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Research Article

Effect of Kangaroo Mother Care on neonatal health outcomes in rural Pakistan, A Randomized Controlled Trial

Muhammad Atif Habib[1, 2], Kirsten I Black[1], Shabina Ariff [2], Sajid Bashir Soofi[2], Mushtaq Mirani[2], Fariha Shaheen[2], Amjad Hussain[2], Zulfiqar A Bhutta[2], Camille Raynes-Greenow[3]

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Correspondence to:
Dr. Muhammad Atif Habib, Pakistan

Author's Affiliation:
1- Discipline of Obstetrics, Gynaecology and Neonatology, Central Clinical School, University of Sydney, Sydney NSW, Australia 2006.
2- Women and Child Health Division, Aga Khan University, Karachi, Pakistan.
3- Sydney School of Public Health, University of Sydney, Sydney NSW, Australia 2006.

Abstract:

Background:

Neonatal infections contribute significantly to neonatal mortality especially in developing countries. Delivering simple evidence based interventions has the potential to reduce the burden of neonatal infections and consecutively of neonatal mortality.

Objective

We assessed the effect of a neonatal intervention package comprised of Essential Neonatal Care (ENC), application of chlorhexidine on umbilical cord and Kangaroo Mother Care (KMC) on neonatal outcomes including neonatal infections, omphalitis, exclusive breast feeding, neonatal weight gain and neonatal mortality.

Methods

In this three arm Randomized Controlled Trial; we compared intervention A (ENC, application of chlorhexidine on umbilical cord and KMC) with intervention B (ENC and application of chlorhexidine on umbilical cord) and control arm C (ENC only). Eligible mother-baby pair were recruited from the tertiary care hospital and followed up till day 28.

Results

The neonates that received the intervention A had a reduced risk of neonatal infections (RR 0.36, 95% CI 0.27-0.63) and omphalitis (RR 0.24, 95% CI 0.15-0.36) and were more likely to gain weight (RR 2.27, 95% CI 1.54-3.46) compared to intervention B and control arm. Overall the intervention A was found to be superior to intervention B and control arm.

Conclusion

ENC and chlorhexidine were effective in improving neonatal outcomes compared to usual care but the effect was significantly augmented when KMC was added to the intervention package. Despite anecdotal evidence, acceptability data of KMC in this study is reassuring and provides evidence that it can be integrated into routine neonatal care to achieve significant reductions in adverse neonatal outcomes.

Key Words:

Kangaroo Mother Care, Essential Neonatal Care, Chlorhexidine, Neonatal Infections, Omphalitis, Neonatal Mortality Rate

Introduction:

Recent neonatal mortality and morbidity estimates from Pakistan depict a dismal picture where a negligible change in the neonatal mortality has been observed since 1990.[1] Pakistan has the third highest global burden of neonatal mortality with approximately 200,000 newborns dying annually and a current neonatal mortality rate of 42 per 1000 live births.[1-3] The majority of these neonatal deaths are attributed to neonatal infections, low birth weight, hypothermia and asphyxia.[4,5] Studies from Pakistan have shown that the risk of neonatal morbidity and mortality is higher in rural areas[1,3,6] reflecting the reduced access to maternal and neonatal health care services, continued use of unsafe newborn care practices and community beliefs preventing early uptake of best practices such as feeding of colostrum, early initiation of breastfeeding and delayed bathing.[3,6,7] A greater number of adverse neonatal outcomes could be prevented by better access to, and use of evidence based interventions.[4,8-11] In settings similar to Pakistan essential neonatal care (ENC), which is comprised of cleanliness, thermal protection, delayed bathing, early and exclusive breast feeding, initiation of breathing, eye care and immunisation[12] has been effective in reducing neonatal morbidity and mortality.[13,15] Likewise application of 4% chlorhexidine has been shown to be beneficial in reducing the incidence of omphalitis and is associated with a reduction in neonatal mortality in many developing countries including Pakistan.[16-19] Studies have also demonstrated that Kangaroo Mother Care (KMC) is beneficial in reducing neonatal morbidity and mortality, improving weight gain and exclusive breast feeding.[11,20-24] Despite the advantages of these low cost and easy to use interventions, they are still not widely practiced in Pakistan.[3,6-7] ENC has been incorporated into the maternal, neonatal and child health program of Pakistan since 2004, and the World Health Organization (WHO) added chlorhexidine as an essential drug for neonates in 2012[25] however coverage and use of both in Pakistan has not been scaled up.[326] KMC is also a neglected intervention in Pakistan; this

has been attributed to the practice being considered culturally unacceptable.[27,28] However specific data on the acceptance and effectiveness of KMC in Pakistan's community settings is lacking,[6,29] therefore, despite the intervention being evidence based in other similar settings, local evidence is required.

In this trial three low cost interventions are integrated into a single package. Each intervention has individually been shown to reduce neonatal morbidity and mortality, although has not yet been combined either in Pakistan or elsewhere. The package comprises of home based ENC, application of 4% chlorhexidine solution on the umbilical cord and KMC. We aimed to assess the effect on neonatal infections, omphalitis, exclusive breast feeding, neonatal weight gain, hospital referrals and neonatal mortality. We also measured the acceptability of KMC in the community setting. We hypothesized that the combined package of three interventions would reduce the incidence of neonatal infection to 30% compared to the control arm during the neonatal period of 0-28 days.

Methodology

We conducted a randomised controlled trial with three arms, for ease of reading we refer to the three arms as A, B and C; neonates in intervention arm A received routine ENC, application of 4% chlorhexidine for umbilical cord care and KMC for sustained skin to skin contact. Neonates in intervention arm B received routine ENC and application of 4% chlorhexidine for umbilical cord, and neonates in the control arm received only routine ENC.

Study Site:

We conducted this trial in the district of Dadu of Pakistan which is a rural district between October 2014 and July 2015. We enrolled mothers and neonates from the maternal unit of a tertiary care hospital. This hospital has an average of 200 births per month. Follow-up to 28 days was conducted in the participant's home.

Eligibility Criteria:

Live born infants from all pregnancies within participating Union councils were eligible for enrollment in the study. All healthy newborns born and their mothers in the study settings were enrolled in the trial after prior consent. Mothers and infants with serious complications and Infants with congenital defects were excluded from the study.

Study team and trainings:

We developed a local team at the district level comprising of a study supervisor, three experienced female medical officers and 15 lady health visitors. Senior research staff from Aga Khan University trained the study team in a five day workshop on all study related aspects including consenting procedures, intervention delivery (practicing ENC, KMC and chlorhexidine use), follow-up, data collection and good clinical practice. Further certified trainers from The Aga Khan University and The Ministry of Health trained the study team in comprehensive Emergency Medical and Obstetric Care and Integrated Management of Childhood and Neonatal Illnesses for the identification of neonatal infections, omphalitis, other complications and prompt referral.

Sample Size Calculation:

We calculated the sample size of the trial on the incidence of severe neonatal infection in Pakistan estimated to be ~25%.[30] We hypothesized a reduction of 30% between the combined package of three interventions and the control arm during the neonatal period of 0-28 days with 80% power and 0.05 as the value of alpha, a total sample 1398 (466 per arm) was required.

Study Procedures:

Consent and Randomisation:

All pregnant women intending to give birth in the hospital, residing in the catchment area (five adjacent union council with a total population of 158,000) and having no signs of complications

were eligible for recruitment. The female medical officer assessed the eligibility of the pregnant women and obtained written informed consent when the women arrived for their delivery. Following consent the study supervisor assigned the participants to the treatment arm using the randomly generated treatment allocations from sealed opaque envelopes using a hidden entry envelope randomisation technique. The envelopes were stored under lock and key under the charge of the study supervisor. Randomisation lists and envelopes were prepared by an independent research officer at the Clinical Trials Unit of Aga Khan University. Treating clinicians were blinded to the randomisation schedule, however due to the nature of the intervention neither the clinician nor the patients were blinded to the treatment arm. Following randomisation the medical officer collected data on pregnant women's sociodemographic and reproductive health information and this was entered into the study database.

Intervention delivery

After the baseline data collection was completed the study team provided education to the pregnant woman about her intervention according to her randomised allocation. The participants in intervention A received information and training on the practice of KMC using pictorial aids, practical demonstrations and a locally adapted video, which included education on how to practice KMC, including timing, feeding and monitoring her baby during KMC. The study team provided two sets of two piece KMC clothing which was comprised of a widely used KMC wrap known as the Thari wrap[31] and an open button shirt to make the Thari wrap more culturally acceptable and comfortable for the women to use in their communities. The study team encouraged the participants to use KMC until day 28 following birth as per the WHO guidelines.[32] The study team also provided information and training on how to use 4% chlorhexidine for cord care using pictorial aids and practical demonstration. The participants were encouraged to apply chlorhexidine twice daily until day 10. The study team provided a 15ml solution of 4% chlorhexidine and a pack of 20 cotton balls to the mothers for home

application. Participants in arm A also received education on the practice of ENC through a pictorial flip chart. The participants in arm B received the ENC and chlorhexidine education, and the control arm received only the ENC education.

Neonatal assessment

Soon after birth, a female medical officer undertook a physical examination of the neonate to ascertain eligibility. Neonates requiring urgent medical care and referral or having a gross congenital abnormality were not eligible for recruitment. APGAR scores were recorded using the standard APGAR score checklist and neonatal birth weight was measured. The neonatal data were recorded on the recruitment form. Once it was established that the child was eligible the intervention was initiated. All mother and baby pairs were kept in the hospital for at least eight hours postpartum and during this period the medical officer encouraged the women to use the assigned intervention especially KMC. After eight hours if the mother baby pair were stable, both were discharged home.

Follow-up:

The lady health visitor conducted home visits on day 3, 5, 7, 14, 21 and 28 to assess the newborn for the study outcomes to all participants. Using a structured questionnaire the lady health visitor collected and documented the information on newborn care practices, breast feeding, morbidity, adherence to the intervention, neonatal examination, and any referral. Neonates were assessed for signs of infection and omphalitis (see below). In the case of any serious complication the lady health visitor referred the neonate to the study physician for clinical care. The lady health visitor also collected data on adherence to the intervention and provided routine postnatal education and encouraged the mothers to use the intervention as per their assignment.

Outcome assessment:

The primary and secondary outcomes of the study are explained in Table 1. All outcomes were recorded on a structured questionnaire which was developed using standard questions for

specific outcome measures. For neonatal infection and omphalitis a detailed neonatal examination was performed on day 3, 5, 7, 14, 21 and 28 and information about outcome was recorded. For the assessment of neonatal infection the lady health visitor observed the respiratory rate and looked for chest retraction, measured axillary temperature and also asked about feeding history and convulsions since the last follow-up (Table 1). The lady health visitor recorded an episode of neonatal infection if any of the signs were found. The neonate was weighed once on day 0, 14 and 28. We took three readings and recorded the mean weight in grams. For weight gain we calculated the mean difference in weight between day 28 and day 0, we also calculated the mean weight gain per day by dividing the difference in weight by number of days (28 days). Information about exclusive breast feeding was collected from mothers on day 3, 5, 7, 14, 21 and 28 using the standard exclusive breastfeeding questions taken from the WHO Infant and Young Child Feeding guidelines.[33] Neonatal mortality was recorded as death occurring due to any cause during the neonatal period. Since there is no standard definition for KMC compliance and its acceptance[32,34] we defined acceptability as adherence to KMC as per the WHO protocol. Adherence to KMC was assessed using the standard checklist for KMC implementation and recorded as hours/day as reported by the mother.[32] Chlorhexidine use was checked by observing the level of solution remaining in the bottle, the number of used cotton balls and the number of applications/day as reported by the mother.

Data Processing and analysis:

Data entry and analysis were performed by the data management unit of Aga Khan University. Recruitment and follow-up forms for mother and neonate pairs were collected on paper. Prior to data entry, all forms were checked for completeness and consistency. Data entry was done using specifically designed data entry screens on visual Fox Pro for the study with built in range and consistency checks. Data were analysed using intention to treat analysis through IBM SPSS 19[35]

software. The primary analyses compared incidence of neonatal infection and their 95% confidence interval in each arm. Secondary analyses examined each outcome variable using separate mixed models. We used generalized linear mixed models for non-continuous outcomes (e.g. Cox proportional hazards mixed models for mortality outcomes). Models included the intervention arm as a fixed effect. We estimated the relative risk and compared among arms for neonatal infections, omphalitis, weight gain, exclusive breast feeding, hospital referrals and neonatal mortality between day 0 and day 28 recorded during the follow-ups. For the acceptability of KMC and chlorhexidine we used means and standard deviation to present duration in hours/day and applications/day respectively.

Ethical Approval and consent process

The Ethical Review Committee of the Aga Khan University granted the approval. We obtained written informed consent from the mothers. In the case of illiterate women, consent was documented by a thumbprint on the consent form as well as a signature by a literate witness. All activities followed the guidelines of Good Clinical Practice; the trial protocol was registered with the clinicaltrials.gov, NCT02279381.

Results:

We assessed 1902 pregnant women for eligibility. Of these 360 (18.9%) were not enrolled because they did not consent or were ineligible (Figure 1). We randomly assigned 1542 mother and neonate pairs into either intervention arm A (n=511), intervention arm B (n=515) and control arm C (n=516) respectively. A total of 1436 (93.1%) mother and neonate pairs completed the follow-up to day 28 (intervention arm A, n=477, intervention arm B, n=476, control arm C, n=477, Figure 1). All three arms were similar in terms of maternal and neonatal attributes at baseline (Table 2).

Neonatal Infection- Primary outcome

Our primary comparison was between intervention arm A, the package of three interventions and the control, and we found that neonates who received intervention A were at reduced risk of having neonatal infection compared to the neonates in the control arm (RR 0.36, 95% CI 0.27-0.63), and intervention A was superior to intervention B (RR 0.59, 95% CI 0.44-0.63). However, any intervention was better than usual care and intervention B also had fewer episodes of infection than the control group, (RR 0.57, 95% CI 0.43-0.72, Table 3).

Omphalitis (secondary outcome)

For omphalitis, neonates who received intervention A (RR 0.24, 95% CI 0.15-0.36) and intervention arm B (0.43, 95% CI 0.34-0.72) were at reduced risk of having omphalitis compared to neonates in the control. However, again neonates in intervention arm A with the addition of KMC were at reduced risk of having omphalitis compared to intervention arm B (RR 0.54, 95% CI 0.38-0.86, Table 3).

Weight gain (secondary outcome)

We examined the weight data and found that the neonates in either intervention arm weighed more on day 28 compared to the control, intervention A (RR 2.27, 95% CI 1.54-3.46) and intervention B (RR 1.47, 95% CI 1.04-1.74, Table 3). Further analysis of the neonatal weight data found that the mean weight on day 28, mean difference in weight gain and average rate of change in weight per day was significantly higher ($p < 0.001$) among neonates in intervention am A, compared to neonates in intervention arm B and control arm (Table 4).

Exclusive breastfeeding (secondary outcome)

All three arms maintained high exclusive breastfeeding throughout the study period and the proportion of neonates that were exclusively breastfed at day 28 were 90.9%, 88.2% and 87.4% in intervention arm A, intervention arm B and the control arm respectively. Although there was a small difference between proportions among arms this was not statistically significant.

Neonatal mortality (secondary outcome)

We also calculated the neonatal mortality rates (NMR) per 1000 live births (Table 5) and found that the NMR was 27.3, 33.0 and 36.8 (per 1000 live births) in intervention arm A, intervention arm B and control arm respectively. Similar to the exclusive breast feeding data, although we observed a difference it was not statistically significant. Post-hoc analysis of the mortality data for cause specific NMR for low birthweight infants found that the cause specific NMR for low birthweight was lowest 37.9 (per 1000 live births) in intervention A and highest in control (136.9). Further analysis showed that the low birthweight neonates in intervention A were at reduced risk (RR 0.28, 95% CI 0.079-0.95) of neonatal mortality compared to the control arm. No difference in cause specific mortality for low birthweight was observed between the two intervention arms.

Hospital referrals (secondary outcome)

The data on hospital referrals were also analysed. The total number of referrals was 12, 12 and 14 in arm A, B and C respectively. We did not find any difference in hospital referrals among intervention arm A (RR 0.88, 95% CI 0.41-1.88) and intervention arm B (RR 0.87, 95% CI 0.40-1.87) when compared to control arm there was also no difference in hospital referrals when the two intervention arms were compared (RR 1.00, 95% CI 0.45-2.22).

Adherence of chlorhexidine and KMC protocol (secondary outcome)

We analysed adherence of the mothers for both chlorhexidine and KMC (Table 6), and found that the mean duration of chlorhexidine use was very similar in both arms, intervention arm A 7.77 days (±1.92) and intervention arm B 7.78 days (±1.86), and the number of applications per day was also similar 1.97 (±2.63) and 1.93 (±2.50) respectively. We defined acceptance as the duration of use, and found that the mean duration of use for KMC was 24.8 days (±2.32) and mean duration per day was 7.45 hours (±1.3).

Discussion

The study provides evidence in favor of a package of interventions that are low cost, simple, community-based and thus suitable for immediate adoption into neonatal care in Pakistan. We demonstrated that a package of interventions that included ENC, chlorhexidine and KMC reduced the risk of neonatal infection and omphalitis and had a positive impact on weight gain, though it did not impact overall neonatal mortality. However, in low birthweight neonates for cause specific neonatal mortality a significant difference was observed in favour of intervention package. The intervention package with KMC was superior compared to the arm without KMC and also to the control arm. The findings of our study are consistent with a recent review of interventions to improve neonatal health and survival that included 26 trials suggesting that packaged interventions delivered within a health system have beneficial effects on neonatal morbidity and mortality.[11]

The interventions in our study appeared to be well accepted as defined by high adherence by the study participants. The majority of the women immediately breast fed their neonates within the first hour of birth and maintained high exclusive breastfeeding. The mean duration of chlorhexidine use on the stump in our study was 7.7 days, and 1.9 applications/day compared to 11.1 days with a mean 2.4 applications/day which has been documented in a previous cluster randomised trial in Pakistan.[16] Similar to the chlorhexidine finding, KMC also appeared to be well liked by the mothers, with the mean length of daily KMC practice at 7.5 hours/day and the mean duration of 25 days. Although there is no standard definition for length and duration of KMC, the WHO recommends using it as long as possible to gain maximum benefit.[32,34] Data on length and duration of KMC is limited and is missing in many studies. A recent systematic review of 260 studies of KMC conducted by Chan et al.[36] showed that 44.1% did not report length of KMC, 35.5 % reported <4 hours/day, 5.2% reported 4-22 hours while 15.2% reported >22hrs. In the same review, 64.8% of the studies did not report the duration of KMC while 31%

reported the duration of between 1 to < 30 days and 4.2% of > 30 days. Considering the community based setting, the length and duration of KMC in our study is quite impressive and is supported by the beneficial effects of the intervention that included KMC.

KMC has never been used or evaluated for its effects on neonatal outcomes in Pakistan and this study is the first study to implement KMC and evaluate its acceptability and efficacy. During the implementation the study team encountered some cultural and religious barriers and reluctance to carry the babies using KMC by the mothers. We overcame this challenge by customising a KMC wrap and shirt[31] to make it more culturally acceptable, provided extensive counseling and reassurance to mothers and families along with extensive training of the research team staff on the implementation, communication and counseling about the use of KMC. Although the cost of the Thari wrap and open button shirt was about US$1.5 this could be further reduced when produced at scale. Adopting KMC into routine practice of mothers and scale up in Pakistan will require some initial support but our findings suggest that hospital staff can train women; women can use it and do find it acceptable. This is consistent with studies carried out in similar settings to Pakistan.[20-24]

Our study did not find any significant effect on exclusive breastfeeding as all arms maintained a high proportion of exclusive breastfeeding to follow-up at 28 days. Exclusive breast feeding, tends to decrease rapidly within the neonatal period when it should remain high[37] and this trend is also seen in the Pakistan demographic and health survey data which shows an exclusive breastfeeding rate of 54.7% in the first month of life gradually decreasing to 24.1% by the end of the fifth month.[3] The high exclusive breastfeeding rates, and only a small reduction of these rates in our study, may be explained by thorough follow-up and continued counseling of the benefits of exclusive breastfeeding to all mothers by the lady health visitors.

In this study the interventions did not reduce the overall neonatal mortality rate but had a significant effect on cause specific mortality for low birth weight. Although there was a

difference in the overall mortality between arms, favoring intervention A, that difference was not statistically significant. This finding is not consistent with the available literature[11,38] and most likely can be explained by the different design and size of the studies which were specifically powered for mortality outcomes.[39] Similar differences in mortality among low birthweight neonates were observed in studies of similar sample size that used KMC either alone or as a part of an intervention package elsewhere.[11,20-21] However this incidental finding in our study should be dealt with caution as we did not power the study for mortality estimates.

There are some potential limitations. Firstly, the study team and participants were not blinded and thus it was possible that participants might have over or under reported the outcomes and adherence; however this was dealt with regular monitoring visits and direct observation of practicing interventions in the homes. This is also likely to be non-differential between the two intervention arms. Secondly, the data were collected using paper based questionnaires and some questions were retrospective which were subject to recall bias, however, we believe that this bias was also non-differential. Finally, the study evaluated a combined intervention package and it was not possible to establish which component of the intervention package had the greatest effect on outcomes, although the intervention with KMC had the greatest effect in all outcomes.

Our study demonstrates that improved neonatal outcomes such as reduction in neonatal infection and omphalitis, improvement in weight gain and reduction in cause specific mortality for low birthweight infants in community settings is achievable by packaging simple interventions together. This study also provides important insights into developing an intervention package for the care of neonates in community settings in a country like Pakistan where significant reductions in neonatal morbidity and mortality still have not been achieved. The study also illustrates the acceptability and feasibility of implementing KMC in community settings which has never been used in Pakistan prior to this research.

Conclusion

Our study demonstrates that a package which comprised ENC and chlorhexidine had favorable outcomes compared to the control group but this effect was significantly augmented when KMC was added to these two interventions. It was believed that Pakistani women would not use KMC but the acceptability data of KMC in this study is reassuring and provides evidence that it can be integrated in to routine neonatal care to achieve significant reductions in adverse neonatal outcomes. Moreover this study also offers an impetus for scale-up of these interventions in Pakistan and furthers supports the need to evaluate the effectiveness of intervention in local settings.

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Table 1: Study outcomes and operational definitions

Outcome	Definition
Primary Outcome	
Incidence of neonatal infections*	A) Convulsions; or B) Fast breathing (60 breaths per minute or more); or C) Severe chest in drawing; or D) Movement only when stimulated or no movement at all; or E) Not feeding at all for at least 12 hours; or F) Hypothermia (35C to 36C); or G) Hyperthermia (>39C)
Secondary outcomes	
Incidence of omphalitis*	A) None (no redness or swelling); B) Mild (inflammation limited to the cord stump); C) Moderate (inflammation extending to the skin at the base of the cord stump less than 2 cm); or D) Severe (inflammation extending more than 2 cm from the cord stump)
Weight	A) Proportion of neonates that gained weight at day 28; and B) Mean weight on day 28; and C) Mean difference in weight gain; and D) Average rate of change in weight per day
Exclusive Breastfeeding*	Exclusive breastfeeding was defined as no other food or drink, not even water, except breast milk, but allows the infant to receive ORS, drops and syrups (vitamins, minerals and medicines).
Neonatal mortality	Death from any cause in the first 28 days of life
Acceptability of KMC	Adherence of KMC as per the WHO guidelines (as long as possible)
Acceptability of CHX	Application of CHX as per the WHO guidelines (twice daily for ten days)

**WHO Standard definitions were used*

Table 2: Baseline maternal and neonatal characteristics by study arms

Characteristics	Intervention arm A (N = 511)	Intervention arm B (N =515)	Control arm C (N = 516)
Maternal	n (%)	n (%)	n (%)
Maternal age in years (Mean/SD)	25.3 (4.7)	25.4 (4.5)	25.5 (4.4)
Parity (Mean/SD)	2.8 (2.1)	2.6 (2.0)	2.8 (2.2)
Previous miscarriages/abortions	102 (19.9)	105 (20.3)	106 (20.5)
Previous stillbirth	27 (5.2)	25 (4.8)	24 (4.6)
Hypertension during current pregnancy	85 (16.6)	86 (16.6)	88 (17.0)
Gestational Diabetes during current pregnancy	4 (0.78)	5 (0.97)	6 (1.16)
Received Antenatal care during current pregnancy	484 (94.7)	483 (93.7)	493 (95.5)
Received Antenatal care >= 4 times	273 (53.4)	276 (53.6)	274 (53.1)
Received Iron folic acid supplementation during pregnancy	275 (53.8)	268 (52.0)	272 (52.7)
Type of delivery (Normal vaginal delivery)	481 (94.1)	479 (93.0)	484 (93.7)
Type of delivery (Instruments/ forceps)	30 (5.9)	36 (6.9)	32 (6.2)
Mean Gestational age (Mean/SD)	38.2 (2.5)	38.4 (2.2)	38.5 (2.6)
Gestational age at delivery (< 37 weeks)	40 (7.9)	42 (8.2)	41 (8.0)
Gestational age at delivery (37-40 weeks)	403 (78.8)	408 (79.2)	410 (79.5)
Gestational age at delivery (> 40 weeks)	68 (13.3)	65 (12.6)	65 (12.5)
Neonatal			
Male	251 (49.1)	262 (50.8)	273 (52.9)
Mean birth weight (grams)	2810 (440.8)	2843 (442.3)	2821 (445.9)
Birth weight <2500 (grams)	79 (15.4)	75 (14.5)	73 (14.2)
Received colostrum (n/%)	452 (88.2)	457 (88.7)	456 (88.3)
Received breast milk immediately after birth	492 (96.2)	495 (96.1)	497 (96.3)
APGAR score after five minutes of delivery (Mean/SD)	8.8 (1.2)	8.9 (1.3)	9.1 (1.0)
APGAR score after five minutes of delivery (Scored of 7-10)	493 (96.4)	486 (94.3)	489 (94.7)

Table 3: Comparison of primary and secondary neonatal outcomes by study arms (day 0-28)

Outcome variable	Study Arm	n (%)	Relative Risk	95% CI	p-value
Incidence of Neonatal Infections (0-28 days)					
	Intervention arm A	61 (12.7)	0.36	0.27 – 0.63	0.01
	Intervention arm B	90 (18.9)	0.57	0.43 – 0.72	0.01
	Control arm C	135 (27.9)	Ref	-	
	Intervention arm A	61 (12.7)	0.59	0.44 – 0.63	0.027
	Intervention arm B	90 (18.9)	Ref	-	
Incidence of Omphalitis (0-28 days)					
	Intervention arm A	30 (6.4)	0.24	0.15 – 0.36	<0.0001
	Intervention arm B	52 (11.2)	0.43	0.34 – 0.72	<0.0001
	Control arm C	105 (22.4)	Ref	-	
	Intervention arm A	30 (6.4)	0.54	0.38 – 0.86	0.01
	Intervention arm B	105 (22.4)	Ref	-	
Proportion of neonates whose weight was increased at day 28					
	Intervention arm A	389 (89.6)	2.27	1.54 – 3.46	<0.0001
	Intervention arm B	370 (84.8)	1.47	1.04 – 1.74	0.028
	Control arm C	346 (79.2)	Ref	-	
	Intervention arm A	389 (89.6)	1.54	1.03 – 2.11	0.035
	Intervention arm B	370 (84.8)	Ref	-	
Exclusive breast feeding at Day 28					
	Intervention arm A	434(90.9)	0.74	0.51 – 1.08	0.07
	Intervention arm B	420(88.2)	0.93	0.66 – 1.31	0.72
	Control arm C	417(87.4)	Ref		
	Intervention arm A	434(90.9)	0.75	0.51 -1.08	0.12
	Intervention arm B	420(88.2)	Ref	-	
Hospital referrals (0-28 days)					
	Intervention arm A	12(2.3)	0.88	0.41-1.88	0.74
	Intervention arm B	12(2.3)	0.87	0.40-1.87	0.72
	Control arm C	14(2.5)	Ref		
	Intervention arm A	12(2.3)	1.00	0.45-2.22	0.98
	Intervention arm B	14(2.5)	Ref	Ref	

Table 4: Comparison of weight gain by study arm (day 0 and day 28)

	Intervention arm A	Intervention arm B	Control arm C	p-value
Weight at Day 28 (grams, SD)	3350 ± 480.2	3310 ± 550.6	3130 ± 570.4	<0.0001
Difference in weight (grams, SD) (day 28 to day 0)	530±370	460±440	370±440	<0.0001
Mean rate of change in weight (day 28 to day 0)	15.07±10.84	12.82±13.07	10.64±13.32	<0.0001

Table 5: Comparison of Neonatal Mortality (all cause and low birthweight specific) by study arms (day 0-28)

Neonatal mortality Rate (All Neonates)	Study Arms	Neonatal Deaths	NMR	Relative Risk	95% Confidence Interval	p-value
	Intervention arm A	14	27.3	0.83	0.41 – 1.66	0.60
	Intervention arm B	17	33.0	0.90	0.48 – 1.72	0.72
	Control arm C	19	36.8	Ref	-	
	Intervention arm A	14	27.3	0.89	0.47 – 1.69	0.73
	Intervention arm B	17	33.0	Ref	-	
Neonatal mortality Rate (Low birthweight Neonates)						
	Intervention arm A	3	37.9	0.28	0.079 – 0.95	0.044
	Intervention arm B	5	66.7	0.56	0.14 – 2.30	0.42
	Control arm C	10	136.9	Ref	-	
	Intervention arm A	3	37.9	0.29	0.14 – 2.32	0.48
	Intervention arm B	5	66.7	Ref	-	

Table 6: Compliance of KMC and chlorhexidine application

	Kangaroo mother care		Application of 4% Chlorhexidine	
	Days (Mean/SD)	Duration hours/day (Mean/SD)	Days (Mean/SD)	Number of Applications/ day (Mean/SD)
Intervention arm A	24.8 (±2.32)	7.45 (±1.3)	7.77 (±1.92)	1.97 (±2.63)
Intervention arm B	-	-	7.78 (±1.86)	1.93 (±2.50)

Figure 1: Consort diagram