4833 deliveries) | p value |
|-----------------------|----------------------------------|--|--|---------|
| Cesarean delivery | 12 | 24.3 | 37.9 | <.01 |
| Fever during delivery | 0.1 | 0.3 | 0.1 | <.01 |
| Chorioamnionitis | 0.4 | 1.6 | 3 | <.01 |
| Infection | 0.4 | 1.5 | 1.9 | <.01 |
| Post-partum fever | 0.3 | 0.6 | 1.2 | <.01 |
| Antibiotics treatment | 2.5 | 12.3 | 12.8 | <.01 |
| Postpartum hemorrhage | 0.6 | 0.4 | 0.7 | <.01 |
| Blood transfusion | 1.2 | 1.6 | 5.1 | <.01 |
| Maternal anemia | 26.4 | 27.8 | 36.2 | <.01 |

Data are presented as percentage.

Table 4. Neonatal outcomes.

| Variable | Term (N = 242,286 deliveries) | Spontaneous (N = 10,063 deliveries) | Medically indicated (N = 4,833 deliveries) | p value |
|---|----------------------------------|--|---|---------|
| Gestational age (weeks) | 40 (37; 45) | 36 (34; 36.6) | 36 (34; 36.6) | <.01 |
| Birthweight (g) | 3262.6 ± 448.3 | 2630.8 ± 456 | 2446.8 ± 502.4 | <.01 |
| Male | 51.1 | 53.7 | 52.2 | <.01 |
| Intrauterine growth | | | | <.01 |
| SGA | 5.1 | 3.9 | 15.8 | |
| AGA | 85.4 | 83.8 | 76.2 | |
| LGA | 9.6 | 12.3 | 7.9 | |
| Non-reassuring fetal heart rate tracing | 1.4 | 0.4 | 5.6 | <.01 |
| Apgar 1' < 5 | 1.4 | 2.7 | 6.3 | <.01 |
| Apgar 5' < 7 | 0.3 | 1 | 1.9 | <.01 |
| Umbilical cord pH < 7 | 0.3 | 0.6 | 1 | <.001 |
| Respiratory distress syndrome | 0.1 | 2.5 | 2.9 | <.01 |
| Intraventricular hemorrhage | 0.0 | 0.1 | 0.1 | <.001 |
| Necrotizing enterocolitis | 0.0 | 0.1 | 0.2 | <.001 |
| Bronchopulmonary dysplasia | 0.0 | 0.0 | 0.0 | n/a |
| Retinopathy of prematurity | 0.0 | 0.0 | 0.0 | n/a |
| Jaundice | 1.2 | 18.6 | 24.2 | <.01 |
| Hypoglycemia | 0.6 | 4.5 | 6.5 | <.01 |
| Transitory tachypnea | 0.8 | 7.8 | 7.4 | <.01 |
| Antibiotics administration | 2.8 | 13.6 | 13.8 | <.01 |
| Hospitalization, days | 2 (0; 679) | 3 (0; 364) | 5 (0; 400) | <.01 |
| Median (min; max) | | | | |

Data are presented as median (range), percentage (number), mean ± standard deviation.

n/a: not available; SGA: small for gestational age; AGA: adequate for gestational age; LGA: large for gestational age.

Table 5. Neonatal complications – spontaneous versus medically indicated late preterm birth.

| Variable | Spontaneous (N = 10,063 deliveries) | Medically indicated (N = 4833 deliveries) | p value |
|--|---|--|---------|
| Apgar 1' < 5 | 2.7 (265) | 6.3 (294) | <.01 |
| Apgar 1' < 7 | 1 (92) | 1.9 (89) | <.01 |
| Jaundice | 18.6 (1689) | 24.2 (3370) | <.01 |
| Hypoglycemia | 4.5 (410) | 6.5 (288) | <.01 |
| Packed cell transfusion | 0.8 (77) | 1.4 (62) | .003 |
| Convulsions | 0.2 (22) | 0.7 (31) | <.01 |
| Asphyxia | 0.5 (46) | 1.3 (57) | <.01 |
| Acidosis | 0.6 (53) | 1.1 (50) | .001 |
| Chorioamnionitis affecting fetus | 1.7 (155) | 3 (135) | <.01 |
| Anemia | 30.1 (2741) | 37.6 (1685) | <.01 |
| Composite prematurity complications ^a | 2.4 (240) | 3 (148) | .018 |
| Hospitalization, days | 3 (9072) | 5 (4445) | <.01 |
| | 0 ; 364 | 0 ; 400 | |

^aComposite prematurity complications: account for all neonates with RDS. IVH: intraventricular hemorrhage; NEC: necrotizing enterocolitis; BPD: bronchopulmonary dysplasia; ROP: retinopathy of prematurity. Data are presented as percentage (number), mean ± standard deviation, median (range).

Table 6. Composite neonatal morbidity stratified for gestational age^a.

| Variable | 34 weeks | 35 weeks | 36 weeks |
|------------------|------------------|------------------|------------------|
| Maternal age | 1.01 (0.98–1.05) | 1.02 (0.99–1.05) | 1.02 (0.99–1.05) |
| Induced delivery | 1.52 (0.97–2.37) | 1.55 (1.01–2.37) | 2.16 (1.53–2.30) |
| Male gender | 1.44 (0.91–2.28) | 1.14 (0.75–1.75) | 1.35 (0.96–1.90) |
| Bedouin origin | 1.62 (1.01–2.59) | 1.67 (1.08–2.57) | 1.81 (1.27–2.59) |

Data are presented as adjusted odds ratio (OR) (95% CI).

^aComposite neonatal morbidity: accounts for all neonates with- low Apgar score at 5', seizures, asphyxia, acidosis; after adjustment for confounding factors (maternal age, neonatal origin and gender), and stratified according to gestational age.

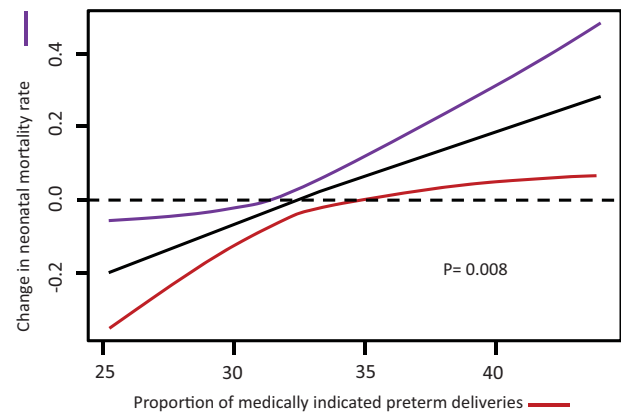


Figure 5. The change in neonatal mortality according to the rate of indicated late preterm delivery. Caption: Linear association between these changes in neonatal mortality rate and proportion of indicated preterm deliveries. As shown in the figure, up to a rate of 35% of indicated late preterm deliveries, there was a decrease in neonatal mortality, while a higher rate of indicated late preterm deliveries was associated with an increased neonatal mortality.

and 36 weeks of gestation, the tool of medically indicated late preterm delivery may have been overused. Indeed, a survey in 2009 indicated that about 23% of late preterm delivery in the USA had no indication for delivery [20].

This is also reported by Bouchet et al. [12] that employed a categorization to understand if medically indicated late preterm birth was based on evidenced-based or non-evidence-based indication. These authors conducted an 11-year retrospective cohort study and

observed that 54% of all medically indicated late preterm deliveries were non-evidenced based, meaning that the tool of late preterm delivery was overused.

In the recent decades, there is a substantial increase in the rate of medically indicated late preterm deliveries [30]. Indeed, the findings regarding our tertiary center reflect this tendency, with an increase in the rate of medically indicated late preterm delivery until the early 2000s (Figure 3(a,b)).

This was based on two accounts: (1) the reports suggesting that medically indicated late preterm delivery reduces the overall perinatal mortality. Ananth et al. [30,31] observed a relative decline of 35% in perinatal mortality rate that was subsequent to the increase in medically indicated preterm delivery. The neonatal mortality rate decreased from 7.8 per 1000 total deliveries in 1989 to 5.4 per 1000 total deliveries in 2000 (RR 0.70, 95% CI 0.69–0.71), while the rate of medically indicated preterm delivery increased from 2.6% to 3.8% during the same period [31–33]; and (2) the paradigm that only moderate and severe prematurity are associated with substantial neonatal morbidity. Evidence in support of that is the fact that the prevention of preterm delivery actually includes or sets as a goal the reduction of preterm births prior to 34 weeks or earlier [34] and the fact that the current recommendations of the professional societies is to deliver patients with preterm PROM between 34 and 37 weeks [35,36].

What is the price of medically indicated late preterm delivery

Accumulating reports suggest that late preterm delivery is associated with higher rates of neonatal morbidity (mainly respiratory) [37], long-term sequelae like cerebral palsy [38], and even mortality [19] than those observed in neonates delivered at term [39]. These findings led to the notion that induction of labor during the late preterm period may sometimes be associated with adverse neonatal outcomes and should be carefully considered [19,37,38,40–42]. Moreover, many of these reports study outcomes of late preterm delivery as an unique population, without dividing spontaneous from medically indicated late preterm delivery, and those who do that do not provide a clear definition for these phenotypes of late preterm parturition [20–24].

Medically indicated late preterm delivery carries, as every medical intervention, a certain price to pay and in this case it is shared between the mother and her newborn. As we demonstrate herein, medically indicated late preterm delivery is associated with a higher

rate of maternal anemia, blood transfusion, cesarean section, infection, chorioamnionitis, endometritis, postpartum fever and sepsis, compared with spontaneous late preterm delivery. Moreover, women who had medically indicated late preterm delivery suffered from a higher rate of adherent placenta, manual removal of the placenta and peripartum hysterectomy. In addition, newborns of women with medically indicated late preterm delivery had a higher rate of low Apgar scores, jaundice, hypoglycemia, anemia and blood transfusion, seizures, asphyxia, acidosis, composite prematurity outcome, a longer median duration of hospitalization, and a higher risk for composite neonatal morbidity. These findings are in accord with other recent studies that compared the outcomes of medically indicated late preterm delivery versus labor and delivery at term [21,43].

What is the optimal rate of medically indicated late preterm delivery in term of neonatal mortality?

To address this issue, we designed a quasi-Poisson model that included the rate of medically indicated preterm delivery, neonatal mortality, and adjustment for gestational age at delivery. This analysis demonstrated that if the rate of medically indicated late preterm deliveries out of all late preterm deliveries exceeds 35% it is associated with increased neonatal death, while lower rates are associated with decreased neonatal mortality, suggesting that medically indicated late preterm delivery can be a double edged sword. Indeed, this novel finding suggests that medically indicated late preterm delivery should be used carefully, for selected indications, in order to avoid that point where we do more harm than good. Recently active measures have been taken in some countries to assure better justification for medically indicated late preterm delivery, and clinical opinions and guidelines referring to who should be induced at the late preterm period have been published [44].

Strength and limitations of the study

This is a large population-based study including a large cohort of more than 200,000 deliveries over a period of more than 20 years, that gives true representation of even rare complications of late prematurity. The fact that our study is based on a database registry has its limitations: for example, we do not have the information regarding the cervical conditions in which induction was started and data regarding the process of parturition in spontaneous late preterm delivery

and medically indicated late preterm delivery are missing. Nevertheless, the information included in this database was collected from a specially designed collecting form that will allow highly trained secretaries to truly represent the clinical diagnosis of the patient with high degree of accuracy in order to overcome the pitfall of inconsistency existing in other large databases that has been collected over time. This is in agreement with Iams' editorial suggesting that distinguishing spontaneous and medically indicated preterm deliveries is a challenge, when using large retrospective databases, since it poses a limitation in elucidating the reasons for obstetrical intervention [45].

Conclusions

Our study shows that medically indicated and spontaneous late preterm deliveries differ in their demographic and clinical characteristics. In addition, medically indicated late preterm delivery is independently associated with adverse composite neonatal outcome, in agreement with the recent literature. Of interest, neonatal mortality increases when the rate of medically indicated late preterm delivery exceeds 35% of all late preterm deliveries. A further verification of this cutoff is needed but, if verified, it might be useful as a parameter in the assessment of the quality of perinatal care.

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