

## Risk factors for Perinatal Mortality Due to Asphyxia Among Emergency Obstetric Referrals in a Tertiary Hospital

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**Objectives:** To evaluate the clinical, behavioral and health-care associated risk factors of intrapartum perinatal mortality (IPPM).

**Design:** Prospective cohort study.

**Setting:** Labor room and postnatal wards of a teaching hospital in North India.

**Participants:** Pregnant women were eligible for enrolment in the study if period of gestation at delivery was 35 weeks or more or baby weighed at least 2000 g at birth, index pregnancy was not booked in antenatal clinic of the study hospital and fetus was delivered within 24 h of admission in the hospital.

**Methods:** Information about antenatal care and events surrounding labor and delivery were retrieved from antenatal care records, referral notes, hospital clinical records and interview of mothers. Multivariate analysis was conducted using forward stepwise logistic regression analysis.

**Main Outcome Measure:** IPPM was defined as asphyxia-specific stillbirth or asphyxia-specific early neonatal death.

**Results:** Among 248 emergency obstetric referrals during the study period, rate of IPPM was 8% (20/248, 18 fresh stillbirths and 2 asphyxia-specific neonatal deaths). District hospitals and community health-centers/first referral units contributed three-fourths of all referrals. On logistic regression analysis significant risk factors for IPPM were presence of obstructed labor (OR: 23, 95% CI: 1.9-275.8), father engaged in unskilled labor (OR: 10, 95% CI: 1.3-77.7) and absence of urine examination during antenatal period (OR: 5.5, 95% CI: 1.8-16.3).

**Conclusions:** Low socioeconomic status, inadequate antenatal care and poor intrapartum care due to unskilled birth attendance are risk factors of IPPM.

**Key words:** *Asphyxia, Mortality, Neonate, Stillbirth.*

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Stillbirths and neonatal deaths due to asphyxia together constitute the intrapartum related perinatal mortality (IPPM) which can be reduced by facility-based intrapartum care and neonatal resuscitation [1,2]. In middle-and low-income countries, despite strong advocacy and provision in national health programs for health facility births large proportion of women deliver at home or reach health facilities late during labor. In addition, limited round-the-clock coverage, lack of trained health care personnel and non-adherence to standard management protocols may mitigate the potential beneficial impact of health facilities in preventing IPPM. Prolonged intrauterine asphyxia due to delay in receiving appropriate intrapartum care can result in stillbirth or asphyxial organ damage in neonate. A systematic evaluation of clinical, behavioral and health-care associated risk factors of IPPM can identify domains for behavior change communication in community and detect limitations of current health system and programs in preventing IPPM. This study was planned to investigate risk factors of intrapartum stillbirths and

neonatal deaths due to asphyxia among emergency obstetric referrals.

### METHODS

This prospective cohort study was conducted in labor ward and neonatal care areas of a teaching hospital in north India from May to October 2009. Study protocol was approved by Research Committee of the hospital and written informed consent was obtained before enrolment.

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Pregnant woman were eligible for enrolment in the study if all of the following criteria were fulfilled: (i) period of gestation at birth 35 weeks or more or baby weighed at least 2000 g at birth (ii) index pregnancy not booked in antenatal clinic of the study hospital and (iv) fetus delivered within 24 h of admission to the study hospital. Delivery was conducted by or under direct supervision of a senior registrar or consultant-on-call. Neonatal resuscitation was conducted by pediatric registrar as per standard guidelines.

A fetus was declared as fresh stillbirth if at birth and during resuscitation there was no evidence of cardiac activity or breathing movements, and skin of the fetus was intact [2]. IPPM was defined as asphyxia-specific stillbirth or asphyxia-specific early neonatal death. Asphyxia-specific stillbirth was defined as death of fetus born at or after 35 completed weeks of gestation or weighing more than 2000 g if fetus was born with intact skin (implying death less than 12 hours before delivery) and without severe lethal congenital malformation visible on external examination or detected in antenatal fetal imaging. Asphyxia-specific early neonatal death was defined as death of fetus born at or after 35 completed weeks of gestation or weighing more than 2000 g within first 7 days of life if asphyxia was assigned as primary cause of death by attending neonatologist.

Information about antenatal care and events surrounding labor and delivery were retrieved from antenatal care records, referral notes and hospital clinical records. In addition, enrolled women were interviewed within 24 h of termination of pregnancy. Interview was conducted by an obstetric registrar using a pre-tested structured data collection form. Specific information was collected to evaluate delay at different levels in getting medical care: delay in seeking care (duration from onset of labor or rupture of membranes or sentinel perinatal event to contact with first birth attendant), delay in reaching referral hospital (duration from referral by last birth attendant to reaching study hospital) and delay in delivery of fetus (duration from reaching referral hospital to termination of pregnancy).

**Statistical analysis:** For statistical robustness 10-15 subjects are needed to identify one risk factor and include in the regression analysis. With a target to identify and analyze 10-15 risk factors we planned to enroll 225 eligible subjects over a period of 6 months. Data were entered in Microsoft Access (Microsoft Corporation, Redmond, WA, USA) and analyzed using Epi-Info (Center for Disease Control, Atlanta, US). Continuous data with normal distribution were analyzed by student t-test and non-normally distributed data by Mann-Whitney U test. Categorical data were analyzed by chi-square or Fischer exact test. A *P* value of <0.05 was considered significant. Multivariate analysis was conducted using forward stepwise logistic regression analysis. Risk factors with *P* value <0.1 were entered in empty model and final model included variables with *P* value <0.05.

## RESULTS

A total of 248 emergency obstetric referrals were enrolled during the study period. District hospitals (115, 46.8%) contributed almost half of the referrals followed by

community healthcenters/first referral units (57, 23.2%), private hospitals (45, 18.3%), health facilities of employee's health scheme (19, 7.7%) and primary health centers (10, 4.1%). Among all referrals, 129 (52%) were delivered by unassisted vaginal delivery, 111 (44.8%, 107 with labor and 4 without labor) by cesarean section, and 8 (3.2%) by forceps delivery.

Among fetuses delivered to all the emergency obstetric referrals, 18 fresh stillbirths without external malformation and 2 deaths in neonatal period were assigned to be due to birth asphyxia. Therefore, rate of IPPM was 80/1000 births. On univariate analysis, socio-economic risk factors of IPPM included father engaged in unskilled labor (95% versus 59%, *P*=0.01) and absence of television in household (15% vs. 41.2%, *P*=0.03) (**Web Table I**). Health-care seeking or health-care delivery associated risk factors included traditional birth attendant being antenatal care provider (10.5% vs 0.4%, *P*=0.003) and not having hemoglobin estimation (35% vs 7.9%, *P*<0.001) or urine examination (35% vs 8.4%, *P*<0.001) during antenatal care (**Web Table II**). Clinical risk factor of IPPM was presence of obstructed labor (10% vs 0.4%, *P*=0.02). (**Web Table III**). There was no difference in durations between onset of labor and reaching first birth attendant (minutes, median [IQR]: 60 [30-540] vs 150 [0-600], *P*=0.47), between time of referral and time of reaching referral centre (minutes, median [IQR]: 158.5 [109.5-232.5] vs 150 [90-255], *P*=0.76) or between time of reaching referral centre and time of delivery (minutes, median [IQR]: 260.5 [65-426] vs 202 [68-468], *P*=0.72).

On forward stepwise logistic regression analysis significant risk factors for IPPM were presence of obstructed labor (OR: 23, 95% CI: 1.9-275.8, *P*=0.013), father engaged in unskilled labor (OR: 10, 95% CI: 1.3-77.7, *P*=0.027) and absence of urine examination during antenatal period (OR: 5.5, 95% CI: 1.8-16.3, *P*=0.002).

## DISCUSSION

In this prospective cohort study, low occupational status of father, absence of urine examination during pregnancy and presence of obstructed labor were observed to be significant risk factors for IPPM. These risk factors are markers of low socioeconomic status, inadequate antenatal care and poor intrapartum care due to unskilled birth attendance.

Observations made in this study are in agreement with those reported by other investigators. In the NICHD sponsored First Breath study, outcomes of all community deliveries in 5 resource-poor countries (Democratic Republic of Congo, Guatemala, India, Zambia, and Pakistan) and in 1 mid-level country (Argentina) were

**WHAT IS ALREADY KNOWN?**

- Birth asphyxia is a major cause of perinatal mortality despite advocacy and support for institutional births.

**WHAT THIS STUDY ADDS?**

- Low occupational status of father, absence of urine examination during pregnancy, and presence of obstructed labor were significant risk factors for intrapartum-related perinatal mortality among emergency obstetric referrals.

evaluated prospectively over an 18-month period [4]. Stillbirth rates ranged from 34 per 1000 in Pakistan to 9 per 1000 births in Argentina. Increased stillbirth rates were associated significantly with lower skilled providers, out-of-hospital births, and low caesarean section rates. Maceration was uncommon, which indicated that most of the deaths probably occurred during labor. In South Africa, perinatal mortality rate from intrapartum-related birth asphyxia was 4.8/1000 births in 27 state hospitals [5]. The most frequent avoidable factors were delay by mothers in seeking care during labor, signs of fetal distress interpreted incorrectly, inadequate fetal monitoring and no response to poor progress of labor. Contribution of birth asphyxia to perinatal mortality was higher in rural hospitals as compared to metropolitan hospitals (26.4% vs 10.8%). In a retrospective analysis from a tertiary care hospital in Nigeria, stillbirth rate of 89 per 1000 births was observed during the study period spanning 9 years [6]. Intrapartum stillbirth rate was 52.1 per 1000 births. Nonmedical factors contributing to stillbirths included delays in receiving appropriate management, inadequate intrapartum monitoring, inappropriate interventions, and wrong diagnosis. Most common risk factors for stillbirths in developing countries identified in Lancet stillbirth series included lack of adequate antenatal care, lack of a skilled attendant at delivery, low socioeconomic status, poor nutrition, prior stillbirths and advanced maternal age [3].

Reducing asphyxia-related perinatal deaths in middle- and low-income countries is not an easy task because of many contributing factors. First, in rural or slum areas proportion of pregnant woman receiving adequate antenatal care is low [7,8]. Large proportions of deliveries still occur at home and are conducted by untrained traditional birth attendants (*Dai*). *Janani Surksha Yojna* (JSY) has resulted in an increase in number of health facility-births [9]. However, cash-incentive in JSY is based on site of delivery and not site or quality of antenatal care received. Therefore, potential beneficiaries may not be motivated to receive optimum antenatal care. Second, health care workers conducting delivery at home or in hospitals are either not trained for doing neonatal resuscitation or are too pre-occupied managing the mother [10,11]. Third, primary-and secondary-level health facilities which conduct majority

of institutional births may still be lacking equipment and manpower to efficiently run these services round-the-clock. Fourth, non-reporting of stillbirth or misclassification of asphyxia neonatal death as stillbirth are not uncommon and can be potential sources of bias in a study evaluating impact of birth asphyxia on reproductive outcome [12]. Lastly, factors operating before labor or even before pregnancy have a large influence of risk of IPPM. Risk factors like low socioeconomic or education status cannot be modified in short- or medium-term.

Delay in seeking care or receiving appropriate care on reaching the health facility may also contribute to increased risk of IPPM. In our study, mother with or without IPPM had similar durations of seeking care, travelling to referral health facility and delivering the baby on reaching the health facility. However, durations spent travelling to referral centre and then getting baby delivered were relatively long. This could have contributed to high incidence of IPPM among emergency obstetric referrals in our study. Although, we could not find any difference in day of referral (weekday vs weekend) or time of referral (office hours vs off-hours), it is important to operationalize round-the-clock obstetric and newborn services in district hospitals and first referral units. Prolonged intrapartum asphyxia can also adversely affect the potential benefits of neuroprotective therapies like systemic hypothermia in asphyxiated neonates [13].

Strengths of the study include prospective design, inclusion of both stillbirths and neonatal deaths as outcome of birth asphyxia and collection of information on risk factors in different domains encompassing large part of emergency obstetric care dynamics. Our study also has certain limitations. Most importantly, a population-based study with tracking of reproductive outcome in all pregnant women across all levels of health facilities in the sampling frame would have provided better information about incidence of IPPM and factors affecting the latter. Fetal death can occur due to complex interaction between co-existing morbidities e.g. infection and asphyxia. Detailed histopathological evaluation may be able to diagnose the primary reason of IPPM. Due to logistic constraints placental histopathology and fetal or

neonatal autopsy could not be conducted in the present study. However, we used a standard operational definition to identify asphyxia-specific IPPM [2]. Small sample size and lack of information about obstetric events other than delivery after reaching the referral centre are other weaknesses of the study. However, observations made in this study can help in planning larger population-based studies to confirm and target the risk factors of intrapartum mortality.

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