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Impact of Newborn Skin-Cleansing With Chlorhexidine on Neonatal Mortality in Southern Nepal: A Community-Based, Cluster-Randomized Trial

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Abstract

OBJECTIVE—Hospital-based data from Africa suggest that newborn skin-cleansing with chlorhexidine may reduce neonatal mortality. Evaluation of this intervention in the communities where most births occur in the home has not been done. Our objective was to assess the efficacy of a 1-time skin-cleansing of newborn infants with 0.25% chlorhexidine on neonatal mortality.

METHODS—The design was a community-based, placebo-controlled, cluster-randomized trial in Sarlahi District in southern Nepal. Newborn infants were cleansed with infant wipes that contained 0.25% chlorhexidine or placebo solution as soon as possible after delivery in the home (median: 5.8 hours). The primary outcome was all-cause mortality by 28 days. After the completion of the randomized phase, all newborns in study clusters were converted to chlorhexidine treatment for the subsequent 9 months.

RESULTS—A total of 17 530 live births occurred in the enrolled sectors, 8650 and 8880 in the chlorhexidine and placebo groups, respectively. Baseline characteristics were similar in the treatment groups. Intention-to-treat analysis among all live births showed no impact of the intervention on neonatal mortality. Among live-born infants who actually received their assigned treatment (98.7%), there was a nonsignificant 11% lower neonatal mortality rate among those who were treated with chlorhexidine compared with placebo. Low birth weight infants had a statistically significant 28% reduction in neonatal mortality; there was no significant difference among infants who were born weighing ≥ 2500 g. After conversion to active treatment in the placebo clusters, there was a 37% reduction in mortality among low birth weight infants in the placebo clusters versus no change in the chlorhexidine clusters.

CONCLUSIONS—Newborn skin-wiping with chlorhexidine solution once, soon after birth, reduced neonatal mortality only among low birth weight infants. Evidence from additional trials is

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needed to determine whether this inexpensive and simple intervention could improve survival significantly among low birth weight infants in settings where home delivery is common and hygiene practices are poor.

Keywords

chlorhexidine; mortality; neonatal; Nepal

DEVELOPING COUNTRIES HAVE made significant progress in reducing mortality for children who are younger than 5 years through the implementation of a variety of maternal and child health interventions in the past 3 decades. Little progress has been made, however, in reducing perinatal and neonatal mortality,^{1,2} and neonatal deaths now comprise nearly 40% of all mortality in children who are younger than 5 years.³ Ninety-nine percent of neonatal deaths occur in developing countries, mostly at home, and are attributable primarily to infections, birth asphyxia, and complications of prematurity.^{3,4} Low birth weight (LBW) is an important underlying factor for neonatal mortality and contributes to an estimated 60% to 80% of neonatal deaths in low-resource settings.¹ LBW is particularly important in south Asia, where the prevalence is ~30%.² Recent research suggests that improved care of LBW infants has the potential to improve survival significantly.^{5,6}

Early neonatal sepsis is associated with colonization of infant skin by organisms that are present in the vaginal canal. This is supported by studies from developed countries that demonstrated reduced neonatal colonization when the vaginal canal is cleansed with antiseptic solution.^{7–13} Two hospital-based studies from developing countries also have addressed this issue. In nonrandomized, unmasked trials that were conducted in Malawi¹⁴ and Egypt,¹⁵ pregnant women received vaginal cleansing with 0.25% chlorhexidine during labor and their newborns were given full-body skin-cleansing with the same solution. Compared with nonintervention time periods, neonatal mortality was reduced 22% in Malawi and 33% in Egypt. However, the combination of treatment to both mother and child prevents differentiating the contribution of each intervention to these results. Generalizing these findings to other populations with high neonatal mortality also is problematic because other factors may modify the effect of such an intervention. For example, in rural Nepal, the rates of sexually transmitted infections and bacterial vaginosis are low compared with many places in Africa,^{16,17} and the vast majority of deliveries occur at home, a highly contaminated environment. Therefore, colonization of the infant with potential pathogens from the mother during delivery may play a smaller role in South Asia than in Africa. The causative organisms for neonatal infections also suggest that environmental sources are common.^{18,19} Furthermore, the treatment effect could be modified by the birth weight distribution of the population, because skin barrier function is compromised in preterm, LBW infants, leading to increased risk for infection.^{20–22} Given the marked differences in LBW rates in Asia and Africa, it is important to understand the impact of the intervention in both contexts. On the basis of the potential for skin-cleansing of newborns with chlorhexidine to be a simple, inexpensive, and safe intervention for improving neonatal survival, we conducted a community-based trial of this intervention on neonatal mortality.

METHODS

The Nepal Newborn Washing Study was a cluster-randomized, placebo-controlled, community-based trial that began in September 2002 among newborn infants who were delivered to women who lived in Sarlahi District in south-central Nepal. This area is typical of much of the Indian subcontinent. The population is considered poor, even in Nepal; almost three fourths of families live below the poverty line.²³ The area was divided into sectors ($N = 413$) on the basis of the population that 1 local female worker (ward distributor [WD]) could service, ~40 to 50 households.

Pregnancies in the study area were identified by the WDs, who went door to door on a monthly basis. At ~6 months' gestation, women were recruited for participation. At the time of recruitment, all women received weekly vitamin A supplementation, iron–folic acid supplements, and albendazole. These benefits were provided because previous research in this area had demonstrated their efficacy. Tetanus immunization history was assessed and, when deficient, provided by study staff, and all women were provided with a clean birthing kit. Workers provided education regarding proper nutrition during pregnancy and hygienic delivery and neonatal care, including clean cord care and prevention of hypothermia. Although the prevalence of HIV infection and group B streptococcal colonization in pregnant women is not known in this area, they are likely to be very low.

Eligibility and Randomization

Infants in this population typically are delivered by family members or untrained, traditional birth attendants, and >95% of births occur in the home. The WD was notified by families as soon as possible after the birth of a child. The WD then walked to the home to enroll the newborn infant and conducted the skin-cleansing.

Randomization was conducted at the sector level, stratified by geographic area and tertiles of infant mortality risk as measured during an antenatal micronutrient supplementation trial that was completed in the same area 1 year before the start of this study.²⁴ Concurrent with this trial, a subset of infants were included in a nested trial of 3 approaches to care of the umbilical cord using omphalitis and mortality as end points (Fig 1). Details of this trial were presented in a separate article.²⁵

Informed consent was obtained at the community, household, and individual levels. Community consent was obtained during meetings with community leaders. In addition, verbal consent was obtained at the household level from the parents of enrolled infants.

Intervention

Newborn infants were sector-randomized to receive 1 of 2 skin-cleansing regimens when the WD arrived at the house after delivery: (1) wiping of the total body excluding the eyes and ears with Pampers infant wipes (Procter and Gamble Co, Cincinnati, OH) that released a solution that contained 0.25% free chlorhexidine (equivalent to 0.44% chlorhexidine digluconate) or (2) wiping with the same infant wipes that lacked chlorhexidine (placebo). All wipes were alcohol-free, produced by Procter and Gamble Co, and packaged in sterile plastic sachets that contained 6 wipes. The allocation codes were kept at Procter and Gamble, and investigators and all study staff were masked to the treatment assignment. Demonstrations with life-sized dolls and an instructional video were used to train WDs to deliver the intervention using a standard protocol.²⁶

Definition and Measurement of Outcome

The primary outcome was all-cause mortality within the first 28 days of life. Cause of death was assessed by verbal autopsy and classified by an algorithmic approach defined previously.²⁷ Sepsis deaths were defined by the presence of 2 or more of the following signs or symptoms: (1) caregiver's report of fever; (2) vomiting more than half of feeds; (3) unconsciousness; (4) bulging fontanelle; (5) feeding difficulty (not able to suck before death or feeding less than normal); (6) skin or umbilical cord infection (pus discharge from the cord stump); (7) jaundice; and (8) difficulty breathing and either rapid breathing or chest indrawing. A hierarchy of diagnoses was applied during cause-of-death analysis as follows: congenital abnormality, tetanus, prematurity, birth asphyxia, sepsis, acute lower respiratory infection, and diarrhea.²⁷ For deaths that were attributed to congenital abnormality or tetanus, a confirmation by physician review of the verbal autopsy record was required.

Data Collection

Community-level data on the presence of economic, educational, and health facilities were collected during interviews with community leaders. Household-level data on socioeconomic status, education, maternal health indicators including reproductive history, and household structure were collected during a household interview. After the intervention visit to the home, a staff member (not the WD) visited to collect data on the delivery process and the condition and immediate care of the newborn infant and to weigh the infant using a digital infant scale. Visits were conducted on days 2, 3, 4, 6, 8, 10, 12, 14, 21, and 28 to assess infant vital status and morbidity. At each visit, the staff member examined the infant for signs of umbilical cord and skin infection, measured the axillary temperature and respiratory rate, and recorded other morbidity symptoms and signs. On day 14, an interview was conducted with the mother on newborn care practices. Infants who had specific sets of signs and symptoms at the time of household visits were referred to the local health system for care. All infants who were alive at 28 days were discharged from the study.

Sample Size

The study originally was designed to detect a minimum reduction in all-cause neonatal mortality of 20% (relative risk [RR]: 0.80) given 80% power, a 2-sided type I error of 5%, 5% loss to follow-up, and a neonatal mortality rate of 50 per 1000 live births in the placebo group. Because neonatal mortality did not cluster at the sector level during a previous study,²⁴ no adjustment was made for intracluster correlation. This resulted in a sample size of 13 500 live births. A lower-than-expected neonatal mortality rate by the time of the first Data and Safety Monitoring Board (DSMB) meeting prompted the recommendation that the sample size be expanded to ~17 000 live births.

Statistical Analysis

Statistical analysis was performed using Stata 8.0 (Stata Corp, College Station, TX). Treatment groups were compared on baseline household, maternal, and delivery characteristics. Treatment effect on neonatal mortality was done on 2 populations. The first used all live births that occurred in the cluster irrespective of whether they received their assigned intervention. The second used only newborns who were alive at the time of the WD visit to the home and who received their assigned intervention. Mortality was compared using live births as the denominator and deaths within the first 28 days as the numerator. Survival analysis, including Kaplan-Meier survival curves, also was conducted. Multivariable binomial regression with a log link function was used to model the risk for mortality adjusted for potentially confounding factors imbalanced across treatment groups and to model effect modification. Estimates of the RRs and their SEs were adjusted to account for the clustered randomization using generalized estimating equations with an exchangeable correlation structure.²⁸

Children who migrated out of the study area or whose parents refused additional participation before day 28 were censored at the time when they left the study. Stratified analyses were planned for selected variables that are known to be important risk factors for neonatal mortality, such as LBW, previous child death in the family, gender, and ethnic group.

Ethical Review and Data and Safety Monitoring

This study received approval from the Nepal Health Research Council and the Committee on Human Research of the Johns Hopkins Bloomberg School of Public Health. It is registered at www.clinicaltrials.gov (NCT00109616). An independent DSMB met 3 times to review the protocol and the data for safety and efficacy. At the meeting in January 2005, the DSMB recommended that the study be stopped because of adequate evidence for a beneficial effect of chlorhexidine newborn skin-cleansing among LBW infants. The ethical committees

approved this decision, and from March 8, 2005, through January 2006 (end of enrollment), all newborn infants in the study area received skin-cleansing with the chlorhexidine solution.

Role of Funders

Financial supporters and the commodity supplier played no role in the design, conduct, management, analysis, or interpretation of the results or in the preparation, review, or approval of this article.

RESULTS

Study Population

Between September 1, 2002, and March 8, 2005, there were 17 530 live-born infants from women who agreed to participate during their pregnancy (Fig 2). Parents of 18 (0.2%) infants in each group refused to participate when asked again at the time of infant enrollment. More infants did not receive their assigned intervention in the chlorhexidine group, 27 for other reasons and 86 because the infant died before the time the WD arrived to conduct the intervention (total = 113 [1.3%]) vs 20 for other reasons and 55 pretreatment deaths in the placebo group (total = 75 [0.8%]; Fig 2). The reason for this imbalance is unclear because the distribution of the time between birth and intervention was the same in the 2 treatment groups.

Baseline characteristics of the families, deliveries, and newborn infants who were enrolled in the trial were well balanced across treatment groups (Table 1). More than 90% of deliveries occurred at home. Approximately 60% of birth attendants washed hands with soap and water before the delivery; 80% of infants were fed colostrum, but only approximately half began breast-feeding within 12 hours after delivery. Birth weight distributions in the treatment groups were similar as were a number of other characteristics related to delivery hygiene and status of the infant at birth (Table 1). The LBW rate was 30%.

Intervention Delivery

Because study staff typically were not in attendance at the delivery, WDs traveled to the house where the delivery took place. Despite this inherent delay, newborn skin-cleansing occurred soon after delivery at a median time of 5.8 hours after birth (interquartile range: 2.1– 11.8 hours); 91.4% of infants were cleansed within the first 24 hours. No adverse reactions to the intervention were reported.

Safety

A concern regarding this intervention was the potential for hypothermia as a result of the wetting action of the wipes, especially because the World Health Organization (WHO) recommends that bathing after birth be delayed for at least 6 hours.²⁹ Previous research in our study area showed that 95% of families conduct a wet wash of the newborn within the first 12 hours after delivery.³⁰ This suggested that an additional skin-wiping followed promptly by wrapping of the infant and accompanied by behavioral messages to limit exposure and manage hypothermia would be unlikely to produce additional risk as a result of hypothermia. A pilot study of the wiping procedure confirmed that little moisture was left on the skin, little to no vernix was removed, and a small drop in body temperature (mean: 0.4°C) resulted.²⁶ A previous trial of antenatal micronutrient supplementation on birth weight and early infant health that was conducted in the same study area used an identical method for measurement of infant temperature (P. Christian, DrPH, written communication, 2005). This allowed a comparison of rates of hypothermia between these studies. Adjusted for month of birth, there was a 12% (95% confidence interval [CI]: 5%–19%) increased odds of mild hypothermia (36.5°C–35.8°C

C) and a 16% (95% CI: 22%–10%) reduced odds of moderate to severe hypothermia ($<35.9^{\circ}\text{C}$) in the skin-cleansing trial compared with the previous study.

Intervention Impact

On the basis of the intention-to-treat analysis of all live births, there was no difference in neonatal mortality (RR: 1.04; 95% CI: 0.87–1.24; Table 2). Among those who actually received their assigned intervention, there was a nonsignificant 11% lower neonatal mortality rate in the chlorhexidine group compared with placebo (Table 2). However, among LBW infants, the chlorhexidine group had a significant, 28% lower mortality than the placebo group (RR: 0.72; 95% CI: 0.55–0.95). Infants who weighed ≥ 2500 g showed no significant difference in mortality (Table 2; Fig 3). Among LBW infants, baseline comparisons between the treatment groups also were well balanced (data not shown). Alternative definitions of LBW, such as <2000 g, showed similar treatment effects as for those <2500 g (data not shown). There was no evidence of interaction between the skin-cleansing intervention and the treatments in the umbilical cord care trial; both chlorhexidine treatments acted independently.²⁵ There was no evidence that other factors modified the effect of skin-cleansing with chlorhexidine on mortality risk (Table 2). Among LBW infants, chlorhexidine skin-cleansing was equally effective when stratified by whether the birth attendant washed her hands before delivery (washed hands RR: 0.77 [95% CI: 0.51–1.18]; did not wash hands RR: 0.78 [95% CI: 0.53–1.16]). Among LBW infants, there was a trend toward reduction in sepsis-specific deaths in the chlorhexidine group (RR: 0.83; 95% CI: 0.53–1.29).

Once the DSMB recommended that the randomized-trial portion of the study be stopped, all subsequent live births ($n = 6055$) were eligible to receive the active treatment. After conversion of the placebo clusters to chlorhexidine, there was a statistically nonsignificant 6% reduction in overall mortality as compared with no change in the chlorhexidine clusters (Table 3). Among LBW infants, there was a 37% reduction in mortality among infants in the placebo clusters, whereas no change was found from before conversion to after conversion in the chlorhexidine clusters.

DISCUSSION

Overall, there was no evidence that chlorhexidine cleansing of the skin was associated with reduced neonatal mortality in this population. However, among LBW infants who actually received their assigned intervention, there was a 28% reduction in neonatal mortality among those whose skin was wiped with chlorhexidine as soon as possible after birth. The causal evidence for the LBW results were strengthened by the observation of a significant decline in mortality among LBW infants after the randomized portion of the study among sectors that originally were assigned to the placebo group, whereas mortality in the clusters that originally were assigned to chlorhexidine did not change. These data suggest that, in a high-risk subgroup of infants, early postdelivery skin-cleansing with chlorhexidine may reduce the risk for neonatal mortality. This finding needs confirmation, however, from other studies of LBW infants in settings where home deliveries are common. These data lend partial support to 2 previous, nonrandomized, hospital-based studies in Malawi and Egypt, where significant reductions in early neonatal mortality were found among infants who were washed with 0.25% chlorhexidine and whose mothers received vaginal cleansing with the same solution.^{14,15} Whether the combined use of vaginal and newborn skin-cleansing would have produced greater benefit or spread the benefit across all infants in our study population is unknown. More than 90% of births in Nepal occurred at home, where there is a much higher potential for environmental contamination of the newborn infant than in hospital settings.

As expected for an intervention that focuses on reducing the risk for infection, fewer deaths among LBW infants as a result of sepsis were observed in cause-specific analysis. However,

results of verbal autopsies for very young infants must be viewed with caution because many of the signs and symptoms that were used in the algorithms for cause of death can apply to a variety of causes. A reduction in sepsis deaths also was observed in the Malawi study, in which there was a two-thirds reduction in clinically diagnosed early neonatal sepsis deaths.¹⁴

The results from these studies suggest that the importance of a well-developed and healthy skin barrier to infection may have been underestimated to date, especially in settings where environmental contamination and the prevalence of LBW are high. This idea is supported by recent results from trials of therapy with topically applied emollients (eg, sunflower oil), which showed 54% and 41% reductions in nosocomial sepsis among preterm infants in Egypt²¹ and Bangladesh,²² respectively. Moreover, invasion through the skin of pathogens in neonatal sepsis among very LBW infants in developed countries has been documented.^{31–33} Evidence suggests that chlorhexidine-mediated reductions in numbers of colonizing pathogens, alternations in the local balance of microbes, and/or in skin barrier immune function may act to reduce risk for development of systemic infections via cutaneous and/or umbilical portals of entry.^{34–37}

Chlorhexidine was chosen for this study because of its established safety profile at concentrations well above those used in this trial and because it leaves a residual bactericidal effect on the skin.³⁸ It is included on the WHO essential drug list, and the WHO recommends it when antiseptic applications to the umbilical cord are indicated.³⁹ We found no adverse effects as a result of its use as a skin-cleansing agent.

This study does have limitations. Specifically, there was imbalance in the number of deaths that occurred between birth and the time when our local worker arrived at the house to enroll the infant officially and provide the assigned skin-cleansing. We have no explanation for this difference in preenrollment mortality because the distribution of time between birth and the application of the assigned treatment was identical in the 2 treatment groups. Treatment groups also were well balanced on a variety of other factors that are associated with early infant mortality.

The results from this trial in rural Nepal and the hospital-based studies in Africa suggest that a simple, safe, and inexpensive newborn chlorhexidine skin-cleansing may reduce significantly neonatal mortality among infants in these low-resource settings. However, the limitation of a positive treatment effect to a subgroup of this study population requires that additional data that directly address the role of chlorhexidine skin-cleansing among LBW infants be collected in populations with high risk for neonatal mortality before this intervention can move from research to programs and policy.

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Abbreviations

LBW, low birth weight; WD, ward distributor; RR, relative risk; DSMB, Data and Safety Monitoring Board; WHO, World Health Organization; CI, confidence interval.

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FIGURE 1.

Study design. Results of the nested trial of umbilical cord care treatments (gray boxes) are reported separately.²⁵

FIGURE 2.
Participation flow chart.

FIGURE 3.

Kaplan-Meier survival curves according to treatment group among LBW (<2500 g) and normal birth weight (≥2500 g) infants. Log rank test: ≥2500 g $\chi^2 = 0.79$, $P = 0.37$; <2500 g $\chi^2 = 5.26$, $P = .02$.

TABLE 1

Selected Baseline Characteristics According to Treatment Group

Baseline Variable	Chlorhexidine		Placebo	
	<i>n</i>	%	<i>n</i>	%
Total clusters	207	100.0	206	100.0
Cluster size of infants, mean (SD)				
Total live-born infants	8650	100.0	8880	100.0
Maternal age, y				
<20	2151	24.9	2211	24.9
20–24	3503	40.5	3459	39.0
25–29	1860	21.5	2035	2.9
30–34	777	9.0	841	9.5
≥35	359	4.2	334	3.8
Gender				
Male	4443	51.4	4533	51.1
Female	4207	48.6	4347	49.0
Ethnic group ^a				
Pahadi	2375	27.9	2596	29.8
Madeshi	6124	72.1	6109	70.2
Caste ^b				
Brahmin	528	6.6	585	6.7
Chetri	581	6.8	562	6.5
Vaiysha	5379	63.2	5521	63.3
Shudra	1113	13.1	1267	14.5
Muslim/other	876	10.3	781	8.9
Paternal literacy ^c	4862	56.3	4920	55.5
Maternal literacy ^d	2198	25.4	2262	25.5
Paternal occupation ^e				
Farmer	3732	43.2	3961	44.6
Laborer	2933	33.9	2874	32.4
Business	1063	12.3	1121	12.6
Private service	593	6.9	639	7.2
Government	228	2.6	195	2.2
None	88	1.0	75	0.8
Previous child mortality ^f				
≥1 previous child deaths	1767	20.4	2019	22.6
Electricity in house ^g	2039	24.0	2081	23.9
Ownership				
Bicycle ^h	4603	53.2	4744	53.4
Radio ⁱ	2533	29.8	2593	29.8
Television ^j	1538	18.1	1517	17.4
Paddy farm land ^k	4201	49.8	4433	51.5
Nonpaddy farm land ^l	3673	43.5	3857	44.8
Cattle ^m	5122	60.3	5326	61.2
Goats ⁿ	3872	46.7	4065	46.8
House roof material ^o				
None	40	0.5	36	0.4
Thatch	1315	15.5	1457	16.7
Tile/tin	6804	80.0	6878	78.9
Concrete	341	4.0	341	3.9
Latrine at house ^p	972	11.5	1019	11.6
Water source ^q				
Tube well	7226	85.0	7376	84.8

Baseline Variable	Chlorhexidine		Placebo	
	n	%	n	%
Ring well	1236	14.5	1256	14.5
Other	42	0.5	80	0.7
Place of delivery ^r				
Home	7417	90.2	7620	90.2
Outdoors	33	0.4	40	0.4
Health post/clinic	270	3.3	282	3.3
Hospital	441	5.4	450	5.3
Other	63	0.8	56	0.7
Birth weight, g ^s				
Mean (SD)	2704 (437)		2706 (450)	
Median (IQR)	2700 (2414–3000)		2700 (2408–3000)	
<2000	400	4.3	433	5.1
2000–2499	2048	24.8	2058	24.2
2500–2999	3687	44.6	3809	44.8
≥3000	2128	25.8	2201	25.9
Unclear amniotic fluid at delivery ^t	2201	28.7	2292	29.0
Birth attendant washed hands before delivery ^u	4981	63.5	4804	59.8
Used new blade to cut umbilical cord ^v	7753	97.6	7987	98.0
Breastfed within 12 h after delivery ^w	4009	47.8	4095	47.4
Infant given colostrum ^x	6735	80.1	7038	81.2

IQR indicates interquartile range.

^a A total of 326 were missing ethnicity data.

^b A total of 307 were missing caste data.

^c A total of 19 were missing paternal-literacy data.

^d A total of 11 were missing maternal-literacy data.

^e A total of 28 were missing paternal-occupation data.

^f None were missing previous child-death data.

^g A total of 329 were missing data on electricity in the house.

^h None were missing bicycle ownership data.

ⁱ A total of 330 were missing radio-ownership data.

^j A total of 330 were missing television-ownership data.

^k A total of 472 were missing paddy-land data.

^l A total of 472 were missing nonpaddy-land data.

- ^m A total of 332 were missing cattle-ownership data.
- ⁿ A total of 370 were missing goat-ownership data.
- ^o A total of 318 were missing house roof material data.
- ^p A total of 348 were missing latrine data.
- ^q A total of 314 were missing water-source data.
- ^r A total of 858 were missing place-of-delivery data.
- ^s A total of 766 were missing birth weight data.
- ^t A total of 2055 were missing amniotic fluid data.
- ^u A total of 1653 were missing hand-washing data.
- ^v A total of 1432 were missing blade data.
- ^w A total of 493 were missing breastfeeding data.
- ^x A total of 449 were missing colostrum data.

TABLE 2

Mortality According to Treatment Group

Parameter	Placebo Wash		Chlorhexidine Wash		RR	95% CI
	Live Births	Deaths	Live Births	Deaths		
Total	8880	263	8650	264	1.04	0.87–1.24
Received assigned intervention						
No	93	55	131	86	1.11	0.90–1.36
Yes	8787	208	8519	178	0.89	0.72–1.10
Gender						
Male	4533	133	4443	142	1.08	0.86–1.38
Female	4347	130	4207	122	0.98	0.76–1.28
Ethnic group ^a						
Pakistani	2596	49	2375	55	1.24	0.83–1.86
Madeshi	6109	205	6124	203	0.99	0.81–1.21
History of child death in family ^b						
No	6861	178	6883	202	1.14	0.92–1.41
Yes	2018	85	1763	62	0.84	0.59–1.19
Birth attendant washed hands before delivery ^c						
No	3232	107	2860	98	1.04	0.78–1.37
Yes	4804	124	4981	135	1.06	0.82–1.36
Birth weight, g ^d						
<2500	2491	117	2448	83	0.72	0.55–0.95
≥2500	6010	42	5815	49	1.20	0.80–1.81

Rate shown is per 1000 live births.

^a A total of 326 were missing ethnicity data.^b A total of 5 were missing previous child-death data.^c A total of 1653 were missing hand-washing data.^d A total of 766 were missing birth weight data.

Mortality According to Treatment Group During Randomized-Trial Phase and After Switch-over of Placebo Clusters to Chlorhexidine Skin-Cleansing

TABLE 3

Parameter	Placebo Wash			Chlorhexidine Wash		
	Live Births	Deaths	Rate (per 1000 Enrolled Live Births)	Live Births	Deaths	Rate (per 1000 Enrolled Live Births)
Total						
Randomized-trial period, <i>n</i>	8880	263	29.6	8650	264	30.1
Placebo converted to chlorhexidine, <i>n</i>	3136	87	27.7	2919	94	32.2
RR after conversion vs before conversion		0.94			1.04	
95% CI		0.74–1.19			0.83–1.31	
Birth weight <2500 g ^a						
Randomized-trial period, <i>n</i>	2491	117	47.0	2448	83	33.9
Placebo converted to chlorhexidine, <i>n</i>	952	28	29.4	877	32	36.5
RR after conversion vs before conversion		0.63			1.08	
95% CI		0.42–0.94			0.72–1.61	
Birth weight ≥2500 g ^a						
Randomized-trial period, <i>n</i>	6010	42	7.0	5815	49	8.4
Placebo converted to chlorhexidine, <i>n</i>	2114	12	5.7	1978	14	7.1
RR after conversion vs before conversion		0.81			0.84	
95% CI		0.43–1.54			0.47–1.52	

^aBirth weight data were missing for 134 infants during the postconversion data-collection period.