Original Article

Incidence of umbilical cord infection in neonates receiving 7.1% chlorhexidine gel and methylated-spirit in ibadan

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A B S T R A C T

Background: The optimal method of umbilical cord care after birth is still a controversial issue, as umbilical stump has remained a focus of infection in newborns. Use of topical antiseptics is one intervention that could reduce the incidence of infection by preventing or reducing the bacterial colonization of the umbilical cord in neonates.
Aim: To compare the incidence of umbilical cord infection between neonates receiving 7.1% chlorhexidine gel (CHG) and Methylated-spirit (MTS) in Ibadan.
Method and subjects: This study was a prospective-comparative study. The study settings were selected by a multistage sampling technique from the 11 local governments in Ibadan. A total of 179 newborns (93 in the Chlorhexidine group and 86 in the Methylated spirit group) were enrolled into the study from three primary health centers (PHC) in Ibadan and analyzed for the incidence of umbilical cord infection.
Results: There was no statistical significant difference in the incidence of umbilical cord infection between the two groups [p = 0.447]. There was a higher non compliance rate in the CHG group (21.1%) than in the MTS group (9.6%) [p = 0.001]
Conclusion: There is no difference in incidence of umbilical cord infection with the use of Chlorhexidine or methylathed spirit in newborns.

Introduction

Each year 3 million newborns die globally (Liu et al., 2012) accounting for 40% of global under-five mortality (Nangia et al., 2016). Annually, serious infections account for nearly 30% of the 3 million neonatal deaths (Sankar et al., 2016). In settings with high-mortality rates, this proportion is closer to 50% (Oestergaard et al., 2011; Lee et al., 2014). Such high-infection-related death rates make it imperative to identify simple and cost-effective interventions that can be implemented in different settings across the globe. Use of topical antiseptics is one such intervention that could reduce the incidence of infections by preventing or reducing the bacterial colonization of the umbilical cord in neonates. While the use of clean delivery kits, hand washing and careful attention to cleanliness in the postnatal period may all be important measures to reduce neonatal infection; however, none of these have to date provided unequivocal evidence that they can reduce infection-related neonatal deaths (Blencowe et al., 2011).

In Nigeria, an estimated 276,000 neonatal deaths occur annually 60,000 of these deaths stem from infection, and about 20,000 of these deaths are umbilical cord-related (Orobaton et al., 2015). Most of these deaths occur in rural areas and northern Nigeria (Akinyemi et al., 2015). Nigeria has the second highest number of neonatal deaths in the world after India (Lawn et al., 2014). In settings with high neonatal mortality rate (30 or more neonatal deaths per 1000 live births), the World Health Organization (2014) recommended daily chlorhexidine (7.1% chlorhexidine digluconate aqueous solution or gel, delivering 4% chlorhexidine) application to the umbilical cord stump during the first week of life for newborns that are born at home. Clean, dry cord care was recommended for newborns born in health facilities and at home in low neonatal mortality settings. Use of chlorhexidine in these situations was considered only to replace application of a harmful traditional substance, such as cow dung, to the cord stump.

Traditionally, there is a general desire to actively care for the umbilical cord of newborns as observed by the variety of cord care practices and beliefs in Nigeria (Coffey and Brown, 2017); some of these practices range from the use olive oil to engine oil, using red toothpaste and Mentholatum in the south; and herbs, salt, and even cow dung in the north (Goldman, 2017), with the intention of promoting healing and/or hastening umbilical cord separation time (Coffey and Brown, 2017; Goldman, 2017). Convincing families that such approaches expose the neonate to infection is not an easy task particularly, when the grandparents are not convinced.

Three randomized controlled trial reviewed by Imdad et al. (2013) provided substantial evidence that umbilical cord stump treatment with 4% Chlorhexidine digluconate reduces both omphalitis and neonatal mortality, with the impact likely greater in preterm and low birth-

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weight infants (Goldenberg et al., 2014). This group of newborns is particularly prone to infection because of their relatively immature immune system, also because they are likely to receive one or more invasive interventions. A study by Lyngdoh et al. (2018) showed that CHG was very effective in reducing pathogenic bacteria colonization of the cord in preterm babies. However, the time for umbilical cord separation was longer in the CHG group. Also, in a bid towards achieving the targets of the Sustainable Developmental Goal 3 (SDG 3), Herrick et al. (2017) modeled the potential impact of some emerging innovations on achievement of SDG 3. Of the eight (8) innovations studied, use of Chlorhexidine gel or aqueous Chlorhexidine ranked second with the largest projected health impact. Number of lives saved was estimated to be one (1) million. A new tool for small-scale water treatment for diarrhea ranked first.

Documentation of cord-care practices is not consistent throughout low-and middle-income countries, yet existing literature depicts a firm tradition of umbilical cord care in every culture studied (Coffey and Brown, 2017). Various health institutions and cultures adopt different methods of umbilical cord care. The standard of practice in most health institutions in Nigeria was the use of Methylated spirit. There is paucity of studies conducted on the effect of 7.1% Chlorhexidine gel on umbilical cord infection in Nigeria; two randomized controlled trials conducted so far in Africa (Tanzania and Zambia) showed no difference in reduction of omphalitis when compared with dry cord care (Sazawal et al., 2016; Semrau et al., 2016). Use of Methylated spirit is the known standard cord care agent in Ibadan; hence, this study compared the incidence of umbilical cord infection between neonates receiving 7.1% chlorhexidine gel and methylated spirit in Ibadan.

Brief description of the cord care agents employed in the study (methylated spirit and chlorhexidine)

Methylated spirit is a denatured alcohol that has additives to make it poisonous, bad tasting and nauseating so as to discourage recreational consumption. The product used for this study (Moko Methylated spirit) contains isopropyl alcohol B.P 95%. It is also used for disinfecting the skin prior to injection or minor surgery. Chlorhexidine digluconate on the other hand, is the gluconate salt form of chlorhexidine, a biguanide compound used as an antiseptic agent with topical antibacterial activity. Chlorhexidine gluconate is positively charged and reacts with the negatively charged microbial cell surface, thereby destroying the integrity of the bacterial cell membrane (National Center for Biotechnology Information, 2016). The bacterial uptake of the chlorhexidine is very rapid, typically working within 20 s (McDonnell and Denever, 1999). In low concentrations it affects the integrity of the cell wall. Once the cell wall is damaged, chlorhexidine then crosses into the cell and attacks the cytoplasmic membrane. Damage to the cytoplasm's delicate semipermeable membrane allows for leakage of cell components leading to cell death. In high concentrations, chlorhexidine causes the cytoplasm to congeal or solidify (Kaye, 2012).

The peculiar mechanism of action of chlorhexidine in healthcare applications is that in topical application, chlorhexidine is shown to have the unique ability to bind to the proteins present in human tissues such as skin and mucous membranes with limited systemic or bodily absorption (WHO, 2009). Protein bound chlorhexidine releases slowly leading to prolonged activity known as substantivity (Mohammadi and Abbott, 2009). This allows for a longer duration of antimicrobial action against a broad spectrum of bacteria and fungi. In fact, chlorhexidine's antimicrobial activity has been documented to last at least 48 h on the skin (Hibbard, 2005). Unlike povidone-iodine, chlorhexidine is not affected by the presence of body fluids such as blood (Lim and Kam, 2014). The product used for this study (chlorxy-G gel) contains 7.1% chlorhexidine digluconate, delivering 4% Chlorhexidine.

The current situation on the implementation and uptake of 7.1% chlorhexidine gel for cord care in Nigeria

Nigeria adopted the use of CHG for newborn cord care at the 56th National Council on Health meeting in 2013. With the support of USAID, Sokoto State government launched its procurement in March, 2013 and was the first government in Africa to launch the use of CHG (Orobaton et al., 2015). Later, Bauchi, Ogun, Kogi and six other states emulated this action and included CHG procurement in their drugs for free health services.

Examining the trends in umbilical cord care practices between 2012 and 2015 in Bauchi and Sokoto state, Abegunde et al. (2017) observed that in Bauchi State, the application of chlorhexidine gel accelerated from 0.7% in 2012 to 21.5% in 2015; while methylated spirit decreased from 17.0% in 2012 progressively to 6.3% in 2015. Similarly, in Sokoto State, the use of chlorhexidine gel for cord dressing rose from 0.8% in 2012 to 17.1% in 2015. In contrast, the use of Methylated sprit dropped from 10.0% in 2012 to 2.6% in 2015. Their study also found that the substitution of methylated spirit with chlorhexidine was mainly by health workers in public health facilities; while there was little or no change in cord care practice among the traditional birth attendants.

In spite of the promising benefits anticipated from the use of Chlorhexidine gel; its implementation is not without challenges. Some of the obstacles pointed out by Goldman (2017) include: the task of establishing a reliable supply chain CHG from the manufacturer. A second problem is the lack of demand for CHG; since most mothers, TBAs and some clinicians are still not aware of CHG and its benefits. Additionally, patent medicine vendors are not willing to stock products with little or no demand. A third challenge is storage and handling. Chlorhexidine gel has a short shelf-life of three years within a normal temperature range; and Nigeria lacks a steady power supply. Fourthly, doctors are sometimes adamant when it comes to changing standard of practice, they always insist on a higher level of proof for implementation. Finally is the challenge of the government bearing the financial cost of procurement and implementation until people are willing to pay for it themselves. The national strategy estimates that it will cost US$32 million to reach its five-year goal of 52 percent chlorhexidine uptake.

Methods

Study design and population

A prospective comparative research design was employed to compare the incidence of umbilical cord infection between neonates receiving 7.1% chlorhexidine gel and methylated spirit in Ibadan, the capital city of Oyo State. Ibadan is the most populous city in the state, and the fourth most populous city in Nigeria, after Lagos, Onitsha and Kano (Dhaka, 2017). It is the country's largest city by geographical area. The principal inhabitants of the city are the Yorubas. There are eleven (11) Local Governments in the Ibadan Metropolitan area. A multistage sampling technique was used to arrive at the required sampling units required for the study and are as follows:

Stage one: Three (3) local governments were randomly selected from the existing eleven (11) local governments in Ibadan. The randomly selected local governments were Egbeda, Onara and Ibadan southeast.

Stage two: Two (2) Primary Health Centers (PHC) with the highest number of births was selected from each of the three local governments.

Stage three: The six (6) selected PHCs were clustered into two groups according to the cord care agent utilized at the center: either Chlorhexidine gel (CHG) or Methylated spirit (MTS). One health center using CHG and had a good number of births per month was selected, while two health centers with the highest births per month using Methylated spirit was selected (Two health centers were selected in this group so as to make up the required sample size). Orayan health center was selected because of the large number of newborns delivered per

month and also, the use of CHG has been well established in this center; while Sarat Adesina health center and Alakia model health center still uses MTS (still on the verge of introducing CHG). The researchers considered that sampling the primary health centers based on the cord care agent they have been using (either CHG or MTS), would enhance compliance.

Stage four: In the three selected PHCs, all babies who meet with the inclusion criteria in the three selected PHCs, and whose mother consented to participate in the study were continuously recruited from March to August 2017.

Inclusion/exclusion criteria

The inclusion criteria were healthy neonates with first contact at/ less than 24 h of life, babies with normal circumferential diameter of umbilical cord and birth weight between 2.0 and 4.0 kg. Exclusion criteria included neonates with respiratory distress, metabolic disease, perinatal asphyxia, those with major congenital abnormalities, neonates requiring resuscitation or admission to neonatal intensive care unit and neonates with immediate need of evaluation and treatment. These groups of neonates were excluded because they may have been referred for intensive care in a tertiary facility outside the study area. Also, if the mother and baby were not residing in Ibadan for the first 28 days of life, the neonate was excluded from the study (to facilitate follow-up visits).

Health education

Mothers whose babies were enrolled into the study were instructed to apply CHG twice daily (for the CHG group) and MTS four times daily (for the MTS group) at home. All mothers received information on the importance of hand washing and umbilical cord hygiene, and how to recognize and report signs of infection (pus, redness, abnormal color, tenderness or offensive odor).

Sample size estimation

The minimum sample size was set at 80% power and a 0.05 level of significance was estimated to include 136 newborns (i.e. 68 newborns in each of the study groups). A total of 238 newborns were invited to participate in the study over a 6 months period (134 in the CHG group and 104 in the MTS group). Of the 134 newborns in the CHG group, 15 (11.2%) were lost to follow-up (due to wrongly copied phone number/ or no house number); 1 (0.7%) died before cord separation, although the death was not related to the umbilical cord care practice. Also, of the 104 newborns in the MTS group 10 (9.6%) were lost to follow-up (also due to wrongly copied phone number/or no house number). Therefore, 212 neonates (I18 newborns in the CHG group and 94 newborns in the MTS group) were followed-up (see Fig. 1). Data collection procedure.

Participants were enrolled into the study at birth after consent was obtained from the mother. The researcher or any of the three (3) trained
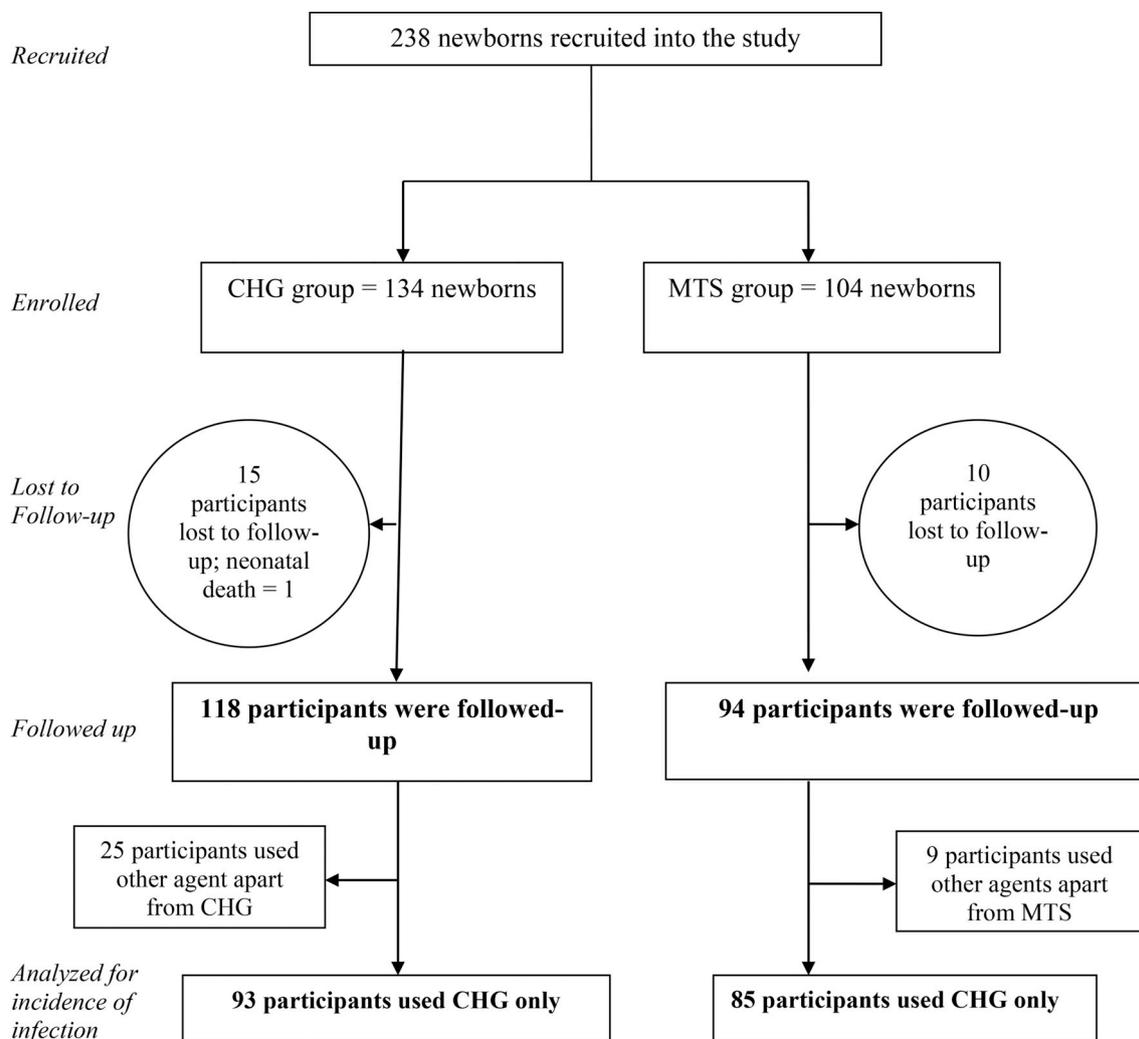

Fig. 1. Study participants flow diagram.

Table 1
Socio-demographic Characteristics of the study participants' mothers in the two study groups.

	CHG group (%)	MTS group (%)	p-value
Mother's age (years)			
15-25	45 (38.1)	23 (24.5)	0.003
26-35	61 (51.7)	50 (53.2)	
36-45	12 (10.2)	21 (22.3)	
Mean ± SD	27.87 ± 5.407	30.17 ± 5.876	
Minimum age	17	20	
Maximum age	42	43	
Parity (Number of children)			
1	38 (32.2)	32 (34.0)	0.438
2	31 (26.3)	30 (31.9)	
3	26 (22.0)	17 (18.1)	
4	17 (14.4)	9 (9.6)	
5	4 (3.4)	6 (6.4)	
Above 5	2 (1.7)	0 (0.0	
Range	5	4	
Highest level of education			
No formal education	2 (1.7)	2 (2.1)	0.000
Primary	9 (7.6)	2 (2.1)	
Secondary	84 (71.2)	46 (48.9)	
Tertiary	23 (19.5)	44 (46.8)	
TOTAL	118	94	

research assistants collected information on socio-demographic and vital statistics of the participants at birth, before discharged from the health facilities. Study participants were recruited on a daily basis by the researcher or the trained research assistants from March to August 2017. Follow up was made via phone calls and/or home visits and during visits to the clinics. The researcher collected the name, nickname, phone numbers of the mother and any other significant person; and house address of the subjects which was recorded in a proforma. Each subject was assigned a serial number based on the study setting and study group; this serial number was entered in each subject's questionnaire. The researcher also gave her phone number to the mothers; they were encouraged to beep the researcher immediately they notice any sign of cord infection (pus, redness, abnormal color, tenderness or offensive odor) before follow-up visit. But where phone calls were not possible; a home visit was made on day of life 7 to assess and collect information. For babies whose umbilical cord did not fall by day 7, the researcher followed-up with the mothers on day of life 14, 21, 28 (every 7 days) The remaining sections of the questionnaire were filled in for each subject by the researcher at the follow-up visit and after the cord had fallen off. The questionnaire was considered 'complete' two days after the umbilical cord separated.

Data management and analysis

Data analysis was performed using IBM SPSS version 22. Numeric variables were expressed as frequencies, percentages, ranges, means and standard deviations; while categorical data were expressed as frequencies and percentages. For quantitative data, χ^2/Fisher exact test were used for non-parametric data at 0.05 level of significance. The study proposal was approved by University of Ibadan/University College Hospital Ethics committee **UI/EC/17/0047.** The purpose of the study was explained to the participant's mothers and they were told of their right to withdraw from the study at any time. Confidentiality was maintained, and anonymity ensured.

Results

A total of 212 neonates (118 in the CHG group and 94 in the MTS group) were enrolled during this period (see Fig. 1). The baseline comparison of the socio-demographic characteristics of mothers in the two study groups showed the mean age in the CHG group to be

Table 2
Vital statistics of the study participants at birth.

	CHG group N (%)	MTS group N (%)	p-value
Gestational age at birth (weeks)			
30-35	14 (11.9)	0 (0.00)	0.000
36-40	98 (83.0)	80 (85.1)	
41-45	6 (5.1)	14 (14.9)	
Mean ± SD	37.64 ± 1.973	38.84 ± 1.675	
Birth weight (kg)			
2.00–2.50	8 (6.8)	13 (13.8)	0.224
2.60–3.00	60 (50.8)	29 (30.9)	
3.10–3.50	42 (35.6)	34 (36.2)	
3.60–4.00	8 (6.8)	18 (19.1)	
Mean ± SD	3.050 ± 0.366	3.122 ± 0.492	
Sex of newborn			
Male	63 (53.4)	38 (40.4)	0.062
Female	55 (46.6)	56 (59.6)	
Total	**118 (100%)**	**94 (100%)**	

Table 3
Cord care practices of the study participants' mothers in the two groups.

	CHG group	MTS group	p-value
Time of commencement of cord care agent			
a. At birth	109 (92.4%)	72 (76.6%)	0.002
b. 6–12 h after birth	0 (0.0%)	5 (5.3%)	
c. 12–24 h after birth	9 (7.6%)	17 (18.1%)	
Use of cord care agent at home after discharge			
a. Yes	111 (94.1%)	94 (100%)	0.016
b. No	7 (5.9%)	0 (0.0%)	
Additional cord care agents applied			
a Chlorhexidine	–	8 (8.5%)	0.001
b Methylated spirit	24 (20.3%)	–	
c Dusting powder	1 (0.8%)	0 (0.0%)	
d Oil	0 (0.0%)	1 (1.1%)	
Reasons behind application of other cord care agents			
a. To quicken cord separation	7 (28%)	1 (11.1%)	
b. No special reason	1 (4%)	1 (11.1%)	
c. Other reasons	17 (68%)	7 (77.8%)	
• Grandparent advice	15 (60%)	0 (0.0%)	
• For prior cleansing of the cord	7 (28%)	0 (0.0%)	
• To enhance drying of the cord	3 (12%)	0 (0.0%)	
• Friend's advice	–	7 (77.8%)	

27.87 ± 5.407 years, while the MTS group was 30.17 ± 5.876 years. The Majority (above 50%) of the participant mothers in both groups was between 26 and 35 years of age and had one or two children (see Table 1).

The majority of the study participants (above 80%) in both groups were born at a gestational age between 36 and 40 weeks. The mean birth weight in the CHG group was 3.050 ± 0.366 Kg and 38.84 ± 1.675 Kg in the MTS group (see Table 2).

Table 3 shows the umbilical cord care practices of the study participants' mothers in the two groups. The results showed that a majority in each group: CHG 109 (92.4%) and MTS 72 (76.6%) began cord care at birth. Only 7 (5.9%) of the 118 mothers who used CHG did not continue using it at home, while all the study participants 94 (100%) in the MTS group continued its use at home. There was a statistically significant difference between the substance of care used and the continuity of its use at home [χ2 = 5.767, p = 0.016], implying higher satisfaction and compliance in the MTS group compared to the CHG group.

Some mothers in both groups used other substances in addition to the primary substance; the CHG group, 25 (21.1%) used CHG along with Methylated spirit and dusting powder, while the MTS group, 9 (9.6%) used MTS along with oil and CHG. Other non-study substances/ practices used by the mothers include mentholatum balm, hot water

Table 4
Signs of umbilical cord infection in the two study groups.

	CHG N (%)	MTS N (%)	Total	p-value
a. Drainage of pus	0 (0.0)	0 (0.00)	0 (0.0)	–
b. Drainage of serous fluid	1 (1.1)	3 (3.5)	4 (2.2)	0.320
c. Tenderness	0 (0.0)	0 (0.0)	0 (0.0)	
d. Redness	0 (0.0)	1 (1.2)	1 (0.6)	0.445
e. Foul smelling	9 (9.7)	10 (11.6)	19 (10.6)	0.701
f. Abnormal color	3 (3.2)	5 (5.8)	8 (4.5)	0.512
Total	**13 (14.0)**	**19 (22.1)**	**32 (17.9)**	

fomentation and burning with lantern (though these practices were initiated after the umbilical cord had fallen, which they said was aimed at preventing abdominal pains in newborns). Since these practices were employed after umbilical cord separation, they were not excluded from analysis. For those who used other substances (before umbilical cord separation) apart from their primary substance of umbilical cord care, prolonged cord separation, to quicken drying of the cord, to cleanse the cord and mother-in-law's advice/persuasion were their reasons (see Table 3). There was a significant association between the substance of care and the addition of other substances to the primary substance of cord care [$\chi^2 = 106.32$, p = 0.001].

Drainage of pus and tenderness were not reported by any participant in either of the two groups. The most reported sign of cord infection was foul smell; CHG group 9 (9.7%), while 10 (11.6%) in MTS group (see Table 4). This difference was not statistically significant [p = 0.701]. Those who used other umbilical cord care agent apart from their primary agent were excluded from the analysis.

Discussion

The use of topical antibacterial agents is known to reduce bacterial colonization of the umbilical cord; however, some of these anti-infective agents have higher potency than others.

Of the 118 study participants in the CHG group, 7 participants did not continue with the use of CHG at home, while all the participants in the MTS group continued with its use at home. This shows a higher compliance with the use of MTS than CHG. One-quarter of the study participants in the CHG group used other substances in addition to CHG before cord separation; with major reasons due to mother-in-law's persuasion; to clean the cord before applying CHG and to quicken cord drying and separation. This again could be due to its novelty; mother-in-laws (grandparents) were not aware of the CHG product and they preferred to use what they have traditionally used. Also, CHG when applied to the umbilical cord dries and leaves yellowish flakes on the surface of the cord, causing some mothers to use MTS to clean off the flakes before applying the gel. There was no literature found to back this finding up.

There were other non-studied umbilical cord care practices that were observed among the study participants after the cord has separated such as: the application of mentholatom/Rob at the point of detachment of the umbilical cord, burning the raw area with lantern and cloth; and hot water fomentation: the reason given by majority of the mothers was to prevent the common colicky abdominal pains experienced by newborns.

In the MTS group, over 90% used MTS alone; suggesting a more acceptable practice and subsequent compliance than the use of CHG. Eight (8) out of the 94 participants in the MTS group that used CHG in addition to MTS, did so because it was introduced to them either by a friend after birth or during the infant's immunizations given by the community health extension worker.

Of the six (6) cardinal signs of umbilical cord infection that was considered in this study, there was no incidence of purulent discharge and tenderness reported by either of the study groups. Foul smelling umbilical stump was the most reported sign of umbilical cord infection

with no statistically significant differences between the two groups. In the course of this study, it was observed that most of the mothers burrow the umbilical stump inside their baby's diaper as it is a common belief among the Yorubas (the primary inhabitants of the study area) that "air" will enter into their baby if the cord is exposed. The delayed drying and consequently prolonged cord separation that occurs with this practice could be a potential cause for the foul smell. Abnormal color was the next most reported sign (3/93 in the CHG group and 5/85 in the MTS group), which was not statistically significant. There was no incidence of peri-umbilical redness in the CHG group. Only one participant developed a very mild peri-umbilical redness in the MTS group, which resolved after two days, and there was no associated delayed in cord separation, infection or child morbidity.

In line with the findings of this study, Elsobky et al. (2017) reported that in study participants using ethanol, 6% observed moderated to severe peri-umbilical redness. A study by Golshen and Hossein (2013) demonstrated that 2% of the study participants had a general incidence of omphalitis among neonates using ethanol. However; contrary to the findings of this study, Mullany et al. (2006) reported that neonates using CHG were 3.6 times more likely to have umbilical cord separation after 7 days, but separation time was not associated with omphalitis. Also, in a meta-analysis by Sankar et al. (2016), their results showed no incidence of umbilical cord infections with the use of CHG in hospital settings. The variation in findings on the incidence of umbilical cord infections in the various studies reviewed might be due to different definitions of umbilical cord infection. This study defined umbilical cord infection as discharge such as pus, redness, swelling, warmth, tenderness or foul odor arousing from the umbilical stump. Mullany et al. (2006) defined umbilical cord infection as presence of pus, redness or swelling, while Golshen and Hossein (2013) defined it as infectious discharge or erythema or rigidity around the umbilicus or on the anterior abdomen. There was no statistical significant difference in the incidence of umbilical cord infections between the two groups. This could be because MTS and CHG have equal antibacterial effects.

Conclusion

This study has shown that there is no significant difference in the incidence of umbilical cord infections between groups of infants treated with CHG compared to MTS. Mothers in the CHG group were not compliant with CHG use as compared to mothers in the MTS group. To increase maternal compliance with the use of CHG, the researchers recommend that CHG be formulated in an aqueous form rather than in its present jelly form which leaves dry flakes on the cord when dried; necessitating cleansing with another agent before application. It was also found that cultural differences and family members can greatly influence beliefs and practices related to how the umbilical cord is cared for. Therefore, health education should be geared towards not only mothers, but also to the grandparents and other caregivers.

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