**Birth asphyxia is under-rated as a cause of preterm neonatal mortality in low- and middle-income countries: A prospective, observational study from PURPOSe**

Robert L Goldenberg, MD1, Sangappa Dhaded, MD, DM2, Sarah Saleem, MBBS, DCH, FCPS3, Shivaprasad S Goudar, MD, MHPE2, Shiyam Sunder Tikmani, MBBS3, Marissa Trotta, MS4, Kay Hwang Jackson, BS4, Gowder Guruprasad, MD, DM5, Vardendra Kulkarni, MD5, Sunil Kumar MD5, Zeesham Uddin, MD3, Sayyeda Reza, MBBS3, Jamal Raza, MD6, Haleema Yasmin, MD7, S. Yogeshkumar, MD2, Manjunath S. Somannavar, MD2 Anna Aceituno, MSPH4, Lindsay Parlberg, BS4, Robert M. Silver, MD8 and Elizabeth M McClure, PhD4 on behalf of the PURPOSe Study Group

1Columbia University, New York, NY

2KLE Academy of Higher Education and Research’s, J N Medical College, Belagavi, Karnataka, India

3Aga Khan University, Karachi, Pakistan

4RTI International, Durham, NC

5Bapuji Educational Association’s J.J.M. Medical College, Davangere, Karnataka, India

6National Institute of Child Health, Karachi, Pakistan

7Jinnah Postgraduate Medical Centre, Karachi, Pakistan

8University of Utah School of Medicine, Salt Lake City, UT

Corresponding author:

Elizabeth M McClure, PhD

RTI International

Durham, NC 27709

# Abstract

**Objective:** Among preterm neonatal deaths, to assess respiratory distress syndrome (RDS) compared to birth asphyxia as the cause of death assigned by the neonatal intensive care unit (NICU) physician at the time of death to the cause of death assigned by a panel with complete obstetric history, placental evaluation, tissue histology and microbiology.

**Design:** Prospective, observational study

**Settings:** Study NICUs in India and Pakistan

**Population:** Preterm infants delivered in study facility

**Methods:** 410 preterm infants who died in the NICU with cause of death ascertained by the NICU physicians and independently by expert panels. We compared the percentage of cases assigned RDS vs. birth asphyxia as cause of death by the physician and the panel.

**Main outcome measures:** RDS and birth asphyxia.

**Results:** Of 410 preterm neonatal deaths, the discharging NICU physicians found RDS as a cause of death among 83.2% of the cases, compared to panel’s finding RDS in only 51.0%. In the same neonatal deaths, the NICU physicians found birth asphyxia as a cause of death in 14.9% of the deaths, while the panels found birth asphyxia in 57.6% of the deaths. The difference was greater in Pakistan were the physicians attributed 89.7% of the deaths to RDS and <1% to birth asphyxia while the panel attributed 35.6% of the deaths to RDS and 62.7% to birth asphyxia.

**Conclusions:** NICU physicians who reported cause of death in deceased preterm infants less often attributed the death to birth asphyxia, and instead more often chose RDS, while expert panels with more extensive data attributed a greater proportion of deaths to birth asphyxia than did the physicians.

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**Summary/Tweetable abstract:** In preterm infant deaths, RDS was more often chosen as the cause of death by the NICU physician, while a panel evaluating the same cases, with more extensive data, attributed a greater proportion of deaths to birth asphyxia than did the physician.

**Introduction**

In many, if not most, reports of neonatal death in preterm infants in low and middle-income countries (LMIC), complications of prematurity are listed as the most common cause of death (COD).1-4 Of these complications, respiratory distress syndrome (RDS) is often listed as the leading cause of *preterm* neonatal death and a major contributor to all neonatal deaths.5-7 These reports are generally based on the presence of breathing difficulty noted by the clinician or on verbal autopsy. However, breathing difficulty may result from other conditions, most notably birth asphyxia.8 Ideally, to attribute RDS as a COD, evidence of respiratory difficulty soon after birth together with x-ray findings pathognomonic for RDS, and/or hyaline membranes on pulmonary histology are needed.

In contrast, few, if any, x-ray or pulmonary histological findings are pathognomonic for birth asphyxia.9,10 Birth asphyxia may be considered a COD based on a constellation of findings including prolonged labor, maternal preeclampsia, placental abruption or previa and low Apgar scores.11 Other suggestive findings, based on placenta examination, include signs of abruption and lesions associated with fetal or maternal vascular malperfusion.11 Lower than expected newborn and placental weights may also suggest birth asphyxia.12 Signs of aspiration, especially with meconium present on histologic lung evaluation, also indicate asphyxia. If available, abnormal umbilical cord gases and evidence of brain injury may suggest birth asphyxia. Thus, this group of findings is highly suggestive of asphyxia as a COD. This is especially true when microbiology and histology evaluations rule out pneumonia or sepsis.

While complete clinical and diagnostic information are rarely available for most neonatal deaths, especially in LMICs,13 the more information available, the more likely an accurate COD will emerge. Unfortunately, in most COD studies, these data were unavailable to inform the COD; this is a well-documented limitation in COD studies involving verbal autopsy and clinical opinion.14,15

A related limitation in neonatal COD studies is individual physician bias in reporting COD.15 To overcome this bias, many studies assessing COD use computerized algorithms16,17 or expert panels to determine COD.18-20  However, for the algorithm or panel’s COD attribution to be accurate, appropriate clinical and laboratory data should be available.

To improve cause of preterm neonatal death ascertainment, recent advances have occurred. First, more complete, accurate data, generally in a standardized format, has been encouraged for COD examinations.20,21 Also, minimally invasive tissue sampling (MITS) to evaluate various organs, especially the lung, for histology and organism identification has enabled investigators to better assess infectious COD.22-24 Finally, placental histology, including assessment of placental malperfusion and inflammation, are now more widely available.11,23

For this study, our objective was to compare the assignment of RDS and birth asphyxia by the NICU physician at the time of death with the proportion of causes identified by a panel with more complete obstetric history, the placenta evaluation, tissue histology and microbiology. Our hypothesis was that discharging physicians, relying on data only available at time of death, would more often report RDS as the cause of preterm neonatal death, while the panel, with more comprehensive information available, and perhaps being less biased because they were not involved in the clinical care, would more frequently designate birth asphyxia as the COD. We believe this distinction is not only of academic interest, but crucial for medical practice and research direction, since death from birth asphyxia is often preventable by better obstetric care and appropriate neonatal resuscitation, while death from RDS requires different strategies to reduce mortality.

**Methods**

The data in this report were derived from data collected for the PURPOSe study.24 Briefly, the PURPOSe study was a prospective, observational cohort study performed in India and Pakistan from 2018 to 2020 to determine COD in preterm neonates and stillbirths. This study evaluated only the preterm neonatal deaths among liveborn infants who were admitted to a study neonatal intensive care unit (NICU) and died prior to discharge, up to 28 days post-delivery. The study NICUs included a large children’s hospital in Karachi, Pakistan and 3 NICUs within one health system located in Davangere, India.

The planned study sample size was 350 preterm neonatal deaths in both India and Pakistan to provide sufficient precision to detect COD that contributed to 20% or more of the deaths. To reach that target, assuming the reported mortality rates, we attempted to screen and enroll all eligible women admitted to study hospitals. Pregnant women of the local age of consent were eligible if they presented in preterm labor or for preterm delivery over the 18-month study period.

For each woman enrolled and consented, we prospectively obtained clinical information, including medical history, delivery information and collected a maternal rectovaginal culture for group B streptococcus (GBS) and the placenta. Staff then followed their infants admitted to the study NICU until day 28, or death if prior to day 28. Trained research staff collected information on the neonatal conditions daily. Following a neonatal death in the NICU, the attending physician determined major cause(s) of the neonatal death based on the clinical course and any other information available at the time of death. Because infants <1000g , even if born alive, are frequently labeled as miscarriages or abortions in these sites, with less stringent attempts at salvage, the panels only determined COD in infants born weighing >1000g.

The panels assigned primary and contributing COD using the International Classification of Disease (ICD-10 PM) classification. The panelists received training in COD ascertainment and were given and referred to the PURPOSe Determining Cause of Death (DeCODE) manual developed for PURPOSE26, as adapted from the Child Health and Mortality Prevention (CHAMPS) project.20 The DeCODE manual defines all potential COD in neonates including RDS and birth asphyxia based on ICD10-PM criteria. As an example, the manual states: “The ICD-10 code is specific to RDS/HMD and should not be used for respiratory distress in general.” To determine RDS as a COD, the guidance focuses on the infant being preterm, having respiratory distress, an x-ray with typical RDS characteristics and specific findings at autopsy. For birth asphyxia to be considered the COD, the presence of various maternal conditions, abnormal placental pathology, respiratory distress at birth and evidence of altered neonatal neurologic status, with many of the prior findings summarized by low Apgar scores should be present. These definitions are based on the WHO and the US Centers for Disease Control (CDC) guidance.20 Panelists had all available information on the obstetric history, delivery, NICU clinical course which included the physician’s cause of death classification, and the histologic and PCR investigations derived from the placenta and for fetal samples obtained by MITS.

**Statistical analyses**

The primary outcome was comparison of RDS and birth asphyxia as a COD determined by the discharging physicians vs. the panels. For these analyses, we classified RDS as a COD if RDS was listed as a either a “primary” or “contributing” COD with the same criteria used to classify birth asphyxia. We grouped the primary and contributing causes because we were primarily interested in whether the NICU physician or panel noted that RDS or birth asphyxia was present and contributed to the death. Related conditions such as hypoxic ischemic encephalopathy for birth asphyxia or hyaline membrane disease for RDS were grouped with either birth asphyxia or RDS, as appropriate. We also determined when RDS and birth asphyxia were both listed as a primary or contributing COD. Other causes of neonatal death were present in about 10% of the cases, but were not further analyzed for this report. Differences between the proportions of birth asphyxia and RDS attributed by the NICU physicians and by the panelists were evaluated using chi-square tests. We assessed the results overall and separately by study site.

**Ethical considerations**

This study was reviewed and approved by the ethics review committees at Aga Khan University, Karachi, Pakistan; KLE Academy of Higher Education and Research, Belagavi, India; J.J.M. Medical College, Davangere, India; and RTI International, Durham, NC US. All women provided informed written consent prior to participation in the study.

**Results**

Table 1 describes the study population. Of deaths in infants >1000 g, 602 were admitted to a NICU, 262 in India and 340 in Pakistan. Of these, we had both a physician and panel cause of death determination available for 177 of the deaths in India and 233 in Pakistan for a total of 410 cases, comprising the analytic sample for this study. Of these, about half the cases did not have a MITS procedure (51.2%) or PCR evaluation (52.6%) and 4.8% did not have a placental evaluation.

Table 2 summarizes the maternal and newborn characteristics of the 410 cases. The mothers in India were most often age 20 to 25 while the Pakistani mothers’ ages were more widely distributed. The mothers in Pakistan had far less schooling than the mothers in India. Few mothers had parity greater than 3 in India but nearly a quarter of the mothers in Pakistan were of higher parity. The gestational age at birth in the India site was most commonly 32-36 weeks, while in Pakistan, the most common gestational age at birth was 28-32 weeks. Most babies in the Indian sample were 1000 to 1499 g while a greater percentage in Pakistan were 1500-2499 g. Of the 410 infants in the study sample, 86.8% were noted to have signs of respiratory distress in the NICU. Overall, 58.3% of the infants included in the study were male.

Table 3 shows the COD as determined by the physicians and by the panels, overall and stratified by site. Results are categorized as RDS only, birth asphyxia only, cases with both RDS and birth asphyxia or cases with neither condition. We also calculated whether any RDS, or any birth asphyxia was determined as a COD by the NICU physicians or the panels.

Focusing on the overall findings, the NICU physicians determined that RDS alone was present in 71.7% of the cases, while the panel judged that only 27.3% of the cases had RDS alone. Birth asphyxia alone was found in 3.4 % of the cases by physician determination and alone for 33.9% of the cases by the panel’s judgement. The physicians also determined that 11.5% of the deaths had both RDS and birth asphyxia, while the panel concluded that 23.7% of the cases had both RDS and birth asphyxia. When the physician and panel opinions were compared for any RDS or any birth asphyxia, the physicians found that 83.2% of the deaths had evidence of RDS as a COD, while the panel concluded that only 51.0% of the cases had evidence of RDS. On the other hand, the physicians observed that 14.9% of the deaths had evidence of birth asphyxia, while the panel noted that 57.6% of the deaths had evidence of birth asphyxia.

We next performed the same analyses stratified by site. In the India site, by physician determination, RDS was present alone in 48.0% vs. 36.2% by the panel’s assessment. Birth asphyxia, on the other hand, was present alone in 7.3% of the cases by physician determination, but in 15.8% by the panel’s judgement. By physician assessment, 26.6% of the deaths had both RDS and birth asphyxia, while the panel identified that 35.0% of the cases had both COD. When the physicians and panel were compared about the presence of any RDS, the physicians believed that 74.6% of the deaths had RDS while the panel believed that 71.2% had RDS. On the other hand, the physicians believed that only 33.9% had any birth asphyxia while the panel noted that 50.8% of the deaths had birth asphyxia.

For the same analysis restricted to the Pakistani site, RDS was determined as present alone in 89.7% by the physician but only in 20.6% of the same cases evaluated by the panel. Birth asphyxia, on the other hand, was determined as present alone in only 0.4 % of the cases by the physician, but in 47.6% by the panel’s judgement. The physicians in Pakistan did not find both RDS and birth asphyxia as a COD in any cases, while the panel determined that 15.0% of the cases had both. Comparing assessments of any RDS, the physicians believed that 89.7% had RDS, while the panel believed that only 35.6% had any RDS as a COD. However, the physicians noted that 0.4% of the deaths had any birth asphyxia while the panel noted that 62.7% of the deaths had birth asphyxia as a primary or contributing COD.

Finally, we present the percent of deaths in India and Pakistan attributed by the panels to RDS and birth asphyxia. The panels in Pakistan noted that asphyxia was present in a greater proportion of the deaths (62.7%) than the panels in India (50.8%). Conversely, the panels in India more often attributed the COD to be RDS (71.2%) than the panels in Pakistan (35.2%). In both sites, the panels attributed a greater percentage of deaths to birth asphyxia than did the physicians.

**Discussion**

Main Findings

Regardless of whether we compared deaths attributed to RDS to birth asphyxia overall, or by site, there were substantial, statistically significant differences. Although most preterm infants who died had some component of respiratory difficulty in their clinical course, the NICU physicians, only using information available at the time of death, far more often chose RDS as the COD, while the panels, using additional information, including obstetric history, evaluation of the placenta, histologic examination of fetal tissues, and PCR evaluation of the placenta and tissues, often came to a substantially different conclusion. Thus, with more information available to determine the cause of a preterm neonatal death, more often birth asphyxia was chosen, while with minimal clinical data, the COD was more likely attributed to RDS.

There were differences between India and Pakistan in the percent of deaths attributed to RDS and birth asphyxia with RDS more commonly chosen as a COD in India while birth asphyxia was more commonly chosen in Pakistan. These differences seem plausible given the difference in medical care availability between the sites.  For example, a higher level or availability of care (as in India) might have a greater impact on reducing death from asphyxia than death from RDS. In any case, in both sites, the panel attributed a greater proportion of the deaths to birth asphyxia than did the discharging NICU physician.

Study in Context

Similar findings to the present study are found in other studies, although usually not emphasized. For example, the Study of Illness in Preterms, which included MITS but not placental evaluations to assess COD among preterm neonates in Ethiopia from 2016 to 2018, found that no preterm neonatal deaths were attributed to birth asphyxia by physicians, while the panel, with more data, assigned birth asphyxia as a COD for 14%.7 The CHAMPS multi-country study, which evaluated all neonatal deaths using MITS (in contrast to PURPOSE which only evaluated preterm neonatal deaths) and generally did not include placental evaluations, found that complications of preterm birth accounted for 38% of all neonatal deaths.19 They also found that 26% of the deaths were attributed to birth asphyxia. A study from Matlab, Bangladesh that also evaluated the causes of all neonatal deaths, found that birth asphyxia was the cause of 44.9% of the deaths, while the combination of low birthweight, prematurity and RDS accounted for only 22.0% of the deaths.29 These two studies were typical of many, in that a number of conditions were grouped into a category of complications of prematurity, rather than defining RDS specifically. In a different approach that modeled interventions to prevent neonatal death, the most effective interventions were shown to be related to better obstetric care and neonatal resuscitation, interventions thought to impact most strongly on deaths from birth asphyxia.30 We could find no published study comparing the attribution of cause of preterm neonatal death by different assessors with access to varying types and amounts of data, although a study by Bhutta et al from Pakistan noted that compared to the discharge COD listed by the NICU physician, they believed the COD determined by verbal autopsy was more accurate.

We have considered why there was less attribution of birth asphyxia as a COD by the physicians as compared to the panels and conversely why the panels found less RDS. While we have limited data to support our hypothesis, it appears that some physicians associate breathing difficulty in a preterm neonate with RDS. In the absence of much other data to contradict this belief, the fallback position was RDS. Attributing birth asphyxia to be the COD often requires more detailed information abstracted from multiple sources. Not assessed immediately after death, but only when placental, histologic and PCR data become available, the panel’s COD determination is generally more extensive. Another reason why birth asphyxia may be chosen less often as the COD by the physician may be because birth asphyxia may imply mismanagement by the obstetric provider, the neonatal provider, or both.31,32 On the other hand, because RDS may be perceived as a common, naturally occurring condition among preterm infants, when deaths attributed to RDS occur, there may be little or no implication of physician mismanagement. Also, since the person assigning cause of a neonatal death occurring in an NICU is likely to be a pediatrician, the obstetrical history suggesting birth asphyxia might not have been available or incorporated when considering the cause of death. We have also considered why RDS was more often chosen as the COD in Pakistan. Because of the limited data available in that site prior to delivery and the heavy clinical load, we believe that only when the panel focused on all the data – much of it only available after death, did the importance of birth asphyxia at that site become apparent.

Strengths and Limitations

This study had strengths and weaknesses. First, the study was performed in two sites with different levels of care and neonatal mortality rates. They had similar oversight and data forms but separate investigators. The pathologists in both sites had similar training, but again were completely independent of one another. The panels received the same training on COD determination, but reviews were conducted independently of each other. The fact that findings were in the same direction in both sites supports our conclusions, as does the findings from the SIPS study and others. Weaknesses include the fact that because the preterm infants in this study were >1000 grams at birth, admitted to, cared for, and died in an NICU, we cannot generalize to smaller babies or those cared for outside NICUs. The study subjects were recruited at presentation for delivery and therefore some prenatal information may have been lost. However, the infants were all followed during their stay in the NICUs. In addition, the study was performed in a single NICU in Pakistan and three smaller NICUs in a single health system in India. The results, therefore, may not be representative of all neonatal deaths in NICUs in those countries. Another issue is the relative accuracy of COD determination by physicians and the panels. In virtually all determinations of COD, the outcome is an opinion based on the review of available information.34 We could find no definitive study saying that the COD determined by a panel with more extensive information is more accurate than the COD determined by a single physician with less information. However, in an increasing number of studies, using a panel with more extensive information is the methodology used to determine COD.18,20,34-36 We adopted that strategy for the PURPOSe study.

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**Conclusions**

Respiratory conditions are very common in deaths among preterm neonates. Knowing the distribution of respiratory causes of preterm neonatal death is crucial if interventions to reduce those deaths are to be implemented successfully. If RDS is the most frequent cause of preterm neonatal death, a program focused on maternal corticosteroids and the use of CPAP and oxygen in the neonate might be implemented. On the other hand, if birth asphyxia was found to be the most common cause of preterm neonatal death, this would suggest implementing interventions focused on improving obstetric care and neonatal resuscitation. Of course, improving care in both areas, and doing both well, would be ideal, but in many LMIC, because of very limited resources, choices among interventions often must be made. It is especially concerning if among preterm neonatal deaths, because of limited information, infants dying with respiratory distress are automatically assigned RDS as the COD. With the availability of more extensive data, we now can better understand the causes of neonatal death, especially in preterm infants, and to choose interventions likely to have the greatest chance of improving outcomes. In prior years, in COD studies for neonates, if the infant was premature, prematurity was often listed as the cause of death. More recently it has become apparent that preterm infants die from a variety of causes and distinguishing among them is not only possible but crucial. Thus, it is important to use all available information to delve deeply into the causes of preterm neonatal deaths and especially, to distinguish between the COD in preterm infants with respiratory distress.

Assuming these results are replicated among other studies assessing COD among preterm newborns, birth asphyxia should be acknowledged as a major COD in preterm neonates. Therefore, we believe that far more attention should be directed at reducing birth asphyxia in preterm neonates in LMIC by improving obstetric care and neonatal resuscitation.

Declarations of Interest: The authors declare no conflicts of interest.

Authors’ contributions: RLG conceived the study and with EMM wrote the initial draft with additional input from SSG, YG and RMS. SD, SS, SSG, SST, MT, GG, VK, SK, ZU, SR, JR, HY, SY, and MSS implemented the study. SD, SS, SSG, SST, MT, GG, VK, SK, ZU, SR, JR, HY, SY, AA, LP, KH EMM and MSS monitored the study. RLG, SSG, SS, RMS developed the initial study protocol. KH performed the statistical analyses. All authors reviewed and approved the final manuscript.

Details of Ethics Approvals: This study was reviewed and approved by the ethics review committees at all participating institutions (Aga Khan University, Karachi, Pakistan; KLE Academy of Higher Education and Research, Belagavi, India; J.J.M. Medical College, Davangere, India; and RTI International, Durham, NC US). All women provided informed written consent prior to participation in the study.

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**Table 1. Study enrollment and among those enrolled, those with missing data**

|  | **Overall** | **India** | **Pakistan** |
| --- | --- | --- | --- |
| Preterm women enrolled (N) | 4,161 | 2,262 | 1,899 |
| Preterm infants born (N) | 3,471 | 2,032 | 1,439 |
| Preterm infants admitted to NICU (N) | 1,673 | 1,084 | 589 |
| Of admitted, preterm infant died <28 d (N) | 602 | 262 | 340 |
| Of infants who died, both panel and physician COD available (N) | 410 | 177 | 233 |
| Among infants evaluated for COD, missing post-partum investigations: |  |  |  |
| Missing MITS evaluation, n (%) | 210 (51.2) | 55 (30.9) | 155 (66.5) |
| Missing PCR evaluation, n (%) | 216 (52.7) | 58 (32.6) | 158 (67.8) |
| Missing placental evaluation, n (%) | 20 (4.7) | 3 (1.1) | 17 (7.3) |

|  |  |  |  |
| --- | --- | --- | --- |
| **Table 2. Maternal and Neonatal Characteristics Overall and by Site** | | | |
| **Characteristic** | **Total** | **India** | **Pakistan** |
| Maternal age, n (%) | 410 | 177 | 233 |
| < 20 | 31 (7.6) | 17 (9.6) | 14 (6.0) |
| 20 – 25 | 182 (44.4) | 94 (53.1) | 88 (37.8) |
| 26 – 30 | 142 (34.6) | 51 (28.8) | 91 (39.1) |
| > 30 | 55 (13.4) | 15 (8.5) | 40 (17.2) |
| Maternal education, n (%) |  |  |  |
| No formal schooling, illiterate | 72 (17.7) | 15 (8.7) | 57 (24.5) |
| No formal schooling, literate | 59 (14.5) | 2 (1.2) | 57 (24.5) |
| 1-4 years | 15 (3.7) | 7 (4.0) | 8 (3.4) |
| 5-8 years | 99 (24.4) | 52 (30.1) | 47 (20.2) |
| 9-12 years | 139 (34.2) | 81 (46.8) | 58 (24.9) |
| > 12 years | 22 (5.4) | 16 (9.2) | 6 (2.6) |
| Gravida, n (%) |  |  |  |
| 0 | 143 (34.9) | 72 (40.7) | 71 (30.5) |
| 1-3 | 207 (50.5) | 98 (55.4) | 109 (46.8) |
| >3 | 60 (14.6) | 7 (4.0) | 53 (22.7) |
| Maternal conditions |  |  |  |
| Hypertensive disorders | 123 (30.1) | 58 (33.1) | 65 (27.9) |
| Hemorrhage | 51 (12.5) | 15 (8.6) | 36 (15.5) |
| Diabetes | 19 (4.7) | 7 (4.0) | 12 (5.2) |
| **Neonatal characteristics** |  |  |  |
| Gestational age at birth (wks, days), n (%) |  |  |  |
| 20,0 - 27,6 | 48 (11.7) | 14 (7.9) | 34 (14.6) |
| 28,0 - 31,6 | 183 (44.6) | 67 (37.9) | 116 (49.8) |
| 32,0 - 36,6 | 179 (43.7) | 96 (54.2) | 83 (35.6) |
| Birth weight (g), n (%) |  |  |  |
| 1000-1499g | 215 (52.4) | 111 (62.7) | 104 (44.6) |
| 1500-2499g | 175 (42.7) | 59 (33.3) | 116 (49.8) |
| ≥ 2500g | 20 (4.9) | 7 (4.0) | 13 (5.6) |
| Fetal growth restriction\*, n (%) | 92 (22.5) | 63 (35.6) | 29 (12.5) |
| Respiratory distress n (%) | 354 (86.8) | 135 (77.1) | 219 (94.0) |
| Age at death (days), n (%) |  |  |  |
| < 1 | 58 (14.2) | 24 (13.7) | 34 (14.6) |
| 1-3 | 206 (50.5) | 72 (41.1) | 134 (57.5) |
| ≥ 3 | 144 (35.3) | 79 (45.1) | 65 (27.9) |
| Male gender, n (%) | 239 (58.3) | 111 (62.7) | 128 (54.9) |

\*Fetal growth restriction defined as <10%ile by Intergrowth standards33

| **Table 3. Panel and Physician Cause of Death Determination for Preterm Infants, Overall and by Site** | | | |
| --- | --- | --- | --- |
| **Overall** | **Panel** | **Physician** | **p-value** |
| **Overall, N** | **410** | **410** |  |
| RDS only, n (%) | 112 (27.3) | 294 (71.7) |  |
| Asphyxia only, n (%) | 139 (33.9) | 14 (3.4) |  |
| Both RDS and Asphyxia, n (%) | 97 (23.7) | 47 (11.5) |  |
| Neither RDS Nor Asphyxia, n (%) | 62 (15.1) | 55 (13.4) | <0.05 |
|  | | |  |
| ANY RDS, n (%) | 209 (51.0) | 341 (83.2) | <0.05 |
| ANY Asphyxia, n (%) | 236 (57.6) | 61 (14.9) | <0.05 |
|  | | |  |
|  | | |  |
| **India Site, N** | **177** | **177** |  |
| RDS only, n (%) | 64 (36.2) | 85 (48.0) |  |
| Asphyxia only, n (%) | 28 (15.8) | 13 (7.3) |  |
| Both RDS and Asphyxia, n (%) | 62 (35.0) | 47 (26.6) |  |
| Neither RDS Nor Asphyxia, n (%) | 23 (13.0) | 32 (18.1) | <0.05 |
|  | | |  |
| ANY RDS, n (%) | 126 (71.2) | 132 (74.6) | <0.05 |
| ANY Asphyxia, n (%) | 90 (50.8) | 60 (33.9) | <0.05 |
|  | | |  |
|  | | |  |
| **Pakistan Site, N** | **233** | **233** |  |
| RDS Only, n (%) | 48 (20.6) | 209 (89.7) |  |
| Asphyxia Only, n (%) | 111 (47.6) | 1 (0.4) |  |
| Both RDS and Asphyxia, n (%) | 35 (15.0) | 0 (0.0) |  |
| Neither RDS Nor Asphyxia, n (%) | 39 (16.7) | 23 (9.9) | <0.05 |
|  | | |  |
| ANY RDS, n (%) | 83 (35.6) | 209 (89.7) | <0.05 |
| ANY Asphyxia, n (%) | 146 (62.7) | 1 (0.4) | <0.05 |

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