Waterless Hand Cleansing with Chlorhexidine during the Neonatal Period by Mothers and Other Household Members: Findings from a Randomized Controlled Trial

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Abstract. Observational data suggest maternal handwashing with soap prevents neonatal mortality. We tested the impact of a chlorhexidine-based waterless hand cleansing promotion on the behavior of mothers and other household members. In rural Bangladesh in 2014, we randomized consenting pregnant women to chlorhexidine provision and hand cleansing promotion or standard practices. We compared hand cleansing with chlorhexidine or handwashing with soap before baby care, among mothers and household members in the two groups, and measured chlorhexidine use in the intervention arm. Chlorhexidine was observed in the baby's sleep space in 97% of 130 intervention homes, versus soap in 59% of 128 control homes. Hand cleansing before baby care was observed 5.6 times more frequently among mothers in the intervention arm than in the controls (95% CI = 4.0–7.7). Hand cleansing was significantly more frequently observed in the intervention arm among women other than the mother (RR = 10.9) and girls (RR = 37.0). Men and boys in the intervention arm cleansed hands before 29% and 44% of baby care events, respectively, compared with 0% in the control arm. The median number of grams consumed during the neonatal period was 176 (IQR = 95–305 g), about 7.8 g/day (IQR = 4.2–13.8 g). Promotion of waterless chlorhexidine increased hand cleansing behavior among mothers and other household members. Discrepancy between observed use and measured chlorhexidine consumption suggested courtesy bias in structured observations. A waterless hand cleanser may represent one component of the multimodal strategies to prevent neonatal infections in low-resource settings.

INTRODUCTION

The neonatal period (the first 28 days of life) is highly vulnerable, with 44% (2.8 million) of childhood deaths occurring in the first 28 days of life.¹ Of these, nearly one-quarter are attributable to infectious causes, including sepsis, pneumonia, and umbilical cord infections. Data from observational studies suggest that hand hygiene may reduce the risk of umbilical cord infections by about 25% and mortality by 41%.^{2,3} But, consistent with weak habits and social norms regarding handwashing with soap in many low-income settings, mothers often do not wash their hands despite the vulnerability of the neonatal period.^{4,5} Hand hygiene promotion is a relatively weak component of neonatal care counseling, typically consisting of provision of a bar of soap, a basic explanation of the potential health benefits of handwashing, and instructions on how to wash hands. When applied in a cluster-randomized controlled trial in Pakistan, this approach to hand hygiene promotion did not yield benefits for neonatal mortality prevention, but because handwashing behavior was not systematically assessed, the extent to which the intervention resulted in improved handwashing is unclear.⁶ Indeed, prior evidence suggests that interventions relying primarily on improving awareness of the health effects of washing hands appear ineffective, likely because they do not take into account the critical psychosocial and contextual motivators of and barriers to handwashing with soap.⁵

In qualitative research in two sites in rural Bangladesh, we have found a number of barriers to washing hands with soap and water in the neonatal period.⁵ Mothers of neonates reported being too busy to wash hands. Mothers also perceived a need to avoid contact with water because of humoral

concerns, citing fears that excessive exposure to water for the mother could increase the risk of respiratory infection in the neonate. Even when mothers reported wanting to increase their handwashing behavior and to protect baby from others' germs, they found it difficult to overcome social hierarchies within their homes. Whereas mothers felt that they could ask children and, sometimes their husbands, to wash hands, they usually could not request in-laws or elders to wash hands with soap before touching the neonate.

Given the complex set of barriers to washing hands with soap and water in the newborn period, we identified the need for an innovative solution for hand cleansing that is convenient, portable, waterless, and that would be accepted by mothers and others in the home, including children and elders.

Given its bactericidal and bacteriostatic properties, chlorhexidine is used for antiseptic, topical, and dental uses worldwide; has a favorable safety profile; and is a common component of surgical scrub preparations for hand cleansing.⁷ Chlorhexidine is recommended for umbilical cord cleansing for neonates born at home in high neonatal mortality rate settings on the basis of multiple trials from South Asia demonstrating a reduction in all-cause neonatal mortality.^{6,8,9} Chlorhexidine is listed on the WHO's model list of essential medications for children for antiseptic (5% chlorhexidine digluconate) and umbilical cord care (7.1% chlorhexidine digluconate). A chlorhexidine-based hand cleanser has the potential to overcome numerous barriers to hand cleansing in the neonatal period because it can be delivered in a formulation that does not require rinsing and that can be maintained in a portable pump bottle at the neonate's bedside.

In this study, we sought to evaluate the behavioral effects of a chlorhexidine-based waterless hand cleansing promotion on mothers and other household members of neonates in a randomized controlled trial. Our objectives were to assess the impact of a chlorhexidine-based waterless hand cleansing promotion on the hand cleansing behavior of mothers and other household members in the neonatal period, and to

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describe the acceptability of chlorhexidine to mothers of neonates.

METHODS

Study design and site. The trial was conducted in Mirzapur, Bangladesh, a rural area approximately 60 km northwest of Dhaka that has one tertiary-level private hospital. Demographic surveillance in the region is ongoing and managed by Dhaka Shishu Hospital in collaboration International Centre for Diarrhoeal Diseases Research, Bangladesh.

Participant selection. The demographic surveillance system staff provided a listing of pregnant women at 32–34 weeks of gestation, based on the reported date of the last menstrual period, and living in households in the demographic surveillance area. Trial data collection staff visited each woman included on the pregnancy listing to assess for the following eligibility criteria: pregnant at the time of the data collector's visit, married, between 32 and 34 weeks of gestation, and intending to reside in the demographic surveillance area through the remainder of the antenatal period and the first 4 weeks of the neonate's life. Data collectors described the study to eligible pregnant women and requested signed informed consent. Data collectors then administered a baseline survey and observed household conditions with respect to handwashing materials, water, and sanitation.

Randomization. We used block randomization, using blocks of four, to randomly assign participants to either the chlorhexidine intervention or to standard practices (control).¹⁰ The block randomization approach was used to promote balanced sample sizes across the treatment arms over the enrollment period.

An investigator with no access to study participants constructed the assignment table. A field supervisor consulted the assignment table to assign the participant to intervention or control, after baseline data collection was completed in the participant's household. Data collectors were not blinded to the assignment status of participants because the intervention included a chlorhexidine dispenser, which would have been readily observable during the data collector's visit to the household.

Description of study arms/intervention description. Intervention followed baseline data collection and assignment to the study arm. Health promoters, who were distinct from data collectors, delivered all intervention components

pertinent to each treatment arm in a total of three visits to each participating household (Table 1). Health promoters provided maternal and neonatal health counseling to participants and interested family members in both arms (content shown in Box 1). Both treatment arms received a clean delivery kit, which included sufficient chlorhexidine for one-time application to the umbilical stump. No additional communication regarding hand hygiene was addressed to control participants until the completion of all data collection; in postnatal week 6, participants in both intervention and control arms were counseled on handwashing with soap to prevent diarrhea and respiratory infections in the infant.

Hand cleansing with chlorhexidine was promoted to those in the intervention arm. The goal of the chlorhexidine hand cleansing intervention was to increase hand cleansing among mothers and others who were likely to serve as secondary caregivers, or who were likely to come into direct contact with the neonate; secondary caregivers were typically adult women, other than the mother, or older girls in the home who might provide support to the mother in caring for the newborn. The behavior change promotion focused on identifying the benefits of hand cleansing in general, the barriers faced by some to handwashing with soap, and the advantages of chlorhexidine as a waterless, portable product for hand cleansing. The discussions led by the health promoters mobilized participants to identify motivators and barriers for hand cleansing, solutions to address barriers, and strategies for reminding other household members to wash hands. In the intervention group, soap was neither encouraged nor discouraged during the course of the study.

We previously developed a theoretical model conceptualizing the individual and interpersonal determinants of hand hygiene among mothers of newborns based on the health belief model, the theory of reasoned action/theory of planned behavior, social cognitive theory, and information gleaned from formative research (Figure 1).^{11,12} The chlorhexidine hand cleansing intervention was delivered through an iterative discussion-oriented format that identified barriers to hand cleansing among mothers and other household members and promoted chlorhexidine for hand cleansing on the basis of three distinct benefits: nurture, convenience, and cues. Handwashing is viewed as a nurturing behavior among mothers of neonates in rural Bangladesh.⁵ Our intervention promoted the convenience of hand cleansing with chlorhexidine because it does not require rinsing and because it can easily be maintained at the neonate's bedside. We provided a calendar with images of the recommended times for hand

TABLE 1
Data collection and intervention schedule

	Consent	Baseline	Randomization	Intervention	Rapid assessment	Structured observation	Acceptability and endline survey	In-depth interview
Gestational weeks 34–36	✓*	✓	✓	✓	–	–	–	–
Gestational weeks 37–39	–	–	–	✓	–	–	–	–
Birth								
Postnatal week 1	–	–	–	✓✓†	✓	–	–	–
Postnatal week 2	–	–	–	–	✓	✓	–	–
Postnatal week 3	–	–	–	–	–	–	–	–
Postnatal week 4	–	–	–	–	✓	–	✓	–
Postnatal week 6	–	–	–	Control and intervention arms (handwashing)	–	–	–	Intervention arm

* Activity completed in both treatment arms.

† Two intervention visits were completed during postnatal week 1.

FIGURE 1. Theoretical model conceptualizing individual and interpersonal determinants of hand hygiene among mothers of newborns.

cleansing to serve as a visual cue and asked mothers to tick the dates on which they cleansed hands with chlorhexidine to promote self-reinforcement of behavior.

Among mothers and secondary caregivers (typically other adult women, adolescent girls, fathers, or others who might provide direct care for the neonate), health promoters promoted chlorhexidine hand cleansing before umbilical cord

care and after contact with respiratory secretions. Among all others who might come into contact with the neonate, including children in the household and adult or child visitors from outside the household, health promoters promoted chlorhexidine hand cleansing before touching the neonate and after contact with respiratory secretions. These role-specific times for hand cleansing will hereafter be referred to as “recommended times.” Health promoters also recommended hand cleansing with chlorhexidine among mothers at three fixed times of day (morning, noon, and night) to assure at least a minimum number of hand cleanses per day.

Promoters also demonstrated chlorhexidine use to the pregnant mothers and other family members. Small children were also encouraged to participate in the demonstration events. By engaging participants in role plays with each other, health promoters encouraged mothers and family members to become comfortable with requesting each other to cleanse hands with chlorhexidine at recommended times.

Health promoters provided to each pregnant woman in the intervention group one 500-mL bottle of 4% chlorhexidine (7.1% chlorhexidine digluconate) lotion,⁷ a formulation newly developed for this study by ACI Pharmaceuticals, Ltd. (<http://www.aci-bd.com/aci-pharmaceuticals/>). Participants were informed that chlorhexidine would be replenished as needed. Health promoters recommended using one pump, which, as designed, dispensed approximately 3 mL of the chlorhexidine product.

FIGURE 2. CONSORT diagram. *Intervention visit 1b: because of the extensive content to be covered in the first intervention visit, some content was delivered in a follow-up interaction.

TABLE 2
Description of participants at baseline, by treatment arm, Mirzapur, Bangladesh, 2014

Characteristic	Control (n = 128)	Intervention (n = 130)
Age of respondent (years), median (IQR)	24 (20–29)	25 (20–28)
Median number of years education of respondent (IQR)	7 (5–9)	7 (5–9)
Religion, n (%)		
Islam	118 (92)	115 (88)
Hindu	10 (8)	15 (12)
Household characteristics		
Number of rooms for sleeping, median (IQR)	2 (2–3)	2 (1–3)
Number of people living in home, median (IQR)	4 (3–6)	4 (3–5)
Smoking inside home, n (%)	50 (39)	57 (44)
Drinking water source: shallow tube well, n (%)	115 (90)	108 (83)
Materials present at handwashing station, n (%)		
Water	122 (95)	125 (96)
At least one type of soap (bar, powdered, or liquid)	38 (30)	39 (30)
Materials reported used to wash hands after defecation, n (%)		
Water only	76 (60)	79 (62)
Soap and water	49 (39)	49 (38)
Mud	1 (1)	0 (0)
Cleaning hands reported effective for preventing illness in the baby, n (%)		
Very effective	124 (97)	122 (94)
Somewhat effective	4 (3)	8 (6)
Self-report of always washing hands with soap, n (%)		
Before eating	120 (94)	122 (94)
After eating	126 (98)	129 (99)
Before feeding a child	113 (88)	103 (79)
Before touching a baby	25 (20)	19 (15)
After cleaning a child's anus	114 (89)	110 (85)
After disposing of a child's feces	107 (84)	96 (74)
After defecation	124 (97)	124 (95)
After contact with respiratory secretions	17 (13)	27 (21)
Are you able to ask others to clean their hands?, n (%)		
Always	35 (27)	26 (20)
Sometimes	76 (59)	79 (61)
Never	17 (13)	25 (19)

On completion of the study, intervention staff promoted handwashing with soap to participants in both intervention and control groups because of the ongoing vulnerability of the young infants to infections and the lack of availability of chlorhexidine in the market.

Birth surveillance. Field-workers encouraged birth notification by the household members and called participants once per week in weeks 37–38 and every 2 days thereafter to identify when the birth had occurred. Following birth notification, a data collector visited the home to inquire about details of the birth, use of the clean delivery kit, application of substances to the cord, and the hand hygiene of the birth attendant.

Hand cleansing measurement. Data collectors observed the presence of hand cleansing materials in the baby's sleeping room, such as soap, water, and chlorhexidine. At each of four postnatal visits, data collectors also measured the residual weight of the chlorhexidine bottle as a marker of chlorhexidine consumption.

To compare treatment arms with respect to mothers' hand cleansing behavior in the neonatal period (objective 1), our principal outcome of interest was observation of hand cleansing, which was defined as cleaning hands with chlorhexidine (intervention arm) or handwashing with soap or water (intervention or control arm). Data collectors observed hand cleansing during two 3-hour structured observations in postnatal weeks 1 and 3. The data collector requested to observe the neonate, seated herself in as unobtrusive a

position as possible, and observed all interactions that anyone had with the neonate. She observed neonatal contact and recorded whether or not hand cleansing occurred at times recommended to the intervention group.

Adverse events. Data collectors assessed potential adverse events among all participating households, recording the nature of the event and whether or not hospitalization followed the event. Skin complaints, such as rash, have been cited elsewhere as the most common adverse event resulting from chlorhexidine use.¹³

Acceptability. At the final visit among all intervention participants, the data collector used a structured questionnaire to inquire about the ease of chlorhexidine use, scent, skin comfort, and the occurrence of skin reactions. We conducted in-depth interviews with a subset of intervention mothers to explore barriers and motivators to the use of chlorhexidine, perceived acceptability of the chlorhexidine, and the mother's self-efficacy at asking others to use chlorhexidine before visiting with the neonate.

We conducted purposive sampling for in-depth interviews with intervention mothers according to relatively high or low use. We conducted 20 in-depth interviews including 10 mothers with high chlorhexidine use based on the weight of chlorhexidine used and/or observed use during structured observation (high use mothers) and 10 mothers who did not use chlorhexidine at all, either as observed during the structured observation or based on the weight of chlorhexidine (low use mothers).

TABLE 3
Potential adverse events observed among mothers, fetuses, and neonates, by treatment arm, Mirzapur, Bangladesh, 2014

	Mothers			Fetuses/neonates		
	Control (n = 128) (%)	Intervention (n = 130) (%)	P-value*	Control (n = 122) (%)	Intervention (n = 124) (%)	P-value*
Mortality						
Death	—	—	—	2	2	1.0
Stillbirth	—	—	—	2	4	0.68
Events with hospitalization						
Number of participants with serious events with hospitalization	1	2	1.0	7	13	0.24
Excessive vaginal bleeding	1	1	1.0	—	—	—
Convulsion	—	—	—	0	3	0.25
Diarrhea (with dehydration)	—	—	—	0	1	1.0
Difficulty breathing	—	—	—	2	2	1.0
Hyperthermia (fever)	—	—	—	2	3	1.0
Hypothermia	—	—	—	0	1	1.0
Weak, abnormal, or absent cry	—	—	—	0	1	1.0
Diarrhea (no dehydration)	—	—	—	0	1	1.0
Cough	—	—	—	1	1	1.0
Decreased appetite	—	—	—	0	1	1.0
Lethargic	—	—	—	0	2	0.50
Difficulty breastfeeding	—	—	—	0	1	1.0
Pus discharge from umbilicus	—	—	—	1	0	1.0
Red umbilicus	—	—	—	1	0	1.0
Events without hospitalization						
Number of participants with adverse events without hospitalization	1	1	1.0	19	11	0.12
Perineal pain	0	1	1.0	—	—	—
Severe abdominal pain	1	0	1.0	—	—	—
Severe headache	1	0	1.0	—	—	—
Cough	—	—	—	2	3	1.0
Diarrhea (no dehydration)	—	—	—	1	2	1.0
Difficulty breathing	—	—	—	3	0	0.12
Difficulty breastfeeding	—	—	—	2	0	0.25
Hyperthermia (fever)	—	—	—	4	3	0.72
Pus discharge from both eyes	—	—	—	2	0	0.25
Pus discharge from umbilicus	—	—	—	5	2	0.28
Skin pustules	—	—	—	4	2	0.44
Ulcers or white patches in mouth	—	—	—	1	3	0.62
Yellow skin or eyes	—	—	—	1	1	1.0
Red umbilicus	—	—	—	0	1	1.0
Swollen umbilicus	—	—	—	2	1	1.0
Vomiting	—	—	—	1	1	1.0
Irritable/restless	—	—	—	1	0	1.0

* P-value estimated by Fisher's exact test.

In addition, we conducted four focus group discussions of 22 respondents (12 females and 10 males) in total, one each among female caregivers other than the mother and male caregivers in households with high consumption of chlorhexidine and households with low consumption of chlorhexidine. We selected household members for participation in the focus group discussion by using chain referrals sampling, also referred to as snowball sampling, from among mothers with whom we conducted in-depth interviews.¹⁴

Sample size estimation. To estimate the sample size for assessing the impact of the chlorhexidine-based hand cleansing intervention on maternal handwashing behavior, we assumed that the probability of hand cleansing, that is, cleansing with chlorhexidine or handwashing with soap and water, at a recommended time would be 0.15 in the control arm,¹⁵ as measured by structured observation. We projected that the intervention would result in a 33% relative increase in observed hand cleansing by the mother at the recommended times, either by handwashing with soap or cleansing with chlorhexidine.

To observe a 33% relative increase in hand cleansing in the intervention arm, at the 95% significance level and with 80%

power, we would need to observe 900 recommended times in each study arm, or 1,800 recommended times in total. To account for the effects of repeated measures from structured observation data, we applied a design effect of 2, thus requiring us to observe 1,800 recommended times in each study arm, or 3,600 recommended times in total. Based on preliminary findings of our trial of handwashing promotion in the neonatal period in 2010–2011,¹⁶ we estimated that we would observe two recommended times per hour of structured observation, indicating a need to carry out 1,800 hours of structured observation in total, or 900 hours of structured observation in each study arm. Therefore, we sought to carry out two structured observations of 3-hour duration each among 150 participants in each study arm, or 300 participants in total.

Analytic methods. We used an intent-to-treat approach for the quantitative analyses. Because the primary objective was to evaluate the effect of the intervention on the mother's complete handwashing behavior during the neonatal period, in our intent-to-treat analysis, we excluded those mothers who had fetal loss, stillbirths, or whose newborns died within the first 24 hours postpartum.

The primary outcome of interest was the probability of hand cleansing at a recommended event by the mother of the neonate, as observed during structured observations. The secondary outcome of interest was the probability of hand cleansing at a recommended event by other household members in contact with the neonate, as observed during structured observations.

We applied the log binomial regression method to estimate the effect of intervention on the probability of hand cleansing at recommended times, using generalized estimating equations to account for clustering associated with repeated measures (i.e., numerous events, observed during two different observation periods, and for the same individual). We report risk ratios and 95% CIs. We first compared the intervention and control arms with respect to maternal hand cleansing behavior. Thereafter, we examined the effects of the intervention on the hand cleansing behavior of each of the following groups, accounting for clustering at the household level: adult female caregivers other than the mother (> 12 years old), fathers and other adult male caregivers (> 12 years old), girls, and boys.

Among participants in the intervention arm, we characterized chlorhexidine consumption based on the change in weight of chlorhexidine between visits. We described chlorhexidine consumption according to the overall weight used, the mean number of grams used per neonatal day, and the number of uses per day. Based on our observation that one pump of the chlorhexidine bottle yielded approximately 3 g of the product, we calculated the number of uses per day by dividing the mean number of grams used per day by 3. Among households that received chlorhexidine replenishment during the study period, we manually calculated changes in volume to estimate the number of grams of chlorhexidine used per day. We evaluated the association between chlorhexidine consumption and the observation of maternal hand cleansing with chlorhexidine in structured observations using a generalized linear model, adjusting standard errors for clustering at the individual level.

Using survey data from among mothers in the neonatal period, we described the prevalence of self-reported acceptability of chlorhexidine for hand cleansing among respondents in the intervention arm. For qualitative data analysis, we developed a coding system based on themes commonly identified in the raw data. We examined information from participants from high-use households separately from low-use households.

This clinical trial was registered at www.clinicaltrials.gov (NCT01955317).

RESULTS

Recruitment and demographics. Substantial political unrest in 2013 delayed enrollment of participants into the study and resulted in fewer pregnant women enrolled than targeted. Among 587 women identified as pregnant from the demographic surveillance between January and July 2014, 258 (44%) were found to be eligible and consented to participation (Figure 2). Of these, 128 (50%) were randomly allocated to the control arm and 130 (50%) to the intervention arm. Pregnancies resulted in live births in 95% of the respondents in each arm.

At baseline, respondents in the two treatment arms were similar with respect to age, educational attainment, religion, and household size (Table 2). Most households in both arms were found to have water at the main handwashing station, but only 30% in each were observed to have soap.

Adverse fetal and newborn outcomes. There were no significant differences between intervention and control groups with respect to fetal or neonatal deaths, potential adverse events with hospitalization, and potential adverse events without hospitalization (Table 3). Skin-related complaints were reported for 5% of mothers in the chlorhexidine arm, identical to the frequency in the control arm. Among neonates, skin-related complaints were reported for 41% of neonates in the control arm and 34% of neonates in the intervention arm; the difference in proportion reported in neonates across treatment arms was not statistically significant.

Availability of hand cleansing materials. During the four postnatal visits, soap was observed in the neonate's sleeping space in 59–63% of households of control participants, compared with chlorhexidine observed in 97–99% of intervention households. Notably, soap was less commonly observed in the neonate's sleeping space in intervention households (40–61%).

Observed hand cleansing behavior. Data collectors conducted at least one structured observation in households of 128 controls and 130 intervention participants (Table 4). In both structured observations, mothers in the control arm were more frequently observed than intervention mothers to wash hands with water alone. There was no significant difference between the two arms with respect to frequency of observed handwashing with soap. A majority of mothers in the intervention arm used chlorhexidine at least once for hand cleansing in both structured observations (week 1: 64%; week 3: 68%). Mothers in the intervention arm were 2.3 times as likely as controls to be observed to wash hands with soap or use chlorhexidine during the week 1 observation (95% CI = 1.7–3.2, $P < 0.0001$), with similar findings during the week 3 observation. Observation of hand cleansing by at least one household member other than the mother was 2.4–2.5 times as likely in intervention households compared with control households.

Data collectors observed events of recommended times for handwashing among control mothers ($n = 1,441$) and intervention mothers ($n = 1,471$) (Table 5). Hand cleansing was observed in 5% of 849 baby care events observed in control mothers and 26% of 851 events observed in intervention mothers (RR = 5.6; 95% CI = 3.8–8.2). Intervention mothers were also significantly more likely to be observed washing hands with soap or using chlorhexidine after potential contact with feces from the mother herself, newborn, or any other child (RR = 4.1; 95% CI = 2.9–5.8). Whereas none of the control mothers washed hands with soap after contact with her own or any child's respiratory secretion, hand cleansing was observed among 29% of intervention mothers at such events.

Group differences in hand cleansing were greater among household members than among mothers (Table 6). In intervention households, women other than the mother were 10.9 times more likely to be observed practicing hand cleansing before baby care than their counterparts in the control arm (95% CI = 4.9–24.1). Whereas 40% of girls cleansed hands with chlorhexidine or soap in the intervention arm, only 1% of girls in the control arm did so (RR = 37.0; 95%

TABLE 4
Frequency of hand cleansing during structured observations, among mothers and other household members, by treatment arm

	Mothers									
	Week 1 observation					Week 3 observation				
	Control (n = 107)	Intervention (n = 105)	RR (95% CI) (P-value)	P-value		Control (n = 118)	Intervention (n = 115)	RR (95% CI) (P-value)	P-value	
Handwashing with water ≥ one time, n (%)	75 (70)	60 (57)	0.8 (0.7, 1.0)	0.05		80 (68)	71 (60)	0.9 (0.7, 1.1)	0.19	
Mean number of times (SD)	1.6 (1.5)	1.2 (1.3)	-0.4 (-0.8, -0.04)	0.03		1.4 (1.2)	1.3 (1.4)	-0.02 (-0.3, 0.3)	0.9	
Handwashing with chlorhexidine ≥ one time (SD)	0 (0)	67 (64)	—	< 0.0001		0 (0)	80 (68)	—	< 0.0001	
Mean number of times (SD)	0 (0)	1.4 (1.5)	1.4 (1.1, 1.7)	< 0.0001		0 (0)	1.4 (1.4)	1.4 (1.1, 1.6)	< 0.0001	
Handwashing with soap ≥ one time (SD)	32 (30)	25 (24)	0.8 (0.5, 1.2)	0.3		38 (32)	34 (29)	0.9 (0.6, 1.3)	0.5	
Mean number of times (SD)	0.3 (0.5)	0.3 (0.7)	-0.02 (-0.2, 0.2)	0.8		0.5 (0.8)	0.5 (1.0)	0.005 (-0.2, 0.2)	0.9	
Handwashing with soap or chlorhexidine ≥ one time (SD)	32 (30)	73 (70)	2.3 (1.7, 3.2)	< 0.0001		38 (32)	92 (78)	2.4 (1.8, 3.2)	< 0.0001	
Mean number of times (SD)	0.3 (0.5)	1.7 (1.7)	1.4 (1.1, 1.7)	< 0.0001		0.5 (0.8)	1.9 (1.7)	1.4 (1.1, 1.7)	< 0.0001	
All other household members (non-mothers)										
	Week 1 observation					Week 3 observation				
	Control (n = 105)	Intervention (n = 105)	RR/β (95% CI) (P-value)	P-value		Control (n = 114)	Intervention (n = 117)	RR/β (95% CI) (P-value)	P-value	
	Control (n = 105)	Intervention (n = 105)	RR/β (95% CI) (P-value)	P-value		Control (n = 114)	Intervention (n = 117)	RR/β (95% CI) (P-value)	P-value	
Handwashing with water ≥ one time, n (%)	89 (85)	87 (83)	0.98 (0.9, 1.1)	0.71		89 (78)	95 (81)	1.0 (0.9, 1.2)	0.56	
Mean number of times (SD)	3.8 (3.6)	3.6 (3.7)	-0.2 (-1.2, 0.8)	0.67		3.5 (4.2)	3.0 (2.8)	-0.5 (-1.4, 0.5)	0.32	
Handwashing with chlorhexidine ≥ one time (SD)	0 (0)	53 (50)	—	< 0.0001		0 (0)	43 (37)	—	< 0.0001	
Mean number of times (SD)	0 (0)	0.9 (0.9)	0.9 (0.7, 1.1)	< 0.0001		0 (0)	0.46 (0.7)	0.5 (0.3, 0.6)	< 0.0001	
Handwashing with soap ≥ one time (SD)	26 (25)	23 (22)	0.9 (0.5, 1.4)	0.62		23 (20)	24 (21)	1.0 (0.6, 1.7)	0.95	
Mean number of times (SD)	0.3 (0.7)	0.3 (0.8)	-0.03 (-0.2, 0.2)	0.78		0.3 (0.7)	0.2 (0.5)	-0.1 (-0.2, 0.1)	0.37	
Handwashing with soap or chlorhexidine ≥ one time (SD)	26 (25)	63 (60)	2.4 (1.7, 3.5)	< 0.0001		23 (20)	58 (50)	2.5 (1.6, 3.7)	< 0.0001	
Mean number of times (SD)	0.33 (0.7)	1.2 (1.5)	0.6 (0.4, 0.8)	< 0.0001		0.3 (0.7)	0.7 (0.8)	0.4 (0.2, 0.6)	0.0001	

TABLE 5
Observed hand cleansing among mothers, by treatment arm, Mirzapur, Bangladesh, 2014

Event type	Control	Intervention	RR (95% CI)
Baby care			
Number of events	849	851	—
Proportion with hand cleansing (%)	5	26	5.6 (4.0–7.7)
Fecal contact			
Number of events	261	284	—
Proportion with hand cleansing (%)	12	49	4.1 (2.9–5.9)
Respiratory secretion contact			
Number of events	5	13	—
Proportion with hand cleansing (%)	0	29	—
Food contact			
Number of events	321	323	—
Proportion with hand cleansing (%)	6	8	1.4 (0.8–2.6)
All events			
Number of events	1,441	1,475	—
Proportion with hand cleansing (%)	6	26	4.30 (3.45, 5.35)

CI = 5.1–269.7). None of the men or boys in the control arm cleansed hands before baby care events; 29% of men and 44% of boys in the intervention arm did so.

Chlorhexidine consumption. Data collectors weighed chlorhexidine bottles at two or more visits to 120 (92%) intervention mothers, 11 (9%) of whom had received chlorhexidine replenishment. Among 120 with chlorhexidine weight data, the median number of grams consumed during the neonatal period was 176 (IQR = 95–305 g), representing a median of 7.8 g of chlorhexidine consumed per day (IQR = 4.2–13.8 g). Hence, the estimated number of uses was a median of 2.4 uses (IQR = 1.4–4.6 uses). Chlorhexidine consumption, as measured by weight change, was modestly correlated with the number of times that mothers cleansed hands with chlorhexidine during the structured observation ($R = 0.17$, $P = 0.01$). Chlorhexidine use was significantly more likely to be observed in structured observations in households in the second, third, and fourth highest quartiles of chlorhexidine consumption than in households in the lowest quartile of consumption (Table 7).

Because there is a substantial risk of reactivity among subjects in structured observation, we also evaluated the approximate number of times of hand cleansing with chlorhexidine per day based on observed consumption.¹⁷ If

observed use during the 3-hour structured observation (mean 1.4 times per mother) were representative of approximately 18 waking hours per day, then the daily chlorhexidine consumption would have been approximately 25 g/day (or approximately eight uses). Our analysis of chlorhexidine weight changes indicated a lower median consumption of 7.8 g/day (or 2.4 g uses per day) than that based on structured observations. Based on a mean 0.3 hand washes with soap during the 3-hour structured observation in the control group, we estimate that the number of times control mothers washed their hands with soap in an 18-hour day is 1.8, marginally lower than the 2.4 chlorhexidine uses in the intervention group.

Acceptability of chlorhexidine. In in-depth interviews and group discussions, participants reported that the chlorhexidine works quickly, is easy and convenient to use, and time saving; they appreciated its waterless and antimicrobial properties. Mothers reported that it was easier to ask others to clean hands with chlorhexidine than to wash hands with soap. Barriers to chlorhexidine use included a perceived long drying time, which was reported by a few mothers. Some did not like the feel of the chlorhexidine lotion. In addition, mothers did not like to use chlorhexidine before breastfeeding for several reasons, including a concern about the neonate swallowing chlorhexidine if the mother cleansed her hands before feeding.

TABLE 6
Observed hand cleansing among household members of neonates, by treatment arm, Mirzapur, Bangladesh, 2014

Category of household contacts of neonates	Control	Intervention	RR (95% CI)
Mothers			
Number of events	849	851	—
Proportion with hand cleansing (%)	5	26	5.6 (4.0–7.7)
Fathers			
Number of events	1	3	—
Proportion with hand cleansing (%)	0	66	—
Adult women, other than the mother			
Number of events	224	215	—
Proportion with hand cleansing (%)	3	34	10.87 (4.91–24.05)
Adult men, other than the father			
Number of events	10	14	—
Proportion with hand cleansing (%)	0	29	—
Girls			
Number of events	92	97	—
Proportion with hand cleansing (%)	1	40	36.99 (5.07–269.69)
Boys			
Number of events	40	39	—
Proportion with hand cleansing (%)	0	44	—

TABLE 7

Association between chlorhexidine consumption, as determined by change in weight, and observed handwashing with chlorhexidine among participants in the intervention arm, Mirzapur, Bangladesh, 2015

Quartile of chlorhexidine consumption per day	Association between quartile of chlorhexidine consumption and observed hand cleansing with chlorhexidine
	RR (95% CI)
	All household members
1	Referent
2	1.4 (1.06, 2.1)
3	1.5 (1.02, 2.3)
4	1.8 (1.2, 2.8)
	Mothers of neonates
1	Referent
2	1.8 (1.13, 2.8)
3	1.8 (1.14, 2.74)
4	1.9 (1.3, 2.9)

Male participants felt that the intervention did not adequately involve them, perceiving that the health promoters more readily included other women in the family than themselves. We did not find substantive differences in reported barriers and motivators for chlorhexidine use, among participants in high-use households versus those in low-use households.

DISCUSSION

During the vulnerable and busy neonatal period, a number of barriers prevent hand hygiene among mothers and other household members of neonates. Provision and promotion of a waterless chlorhexidine-based hand cleansing option led to increases in observed hand cleansing among mothers and other household members, compared with standard practices. However, the estimated number of uses of chlorhexidine per day lagged behind the number of times recommended.

These findings underscore the continued challenge in promoting hand hygiene in the neonatal period. Extensive prior research in Bangladesh has documented the lack of a widespread handwashing habit and the dearth of social norms favoring at times of possible pathogen transmission, and mothers have described the challenges they face in improving their own handwashing or that of others in the household during the newborn period.⁵ The improvements we have observed in hand cleansing with provision and promotion of chlorhexidine were likely modest, given the relatively short intervention duration against the backdrop of lifelong habits, and the busy and complex newborn period. The safety profile of the chlorhexidine lotion for hand cleansing was favorable, consistent with that in other studies.^{9,18–21}

Although handwashing with soap before umbilical cord contact has been observed to be protective against umbilical cord infections,²² there is a paucity of information on the effectiveness of hand cleansing at other times of potential pathogen transmission to neonates in low- and middle-income countries. We recommended fixed times for handwashing, at three times in the day, and event-specific times for chlorhexidine use, such as before umbilical contact,²² to reduce the risk of pathogen transmission from mothers and other family members. Adherence to such ambitious recommendations, especially the large number of times to cleanse hands, may be particularly challenging during the busy neonatal period.

Mothers and newborns are closely cocooned with each other, particularly in South Asian cultural context.⁵ Other household members, particularly children, may be responsible for introducing new organisms to the newborn because they are more likely to move in and out of the household environment. Compared with control peers, increases in observed hand cleansing among secondary caregivers and other household members were greater than among mothers in the intervention group. Whereas our prior work suggested that it

Box 1

Maternal and neonatal health counseling

The objectives of the maternal and neonatal health counseling were to do the following:

- Highlight the vulnerability of the neonatal period.
- Inform participant and her family of the schedule recommended by the government of Bangladesh for prenatal care and strongly encourage participants to seek appropriate prenatal care, including tetanus toxoid vaccination. Tetanus toxoid is provided free of cost as part of antenatal care at all government of Bangladesh health facilities.
- Discuss birth plans and encourage participants to develop a birth plan, including location of the birth, materials, persons needed, and an emergency plan.
- Introduce and discuss the use of a clean delivery kit for hygienic delivery to reduce infections. This will include instructions on cutting the umbilical cord. Provide a clean delivery kit to the participant, which will include a clean blade, a clean string for tying the cord, and a clean mat for the mother to lie on, among other items.
- Encourage close family members to motivate or demand hand washing with soap by birth attendants before and during labor and delivery.
- Discuss maternal danger signs with participant and her family and encourage care seeking when recognized.
- Discuss neonatal danger signs with participant and her family and encourage care seeking when recognized.
- Discuss neonatal hypothermia prevention with participant and her family and work with the family to build acceptance of the message.
 - Specifically, recommend immediate drying of the newborn and placement on the mother's belly or chest and then covering.
 - Delay bathing until day 2 of life.
- Discuss the benefit of immediate and exclusive breastfeeding with participant and her family and work with the family to build acceptance of the message.
- Provide chlorhexidine and gauze for umbilical cord cleansing, and explain chlorhexidine cord care to the participant and work with her and her family.

Materials: Each participant was given a clean delivery kit and a culturally appropriate pictorial card depicting each of the danger signs for the mother pre-, during, and post-labor, and for the neonate.

was very difficult to motivate other household members to wash hands with soap, mothers in this study indicated that they were able to request others to use chlorhexidine, perhaps because it was perceived as a medical product to protect the vulnerable neonate.

Chlorhexidine's bacteriostatic properties may delay the recontamination of hands or reduce the intensity of hand contamination, giving it potential advantage over hand cleansing with soap or alcohol-based hand sanitizer.⁷ However, we are not aware of data from heavily contaminated low-income community settings that characterize these potential benefits of chlorhexidine hand cleansing fully. Thus, we cannot know whether chlorhexidine represents a more efficacious product for prevention of neonatal infections than either soap or alcohol-based hand sanitizer. Likewise, we do not yet understand the potential adverse ramifications of frequent topical application of such a bacteriostatic product for the establishment of healthy newborn microbiota.²³

The waterless properties afforded by chlorhexidine can also be provided by alcohol-based hand sanitizers. Chlorhexidine hand cleansing preparations are largely relegated to use in healthcare settings, whereas alcohol-based hand sanitizers are increasingly commercially available in many low- and middle-income countries. Although currently beyond the economic reach of most mothers of neonates in low-income settings such as rural Bangladesh, the pathway to scale may be more achievable for commercially available alcohol-based sanitizers than chlorhexidine hand cleansing preparations. Still, based on our analysis of chlorhexidine consumption, strategies to promote adoption and use of alcohol-based sanitizers will suffer the same challenges that have been characterized for promotion of handwashing with soap¹⁶ or, in this article, hand cleansing with chlorhexidine. Moreover, the protective effects of chlorhexidine, alcohol-based sanitizers, and soap are not entirely interchangeable. Alcohol and chlorhexidine may be poorly effective at reducing hand contamination with some pathogens relevant to the LMIC context, including non-enveloped viruses.²⁴ Handwashing with soap and water is recommended over cleansing with alcohol when hands are grossly soiled, which may occur with some frequency among caregivers of newborns, who produce unformed stools.⁷

There are numerous well-documented challenges to measuring hand hygiene, and none of the widely applied methods are free of validity concerns.^{17,25} Structured observation, which is certainly subject to courtesy bias, yields data rich with detail regarding the timing and nature of hand cleansing behavior. In this study, structured observation allowed for comparisons between groups using very different materials for hand cleansing (chlorhexidine lotion versus bar soap). By using a secondary method of behavior measurement, chlorhexidine consumption as indicated by weight change, we were able to apply a reality filter to otherwise highly optimistic findings of behavior change. A second limitation of the study was that data collectors were not blinded to treatment arm allocation; given the hand cleansing behavioral outcome of this trial, there was no feasible way to introduce a placebo in the intervention arm.

CONCLUSION

Our data suggest the potential for a waterless hand cleanser, chlorhexidine in this study, to facilitate hand cleansing among

mothers and family members of newborns. However, it is not clear whether the frequency of hand cleansing was increased sufficiently to prevent neonatal infections. Assessing health outcomes of hand cleansing promotion necessitates using a robust and costly experimental design. Public health research dollars may be better invested in developing and evaluating multimodal strategies to prevent neonatal infections in low-resource settings, including promotion of hand hygiene and umbilical cord care among families of newborns, and strengthened infection prevention and control practices in health facilities where babies are increasingly delivered.

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