Effect of community initiated kangaroo mother care in low birth weight infants on infant breast milk intake, gut inflammation, maternal depressive symptoms and stress

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Background and Rationale

• KMC key components - early and prolonged skin-to-skin contact (SSC) between the mother and baby PLUS exclusive breast feeding (EBF)

• Evidence from hospital-based trials - KMC improves survival and well-being in low birth weight (LBW) infants, but pathways are unclear

• Plausible impact of KMC on neonatal mortality in the LBW babies may be mediated by pathways beyond preventing hypothermia by SSC, but there is limited evidence

• Key pathways may be: better nutrient intake → growth, reduced pathogen exposure and thereby reduction of risk of infections, improving breast milk output/intake and quality

• Elucidating the pathways through which KMC operates would contribute to the evidence base and may support its widespread implementation
Kangaroo mother care

Skin to skin contact / Appropriate breastfeeding

Vagal stimulation and activation of HP Axis

Maturation of stratum corneum (skin)

Reduced gut inflammation and Establishment of gut microbiome rich in *Bifidobacterium*

Oxytocin ↑; Cortisol ↓ Better mother–infant bonding

Reduced depressive symptoms and stress

Improved breast milk output (infant milk intake) and better breastfeeding performance

Improved infant skin barrier function

Improved survival

Better growth

Reduction of infection/sepsis risk

Better growth

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How KMC may reduce Gut Inflammation

Impaired Immunity – increased chances of repeated infection

Pathogen ingestion / Infections

Malnutrition and poor growth

Gut injury and inflammation

Malabsorption/ Loss of nutrients

Kangaroo Mother Care
Protected environment- skin to skin contact immediately after birth and EBF – less pathogen exposure and infections

Adapted from: http://mal-ed.fnih.org
Hypotheses

In LBW infants, c-KMC leads to:

• Improved infant breast milk intake (at least 60 ml increase)

• Substantial reduction in the prevalence of postpartum moderate to severe depressive symptoms (prevalence ratio ≤0.7) and substantial reduction in salivary cortisol levels (reduction of at least 0.3 SD in mean values) as a reflection of reduced maternal stress

• Reduction of gut inflammatory markers - fecal neopterin, myeloperoxidase, alpha1-antitrypsin (reduction of at least 0.5 SD in mean values)
Primary Objectives:

To estimate the effect of community initiated Kangaroo mother care during the neonatal period in LBW infants on:

• Infant breast milk intake

• Prevalence of moderate to severe postpartum depressive symptoms (Patient Health Questionnaire-9 score ≥10) and stress (measured by salivary cortisol levels)

• Gut inflammation as reflected in levels of fecal neopterin, myeloperoxidase, alpha1-antitrypsin at the end of the neonatal period
Secondary Objectives

- To estimate the effect of c-KMC on prevalence of mild depressive symptoms (PHQ 9 score 5-9) and suicidal ideation in mothers in the postpartum period
- To estimate the effect of c-KMC in mothers of LBW infants during the neonatal period on successful breastfeeding performance (measured by IFBAT score), complete lactation failure, perceived breast milk insufficiency and use of breast milk substitutes
- Association of gut inflammation (fecal neopterin, myeloperoxidase, alpha1-antitrypsin with linear growth in the first 6 months of life

IFBAT-based on 4 parameters i.e. readiness to feed, rooting, latch on and sucking pattern
Complete Lactation Failure- Total absence of milk flow or secretion of only a few drops of milk following regular suckling for a period of at least 7 consecutive days
If the mother perceives that she does not have enough milk then it is defined as perceived breast milk insufficiency as per WHO 2009 IYCF guidelines.
Methods

Study design: Individually randomized controlled trial. This sub-study will be embedded within the main trial titled “Impact of Community-initiated Kangaroo Mother Care on Survival of Low Birth Weight Infants” study (NCT02653534) where 10500 LBW infants will be enrolled

Study site: Semi-urban areas of districts of Faridabad and Palwal, Haryana

Study Population: mother infant dyads with singleton LBW babies weighing ≥1500 g to ≤2250 g enrolled within 3 days of delivery

(Infants unable to feed, breathing problems, major congenital malformations or less active on the day of visit are referred to hospitals. Those intending to move away over the next 6 months or refuse participation are also excluded.)
**Intervention & Control**

**Intervention:** Promotion of and support for Kangaroo mother care, i.e. skin to skin contact and exclusive breastfeeding as soon as possible after birth by study ANMs supported by study ASHAs, in addition to routine visits by government health workers.

The women and babies in the **control** arm of the trial receive routine visits by government health workers.
Sample Size

Calculated separately for each primary outcome.
General assumptions: Confidence level: 95%, Power: 90%, Attrition: \leq 10%

- **Moderate to severe postpartum depressive symptoms** (PHQ 9 \geq 10): Assuming a baseline prevalence of 19% in India (Gelaye et al. 2016), 1950 mother infant dyads (975 in each trial arm) will be sufficient to detect a 30% relative prevalence reduction

- **Infant breast milk intake**: 550 mother infant dyads (275 in each arm), will be sufficient to detect a 0.3 SD, i.e. 60ml, increase in average infant breast milk intake (1SD = 200ml) [here a attrition of 15% was considered]
Sample sizes (contd..)

- **Stress marker – serum cortisol levels**: 550 mother infant dyads will be sufficient to examine a 0.3 SD i.e. 1.5 ug/dl difference in the mean serum cortisol levels (biomarker of stress) between the trial arms considering the baseline mean cortisol levels in the infants of control group to be 4.5 ug/dl and 1SD=5 ug/dL cortisol levels.

- **Gut inflammation**: 250 mother infant dyads (125 in each trial arm) will be sufficient to detect a 0.5 SD difference in the levels of gut inflammatory markers between the KMC and the control arm of the trial.

*Sample size may be revised based on Means and SDs of breast milk parameters, serum cortisol and gut markers after first 100 assays*
## Sample Sizes and time of outcome assessment

<table>
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<th>Outcome measured</th>
<th>Sample/Procedure</th>
<th>Method</th>
<th>Total Sample</th>
<th>Day enrol</th>
<th>Day 1</th>
<th>Day 3</th>
<th>Day 7</th>
<th>Day 13</th>
<th>Day 14</th>
<th>Day 28</th>
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<tr>
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<td>Saliva-Mother</td>
<td>FTIR* / ELISA</td>
<td>550</td>
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<td>✓</td>
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<td>✓</td>
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<tr>
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<td>Infant Saliva</td>
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</tr>
<tr>
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<tr>
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</table>

*FTIR: Fourier Transform Infrared Spectroscopy*
Relevance of the study

What is unclear:

• Knowledge on full benefits of KMC is lacking

• Many pediatricians in India are still unclear about the need for KMC wherever incubators are available - Scale up of KMC even in hospitals - a challenge

• The perception that close skin to skin contact early in life may have profound biological effects beyond thermoregulation is not common
What this study aims to add

- Fill in critical knowledge gaps on the biological effects of KMC on infant breast milk intake, maternal stress indicators and depressive symptom markers and gut inflammation

- Measurement of these biological outcomes will help to develop models to explain the impact of KMC on survival, growth and infection

- Better understanding may lead to better acceptance among pediatricians/policy makers and promotion of KMC

- Addition of substantial scientific value to the main trial – a novel approach to link mechanistic science to any observed clinical effects of c-KMC
Acknowledgements

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Thank You