



Practice of Epidemiology

Pregnancy-related Mortality in Southern Nepal Between 2001 and 2006: Independent Estimates From a Prospective, Population-based Cohort and a Direct Sisterhood Survey

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Initially submitted March 1, 2010; accepted for publication June 3, 2010.

Demographic household surveys in Nepal between 1996 and 2006 indicate potentially large decreases in the pregnancy-related mortality ratio and raise hopes that Nepal may be on track to meet Millennium Development Goal 5. Between 2002 and 2006, 23,478 pregnant women in Sarlahi District, Nepal, were followed through pregnancy to 42 days postpartum. The pregnancy-related mortality ratio (PRMR) was estimated directly, comparing deaths among women during pregnancy or within 42 days of pregnancy termination to livebirths. In a separate household survey, 13,319 married females reported on the pregnancy history of 28,829 sisters, allowing for a concurrent comparison of estimation methodologies. In the prospective study, there were 121 pregnancy-related deaths and 23,662 livebirths (PRMR = 511, 95% confidence interval: 425, 611). In the household survey, participants reported 396 deaths among sisters, 87 (22.0%) of which were pregnancy related, and 116,491 person-years of exposure (PRMR = 529, 95% confidence interval: 419, 638). Two independent estimates collected with different methods in the same geographic area over similar time periods resulted in similarly high estimates of mortality that are approximately twice the current national estimate. Access to life-saving maternal health interventions remains low in rural Nepal, and continued efforts are necessary to ensure equitable and country-wide progress toward Millennium Development Goal 5.

demography; health surveys; maternal mortality; Nepal

Abbreviations: CI, confidence interval; DHS, Demographic and Health Survey; MDG, Millennium Development Goal; NNIPS, Nepal Nutrition Intervention Project-Sarlahi; PRMR, pregnancy-related mortality ratio.

An estimated 350,000–535,000 maternal deaths occur annually—during pregnancy or within 42 days after the termination of the pregnancy—because of causes directly or indirectly associated with pregnancy (1, 2). Over 99% of these deaths are concentrated in developing regions, mostly in sub-Saharan Africa (>50%) and Asia (~45%). Reducing this burden has been a significant global health priority for the past 2 decades (3), and Millennium Development Goal (MDG) 5 calls for a 75% global reduction in maternal mortality between 1990 and 2015 (4). In a recent report tracking maternal mortality in 181 countries, while investigators found overall reductions in global maternal deaths, only 23 countries were found to be on track to MDG 5 (2).

In this context, Nepal has recently received considerable attention following the pregnancy-related mortality estimates released from the 2006 Nepal Demographic and Health Survey (DHS). The results indicate a 48% reduction in the pregnancy-related mortality ratio (PRMR) compared with the previous national estimate obtained in 1996, from 539 per 100,000 livebirths to 281 per 100,000 (5, 6). This rate of decline suggests that Nepal might be included in the short list of countries on track to meet MDG 5. It is, thus, essential to understand as completely as possible whether this change is real and, if so, how this improvement was achieved.

The 2006 Nepal DHS pregnancy-related mortality estimates have been received with some skepticism given the improbable circumstances in which the improvements were observed. In an analysis commissioned to further investigate the decline in PRMR, 2 main areas of progress were noted: a greater than 50% relative increase in antenatal coverage and widespread improvements in family planning (7). Although progress in these indicators is positive, other indicators suggest that Nepal might not have made sufficient progress to support a 50% decline in maternal mortality (8, 9); for example, over four-fifths of women continue to give birth without a skilled birth attendant (6), and only 2.9% of births are delivered by cesarean section (7, 10). Moreover, during the same period in which this apparent reduction occurred, Nepal's population suffered through a decade-long civil conflict, characterized by the displacement of hundreds of thousands of individuals and frequent strikes and road blockages disrupting the distribution of supplies to the peripheral health system and placing considerable further strain on retaining health personnel (11–13). Furthermore, shortly after the release of the 2006 Nepal DHS, the World Health Organization, the United Nations Children's Fund (formerly the United Nations International Children's Emergency Fund; UNICEF), the United Nations Population Fund (formerly the United Nations Fund for Population Activities; UNFPA), and the World Bank released a model-based estimate of the maternal mortality ratio in Nepal of 830 deaths per 100,000 births (1, 14). These conditions call into question the likelihood that the recent estimate reflects a real reduction in pregnancy-related mortality. Additional estimates of pregnancy-related mortality in Nepal would provide valuable complementary data and help to clarify the uncertainty surrounding Nepal's progress toward MDG 5.

We present here 2 independent direct estimates of the pregnancy-related mortality ratio in Sarlahi, a rural district in the southern plains region (*terai*) of Nepal, obtained between 2002 and 2006.

MATERIALS AND METHODS

The data for these analyses were collected for 2 separate studies conducted in Sarlahi District, Nepal, by the Nepal Nutrition Intervention Project-Sarlahi (NNIPS). During the period 2002–2006, NNIPS undertook 2 large, cluster-randomized, community-based trials examining the impact of neonatal and child health interventions on mortality risks; the details of these trials and their results have been extensively disseminated in the literature (15–18). These trials, which identified pregnant women and tracked them to the end of pregnancy and through the postpartum period, provide one source of data from which the PRMR was estimated. In order to examine similarities and differences in the health status of populations outside and inside the portion of the district where these trials were being implemented, an additional large retrospective household survey was conducted including participating and nonparticipating regions of the district. Data from this survey allowed a second estimate using the direct sisterhood method. Each of these data sources and the methods for data collection and analysis are described separately below.

Data source I—population-based prospective cohort

Data collection. In the first approach to estimating PRMR, prospectively collected data from 2 community-based trials were utilized. In the first of these trials, the impact of skin and umbilical cord cleansing with chlorhexidine was examined among 23,662 babies born alive between September 2002 and January 2006 (15, 16). During this period, all pregnant women in the NNIPS surveillance area were asked to participate in the study. Women were identified by locally resident, village-based, project workers at approximately the fifth or sixth month of pregnancy and followed through the pregnancy, delivery and postpartum, and neonatal periods. Mothers of babies surviving to 28 days and permanent residents of the study area were then invited to participate in a second trial; here, infants and young children received iron and/or zinc or placebo supplementation daily through 36 months to examine the potential impact on 1–36 month mortality and morbidity (17, 18). The vital status of infants and their mothers was recorded weekly. Thus, enrollment in the second trial allowed continued following of mothers of the cohort of 23,662 livebirths through 42 days postpartum. Women followed in the neonatal trial, whose pregnancy ended in a stillbirth or neonatal death and thus did not have a baby surviving to 28 days, were not followed beyond the termination of their pregnancy, unless they happened to have a previous child that was concurrently enrolled in the postneonatal trial. Other than the vital status of the women, no other maternal-level information was collected. In each trial, project workers obtained consent for participation prior to initiating follow-up and data collection.

Analysis. The pregnancy-related mortality ratio was calculated directly from the prospective data. The number of pregnancy-related deaths reported during the study was used as the numerator. These deaths included women who either 1) died during pregnancy (no liveborn infant), 2) died during childbirth, or 3) died during the first 6 weeks of follow-up of her infant in the neonatal (trial 1) or postneonatal (trial 2) periods. The total number of deaths was divided by the number of livebirths reported throughout the study (i.e., pregnancy-related mortality ratio), and a 95% exact binomial confidence interval was calculated.

Data source II—retrospective household survey

Direct sisterhood method. The second approach to estimating PRMR utilized the direct sisterhood method, which was developed in 1991 for use in DHSs (19). Since its implementation, over 30 countries have used the DHS maternal mortality module, including Nepal, in both the 1996 NFHS and the 2006 Nepal DHS (5, 6, 20). The method involves collecting a detailed sibling history from each respondent, consisting of the number of siblings born from the same mother, the current age of living siblings, and, for deceased siblings, the age at death and years since death. For deceased female siblings, additional questions are asked to ascertain the timing of death in relation to pregnancy (19). As the cause of death is not collected, “maternal deaths” identified under this method are more accurately termed

“pregnancy-related deaths.” In practice (e.g., in DHS reports), however, the term “maternal mortality ratio” is often applied. That common convention is not followed here; the more accurate term, “pregnancy-related mortality ratio,” is utilized throughout. Several studies have validated pregnancy-related mortality estimates obtained by the sisterhood method against external data (21–23).

Data collection. The sisterhood survey for this study was conducted from February through July of 2006 along with a household child mortality survey. The sampling approach for the retrospective household survey was designed to provide approximately 7,500 households inside and outside the study area. In order to include areas that were broadly comparable, the southernmost 10 village development committees from the study area were chosen as the basic sampling frame for the NNIPS area, while the remaining 64 nonurban village development committees that were south of the original NNIPS study area formed the sampling frame for the non-NNIPS area. In each frame, a 2-stage cluster-sampling approach was followed. In the first stage, wards (administrative subunits of village development committees) were chosen proportionate to population size by using a random start point and a strata-specific interval selected such that universal sampling in the second stage would result in the desired number of households.

Ever-married, female participants aged 15–49 years from these households were selected for interview. After obtaining informed consent from prospective participants, workers first completed a set of initial modules (socioeconomic status, household and demographic information, and child health) that are not further discussed here and then the questions of the direct sisterhood survey. This module was identical to that utilized in the Nepal DHS, except that respondents in this survey were asked to give a history of only their sisters instead of a complete sibling history.

Analysis. Data were combined across all wards for the purposes of estimating maternal mortality by using the direct sisterhood method and were analyzed following standard DHS guidelines (24). Maternal deaths and person-years of exposure, defined as the amount of time a sister spent ages 15–49 years within the period 7 years prior to the survey, were stratified into 5-year age groups. Age-specific, pregnancy-related mortality rates were standardized to the population distribution of respondents and then aggregated to obtain an estimate for the total pregnancy-related mortality rate for all women aged 15–49 years. In the community-based trial, we identified and monitored all pregnant women but did not monitor the person-years contributed by women who did not become pregnant; thus, we did not have a direct measure of the denominator for general fertility rate. Therefore, the general fertility rate for the rural, central/eastern *terai* (plains region) of Nepal was obtained from the 2006 Nepal DHS, which covered a period 1–36 months prior to the survey, and was used to convert the mortality probabilities to a pregnancy-related mortality ratio (24). The PRMRs overall and within each stratum (inside NNIPS, outside NNIPS) were estimated along with 95% confidence intervals.

For sisters with incomplete data, missing values were imputed on the basis of recommended procedures

(24, 25). The primary estimate included all data after imputation for missing values. To explore the impact of the above assumptions and imputations, we recalculated the PRMR after first excluding any sisters with missing data and again after excluding all sister groups where any of the sisters had missing information.

Approvals. The 2 trials and the retrospective household study were approved by the Nepal Health Research Council in Kathmandu, Nepal, and the Institutional Review Board of the Johns Hopkins Bloomberg School of Public Health. The parent trials are registered at clinicaltrials.gov (NCT00109551 and NCT00109616).

RESULTS

Between September 2, 2002, and February 1, 2006, 23,478 pregnancies resulted in 23,662 livebirths (23,296 singletons, 180 sets of twins, and 2 sets of triplets). During the same time period, a total of 121 deaths among women during pregnancy or within 42 days of the termination of their pregnancy were observed. Of these deaths, 95 occurred at or after the delivery of a livebirth. The remaining 26 occurred either among pregnant women prior to labor or during delivery resulting in a stillbirth. Although no detailed information is available surrounding the circumstances of these deaths, all of them were observed after 28 weeks of pregnancy; any pregnancy-related deaths that may have occurred prior to this time (i.e., before the project workers identified and initiated vital status tracking of pregnant women) were not counted. The ratio of pregnancy-related deaths to livebirths was 511 per 100,000 livebirths (95% confidence interval (CI): 425, 611).

Between February and June of 2006, 15,006 households were approached (7,486 inside and 7,520 outside the NNIPS study area), and interviews were conducted with 13,319 married women of reproductive age. Among these, 1,800 women reported no sisters, while the remaining 11,519 respondents reported data for 28,829 sisters. The mean and median numbers of sisters per respondent were 2.2 and 2.0, respectively (range: 0–12). Among all sisters, 6,350 were reported deceased at the time of the survey, and 365 (5.7%) of these deaths occurred in the 7 years preceding the survey among women in the reproductive age range. Eighty-one deaths were reported to occur during pregnancy or within 42 days of the end of pregnancy and, for a further 31 deaths, timing relative to pregnancy was not available. These were allocated as maternal deaths according to the age-specific proportion maternal out of all adult female deaths, resulting in 6 additional pregnancy-related deaths for a total of 87 reported for the period 7 years prior to the survey. Pregnancy-related deaths consisted of 21.9% (87/396) of all deaths occurring among married women of reproductive age.

The all-cause and pregnancy-related mortality rate estimates from the direct sisterhood method are shown in Table 1. The all-cause mortality rate for females, aged 15–49 years, was 339 deaths per 100,000 person-years (95% CI: 302, 376). The pregnancy-related mortality rate was 70.0 pregnancy-related deaths per 100,000 person-years (95% CI: 55.5, 84.5). By use of the DHS-based general fertility rate estimate of 132.4 for the rural, central/eastern region of

Table 1. Direct Sisterhood Estimate of Maternal Mortality for the 7-Year Period Preceding the 2006 Maternal Mortality Survey, Sarlahi District, Nepal

Age group of sisters, years	Deaths, no.	Pregnancy-related Deaths, no.	Person-Years of Exposure	Female Adult Mortality Rates ^a	Pregnancy-related Mortality Rates ^a	95% CI	Proportion Pregnancy Related Among Reproductive-Age Female Deaths
15–19	60	21	20,437	33.4	11.5		0.34
20–24	64	20	24,972	50.7	16.2		0.32
25–29	63	20	23,310	53.0	17.0		0.32
30–34	72	15	20,297	61.4	13.1		0.21
35–39	33	5	14,378	30.1	4.7		0.16
40–44	37	4	8,409	45.4	5.4		0.12
45–49	36	1	4,690	65.1	2.1		0.03
Total	365	87	116,491	339.1	70.0	55.5, 84.5	0.21
PRMR					528.7	419.0, 638.3	

Abbreviation: CI, confidence interval; PRMR, pregnancy-related mortality ratio.

^a Expressed as per 100,000 population.

Nepal, the PRMR was estimated at 529 deaths per 100,000 livebirths (95% CI: 419, 638). Given this risk and current fertility conditions, the estimated lifetime risk of pregnancy-related death (26) was 2.2%; equivalently, 1 of every 46 women will suffer a pregnancy-related death during her reproductive life span. The PRMR estimates were similar for the area inside (558/100,000, 95% CI: 397, 719) and outside (492/100,000, 95% CI: 344, 640) the NNIPS study area. A comparison of the point estimates for PRMR obtained through this analysis and the Nepal DHS is shown in Table 2.

With regard to the quality of sisterhood data, only 0.1% of sisters were reported with unknown vital status, and current age was available for over 99% of living sisters. Among deceased sisters, 16.7% were reported with either unknown years since death or age at death. The overall amount of incomplete data was comparable to that found in a review of DHS maternal mortality indicators (range: 0.4%–32.6%) (27). Imputation of missing data did not significantly change the direct sisterhood estimates of maternal mortality. PRMR declined by only 3% (from 529/100,000 to 512/100,000) when sisters with missing data were excluded from analysis. When entire sister groups for which one or more sisters had any missing data were excluded, the PRMR increased by 7% (from 529/100,000 to 565/100,000). The median years of birth of respondents ($n = 2,033$) and their sisters ($n = 2,034$) were similar; these years in the Bikram Sambat calendar correspond to approximately 1977 in the Western calendar.

DISCUSSION

The risk of pregnancy-related death is high in Sarlahi District, exceeding 500 per 100,000 under 2 separate estimation methods. The prospective and sisterhood studies returned nearly identical estimates of the pregnancy-related mortality ratio and reflect overlapping geographic regions and time periods. The observed PRMR is nearly twice as high as the Nepal DHS estimate, and the 95% confidence

intervals of the 2 PRMR figures presented in this study completely exclude that of the 2006 Nepal DHS estimate, further suggesting a real difference between the 2 PRMR estimates presented in this study and that of the 2006 DHS.

The correspondence of the 2 independently obtained PRMR estimates increases confidence in the accuracy of the level of pregnancy-related mortality calculated in these studies. In addition, the identification and enrollment of pregnant women and the follow-up outcomes through the neonatal period were nearly universal during the prospective study, and measures of data quality obtained through the sisterhood module of the retrospective household survey suggest that its quality is comparable with those of other DHS sisterhood surveys. Furthermore, the large sample size available under both methodologies, in addition to a reduced effect of clustering, allowed for substantially higher precision in the current study ($\pm 20\%$) than that of the national DHS value ($\pm 37\%$).

The results presented in this study represent only 1 district and may not be directly generalizable to the entire country. However, many population health characteristics of Sarlahi are similar to those of much of Nepal. Maternal health indicators and risk factors in Sarlahi, such as the proportion of deliveries in a health facility (9.1%) and skilled attendance at delivery (9.0%), are similar to DHS estimates for women

Table 2. Comparison of Pregnancy-related Mortality Ratios From Nepal DHS Estimates, 1996 and 2006

Year	Study	PRMR	95% CI
1996	Nepal Family Health Survey	539	392, 686
2006	Nepal Demographic and Health Survey	281	178, 384
2006	Prospective study, Sarlahi	511	425, 611
2006	Sisterhood study, Sarlahi	529	419, 638

Abbreviations: CI, confidence interval; DHS, Demographic and Health Survey; PRMR, pregnancy-related mortality ratio.

living in rural areas (6, 28, 29). The overall neonatal mortality rate among livebirths in the 2002–2006 trial was 32.1 per 1,000 livebirths (16), comparable to the country-wide neonatal mortality rate estimate of 33 per 1,000 from the DHS. Likewise, the mortality rate during the postneonatal period (1–11 months) was approximately 16.7 deaths per 1,000 livebirths in Sarlahi, compared with 15.0 deaths per 1,000 nationwide (6, 17). Mortality indicators specific to the *terai* region are available from the DHS for only the 10 years prior (42/1,000 and 23/1,000 for neonatal and postneonatal mortality, respectively) (6).

Given the similarity between these indicators from our study area and corresponding national or regional estimates, the marked difference in PRMR is surprising. The standard, albeit limited, quality checks on 1996 and 2006 DHS data do not provide a direct indication that the 2006 DHS was flawed. These checks include the following: 1) comparison of the median birth year of respondents and their siblings, 2) levels of missing data on all siblings and on deceased siblings, and 3) trend in kinship/sibling group size compared with fertility trends. Although these appear to indicate that the quality was not substantially different between the 2 reporting periods, one possible type of misreporting is found in the 2006 DHS data when examining the distribution of respondents and siblings by year of birth. The median birth year differs by just 1 and 0 years for 1996 DHS and the Sarlahi sisterhood data, respectively, but for the 2006 DHS, the distribution of siblings and respondents across birth-year-specific strata differs. Among 5,271 sibling deaths of any age in the 2006 DHS, there was 100% reporting of both age and death and years since death. Such completeness is somewhat surprising given that an evaluation of sisterhood surveys found a mean missing rate of 10.4%, and no country reported less than 0.4% (27).

It is still possible that the 2006 DHS estimate of PRMR underestimates the true burden, even without obvious data quality issues and even while the majority of other measures demonstrate concordance. Given the rarity of the outcome in comparison to other indicators, the PRMR estimation is subject to substantially more variability as reflected by wide confidence intervals. For example, respondents in the 2006 DHS reported just 39 maternal deaths, while neonatal and postnatal deaths or skilled attendants and facility deliveries are reported in the hundreds or thousands, respectively, and subject to less estimation error. These outcomes are also reported directly based on women's own experience, while PRMR is modeled on the basis of reports about events occurring to siblings, adding to the possibility of misreporting.

The discrepancy between the 2006 DHS estimate and the direct prospective measure of PRMR suggests that the recent DHS number might underestimate the country's true pregnancy-related mortality ratio. It is difficult to attribute the PRMR decline observed between 1996 and 2006 in the national estimates to improvements in family planning and antenatal care: The latter has increased dramatically worldwide between 1990 and 2007, but this has not been associated directly with decreases in the maternal mortality ratio. Nepal has seen substantial declines in fertility in recent years, and although this decrease in population fertility reduces the absolute number of deaths, the impact on PRMR or the ma-

ternal mortality ratio might not be as apparent, given that these ratios approximate the risk associated with each birth. While noted improvements in the rates of cesarean section and skilled birth attendance represent large relative increases, current levels of skilled attendance at birth and cesarean section utilization in Nepal are consistent with very high levels of maternal mortality; no country with a cesarean section rate of less than 2% or less than 30% skilled birth attendance has a maternal mortality ratio less than 500 (10).

The recent estimate of maternal mortality in Nepal from the 2006 DHS has raised hopes that the country can reach MDG 5 by 2015, but our data suggest that this conclusion may be premature. The maternal mortality ratio estimated here is not a country estimate. However, the consistency of these 2 estimates arising through 2 independent methodologies in a district characteristic of much of the rural *terai* region suggests that maternal mortality has not fallen uniformly throughout the country but remains alarmingly high in many areas. The current national DHS estimate of 281 might substantially underestimate the true burden of maternal mortality, might obscure substantial variability by sub-region within Nepal (30), or both. Region-specific strategies may be required to more appropriately target maternal health needs, and they may lead to greater equity in progress toward reduced mortality risk. Continued efforts must be made to improve maternal health in Nepal and throughout the world. Measuring maternal mortality remains challenging, and additional resources should be devoted to its measurement in order to accurately track progress toward achieving MDG 5.

ACKNOWLEDGMENTS

Author affiliations: Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland (David W. Wee, Luke C. Mullany, Joanne Katz, Subarna K. Khatri, Steven C. LeClerq, James M. Tielsch); and Nepal Nutrition Intervention Project-Sarlahi, Kathmandu, Nepal (Subarna K. Khatri, Steven C. LeClerq).

This work was supported by the National Institutes of Health, Bethesda, Maryland (grants HD 553466, HD 44004, and HD 38753); the Bill and Melinda Gates Foundation, Seattle, Washington (grant 810-2054); and Cooperative Agreements between Johns Hopkins University and the Office of Health and Nutrition, US Agency for International Development, Washington, DC (HRN-A-00-97-00015-00 and GHS-A-00-03-000019-00).

The authors thank Dr. Cynthia Stanton, Dr. Kenneth Hill, Dr. David Osrin, and Natasha Mesko for their review of the manuscript and helpful suggestions and comments.

The funding agencies played no role in the concept, design, or implementation of this study and in the subsequent analysis, interpretation, and decision to publish.

The corresponding author had full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. The data set is available from the corresponding author at lmullany@jhsph.edu.

Conflict of interest: none declared.

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