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Respiratory Morbidity in Late Preterm Births

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Abstract

Context—Late preterm births (LPTB, 34 0/7-36 6/7 weeks) account for a growing proportion of prematurity-associated short term morbidities, particularly respiratory, that require specialized care and prolonged neonatal hospital stays.

Objective—To assess short-term respiratory morbidity in LPTB compared to term births in a contemporary cohort of deliveries in the United States.

Design, Setting, and Participants—Retrospective collection of electronic data from 12 institutions (19 hospitals) across the United States on 233,844 deliveries between 2002 and 2008. Charts were abstracted for all neonates with respiratory compromise admitted to a neonatal intensive care unit (NICU) and LPTB were compared to term births in regard to resuscitation, respiratory support and respiratory diagnoses. A multivariate logistic regression analysis compared infants at each gestational week controlling for factors that influence respiratory outcomes.

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Main outcome measures—Respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTN), pneumonia, respiratory failure, standard and oscillatory ventilator support.

Results—Of 19,334 LPTB, 7,055 were admitted to a NICU and 2,032 had respiratory compromise. Of 165,993 term infants, 11,980 were admitted to a NICU, 1,874 with respiratory morbidity.

Respiratory distress syndrome decreased from 10.5% (390/3700) at 34 weeks to 0.3% (140/41,764) at 38 weeks. Similarly, TTN decreased from 6.4% (n=236) to 0.4% (n=155), pneumonia from 1.5% (n=55) to 0.1% (n=62), and respiratory failure from 1.6% (n=61) to 0.2% (n=63). Standard and oscillatory ventilator support had similar patterns. Odds of RDS decreased with each advancing week until 38 weeks compared to 39-40 weeks (adjusted OR at 34 weeks 40.1 [95% CI 32.0-50.3] and at 38 weeks 1.1 [95% CI, 0.9-1.4]). At 37 weeks odds for RDS were greater than 39-40 weeks (3.1 [95% CI, 2.5-3.7]), but the odds at 38 weeks did not differ from 39-40 weeks. Similar patterns were noted for TTN (adjusted OR at 34 weeks 14.7 [95% CI, 11.7-18.4] and at 38 weeks 1.0 [95% CI 0.8-1.2]); pneumonia (adjusted OR at 34 weeks 7.6 [95% CI, 5.2-11.2] and at 38 weeks 0.9 [95% CI, 0.6-1.2]), and respiratory failure (adjusted OR at 34 weeks 10.5 [95% CI, 6.9-16.1] and at 38 weeks 1.4 [95% CI, 1.0-1.9]).

Conclusions—In a contemporary cohort, late preterm birth, compared with term delivery, was associated with increased risk for respiratory distress syndrome and other respiratory morbidity.

Introduction

Late preterm birth (LPTB), 34 0/7 to 36 6/7 weeks gestation, now accounts for 9.1% of all deliveries and three quarters of all preterm births[1] in the United States (U.S.) and has been the focus of multiple investigations as well as an NICHD workshop in 2005[2]. Considerable evidence and expert opinion suggest that short-term morbidities are prevalent [2-5] and that the neonatal mortality rate is higher compared to those born at term.[6] However, much of the supporting data for these conclusions are derived from studies which are over a decade old, from outside the U.S., or which used administrative data such as birth certificate or ICD-9 code data, and many were drawn from small populations. For example, Wang et al[3] studied neonates born at 35-36 6/7 weeks and found a statistically higher proportion had respiratory distress syndrome (RDS) and clinical problems compared to term neonates. However, this case-control study included only 120 LPTB neonates. Rubaltelli et al[4] documented 30.8% incidence of respiratory problems in 34-36 week neonates compared to <1% at term, but also noted in another survey an incidence of respiratory problems of only 3% in LPTB[5]. Both surveys were performed 14-15 years ago in Italy.

Given advances in obstetric and neonatal care over the last 10-20 years, we suspected that many published rates of morbidity may overestimate the clinical burden attributable to LPTB. We were interested in whether high rates of respiratory morbidity would be verified after careful chart review, controlling for possible confounding factors in a large, nation-wide cohort of LPTB infants. Thus, the purpose of this investigation was to evaluate short-term neonatal respiratory morbidity in LPTB compared to term neonates in a recent large nationwide cohort of deliveries in the U.S. using data collected from electronic medical records.

Methods

The Consortium on Safe Labor (CSL) is comprised of 12 clinical centers (19 hospitals) representing 9(of 10) American Congress of Obstetricians and Gynecologists districts, designed to reflect all geographic areas of this country, that contributed data from electronic medical records to a validated comprehensive database. More detailed information regarding the CSL has been published.[7] Centers were urban and included university, tertiary, and community hospitals. The computerized database includes extensive information from deliveries 2002-2008; however, 87% of the births occurred 2005-2007, reflecting when individual institutions initiated their electronic medical record system; data from earlier years were as complete and accurate as data from later years. Data collected included demographics, prenatal complications, labor and delivery information, maternal obstetric and neonatal outcomes, as well as data from neonatal intensive care units (NICU) until discharge of the infant or death. In this study NICU was defined to include Level II, “intermediate” or “step-down” nurseries; any infant requiring more than a regular nursery was included, thus capturing all babies with respiratory compromise in our cohort. All participating centers had approval of and waiver for informed consent for study participants by their Institutional Review Board.

LPTB was defined as delivery from 34 0/7 to 36 6/7 weeks gestational age, while term birth was defined as 37 0/7 to 40 6/7 weeks gestational age. Gestational age was determined by best obstetric estimate: in most cases by last menstrual period with confirmatory sonogram; in those cases where last menstrual period was unknown dating was assigned by earliest sonogram. Maternal data of interest included demographics, order of pregnancy, substance abuse, maternal medical and obstetrical complications, and labor and delivery details. Pertinent neonatal data included birthweight, gender, Apgar scores, admission to NICU, length of NICU stay, and neonatal mortality. The race/ethnicity of individuals at each institution was determined by report of the participant upon initiation of care. Small for gestational age was defined as birthweight $<10^{th}$ percentile.[8] Anomalies were categorically coded if present, but not further defined.

Liveborn neonates 34 0/7-40 6/7 weeks gestational age admitted to the NICU with respiratory compromise were identified when a neonate required delivery room intervention with either oxygen or ventilation and admission to a NICU for further respiratory support. A detailed chart review was performed with data extraction on paper forms for information not available in the overall database, and entered into electronic format via desktop computer. For quality assurance the overall electronic database was compared with chart review data for three variables; information was noted to be highly consistent (97.3-99.7%). Delivery room variables collected included administration of oxygen, bag and mask oxygenation, intubation, presence of meconium, and need for chest compressions. NICU respiratory support included oxygen delivery by enhanced ambient oxygen (e.g., “blow by”) or by nasal canulae, use of continuous positive airway pressure (CPAP), biphasic positive airway pressure (BiPAP) or noninvasive positive pressure, surfactant administration, and endotracheal ventilation. For the latter, the type and duration of ventilation were obtained. Clinical definitions for respiratory disorders were determined as documented in the medical record by NICU providers. RDS/hyaline membrane disease (HMD) was typically defined as respiratory symptoms (e.g., grunting, flaring, tachypnea, retractions), supplemental oxygen requirement, and NICU admission for further respiratory support, with the diagnosis verified by chest x-ray findings of reticulogranular patterns and air bronchograms. Mild, moderate or severe RDS/HMD was determined by chest x-ray impression and clinical diagnosis assigned by the NICU provider. Transient tachypnea of the newborn (TTN), pneumonia with chest x-ray verification, persistent apnea and bradycardia, pulmonary hypertension, pneumothorax, meconium aspiration, pulmonary hypoplasia and respiratory failure were documented through the detailed chart review.

Only the first delivery captured in this study from each participant was included in order to avoid intra-person correlation. Continuous variables were compared using students' t-test. Univariate comparisons for categorical variables were performed using chi square or two-sided Cochran-Armitage trend tests where appropriate. A multivariate logistic regression model was developed to examine infant respiratory morbidities across gestational ages controlling for hospital, onset of labor, mode of delivery, number of fetuses, race, maternal BMI at delivery, infant birthweight, gender, presence of anomalies, and maternal medical disorders including chronic hypertension, pregnancy related hypertension (defined as preeclampsia, eclampsia, gestational hypertension or chronic hypertension with superimposed preeclampsia), preexisting diabetes, gestational diabetes, heart, renal, gastrointestinal disease, seizure disorder, asthma, and substance abuse (likely underreported).[9-11] BMI was included in the model due to increased risk for women with greater BMI to have medical conditions or undergo cesarean delivery which may impact respiratory outcome of the neonates.[12] Maternal medical conditions were included in the model as they have been demonstrated to contribute to morbidity in LPTB as well as need for early delivery[13]. Adjusted odds ratios(OR) and 95% confidence intervals(CI) comparing respiratory outcomes for infants at each gestational week below 39 weeks to those born 39 0/7 to 40 6/7 weeks were estimated from the logistic models. Infants born 39-40 weeks gestational age were used as the referent population because they had the lowest rates of morbidity and mortality on univariate analysis. To exclude bias multivariate logistic regression analyses were repeated for deliveries 2005-07. The incidences of most outcomes were <10%, thus, the OR can approximate risk ratio or relative risk in the current study.[14] The study has 92.6% power to detect a difference in rates of RDS between 35-36 weeks and term infants if the rate in the 35-36 week group exceeds that in the term group by 50% (morbidities with a higher rate in term infants will have even higher power). Two-sided significance was set at a p-value of 0.05 and SAS version 9.1 (SAS Corp., Cary, NC) was used for all analyses.

Results

From 2002-2008 a total of 228,668 women delivered 233,844 infants at CSL centers, of which 21,367 were LPTB (9.14%) and 183,790 were term infants(78.6%). After selecting the first delivery from each mother, 19,334 LPTB and 165,993 term neonates were included in the analysis. Table 1 illustrates maternal demographic data for LPTB compared to term deliveries. Women delivering LPTB had significantly more medical complications in all categories, including chronic hypertension (7.2%, n=1255 vs 2.3%, n=3803), pregnancy-related hypertension (15.8%, n=2767 vs 5.2%, n=8542), preexisting diabetes (5.0%, n=852 vs 1.8%, n=2921), and renal disease (1.2%, n=211 vs 0.6%, n=1022).

Table 2 details neonatal demographics for LPTB compared to term deliveries. Overall, LPTB neonates were more frequently small for gestational age (20.2%, n=3910 vs 10.9%, n=18155), male (52.4%, n=10,081 vs 50.9%, n=84327) and anomalous (10.0%, n=1933 vs 5.9%, n=9866).

NICU admission, median NICU stay, details of neonatal resuscitation in the delivery room, and level of respiratory support in the NICU are displayed in Table III by gestational age. Overall, 36.5% (n=7,055) of LPTB were admitted to the NICU compared to 7.2% (n=11,980) of term infants. Overall 4,701 infants were admitted to the NICU with respiratory compromise. Sixty charts randomly distributed among centers were not available for review. The total number of charts reviewed and extracted in detail was 4,641; 3,906 (20.5% of all NICU admissions) infants met criteria described in the methods and were included in the analysis. LPTB and term infants admitted to the NICU for reasons other than respiratory compromise were not reviewed. Infants delivered at 34 weeks required more oxygen supplementation (8.3%, n=307), delivery of oxygen by bag and mask (4.0%, n=148), intubation (2.9%, n=107) and chest compressions (0.2%, n=9) in the delivery room than infants born at each successive week gestational age until 39 weeks (oxygen supplementation 0.30%, n=184, bag and mask 0.12%, n=77, intubation 0.10%, n=60, and chest compressions 0.03%, n=20). With the exception of intubation for meconium, level of resuscitation required in the delivery room and NICU respiratory support decreased significantly with each advancing gestational week until 39 weeks, $p<0.001$.

Table III presents respiratory morbidity diagnosed at each gestational week. RDS/HMD was the most common respiratory morbidity occurring in 10.5% (n=390) of 34 week deliveries decreasing as gestational age advanced to a low of 0.3% (n=118) at 40 weeks. TTN was the second most common morbidity, 6.4% (n=236) at 34 weeks reaching a low of 0.3% (n=207) at 39 weeks. Also decreasing from 34 weeks were pneumonia, 1.5%(n=55) to 0.1%(n=86) at 39 weeks, persistent apnea and bradycardia, 1.6%(n=58) to 0.02%(n=8) at 40 weeks, pulmonary hypertension, 0.5%(n=19) to 0.06%(n=35) at 39 weeks, pneumothorax, 0.8% (n=29) to 0.07%(n=44) at 39 weeks, and overall respiratory failure 1.6%(n=61) to 0.09% (n=38) at 40 weeks. While these diagnoses were not mutually exclusive, the percent of infants with each diagnosis decreased significantly as gestational age increased until 39 weeks, $p<0.001$, with the exception of meconium aspiration which increased (0 at 34 weeks to 0.2%(n=79) at 40 weeks).

A multivariate logistic regression model was developed to compare morbidities across gestational ages while controlling for potentially confounding factors, as detailed in the methods. The adjusted OR and 95% CI are presented in Table IV, all decreasing 34 to 38 weeks for RDS (40.1, [32.0-50.3], 10.5% to 1.1 [0.9-1.4], 0.3%), TTN (14.7 [11.7-18.4], 6.4% to 1.0 [0.8-1.2], 0.4%), pneumonia (7.6 [5.2-11.2], 1.5% to 0.9 [0.6-1.2], 0.1%), respiratory failure (10.5 [6.9-16.1],1.6% to 1.4 [1.0-1.9], 0.2%), surfactant administration (58.5 [44.1-77.6], 7.4% to 1.1 [0.8-1.4], 0.2%) and standard (13.9 [11.0-17.6], 6.6% to 1.2 [1.0-1.5], 0.5%), or oscillatory ventilator support (18.8 [12.6-28.1], 2.8% to 0.9 [0.6-1.3], 0.1%). The analysis was performed for 2005-2007 deliveries; minimal changes were noted, confirming no bias from year of birth. While all selected morbidities decreased inversely and significantly through gestational week 37 in comparison to weeks 39-40, at 38 weeks none of the morbidities were significantly increased compared with neonates at 39 – 40 weeks.

Discussion

This large, representative American population of gravidas with data from validated medical records in the CSL database had LPTB rates virtually identical to that reported by the CDC[1] from administrative data (9.14% and 9.1% respectively) and provides detailed information regarding respiratory morbidity in this population. To our knowledge this is the largest investigation to date of respiratory morbidity in LPTB using recent medical record data and controlling for multiple factors. While morbidity in the late preterm period is clearly increased compared to term, the magnitude of problems is less than that documented in a number of previous reports[3,5]. Our descriptive data are unique in providing insight into delivery room resuscitation requirements at each gestational age, as well as details of requisite NICU respiratory support compared to infants at term. Unlike many previous investigations, ours used a multivariate logistic regression model to control for a number of factors that influence neonatal respiratory outcomes including maternal medical conditions[13], labor and mode of delivery[9-11], and birthweight. We found that for 34 week neonates the odds of RDS were increased 40-fold and that risk decreased with each advancing week of gestation until 38 weeks. Even at 37 weeks, the odds for RDS were still 3-fold greater than that of a 39- or 40-week infant. Similar patterns were seen for TTN, pneumonia, standard ventilator or high frequency ventilator requirements, as well as respiratory failure. Interestingly on multivariate logistic regression analysis there was no difference in respiratory morbidity in 38 week compared to 39-40 week infants. Moreover, our findings stand in the context of current management, including the fact that many LPTB neonates received surfactant treatment. We did not collect information on reasons for NICU admission other than for respiratory compromise, but it may be that a large percentage of LPTB were admitted as a precaution for more intense observation and evaluation as recommended by the American Academy of Pediatrics[15]. Finally, LPTB infants suffer additional morbidity not assessed in this investigation such as higher rates of sepsis and necrotizing enterocolitis.[9]

It has been suggested that obstetricians, with pressure for early inductions and cesarean deliveries, may too readily deliver LPTB infants, though others have documented that indications for LPTB are justified[16,17]. A recent study noted that 23% of LPTB occur with no recorded indication on the birth certificate[18]. Interestingly, women without a recorded indication for their LPTB were more likely to be of older maternal age, Caucasian and well educated, suggesting patient driven factors may play a role in LPTB.[18] Our data from a large, well documented cohort may be beneficial in counseling women who have a need for early delivery, as well as in discouraging those without indications from requesting early inductions or planned cesarean deliveries. It is crucial to be able to counsel a gravida with accurate information regarding risk for her neonate, even when need for delivery is unequivocal. In the cases of less clear indication for delivery, accurate information may help discourage delivery to a later gestational age. Our results will assist the obstetrician in these tasks. Finally, these results may further assist the obstetrician in assuring that proper level of neonatal support is available in the delivery room and nursery. The results of our study support the recommendation that every effort should be made to delay delivery of infants until at least 38 weeks gestational age in order to decrease respiratory morbidity.

Using well collected data on neonatal morbidity through electronic medical records and chart review, we noted respiratory distress to be present in 5.2% of neonates delivered at 34-36 weeks. This rate differs from that of other studies in which the rates of respiratory distress were as high as 28.9%. Our findings are more in-line with those of Melamed et al[19] who recently described a 4.2% rate of RDS in an Israeli LPTB case-controlled study. Overall, respiratory morbidities occurred in 9% of our LPTB cohort, far less than the 30.8% noted by Rubaltelli et al[5] in one report, but quite similar to a second report by the same investigator[4], as well as that noted in a low-risk military population[20]. Interestingly, at 37 weeks gestation our rate of RDS was still 1.0%, twice as high as that reported by Cheng et al[21], and need for ventilator assistance was similarly high in our cohort. However, these rates represented a 3-fold increase in the odds for RDS and ventilator use for infants born at 37 weeks gestational age compared to those born at 39-40 weeks, consistent with adjusted odds reported by Cheng et al[21].

The strengths of the current report include that data are from 2002-08, with the majority of deliveries from 2005-07, and are derived from 19 academic and community hospitals across the U.S. Also, our data are comprehensive in that they include all gravidas whether low or high risk. Our database is comprised of electronic medical records from all centers, allowing for decreased chance of error in extracting general information regarding pregnancies, deliveries and outcomes. The data regarding neonatal resuscitation and management in the NICU are reliable in that they were obtained from comprehensive chart reviews by trained extractors for every neonate admitted to the NICU with respiratory problems, thus assuring that respiratory data are nearly complete. Only 1% of charts were unavailable, randomly distributed among the 12 clinical centers, decreasing the chance that data were biased. Finally, it is likely gravidas were receiving more up to date obstetric care than cohorts reported from the 1990's including GBS screening and prophylaxis according to ACOG and AAP guidelines, administration of antenatal steroids when indicated, and higher probability of dating by sonography. Detailing elements of prenatal care was beyond the scope of this investigation, but more modern obstetric care might account for some of the differences in morbidity noted compared to older reports.

Our retrospective design precludes collection of information not supplied in the electronic medical record or the NICU chart that underwent review. For example, we would have liked to include information on the impact of administration of steroids for fetal lung maturity on the neonate, but this data was not a discrete field collected in delivery medical records in a significant segment of our population. Overall 38.0% of LPTB and 34.6% of term births did not report information on whether the gravida had received steroids previously at 24 to 34 weeks to improve fetal lung maturity. Finally, we were not able to corroborate gestational age determination for neonates included in this study, but depended upon the clinicians' best estimates.

We suggest that future studies should focus on indications for LPTB. Only by more completely understanding reasons for rising rates of LPTB might we be able to initiate salutary interventions to decrease neonatal respiratory morbidity. Improved pregnancy dating through early ultrasound confirmation of estimated due date may help prevent neonatal morbidity associated with erroneous delivery of a neonate that is actually at an earlier gestational age. Finally, a better understanding of the impact of mode of delivery on the neonate may help with future interventions to decrease morbidity.

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Table 1

Demographics: Maternal

	Late preterm 34-36 weeks N (%) or MEAN (SD)	Term 37-40 weeks N (%) or MEAN (SD)
Total mothers, N	**17474**	**164589**
	Mean (SD) (25, 50, 75 percentile)	Mean (SD) 25, 50, 75 percentile)
Age (yrs) (mean, sd)	27.8 (6.5) (23,27, 33)	27.7 (6.2) (23, 27, 32)
Gravidity (mean, sd)	2.8 (2.0) (1, 2, 4)	2.6 (1.8) (1, 2, 3)
Parity (mean, sd)	1.1 (1.4) (0, 1, 2)	1.1 (1.3) (0, 1, 2)
Race		
Caucasian	8032 (46.0)	83779 (50.9)
African American	4878 (27.9)	34469 (20.9)
Hispanic	2949 (16.9)	28117 (17.1)
Asian	570 (3.3)	7228 (4.4)
Other	1045 (6.0)	10996 (6.7)
BMI		
>=30 kg/m^2	6835 (39.1)	61987 (37.7)
Smoker	1590 (9.1)	10246 (6.2)
Alcohol use	374 (2.1)	2930 (1.8)
Illicit drugs	576 (3.6)	2545 (1.7)
Order		
Singleton	15661 (89.6)	163144 (99.1)
Twins	1751 (10.0)	1431 (0.9)
Triplets	62 (0.4)	14 (0.0)
Onset of labor		
Spontaneous	12364 (70.8)	107524 (65.3)
Induced	5110 (29.2)	57065 (34.7)
Mode of delivery		
Vaginal-spontaneous	10143 (58.0)	111190 (67.6)
Vaginal-operative	632 (3.6)	8649 (5.3)
Intrapartum CS	2619 (15.0)	20608 (12.5)
Pre-labor CS	4080 (23.3)	24142 (14.7)
Medical disorders		
Chronic hypertension	1255 (7.2)	3803 (2.3)
Pregnancy related hypertension	2767 (15.8)	2921 (1.8)
Preexisting diabetes	852 (5.0)	2921 (1.8)
Gestational diabetes	863 (5.5)	5750 (4.0)
Heart disease	181 (1.1)	1123 (0.7)
Renal disease	211 (1.2)	1022 (0.6)
Gastrointestinal	243 (1.5)	1521 (1.0)
Seizure disorder	172 (1.1)	1020 (0.7)
Asthma	1430 (8.5)	10573 (6.7)

SD: standard deviation

+ P value < 0.005,

* P value < 0.001 using chi square and students' t-test as appropriate

Table 2

Demographics: Neonatal

	Late preterm 34-36 weeks N (%) or MEAN (SD)	Term 37-40 weeks N (%) or MEAN (SD)
Total infants N	**19,334**	**165,993**
Gestational age (mean, sd)	35.6 (0.8)	39.0 (1.0)
Birth weight (mean, sd)	2612.9 (483.7)	3334.4 (452.4)
SGA <10th percentile	3910 (20.2)	18155 (10.9)
Apgar 5 min<7	541 (2.8)	1318 (0.8)
Resuscitation in DR	5412 (28.0)	36478 (22.0)
Gender		
Female	9165 (47.6)	81416 (49.1)
Male	10081 (52.4)	84327 (50.9)
Anomalous infants	1933 (10.0)	9866 (5.9)

*P-value < 0.001 using chi square and students' t-test as appropriate

Table 3

Neonatal resuscitation and respiratory morbidity

	Gestational Age (weeks)							
	34	**35**	**36**	**37**	**38**	**39**	**40**	**P-trend**
No. of births	3700	5477	10157	20469	41764	62295	41465	
NICU admission (n, %)	2492 (67.4)	2321 (42.4)	2242 (22.1)	2411 (11.8)	3002 (7.2)	3825 (6.1)	2742 (6.6)	<0.0001
Total reviewed (n,%)	757(20.5)	649(11.9)	626 (6.2)	511 (2.5)	442 (1.1)	525 (0.8)	396 (1.0)	
Mortality (n, %)	29 (0.8)	21 (0.4)	29 (0.3)	36 (0.2)	35 (0.1)	21 (0.1)	17 (0.1)	<0.0001
NICU days^	12.0 (3,24)	8.0 (2,19.1)	6.0 (2,17)	4.6 (1,16)	3.7 (1,12)	3.0 (1,10)	3.0 (1,9)	<0.0001
Data based upon detailed NICU chart reviews: Delivery room resuscitation (n,%)								
Oxygen	307 (8.3)	266 (4.9)	252 (2.5)	176 (0.8)	135 (0.3)	184 (0.3)	136 (0.3)	<0.0001
Bag and mask O_2	148 (4.0)	139 (2.5)	104 (1.0)	89 (0.4)	76 (0.2)	77 (0.1)	59 (0.1)	<0.0001
Intubation	107 (2.9)	84 (1.5)	83 (0.8)	67 (0.3)	62 (0.1)	60 (0.1)	45 (0.1)	<0.0001
Intubation for MSAF	3 (0.1)	4 (0.1)	6 (0.1)	4 (0)	9 (0)	22 (0)	34 (0.1)	0.17
Chest compressions	9(0.2)	7 (0.1)	10 (0.1)	12 (0.1)	14 (0)	20 (0)	18 (0)	<0.0001
NICU respiratory support (n, %)								
O_2 nasal canulae	357 (9.6)	354 (6.5)	340 (3.3)	238 (1.2)	190 (0.5)	235 (0.4)	169 (0.4)	<0.0001
O_2 isolette/blow by	164 (4.4)	143 (2.6)	155 (1.5)	129 (0.6)	91 (0.2)	123 (0.2)	91 (0.2)	<0.0001
CPAP, BiPAP, noninvasive PP	315 (8.5)	274 (5)	228 (2.2)	144 (0.7)	102 (0.2)	116 (0.2)	63 (0.2)	<0.0001
Ventilator	245 (6.6)	247 (4.5)	305 (3)	232 (1.1)	189 (0.5)	188 (0.3)	138 (0.3)	<0.0001
Ventilator Duration								
<24 h	111 (3)	118 (2.2)	124 (1.2)	73 (0.4)	72 (0.2)	72 (0.1)	60 (0.1)	<0.0001
24-48 h	46 (1.2)	62 (1.1)	72 (0.7)	58 (0.3)	44 (0.1)	27 (0)	17 (0)	<0.0001
>48 h	79 (2.1)	56 (1.0)	95 (0.9)	84 (0.4)	57 (0.1)	74 (0.1)	49 (0.1)	<0.0001
Oscillator	104 (2.8)	84 (1.5)	84 (0.8)	66 (0.3)	43 (0.1)	66 (0.1)	48 (0.1)	<0.0001
Surfactant administration	273 (7.4)	237 (4.3)	222 (2.2)	149 (0.7)	68 (0.2)	101 (0.2)	60 (0.1)	<0.0001
Respiratory morbidity (n,%)								
RDS/HMD								
Total	390 (10.5)	329 (6.0)	283 (2.8)	204 (1.0)	140 (0.3)	185 (0.3)	118 (0.3)	<0.0001
Mild	317 (8.6)	285 (5.2)	242 (2.4)	178 (0.9)	125 (0.3)	168 (0.3)	103 (0.2)	<0.0001

	Gestational Age (weeks)							
	34	35	36	37	38	39	40	P-trend
Moderate	56 (1.5)	38 (0.7)	36 (0.4)	23 (0.1)	11 (0)	13 (0)	10 (0)	<0.0001
Severe	17 (0.5)	6 (0.1)	5 (0)	3 (0)	4 (0)	4 (0)	5 (0)	<0.0001
CXR verified cases	325 (83.3)	292 (88.6)	249 (88.0)	178 (87.3)	84 (60.0)	127 (68.6)	66 (55.9)	<0.0001
Transient tachypnea	236 (6.4)	252 (4.6)	251 (2.5)	206 (1)	155 (0.4)	207 (0.3)	159 (0.4)	<0.0001
Pneumonia								
CXR verified cases	55 (1.5)	65 (1.2)	65 (0.6)	59 (0.3)	62 (0.1)	86 (0.1)	83 (0.2)	<0.0001
Apnea and bradycarida	58 (1.6)	24 (0.4)	21 (0.2)	16 (0.1)	14 (0)	14 (0)	8 (0)	<0.0001
Pulmonary hypertension	19 (0.5)	16 (0.3)	46 (0.5)	32(0.2)	35 (0.1)	35 (0.1)	45 (0.1)	<0.0001
Pneumothorax	29 (0.8)	37 (0.7)	64 (0.6)	51 (0.2)	34 (0.1)	44 (0.1)	30 (0.1)	<0.0001
Meconium aspiration	0 (0)	4 (0.1)	9 (0.1)	11 (0.1)	31 (0.1)	54 (0.1)	79 (0.2)	<0.0001
Pulmonary hypoplasia	6 (0.2)	2 (0)	3 (0)	4 (0)	5 (0)	0 (0)	3 (0)	<0.0001
Respiratory failure	61 (1.6)	41 (0.7)	81 (0.8)	65 (0.3)	63 (0.2)	62 (0.1)	38 (0.1)	<0.0001

P-trend: two sided Cochran-Armitage Trend Test, $p < 0.001$ across all weeks until 39 weeks

^ Median (10th percentile, 90th percentile)

MSAF: meconium stained amniotic fluid; CPAP: continuous positive airway pressure, BiPAP: biphasic positive airway pressure; PP: positive pressure, RDS/HMS: respiratory distress syndrome/hyaline membrane disease, C

Table 4

Multivariate logistic regression to compare the morbidities across gestational ages: adjusted OR (95% confidence interval)

GA (wks)	RDS	TTN	Pneumonia	Resp Failure	Surfactant	Ventilator	Oscillator
39 and 40	1 (referent)	1 (referent)	1 (referent)	1 (referent)	1 (referent)	1 (ref erent)	1 (referent)
38	1.1 (0.9, 1.4)	1.0 (0.8, 1.2)	0.9 (0.6, 1.2)	1.4 (1.0, 1.9)	1.1 (0.8, 1.4)	1.2 (1.0, 1.5)	0.9 (0.6, 1.3)
37	3.1 (2.5, 3.7)	2.5 (2.1, 3.0)	1.7 (1.3, 2.4)	2.8 (2.0, 3.9)	4.8 (3.8, 6.1)	2.8 (2.3, 3.4)	2.8 (2.0, 3.9)
36	9.1 (7.5, 11.1)	6.1 (5.1, 7.4)	3.6 (2.6, 4.9)	6.2 (4.4, 8.6)	16.1 (12.7, 20.4)	7.3 (6.0, 8.8)	7.1 (5.1, 9.9)
35	21.9 (17.8, 26.9)	11.1 (9.1, 13.6)	6.6 (4.7, 9.3)	4.9 (3.2, 7.6)	35.2 (27.1, 45.6)	9.8 (7.9, 12.1)	12.3 (8.5, 17.7)
34	40.1 (32.0, 50.3)	14.7 (11.7, 18.4)	7.6 (5.2, 11.2)	10.5 (6.9, 16.1)	58.5 (44.1, 77.6)	13.9 (11.0, 17.6)	18.8 (12.6, 28.1)

Adjusted for onset of labor, mode of delivery, number of fetuses, medical disorders, substance abuse, race, BMI at delivery, birth weight, gender, anomalous infants, and hospital.

GA: gestational age, RDS/HMD: respiratory distress syndrome/hyaline membrane disease, TTN: transient tachypnea of the newborn