Neonatal outcome of pregnancies complicated by hypertensive disorders

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OBSTETRICS

Neonatal outcome of pregnancies complicated by hypertensive disorders between 34 and 37 weeks of gestation: a 7 year retrospective analysis of a national registry

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OBJECTIVE: The objective of the study was to determine the neonatal morbidity in late preterm infants born from mothers with a hypertensive disorder.

STUDY DESIGN: Data were obtained from the national Perinatal Registry in The Netherlands on women who delivered between 34^{+0} and 36^{+6} weeks with gestational hypertension (n = 4316), preeclampsia (n = 1864), and normotensive controls (n = 20,749).

RESULTS: Children from mothers with preeclampsia had an increased risk for admission to the neonatal intensive care unit compared with children from normotensive mothers (odds ratio [OR], 2.0; 95% confidence interval [CI], 1.8–2.2). A cesarean delivery and decreasing gestational age were independent risk factors for neonatal respiratory morbidity. Gestational hypertension or preeclampsia reduced the risk of respiratory distress syndrome compared with the control group (OR, 0.81; 95% CI, 0.64–1.0 and OR, 0.69; 95% CI, 0.49–0.96, respectively).

CONCLUSION: Neonatal morbidity in the late preterm period is considerable. Hypertensive disorders appear to protect for neonatal respiratory morbidity, but higher rates of cesarean section diminish this protective effect.

Key words: newborn, preeclampsia, preterm, respiratory distress syndrome

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The majority of hypertensive disorders of pregnancy (gestational hypertension [GH], preeclampsia [PE]) present at term or late preterm, only 10% occur before 32 weeks.[1] Hypertension in pregnancy is associated with severe complications such as eclampsia, placental abruption, HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome, preterm delivery, or even fetal or maternal death.[1-3] The probability of adverse perinatal outcome increases with lower gestational age.[4,5]

The only causal treatment for hypertensive disorders of pregnancy is to deliver the baby. There is a general consensus that in pregnancies complicated by early preeclampsia (eg, <32 weeks' gestational age), temporizing management with close monitoring of the mother and fetus is justified, and prolongation of pregnancy can be achieved without irreversible maternal morbidity and with improved neonatal outcome.[6,7] In contrast, in women with mild GH or PE at term, induction of labor resulted in a decrease of progression to severe disease or complications as well as a decreased number of cesarean sections compared with temporizing management.[8] Moreover, induction of labor showed a trend to a better neonatal outcome.

Until now, only a few studies have focused on the management of women with hypertensive disorders between 34^{+0} and 36^{+6} weeks of gestational age. The National Institute for Health and Clinical Excellence (NICE) guideline for hypertensive disorders during pregnancy refers in the 2010 consensus statement to the issue of mild or moderate preeclampsia between 34 and 36 weeks of gestation in terms of a gray zone at which the optimal timing of birth is not clear.[9] Babies born late preterm (eg, 34^{+0} to 36^{+6} weeks' gestational age) account for more than 70% of the preterm deliveries (<37 weeks).[10] There are reports

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that these late preterm children have significantly more morbidity than babies born at term.[11-17] However, it is unknown whether this finding also applies to infants born from mothers with a hypertensive disorder because in most studies these women were excluded from analysis. This also makes it difficult to determine the optimal obstetric management for these patients.

To improve our understanding on the neonatal outcome of this specific population and its causative factors, we analyzed the data on neonatal morbidity in infants born from mothers with a hypertensive disorder between 34 and 37 weeks' gestation from the Dutch National Registry, compared with morbidity rates of children born between 34 and 37 weeks' gestation from normotensive mothers.

Materials and Methods

Study population

Data were obtained from the Netherlands Perinatal Registry (PRN registry) between January 2000 and December 2006.[18] Since 2000 all gestation/delivery records (National Delivery Record [LVR]), both home deliveries (LVR-1 registry) and hospital deliveries (LVR-2 registry), are combined with neonatal admission records (National Neonatal Register [LNR]) into a national perinatal register (PRN). Méray et al[19] and Tromp et al[20] have extensively described the technical approach and subsequent validation of the probabilistic linkage of these 3 anonymous population-based registries of the midwives, obstetricians, and neonatalogists.

The LVR-1 and LVR-2 register have a 96% national coverage on all births (approximately 180,000 deliveries per year at more than 16 completed weeks of gestation in The Netherlands). The LNR registry has a 68% coverage of all hospitals in The Netherlands of whom the 10 perinatal centers have a coverage of 100% and the other hospitals have 58%.

For the present study, we included all women who delivered between 34^{+0} and 36^{+6} weeks of gestation. Exclusion criteria were chronic hypertension, multiple pregnancies, noncephalic presentation, congenital malformations, mothers diagnosed with AIDS, diabetes, or drug use (drugs, not cannabis), and more than 24 hours of rupture of membranes (in The Netherlands an expectant monitoring management is often followed for this latter group in the late preterm period).

These exclusion criteria were selected because these specific conditions themselves are related to neonatal morbidities. If neonatal follow-up was not available, data were excluded. From the available data, subjects whom the mothers were diagnosed with gestational hypertension (GH group) or preeclampsia (PE group) were selected in. The other patients were the normotensive control group (preterm delivery without a reason).

GH was defined as de novo hypertension, occurring after 20 weeks' gestational age. Hypertension is defined as a diastolic blood pressure of 90 mm Hg or greater or a systolic blood pressure of 140 mm Hg or greater. PE was defined as de novo hypertension after 20 gestational weeks and proteinuria ($\geq$300 mg/day or a spot urine protein/creatinine ratio of $\geq$30 mg/mmol).[21] Patients could be included based only on their diastolic blood pressure and on the amount of proteinuria. The systolic blood pressure is not an item in this national database. This means that we might have missed a small group of patients that did not reach a diastolic blood pressure of 90 mmHg or greater during their entire pregnancy. According to the national guidelines, calculation of gestational age was based on the first day of the last menstrual period and verified by a routinely performed first-trimester ultrasound in all patients.[22]

Maternal baseline characteristics recorded were maternal age, ethnicity, and parity. Variables recorded were gestational age at delivery, birthweight, small for gestational age (SGA; defined as birthweight below the 10th percentile adjusted for gestational age based on a local reference population), and a 5 minute Apgar score less than 7.0.

Poor neonatal outcome included admission to the neonatal intensive care unit (NICU), metabolic and gastrointestinal morbidity subdivided in hypoglycemia (defined as glucose serum or plasma level $<$2.5 mmol/L), hyperbilirubinemia (indirect hyperbilirubinemia defined as above the phototherapy level, direct hyperbilirubinemia defined as $>$10% of the total serum bilirubine), or any stage of necrotizing enterocolitis (NEC).[23]

Respiratory problems were subdivided in the need for oxygen therapy more than 24 hours, any grade of infant respiratory distress syndrome (RDS; based on radiographic thorax findings according to Giedeon grade I-IV), bronchopulmonary disease (BPD; defined as more than 28 days of oxygen therapy or oxygen therapy after 36 postmenstrual weeks), transient tachypnoe of the newborn (TTN; based on the typical clinical picture [respiratory support that is rapidly weaned within the first 24 hours of life]), and chest radiograph (high lung volume).[24]

Neurologic morbidity was subdivided into intracranial hemorrhage including intraventricular hemorrhage (defined according to Papile [grade I: hemorrhage subependymal–germinal matrix; grade II: intraventricular hemorrhage with normal ventricle size; grade III: intraventricular hemorrhage with ventricular dilation; and grade IV: parenchymal hemorrhage]); cerebral ischemia subdivided in any grade of periventricular leucomalacia (PVL; based on ultrasound images or magnetic resonance imaging) or ischemia other than PVL any stage of hypoxic ischemic encephalopathy (HIE); or convulsions.[25,26] For this study only the first admission data after birth were used.

Analysis

The study population was categorized in 3 groups: GH, PE, and the normotensive control group. In later analysis, the 3 study groups were further subdivided by 3 groups of gestational age (GA) per week: delivered at 34^{+0} to 34^{+6} GA; 35^{+0} to 35^{+6} and 36^{+0} to 36^{+6} GA.

Data are presented as n (percentage) and in mean ($\pm$SD), as appropriate. We used χ^2 to test for categoric data and Student t test or 1-way analysis of variance (in case of more than 2 variables) for continuous variables. Two-sided proba-

TABLE 1
Onset of labor between 34^{+0} and 36^{+6} weeks of gestational age in normotensive control mothers, GH, and PE mothers

Onset of labor	Control				GH				PE				
Gestational age, wks	34^{+0-6}	35^{+0-6}	36^{+0-6}	Total	34^{+0-6}	35^{+0-6}	36^{+0-6}	Total	34^{+0-6}	35^{+0-6}	36^{+0-6}	Total	*P* value
Proportion of deliveries	3238 (16)	5697 (27)	11,814 (57)	20,749 (100)	741 (17)	1243 (29)	2332 (54)	4316 (100)	430 (23)	560 (30)	874 (47)	1864 (100)	
Spontaneous start of labor	2776 (86)	5051 (89)	10,458 (89)	18,285 (88)	352 (48)	705 (57)	1362 (58)	2419 (56)	55 (13)	80 (14)	202 (23)	337 (18)	< .0001
Induction of labor	140 (4.3)	250 (4.4)	689 (5.8)	1079 (5.2)	117 (16)	260 (21)	660 (28)	1037 (24)	135 (31)	262 (47)	486 (56)	883 (47)	< .0001
Primary cesarean section	322 (9.9)	396 (7.0)	667 (5.7)	1385 (6.7)	272 (37)	278 (22)	310 (13)	860 (20)	240 (56)	218 (39)	186 (21)	644 (35)	< .0001

Data are presented as n (percentage) of deliveries. Spontaneous start of labor includes spontaneous start of contractions and/or spontaneous rupture of membranes. Induction of labor includes the use of prostaglandins and/or oxytocin and/or artificial rupture of membranes.
GH, gestational hypertension; *PE,* preeclampsia.

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bility of less than .05 was considered statistically significant. Data are expressed in odds ratio (ORs) and 95% confidence intervals (CIs).

A multivariable logistic regression analysis was performed to examine respiratory morbidity outcomes across maternal subgroups (GH, PE, and control) controlling for gestational age in 3 weeks groups (34, 35, and 36 weeks) and for onset or mode of delivery (in 7 groups). We checked for 2 possible interaction effects; first, we tested for interaction between the study group (GH, PE, and control) and gestational age in weeks and second, between the study group and mode of delivery.

Reference groups were the groups with the lowest risk. In addition, we adjusted in the multivariable analysis for parity, maternal ethnicity, and SGA. Data of the multivariable analysis are expressed in ORs with 95% CIs. All analyses were performed using SAS software (version 9.2; SAS Institute, Cary, NC).

RESULTS

From January 1, 2000, until December 31, 2006, a total of 1,246,440 singleton pregnancies were identified in the PRN database. After application of our inclusion and exclusion criteria, 26,929 deliveries were the study population: 4316 women in the GH group (16%); 1864 in the PE group (7%); and 20,749 in the control group (77%).

Differences in onset of labor between groups are shown in Table 1. Both induction of labor and primary cesarean section occurred more frequently in the PE group compared with the GH group, with ORs of 2.8 (95% CI, 2.5–3.2) and 2.1 (95% CI, 1.9–2.4), respectively. Compared with the control group, the risk of induction of labor and primary cesarean section was increased even more strongly (OR, 16; 95% CI, 15–18 and OR, 7.4; 95% CI, 6.6–8.2).

Baseline maternal and neonatal characteristics of all groups are outlined in Table 2. All data were significantly different among the 3 groups. Birthweight was significantly different between groups: 2686 ± 425, 2482 ± 510, and 2248 ± 461 g in the control, GH, and PE mothers, respectively ($P < .001$). SGA was significantly more diagnosed in the PE group (27%) than in the GH group (18%; OR, 1.7; 95% CI, 1.5–1.9) and the control group (5.3%; OR, 6.7; 95% CI, 5.9–7.5). More children in the PE group were admitted to the NICU compared with the GH and control groups: OR, 1.6 (95% CI, 1.4–1.9) and relative risk 2.0 (95% CI, 1.8–2.2), respectively.

Table 3 presents the neonatal outcome for each gestational age group in the normotensive control, GH, and PE groups.

The incidences of hypoglycemia, hyperbilirubinemia, and NEC were not significantly different between the PE and GH groups. However, there was a small but significant difference between the PE and control groups for hypoglycemia (OR, 1.5; 95% CI, 1.3–1.7) and for NEC (OR, 5.0; 95% CI, 2.1–11). Throughout the groups there was a gestational age effect for hyperbilirubinemia and NEC (decreases with advancing gestational age) but not for hypoglycemia.

The incidence of 24 or more hours oxygen therapy was significantly different between the groups with an OR of 1.9 (95% CI, 1.6–2.2), between the PE and the control group and an OR of 1.6 (95% CI, 1.3–1.9), and between the PE and the GH groups. The incidence of RDS was not significantly different between the 3 groups. The PE group more often experienced TTN compared with the control (OR, 1.5; 95% CI, 1.2–1.9) and with the GH group (OR, 1.5; 95% CI, 1.1–1.9). The incidence of BPD was very low in all 3 groups. The risk for respiratory morbidity was inversely related to the gestational age.

The overall incidence of neurologic morbidity was low. The incidences of HIE, cerebral ischemia (not PVL), PVL, and convulsions were not significantly different between all groups. In the PE group, there was an increased risk for intracranial hemorrhage compared with the control group (OR, 2.2; 95% CI, 1.0–4.8). Compared with the GH group, incidences were not significantly different. The gestational effect was also present in the neurologic morbidity (decreasing with advancing gestational age).

For the multivariable logistic regression analysis, interaction between all independent variables were checked. There were no interaction effects between groups. The incidences of the neurologic and metabolic/gastrointestinal morbidities were very low and therefore not calculated. The multivariable analy-

TABLE 2
Maternal and neonatal baseline characteristics of the cohort per category normotensive (control), GH, and PE mothers

Maternal and neonatal characteristics[a]	Control	GH	PE	Total	*P* value
Deliveries[a]	20,749 (77)	4316 (16)	1864 (6.9)	26,929 (100)	
Gestational age at delivery, wks[b]	35.8 (0.78)	35.7 (0.79)	35.5 (0.84)	35.7 (0.79)	
Maternal characteristics					
Maternal age at delivery, y[b]	29.8 (5.0)	30.6 (4.8)	29.9 (5.1)	29.9 (5.0)	< .0001
White ethnicity[a]	17,430 (84)	3874 (90)	1503 (81)	22,807 (85)	< .0001
Primiparous[a]	11,690 (56)	2853 (66)	1303 (70)	15,846 (59)	< .0001
Neonatal characteristics					
Birthweight, g[b]	2686 (425)	2482 (510)	2248 (461)	2623 (460)	< .0001
SGA	1099 (5.3)	776 (18)	508 (27)	2383 (8.9)	< .0001
5 minute Apgar score <7[a]	735 (3.5)	197 (4.6)	82 (4.4)	1014 (3.8)	.002
NICU admission ≥24 h[a]	2666 (13)	684 (16)	419 (22)	3769 (14)	< .0001

SGA was defined as birthweight below the 10th percentile adjusted for gestational age based on a local reference population.
GH, gestational hypertension; *PE*, preeclampsia; *SGA*, small size for gestational age.
[a] Data are presented as n (percentage) of deliveries; [b] Date are presented as mean ± SD.
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sis showed an increased risk on respiratory morbidity with decreasing gestational age (Table 4). With the control group as a reference, the odds on a respiratory morbidity decreased in case of any hypertensive disorder. The adjusted ORs for RDS were 0.81 (95% CI, 0.64–1.0) and 0.69 (95% CI, 0.49–0.96) in the GH and PE group, respectively.

For TTN the ORs were 0.81 (95% CI, 0.67–0.98) and 0.91 (95% CI, 0.70–1.2) in the GH and PE groups, respectively. The adjusted ORs for 24 or more hours of oxygen therapy were 0.87 (95% CI, 0.76–0.99) and 1.0 (95% CI, 0.84–1.2) in the GH and PE groups, respectively. Cesarean delivery was consistently associated with higher odds on a respiratory morbidity.

COMMENT

In this large retrospective analysis, we analyzed the morbidity on late preterm neonates born between 34^{+0} and 36^{+6} weeks of gestation because of a hypertensive disorder of the mother, compared with normotensive controls. Children from mothers with PE or GH are more often SGA, experience more morbidity and have higher NICU admission rates compared with the neonates born from normotensive mothers. The incidences of gastrointestinal and neurologic morbidity were very low (below 1%) for all 3 groups at all gestational ages.

Neonatal morbidity increased significantly within all 3 groups when gestational age was decreasing. As gestational age was approaching the term period, respiratory morbidity decreased significantly (below 1%). The multivariable analysis confirmed lower gestational age as an independent risk factor for respiratory morbidity. This result is in concordance with the recent publication of Hutcheon et al[27] reporting on neonatal morbidity between 36 and 41 weeks of gestational age in women with gestational hypertension.

From literature we know that the incidence on neonatal respiratory morbidity is increased if mode of delivery is by cesarean delivery compared with a vaginal delivery.[28-30] Also in our study the multivariable analysis indicates a primary cesarean delivery as an independent risk factor for respiratory morbidity. Consequently, the most logical explanation for the lower odds on respiratory morbidity in the multivariable analysis for the GH and PE groups (compared with the non-significant different incidences between the 3 groups in Table 3) is the correction for mode of delivery in the multivariable analysis (thus correcting for an independent factor that increases the risk on respiratory morbidity). The rate of primary cesarean section was much higher in the GH and PE groups, compared with the control group. This is a potential source of bias because cesarean section is probably associated with clinical severity of the hypertensive disorders of pregnancy.

The strength of this study is the size of the cohort, including patients over a long but recent period (2000 until 2006). Data are derived from a reliable and validated population-based data system. It includes almost all deliveries in the country and is therefore a good reflection of current clinical decision making.

Our study also has some limitations. First, the reliability of our data depends on the preciseness of registration of obstetricians and pediatrics. The size of the database minimizes this influence. Second, missing neonatal follow-up in the PRN excluded almost 30% of the cohort. We assume that the incidence of the neonatal morbidity in these hospitals does not differ from those who do have a reg-

TABLE 3
Neonatal outcome of normotensive (control), GH, and PE mothers between 34^{+0} and 36^{+6} weeks of gestation

Neonatal outcome	Control				GH				PE			
Gestational age, wks	34^{+0-6}	35^{+0-6}	36^{+0-6}	Total	34^{+0-6}	35^{+0-6}	36^{+0-6}	Total	34^{+0-6}	35^{+0-6}	36^{+0-6}	Total
Proportion of deliveries	3238 (16)	5697 (27)	11814 (57)	2,0749 (100)	741 (17)	1243 (29)	2332 (54)	4316 (100)	430 (23)	560 (30)	874 (47)	1864 (100)
Metabolic/ gastrointestinal morbidity												
Hypoglycemia	240 (7.4)	504 (8.9)	917 (7.8)	1661 (8.0)	84 (11)	128 (10)	238 (10)	450 (10)	36 (8.4)	60 (11)	118 (14)	214 (11)
Hyperbilirubinemia	940 (29)	1209 (21)	967 (8.2)	3116 (15)	181 (24)	255 (21)	208 (8.9)	644 (15)	93 (22)	83 (15)	104 (12)	280 (15)
NEC	5 (0.15)	8 (0.14)	5 (0.04)	18 (0.09)	3 (0.40)	3 (0.24)	3 (0.13)	9 (0.21)	5 (1.2)	2 (0.36)	1 (0.11)	8 (0.43)
Respiratory morbidity												
Oxygen therapy ≥24 h	527 (16)	469 (8.2)	410 (3.5)	1406 (6.8)	129 (17)	118 (9.5)	90 (3.9)	337 (7.8)	90 (21)	74 (13)	57 (6.5)	221 (12)
RDS	248 (7.7)	141 (2.5)	85 (0.72)	474 (2.3)	50 (6.8)	33 (2.7)	18 (0.8)	101 (2.3)	29 (6.7)	18 (3.2)	4 (0.46)	51 (2.7)
BPD	1 (0.03)	0 (0.00)	0 (0.00)	1 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (0.23)	0 (0.00)	0 (0.00)	1 (0.05)
TTN	175 (5.4)	234 (4.1)	297 (2.5)	706 (3.4)	39 (5.3)	56 (4.5)	53 (2.3)	148 (3.4)	31 (7.2)	31 (5.5)	31 (3.6)	93 (5.0)
Neurologic morbidity												
Intracranial hemorrhage	19 (0.59)	12 (0.21)	9 (0.08)	40 (0.19)	8 (1.1)	2 (0.16)	4 (0.17)	14 (0.32)	3 (0.70)	1 (0.18)	4 (0.46)	8 (0.43)
HIE	15 (0.46)	15 (0.26)	20 (0.17)	50 (0.24)	9 (1.2)	3 (0.24)	4 (0.17)	16 (0.37)	3 (0.70)	0 (0.00)	6 (0.69)	9 (0.48)
Cerebral ischemia (not PVL)	9 (0.28)	5 (0.09)	7 (0.06)	21 (0.10)	5 (0.67)	1 (0.08)	3 (0.13)	9 (0.21)	0 (0.00)	0 (0.00)	2 (0.23)	2 (0.11)
PVL	12 (0.37)	9 (0.16)	2 (0.02)	23 (0.11)	5 (0.67)	2 (0.16)	1 (0.04)	8 (0.19)	2 (0.47)	0 (0.00)	2 (0.23)	4 (0.21)
Convulsions	13 (0.40)	14 (0.25)	16 (0.14)	43 (0.21)	6 (0.81)	10 (0.80)	10 (0.43)	26 (0.60)	0 (0.00)	3 (0.54)	5 (0.57)	8 (0.43)

Data are presented as n (percentage).
BPD, bronchopulmonary disease; *GH,* gestational hypertension; *HIE,* hypoxic ischemic encephalopathy; *NEC,* necrotizing enterocolitis; *PE,* preeclampsia; *PVL,* periventricular leucomalacia; *RDS,* respiratory distress syndrome; *TTN,* transient tachypnea of the newborn.

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istered neonatal follow-up. Both type of hospitals are equally distributed over the country, use the same national guidelines, and are financed similarly. Some data of interest were not available (systolic blood pressure and the administration of corticosteroids).

The lack of the systolic blood pressure may have resulted in missing a small group of patients that did not reach a diastolic blood pressure of 90 mm Hg or greater after 20 weeks' gestational age. These patients might have been included in the control group. Because this is a small group of patients we do not believe this will significantly influence the results.

The lack of information on administered corticosteroids is another omission in the data set. Standard care in The Netherlands is not to give corticosteroids after 34 weeks of gestation, so the number of patients who received corticosteroids (before 34 weeks) is probably a very small group. It might be speculated that patients who are admitted to the hospital before 34 weeks but who delivered after 34 weeks did get corticosteroids. Furthermore, the protective effect of hypertensive disorders on respiratory morbidity was present through all gestational ages.

In what perspective should we see this potential protective mechanism of a hypertensive disorder on neonatal respiratory morbidity? Conflicting results on the true effect of hypertensive disorders on neonatal respiratory morbidity are reported.[31-33] Studies that did not correct for mode of delivery in their analysis report a higher risk on a neonatal respiratory disorder when hypertensive disorders are present.[32] However, the studies that corrected for mode of delivery did not show a higher risk on neonatal respiratory disorders or even a protective effect. [31,33] This latter result is supported by our study.

Because mode of delivery seems to be an important influencing factor on the outcome, one could speculate that in case of a hypertensive disorder of the mother in the late preterm period, induction of labor is preferable before deterioration of the maternal condition occurs and a primary cesarean section is the only solution for fast improvement of the maternal condition. Choosing the right moment for delivery, though, remains a difficult task for the obstetrician. With increasing gestational age, neonatal morbidity will decrease but with increasing risk for maternal deterioration. In this perspective, the superior strategy is a randomized controlled trial comparing induction of labor with temporizing management. A lesser alternative could be a prospective closed cohort study.

In conclusion, neonatal morbidity in babies born from mothers with hypertensive disorders is still considerable in the late preterm period, which is pre-

TABLE 4
Multivariable logistic regression analysis respiratory morbidity across subgroups

Variable	RDS, adjusted OR (95% CI)[a]	TTN, adjusted OR (95% CI)[a]	≥24 hours oxygen therapy, adjusted OR (95% CI)[a]
Gestational age, wk			
36	1.0 (reference)	1.0 (reference)	1.0 (reference)
35	3.6 (2.8–4.6)	1.6 (1.4–1.9)	2.4 (2.1–2.7)
34	11 (8.4–13)	2.0 (1.7–2.4)	4.7 (4.2–5.3)
Maternal group			
Normotensive control group	1.0 (reference)	1.0 (reference)	1.0 (reference)
Hypertensive mothers	0.81 (0.64–1.0)	0.81 (067–0.98)	0.87 (0.76–0.99)
Preeclamptic mothers	0.69 (0.4–0.96)	0.91 (0.70–1.2)	1.0 (0.84–1.2)
Onset and mode of delivery			
Spontaneous start to spontaneous delivery	1.0 (reference)	1.0 (reference)	1.0 (reference)
Spontaneous start to assisted vaginal delivery	0.97 (0.67–1.4)	1.3 (1.0–1.7)	1.3 (1.0–1.5)
Spontaneous start to secondary cesarean	1.9 (1.3–2.8)	2.4 (1.8–3.1)	3.0 (2.5–3.7)
Induced labor to spontaneous delivery	1.5 (1.0–2.1)	1.1 (0.79–1.5)	1.1 (0.91–1.4)
Induced labor to assisted vaginal delivery	1.4 (0.49–3.7)	1.8 (1.0–3.3)	1.1 (0.64–1.9)
Induced labor to secondary cesarean	1.9 (1.1–3.3)	2.8 (2.0–4.0)	2.5 (1.9–3.2)
Primary cesarean	3.1 (2.5–3.8)	3.1 (2.6–3.7)	3.6 (3.2–4.1)

Spontaneous start of labor includes spontaneous start of contractions and/or spontaneous rupture of membranes. Induction of labor includes the use of prostaglandins and/or oxytocin and/or artificial rupture of membranes.
CI, confidence interval; *OR,* odds ratio; *RDS,* respiratory distress syndrome; *SGA,* small size for gestational age; *TTN,* transient tachypnea of the newborn.

[a] Adjusted for parity, ethnicity, and SGA.

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dominantly driven by gestational age and mode of delivery. Very interestingly, in our study the presence of a hypertensive disorder per se seems to protect for neonatal respiratory morbidity. However, this protective effect is diminished by the higher cesarean rate in this group, even resulting in higher incidences of respiratory morbidity in case of a hypertensive disorder. ■

REFERENCES

1. Sibai B, Dekker G, Kupferminc M. Pre-eclampsia. Lancet 2005;365:785-99.
2. Sibai BM. Diagnosis and management of gestational hypertension and preeclampsia. Obstet Gynecol 2003;102:181-92.
3. Schutte JM, Schuitemaker NW, van Roosmalen J, Steegers EA; Dutch Maternal Mortality Committee. Substandard care in maternal mortality due to hypertensive disease in pregnancy in The Netherlands. BJOG 2008;115:732-6.
4. Ganzevoort W, Rep A, de Vries JI, Bonsel GJ, Wolf H: PETRA investigators. Prediction of maternal complications and adverse infant outcome at admission for temporizing management of early-onset severe hypertensive disorders of pregnancy. Am J Obstet Gynecol 2006;195:495-503.
5. Chappell LC, Enye S, Seed P, Briley AL, Poston L, Shennan AH. Adverse perinatal outcomes and risk factors for preeclampsia in women with chronic hypertension: a prospective study. Hypertension 2008;51:1002-9.
6. Sibai BM, Mercer BM, Schiff E, Friedman SA. Aggressive versus expectant management of severe preeclampsia at 28 to 32 weeks' gestation: a randomized controlled trial. Am J Obstet Gynecol 1994;171:818-22.
7. Hall DR, Odendaal HJ, Kirsten GF, Smith J, Grové D. Expectant management of early onset, severe pre-eclampsia: perinatal outcome. BJOG 2000;107:1258-64.
8. Koopmans CM, Bijlenga D, Groen H, et al. Induction of labour versus expectant monitoring for gestational hypertension or mild pre-eclampsia after 36 weeks' gestation (HYPITAT): a multicentre, open-label randomised controlled trial. Lancet 2009;374:979-88.
9. NICE guidelines. Hypertension in pregnancy: the management of hypertensive disorders during pregnancy. Available at: www.nice.org.uk. Accessed Aug. 1, 2010.
10. Davidoff MJ, Dias T, Damus K, et al. Changes in the gestational age distribution among US singleton births: impact on rates of late preterm birth, 1992 to 2002. Semin Perinatol 2006;30:8-15.
11. Escobar GJ, Clark RH, Greene JD. Short-term outcomes of infants born at 35 and 36 weeks gestation: we need to ask more questions. Semin Perinatol 2006;30:28-33.
12. Shapiro-Mendoza CK, Tomashek KM, Kotelchuck M, et al. Effect of late-preterm birth and maternal medical conditions on newborn morbidity risk. Pediatrics 2008;121:e223-32.
13. Lubow JM, How HY, Habli M, Maxwell R, Sibai BM. Indications for delivery and short-term neonatal outcomes in late preterm as compared with term births. Am J Obstet Gynecol 2009;200:e30-3.
14. Melamed N, Klinger G, Tenenbaum-Gavish K, et al. Short-term neonatal outcome in low-risk, spontaneous, singleton, late preterm deliveries. Obstet Gynecol 2009;114(2 Pt 1):253-60.
15. Bird TM, Bronstein JM, Hall RW, Lowery CL, Nugent R, Mays GP. Late preterm infants: birth outcomes and health care utilization in the first year. Pediatrics 2010;126:e311-9.
16. Loftin RW, Habli M, Snyder CC, Cormier CM, Lewis DF, Defranco EA. Late preterm birth. Rev Obstet Gynecol 2010;3:10-9.
17. Consortium on Safe Labor, Hibbard JU, Wilkins I, et al. Respiratory morbidity in late preterm births. JAMA 2010;304:419-25.

18. The Netherlands Perinatal Registry [homepage on the internet]. Utrecht: PRN Foundation. Available at: http://www.perinatreg.nl/home_english. Accessed July 1, 2010.
19. Méray N, Reitsma JB, Ravelli AC, Bonsel GJ. Probabilistic record linkage is a valid and transparent tool to combine databases without a patient identification number. J Clin Epidemiol 2007;60:883-91.
20. Tromp M, Ravelli AC, Méray N, Reitsma JB, Bonsel GJ. The Netherlands Perinatal Registry. Perinatal care in The Netherlands 2006 [Dutch], Utrecht, 2008. An efficient validation method of probabilistic record linkage including readmissions and twins. Methods Inf Med 2008;47:356-63
21. Brown MA, Lindheimer MD, de Swiet M, Van Assche A, Moutquin JM. The classification and diagnosis of the hypertensive disorders of pregnancy: statement from the International Society for the Study of Hypertension in Pregnancy (ISSHP). Hypertens Pregnancy 2001;20:IX-XIV
22. NVOG Richtlijn no 46: "Basis prenatale zorg." 2002 (guidelines no 46: Dutch Society of Obstetrics and Gynaecology: basic prenatal care 2002). 2002, Utrecht. Available at: www.nvog.nl. Accessed July 1, 2010.
23. Bell MJ, Ternberg JL, Feigin RD, et al. Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging. Ann Surg 1978;187:1-7.
24. Shennan AT, Dunn MS, Ohlsson A, Lennox K, Hoskins EM. Abnormal pulmonary outcomes in premature infants: prediction from oxygen requirement in the neonatal period. Pediatrics 1988;82:527-32.
25. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. J Pediatr 1978;92:529-34.
26. de Vries LS, Eken P, Dubowitz LM. The spectrum of leukomalacia using cranial ultrasound. Behav Brain Res 1992;49:1-6.
27. Hutcheon JA, Lisonkova S, Magee LA, et al. Optimal timing of delivery in pregnancies with pre-existing hypertension. BJOG 2011;118:49-54.
28. Hook B, Kiwi R, Amini SB, Fanaroff A, Hack M. Neonatal morbidity after elective repeat cesarean section and trial of labor. Pediatrics 1997;100(3 Pt 1):348-53.
29. Levine EM, Ghai V, Barton JJ, Strom CM. Mode of delivery and risk of respiratory diseases in newborns. Obstet Gynecol 2001;97:439-42.
30. Tita AT, Landon MB, Spong CY, et al. Eunice Kennedy Shriver NICHD Maternal-Fetal Medicine Units Network. Timing of elective repeat cesarean delivery at term and neonatal outcomes. N Engl J Med 2009;360:111-20.
31. Habli M, Levine RJ, Qian C, Sibai B. Neonatal outcomes in pregnancies with preeclampsia or gestational hypertension and in normotensive pregnancies that delivered at 35, 36, or 37 weeks of gestation. Am J Obstet Gynecol 2007;197:406.e1-7.
32. Gouyon JB, Vintejoux A, Sagot P, et al. Neonatal outcome associated with singleton birth at 34-41 weeks of gestation. Int J Epidemiol 2010;39:769-76.
33. Patel H, Beeby PJ, Henderson-Smart DJ. Predicting the need for ventilatory support in neonates 30-36 weeks' gestational age. J Paediatr Child Health 2003;39:206-9.