

Caregivers Perspective Towards Use of Enteral Lactoferrin Supplementation In Newborn Infants; Formative Research Findings

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Abstract

Background: Infection is the second most leading cause of neonatal deaths in Pakistan. Lactoferrin is a naturally occurring protein found in human milk which can prevent neonatal infections and improve the survival of high-risk, low birth weight newborns. Bovine lactoferrin (bLF) has been recognized as a safe nutrient with no adverse effects. The aim of this study was to explore routine newborn care practices, care seeking attitudes, and assess the acceptability and the optimal method of administering bLF at the household level.

Method: Exploratory qualitative research design was adopted. Thirty in-depth interviews with mothers, grandmothers and fathers of low birthweight (LBW) infants were conducted at postnatal wards and the neonatal intensive care unit (NICU) of the Aga Khan University Hospital. Eleven of these families were also recruited for a trial of improved practices (TIPs) to assess the feasibility and the method of administration of bLF prior to the main trial. Interviews were recorded and analyzed using thematic analysis.

Result: Most study participants consider birthweight as a predictor of neonatal health outcomes. Caring of LBW newborns was identified as a physically and emotionally overwhelming experience. Majority of mothers believed that LBW babies are prone to infections, gastrointestinal, respiratory and developmental problems. Fathers and grandmothers were major decision makers in the family and supported the use of bLF in LBW newborns. Parents, who used bLF were satisfied with feeding method and frequency of bLF.

Conclusion: Our formative study found that participants were willing to use bLF for feeding LBW babies. However, educating mothers, fathers and grandmothers is crucial for successful uptake of the intervention. Bovine lactoferrin is a safe and easy to administer according caregivers of LBWs babies. It also has potential to be translated into a safe and effective intervention for LBW babies to prevent sepsis.

Trial registration: ClinicalTrials.gov identifier: NCT03431558.

Background

Pakistan has one of the highest neonatal mortality rate worldwide, recently reported to be 46 deaths per 1,000 live births (1, 2). The majority of these deaths are caused by complications from preterm births (36.7%), severe infections (29.6%) and birth asphyxia (21.5%) (3).

Lactoferrin is the most abundant whey protein in human milk that helps protect infants from infections (4). It is also found in most exocrine secretions and in specific granules of neutrophils. It has a multifunctional role in host defence via a myriad of anti-microbial and anti-inflammatory functions (4-6). Human lactoferrin (hLF) and bovine lactoferrin (bLF) have similar bioactivity as proven in vitro and animal models (7). The US Food and Drug Administration has recognized bLF a safe nutrient to add in infant formula with no adverse effects (8). A pilot study in the United States (US) reported a protective effect of bLF enhanced formula (containing bLF 850 mg/L) on lower respiratory tract illnesses compared

to regular formula in infants (6). Another study described it as a safe product that has the potential to reduce sepsis in low birth-weight (LBW) infants (8, 9). Furthermore, it is considered the most effective intervention contributing towards the reduction in neonatal mortality (10).

We conducted a formative research in order to understand the acceptability, feasibility and optimal mode of administration of bLF to LBW infants. In addition, we also collected information on the knowledge and practices of caregivers regarding care of low birth weight babies.

Our study was novel in this context and aided to identify potential obstacles in the use of bLF among LBW babies in Pakistan.

Methodology

The study was carried out at the Aga Khan University Hospital (AKUH), Karachi, Pakistan from April 2018 to June 2018. AKUH is a private tertiary care hospital providing comprehensive care to people from around Pakistan. Annually, nearly 5000 babies are delivered at AKUH, including about 12-15% LBW neonates.

A qualitative exploratory study design was used to achieve the study objectives. A purposive sample of 30 caregivers of LBW infants were recruited in the study. We enrolled ten of each: mothers, grandmothers and fathers. Fathers and grandmothers were included because they are primary decision-makers in Pakistani society. Out of 30, 11 random participants also consented to use bLF for their infants.

Participants were recruited after obtaining informed written consent. Participants were selected based on the following criteria:

Inclusion Criteria

- Stable neonates with a birth weight less than 2500g and more than 1000g.
- Neonates with a gestational age $\geq 28+0$ weeks - $\leq 36+6$ weeks.
- Family plans on staying in the study area for at least one month.
- Parents/caretakers willing to provide consent.

Exclusion Criteria

- Neonates with congenital anomalies.
- Neonates with early-onset sepsis.
- Neonates with a history of chorio-amnionitis or maternal GBS colonisation.

- Reversed or absent end-diastolic flow on maternal umbilical artery doppler ultrasound, where available.

Data Collection

Prior to in-depth interviews (IDIs) and data collection, a senior social scientist provided an intensive five-days training to the research team. The research team comprised of an interviewer and a note taker. The training focused on the conceptual clarity of instruments, interview guides, probing techniques and general instructions. Mock interviews were carried out with immediate feedback and coaching to gain hands-on experience.

IDIs were conducted by the trained research staff at the hospital before discharge. The purpose of the interview was explained and consent to record the interview was taken from all participants. Each interview lasted between 30 to 60 minutes. Separate interview guides were developed for each caregiver category. These guides were developed based on the following themes:

- Perceptions of newborn care
- LBW infants and their special care
- Breast milk expression
- Care seeking patterns

The research staff demonstrated the preparation (breast milk expression and mixing of bLF in breast milk) and the administration of bLF to newborns to caregivers who consented to use bLF while they were still at the hospital. A pictorial brochure with user instructions was provided to the participants. After the demonstration, caregivers were advised to administer bLF once daily for two weeks to their infant at home. They were followed for four weeks. Study team conducted three home visits during first two weeks. At the end of the second week, each caregiver was interviewed to gather information regarding use of bLF and any problems faced in preparation or administration of bLF using a separate structured interview guide. These participants were further followed up by weekly telephonic calls for last two weeks to obtain information of the newborn's health status.

Data was analyzed using thematic analysis. Interviews were transcribed, and each transcript was thoroughly reviewed. Categories and subcategories were formed by coding the data. The emerged categories were listed under major thematic areas.

Results

The collective findings of formative interviews with mothers, fathers and grandmothers gave three broad themes:

1. Low birth weight infants and their care needs.

2. Perceptions of care practices related to LBW babies.
3. Perceptions and attitude towards use of lactoferrin.

Low birth weight neonates and their care needs

This theme explored participants' understanding about LBW babies, and health problems and care needs associated with LBW babies. Unanimously, family support provided to the mother and baby was also assessed. We explored the challenges faced by caregivers of LBW infants and evaluated their awareness of the treatments offered. The role of key decision makers in care seeking was also assessed.

Characteristics of normal birth weight and LBW babies

Most of the participants were able to distinguish between normal birth weight **and** LBW babies. They identified a LBW baby as "*smaller than normal*" with reduced muscle tone, lean, and with less activity compared to a normal weight baby. Half of the mothers considered a LBW baby to have immature lungs, poor suckle reflex, and at a greater risk to acquire respiratory problems.

"When I hold a small baby, I am afraid and doubt in my mind that baby may slip from my hands because he is very small." (Mother)

Whereas they defined healthy babies as active, well hydrated, bright pink in colour and an ability to demand feed when hungry.

"Normal birth weight babies look pink with chubby cheeks." (Mother).

Some fathers described LBW babies as being pale with fragile and loose skin, having breathing difficulties, feeble cry and poor suckling that resulted in feeding problems. Most grandmothers narrated that LBW babies are unable to maintain their body temperature and have poor ability to suckle.

"They do not have enough strength to suck the breast milk." (Grandmother)

Association of birth weight and health outcomes

Almost all mothers believed that LBW babies have delayed milestones and weak immune systems, which make them vulnerable to infections. A couple of mothers expressed that LBW babies can acquire micronutrient deficiencies and diseases in later life.

"They remain physically and mentally weak, and they learn to sit, walk, hold their neck late." (Mother)

"They catch infections and allergies easily and develop multiple deficiencies like vitamin B and low iron." (Mother)

Similar concerns were shared by fathers and grandmothers. Additionally, few grandmothers highlighted frequent respiratory and gastrointestinal problems among LBW babies. However, most of the

grandmothers were optimistic about health outcomes of LBW babies as one grandmother stated: *"As these babies grow, they gain weight and become like normal weight born babies."* Only a few fathers discussed possibility of hypothermia and hypoglycaemia in early days of life.

Perceptions of LBW babies care practices

Challenges in caring for LBW babies

Almost all mothers expressed a disrupted routine life due to the extra time and effort required for care of LBW babies. Their inability to complete household chores further added stress and made them irritable. They also complained of painful breasts, backaches, and insufficient milk production in their initial days. Majority of the mothers verbalized sleep deprivation and an inability to look after themselves. Undesirable comments from visitors further lead to anxiety and depression.

"When people visit, they usually pass comments like 'your child is very weak and small' which stressed me a lot." (Mother)

Similar views were given by fathers. One father said: *"LBW babies need constant vigilance and mothers stay awake the whole night leading to exhaustion and sleep deprivation."* However, half of the fathers had no idea about the challenges faced in care of LBW babies.

"This is not my problem (It does not concern me), please ask the mother." (Father)

Majority of the women reflected difficulties in bathing and dressing their LBW babies, as one participant stated: *"It is a bit difficult to bathe him and change his clothes."* Fathers also endorsed mothers' opinion that it is difficult to hold, feed, and bathe these babies.

On the other hand, most of grandmothers said that they faced no issues when offering care for LBW babies, as they had previous experience in handling LBW babies.

"We know how to carry, feed, bathe, hold and lift the baby with proper positioning. However, caring for the baby does disturb our daily routine." (Grandmother)

Family support system

A majority of the parents in our study shared that they took decisions themselves. On the other hand, some mothers expressed that grandparents and elders of the family were the main decision makers in their household. All grandmothers stated that both parents and grandparents of the baby usually took joint decisions in seeking health care for LBW babies.

"We must value our parents' and in-laws' experience in caring for low birth weight babies." (Father)

During the early postnatal period, all mothers acknowledge support from their mothers-in-law, sisters-in-law and at times, husbands. Support was usually required during the day as mothers had additional

house chores to complete. Fathers and grandmothers specifically identified support from paternal and maternal grandmothers. Grandmothers added that sisters (of both the mother and father) also extended their support.

Majority of the fathers found it difficult to support mothers in caring LBW babies because of their workload at their places of employment. Very few fathers stated that they support their spouse to care for the baby or do household chores while taking leave from work.

Care seeking behaviors

Majority of the mothers verbalized the need to seek the advice of a doctor for their newborn care, but the others preferred to follow the advice of their partner or elder family member. Those who preferred to seek care from doctors preferred to visit specialized doctors, (*“paediatrician”*) to treat their LBW babies. However, all of the participants believed that medical treatment had some side effects and should be used with caution. Only one mother identified taking advice from recently experienced parents of LBW babies.

“Parents who have had LBW babies can guide properly, like they share their experiences about things to take care off.” (Mother)

Fathers have mixed opinions. Few favoured allopathic treatments and some considered home remedies and spiritual healing as treatment options.

“Doctors are the most reliable individual we trust as they have the education and skills along with their experience to make the correct diagnosis.” (Father)

Unlike parents, all grandmothers preferred home remedies as treatment of minor illnesses. Some home remedies listed by them were herbed syrups, honey, oil massage and exposure to sunlight.

Administration of medications

Most of the mothers had experience in administration of medications to LBW babies and listed spoons, droppers and syringes as useful modalities to administer medications. On enquiring about the duration and frequency to administer medicines, mothers said, *“We do as per doctor’s prescription”*. All participants preferred droppers as they were the best at measuring the quantity and controlling the speed of administration. Further, they said that the baby could swallow the medicine easily with no spillage and with fewer chances of aspiration.

Perceptions and attitude towards use of lactoferrin

Opinions about lactoferrin

Most of the parents were convinced that lactoferrin is beneficial for their LBW babies' growth and agreed to add it in the newborns feeding milk. A few grandmothers feared about the side effects of mixing a nutrient substance in the mother's milk or in formula milk.

"My baby's growth will be enhanced perhaps my milk does not contain sufficient nutrients therefore it's better to give lactoferrin to my baby." (Mother)

"For elders there are food supplements to overcome deficiencies so why not for baby? This nutrient will improve the health of my baby." (Father)

Mode of administration of lactoferrin

Parents preferred the liquid form of lactoferrin instead of the powder, as it was easier to dissolve in milk. However, two grandmothers preferred powder over liquid but gave no reason for it. Parents were of the opinion that it should be preferably be mixed in breast milk and fed via bottles. Few mothers also stated that mixing in formula milk and feeding with droppers and spoons is also acceptable.

Frequency of administration of lactoferrin

Majority of the mothers were in favour of giving Lactoferrin as one single dose while the rest preferred to divide the total dose in small quantities throughout the day. In addition, most mothers idealised daytime hours to give lactoferrin so that they could closely monitor neonates for indigestion, feeding intolerance and other possible side effects. Only a few preferred night-time doses and believed it would help the baby to sleep soundly. Similar views were shared by fathers and grandmothers.

Experience of using bLF

After using bLF for two weeks, most of the mothers expressed their satisfaction. They found that bLF was easy to administer, had no side effects and increased the neonate's weight during the two weeks when bLF was administered. However, a third of mothers did not disclose bLF usage to their family members.

"It was a great experience, I am happy as it increased my baby's weight, it was easy to use and should be given to all LBW babies." (Mother)

Most of the mothers stated that use of the Nifty Cup was convenient and effective as a container for mixing and feeding their baby. They added that 5-10 mL of breast milk was sufficient to dissolve bLF.

A few mothers reported that mixing bLF powder in breast milk was frustrating, and household chores suffered due to time spent in expressing milk and mixing bLF.

Discussion

Our study found that issues of LBW babies were well-understood among parents in urban communities and birth weight was considered a predictor of newborn's health outcomes. We also found that parents believed LBW babies are prone to infections, gastrointestinal, respiratory problems, and have delayed milestones.

Mothers described caring of a LBW newborn has significant stress, both physically and emotionally. Our results revealed that mothers experienced painful breasts, poor suckling, and insufficient milk production. They also felt exhausted due to the lack of time to rest and the inability to take care of themselves along with household chores. Similar results have been reported in studies from Malawi and Iran (11, 12).

In this study, mothers were sufficiently supported to look after her baby by her mother and mothers-in-law. Mothers sought support in bathing, handling, and dressing their babies. Similar findings were reported by study in Indonesia (13). Little support was provided by fathers in care practices of their LBW newborns. They only assisted in feeding during night hours. Similar findings from rural Bangladesh had reported, where mothers are primary care providers and fathers usually do not actively participate in care for their infant (14).

Another significant finding was care seeking behaviours for LBW babies. Majority of the parents lived in an extended family system, where major decision makers were fathers and grandmothers. Although mothers preferred to seek advice from doctors, it was influenced by grandparents' choice. Our study confirmed the finding from studies conducted in other low middle income countries, including Uganda, Bangladesh, and Ethiopia, where mothers-in-laws held traditional beliefs and gave priorities to home remedies over allopathic treatments (15-17).

In the present study, one mother suggested that parents who had looked after LBW babies previously could extend their support to other parents. A qualitative study exploring parent to parent support group experiences in an NICU suggested that it is an effective way of supporting parents (18). Furthermore, findings from a systematic review by Hunt (2019) added that parent to parent support groups can reduce parental anxiety, stress and depression (19). Mothers who received peer support reported satisfaction and felt more confident in being able to care for their LBW baby. Similar groups in our setup can be a valuable source of hope, support and advice for parents of LBW babies.

Parents who used bLF seemed satisfied with the its use and reported no morbidity or adverse effects. They also reported weight gain among their LBW newborns with use of bLF. Most participants agreed to proposed administer a single dose during daytime hours. Similarly, a 2020 Cochrane review also reported no adverse effects with use of bLF (20).

The study is first of its kind to be conducted in Pakistan on the use of bLF in LBW babies. Additionally, no previous qualitative studies have been reported in literature exploring parents' perspective towards use of bLF. This could assist in designing large scale effectiveness trials in LBW neonates. However, a limitation in our study existed; our study had a small simple size and data was collected from urban communities; therefore, these perspectives cannot entirely be generalized to other populations.

Conclusion

Our formative study found willingness of parents to use of bLF for their LBW babies. However, educating fathers and grandmothers is crucial towards the successful uptake of this intervention in Pakistan. Bovine lactoferrin has the potential to be translated into a safe and effective intervention to reduce sepsis in LBW babies. Effectiveness trials can be planned after the achievement of conclusive results of this study.

Declarations

Competing interests:

There are no conflicts of interest between the objectives of the study and the investigators. The authors of this manuscript declare that they have no competing interest (financial or otherwise) in this research.

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Authors contributors

SA, SBS, NA and MJD hypothesize the study design. SA finalized the manuscript. SBS, SK, JK, IH, ZM, MDA, NA & MJD have critically reviewed the manuscript. AA supervised field operation and data collection activity. All authors have read and approved the final manuscript.

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Data availability statement

The data underlying this article will be shared on request to the corresponding author.

Ethics

The Ethics Review Committee of the Aga Khan University has granted approval for the proposed study with ID 4873-Ped-ERC-17. The National Bioethics Committee of Pakistan has granted approval for the

study to be conducted on human subjects. The study was also granted approval from Research Integrity & Ethics Administration, Human Research Ethics Committee, The University of Sydney with ID 2017/420.

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