Exploring the epidemiology, diagnosis, and careseeking related to risk factors for intrapartum-related fetal and neonatal death in rural Sarlahi District, Nepal

Introduction. Neonatal mortality is defined as death in the first 28 days of life. An estimated 3.1 million neonatal deaths occur annually worldwide. Intrapartum-related (during labor and delivery) complication was the second-leading cause of neonatal mortality in 2010. Stillbirth is defined as a fetal death occurring in the third trimester, with birth weight greater than or equal to 1000g or more than 28 completed weeks of gestation. An estimated 2.6 million stillbirths occur each year, a little less than half attributable to intrapartum causes (1.2 million). Intrapartum-related complications have also been associated with long-term morbidity; for instance, Lee et al. estimated that in 2010, 287,000 died, 233,000 had moderate or severe neuro-developmental impairment, and 181,000 had mild impairment from neonatal encephalopathy associated with intrapartum events.

Risk factors for intrapartum-related complications include non-cephalic presentation (fetus delivered other than its head first, e.g. breech), multiple births (e.g. twins), and placenta previa. Perhaps owing to the high prevalence of home births, a dearth of comprehensive emergency obstetric care facilities (having capacity that includes blood transfusions and c-section) in low-resource settings, and the low incidence of these risk factors, there is limited literature on burden or care related to these clinical issues in developing country settings. One report on non-cephalic presentation in developing countries reported that adjusted odds ratios of all-cause neonatal/perinatal deaths ranged from 6-15 for breech and 8-34 for other non-cephalic positioning. Intrapartum-related complications largely require intervention at a facility. The perceived complexity of providing care for such complications in areas where home births are highly prevalent may be why they have largely been overlooked by donors, researchers, and programs, despite being the direct cause of about a quarter of neonatal deaths.

The study has three main objectives: 1) to estimate incidence of third-trimester maternal clinical risk factors and their risk of intrapartum-related complications in rural Nepal, 2) to calculate the validity of assessing non-cephalic presentation, multiple births, and placenta previa, training community health workers to use a portable ultrasound machine in rural Nepal 3) to understand careseeking behavior and perceptions associated with non-cephalic presentation in rural Nepal.

Methods. Study 1. Incidence of third-trimester clinical risk factors and their risk of adverse pregnancy outcomes. This is a community-based prospective cohort study examining the incidence of third-trimester maternal clinical risk factors in rural Nepal, and their associations with adverse pregnancy outcomes. Data will be collected as part of an ongoing study (Nepal Oil Massage Study, PI Luke Mullany). The following exposure data will be collected: vaginal bleeding (linked to placental abruption, placenta previa, ectopic pregnancy, etc.), high blood pressure (linked to preeclampsia / eclampsia), multiple births (associated with obstructed labor / retained second twin, higher rates of preterm birth and fetal growth restriction), and non-cephalic presentation (more likely among preterms, associated with obstructed labor). The former two exposures will be collected on a home visit during the late third trimester, while the latter two will be collected during a home visit immediately after delivery of the child, all data from maternal recall. We will validate a subsample of the responses (5%) on fetal presentation at delivery by referring back to a birth attendant. The outcomes of interest are fresh stillbirth, early neonatal mortality, neonatal encephalopathy, and maternal mortality. All stillbirths will be categorized as macerated or fresh to discern the timing of the stillbirths; most fresh stillbirths are expected to be due to intrapartum causes. Data collectors will make home visits immediately after birth, at day 3, and at day 7, allowing us to obtain an accurate estimate of day/hour of death. We will use the following signs to identify neonatal encephalopathy: seizures or two of the following three neurologic symptoms (lethargy, poor suck, or respiratory depression, defined as <40 breaths per minute).

The sample size was calculated by focusing on non-cephalic presentation as the exposure of main interest, using 3% prevalence (k), an alpha value of 0.05 (two-sided test), power of 0.80, and a risk ratio of five (perinatal mortality probability for cephalic births, p1=0.05, for non-cephalic births, p2 = 0.25). The sample size was 748, a total of 772 after accounting for a 3% loss to follow-up (loss-to-follow-up rate based on previous data).
**Study 2. Valid detection of non-cephalic presentation, multiple births, and poor placental position in rural Nepali communities.** This is a community-based validation study, examining the sensitivity with which auxiliary nurse midwives (ANM, high school graduates with 18 months of basic midwifery training) with limited training can use a portable ultrasound machine in the mid/late third trimester to detect three major risk factors of adverse intrapartum-related pregnancy outcomes: non-cephalic presentation, multiple births, and poor placental position. Women at gestational age 32 weeks or more who are already enrolled in the parent trial will be enrolled in this validation study. ANMs will be sent in pairs to a household of a pregnant woman in her third trimester. The ANMs will independently enter the house to conduct an ultrasound exam and will be asked to identify the fetal position, whether the pregnancy is a singleton or multiple, and basic placental position. The ANMs will be blinded to each other’s results to prevent contamination. The images will be digitally saved, and sent to an obstetrician for a gold standard assessment. Using non-cephalic presentation as the key risk factor, the sample size is 583 women (target sensitivity of 90%, expected true prevalence of non-cephalic presentation in the late third-trimester of 6%). These data will be accompanied by survey data on the use of and knowledge pertaining to ultrasound exams among pregnant women in this community. Survey data collection will be integrated with Study 1. The analysis will consist of calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value between each ANM and the gold standard. We will also calculate the kappa statistic for each pair of assessors (three ANMs will be used total) to estimate inter-rater reliability. Intra-rater reliability will not be calculated due to expected shifts in fetal position between two exams on the same woman that are spaced apart.

**Study 3 – Careseeking / caregiving behavior on and perceptions of etiologies and consequences associated with non-cephalic presentation among rural Nepali populations.** Non-cephalic presentation is expected to be highly predictive of intrapartum-related complications and adverse outcomes. There is limited literature on how non-cephalic presentation is perceived by the community in relation to pregnancy outcomes, and whether and how families choose to seek care when a fetus is presenting in poor position. For instance, an ethnography on Nepal’s Magar ethnic group reported that women would attempt to turn breech babies around in the womb, and if unsuccessful, it was said that the child inside bites the mother’s heart, leading to both maternal and fetal death. We will conduct in-depth interviews with mothers who recently experienced non-cephalic presentation and their mothers-in-law (often the key decision-maker) to discuss their diagnostic and careseeking behavior and perceptions pertaining to etiology and consequences of non-cephalic presentation. We will also conduct focus groups with mothers in the community to obtain community perceptions and norms pertaining to non-cephalic presentation. Such cultural understanding will be critical in designing future referral mechanisms that inspire high referral compliance.

**Significance.** With neonatal deaths attributable to preterm births and infections (first and third leading causes of neonatal mortality) dropping globally, the proportion attributable to intrapartum-related complications is likely to increase rapidly. In the late 1980s, there was a push within the maternal health community to explore the concept of prenatal risk screening to reduce intrapartum-related deaths. Many of the risk factors that were examined were high in prevalence (i.e. first births, maternal short stature, young maternal age), which meant that while the screening successfully captured a large proportion of mothers who later experienced adverse outcomes (high sensitivity), it also captured many who did not require special care (low PPV). This finding essentially ended the pursuit of this agenda at the time. There have since been a few studies that have explored risk factors for intrapartum-related deaths with lower prevalence, high sensitivity, and high PPV, such as multiple births, vaginal bleeding, and non-cephalic presentation. Findings from our study will contribute to this literature, and potentially revive this late pregnancy risk screening agenda. It may be possible to identify a very small subpopulation of women with extremely high obstetric risk, in communities where antenatal care coverage and ultrasound access are low, using health workers with limited training. 50 million women still deliver at home worldwide, and this study will be a part of a concerted effort to link these women to facility-based care.
Budget. The study is being conducted with Nepal Nutrition Intervention Project – Sarlahi (NNIPS) in Sarlahi District, Nepal. I am awaiting responses (as of March 9) from other funding applications to the Department of International Health and the Center for Global Health.

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References