ejpmr, 2015,2(5), 176-183.

SJIF Impact Factor 2.026

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 3294-3211

EJPMR

IMPORTANCE OF BREAST MILK IN IMMUNE SYSTEM DEVELOPMENT OF INFANTS

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Article Received on 23/06/2015 **Article Revised on 17/07/2015** **Article Accepted on 11/08/2015**

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ABSTRACT

It has observed in day to day clinical practice, that morbidity or mortality due to intestinal infections, was higher for formula fed than of breast fed infants. In 1934, a report on 20,000 mother infant dyads in the U S, found that morbidity or mortality due to intestinal infections, was higher for non breast fed infants than for breast fed infants. Many pediatricians and health care nurses actively advocated infant food formula to infant in 1950s and later. This was due to availability of better and improved artificial infant formulas, coupled with improved hygiene, better weight gain, and dramatic reduction in infant mortality rate, many of them thought that this relationship was no longer relevant. However, the studies in many countries; showed that artificially fed infants were at higher risk of disease, especially diarrhea and respiratory infections. Carefully designed studies in developed nations, suggested a significantly lower risk of diseases in breast fed infants, relative to those artificially fed. All these suggest that, the best of the infant's food formulas are lacking in protective and immune modulator activities that are present in human breast milk.

KEYWORDS: Breast, diarrhea, infant, hygiene.

INTRODUCTION

There is tremendous advance in our understanding, of protective components of human milk. It has direct bearing on the immunity of infants. It protects and facilitates development, tolerance, and an adequate inflammatory response. It is said that, milk is the communication channel between the immune system of mother and infant. It actively directs and educates the

immune, metabolic, and micro floral system of the infant, while rendering multiple means of protection from pathogenic organisms.

Immune system of newborn

The new born infant's immune system works in two ways,

1. Innate immune system.

2. Adaptive immune system

The adaptive immune system of new born is relatively new to external antigens, and requires synergy with the innate immune system to protect the intestine. Gut mucosa of the infant secrets mucin, antimicrobial peptides, luminal antigens, chemokine and cytokines that modulates inflammation. In addition to this, they also produce secretes paracrine and endocrine hormones. In addition to above all Components, full protection to the infant, requires human milk.[1] Breast feeding helps in reducing intestinal infection and also reduce incidents of chronic disease in later life. Though human milk contains significant amount of secretory immunoglobulin A, which is protective factors.

Multifunctional milk components in the human milk are nutrients, whose partially digested products inhibit pathogens. Also, Cytokines and its receptors, Toll Like Receptors - agonist and antagonists, anti-inflammatory agents, nucleotides and hormones in milk, modulate inflammatory responses. At birth component of the innate immune system like macrophages, neutrophil, dendritic cells, and IgM and IgG antibodies producing cells are present in the gut mucosa, but mucosa lacks or is deficient in IgA antibodies producing cells. The gut immune system develops rapidly in the immediate postnatal life, as it comes in contacts with dietary and microbial antigens.

New born gut is exposed to a large number of microorganisms, foreign proteins, and chemicals. The resistance to these relies on the protective factors present in the breast milk, and on the infant who develops their own innate and adaptive immunity.

Human milk is rich in glycan. Indigestible glycan in infant gut, stimulate colonization by probiotic organisms, modulates mucosal immunity and protects against pathogens.

Milk components, Promoting tolerance and Priming of the Immune System: In addition to the role of eliminating infectious agents and minimizing the damages caused by them, their immune system must learn the ability to discriminate between antigens that are harmless, and

one which is potentially dangerous. This Induction of tolerance is believed to occur mainly in the gut and is facilitated by the specialized B cells and T cells, production of sIgA, and the skewed Th2 response.[2]

Tolerance is an active process. In vitro studies suggest that the food antigens present in breast milk along with the immune suppressive cytokines aid in promoting tolerance to dietary and micro flora antigens in the gut. There are also clinical data to support breast feeding in infants, tolerate to mother's major histo compatible complex antigens. For example, kidney transplants from mothers were shown to survive better if the recipient had been breast fed by her. In infancy there is a fine balance between antigen responses, those results in tolerance to responses, which results in sensitization. It is hypothesized that, food intolerance, a common occurrence in infancy and is the result of the failure to adequately develop tolerance. The successful development of tolerance, contributes to lower incidences of food related allergies in breast- fed infants.[3, 4]

A systematic review recently, concluded that human milk appears to protect infants from the development of atopic diseases like eczema, food and respiratory allergies, in particular if there is a strong family history. It is also found that breast feeding, reduces incidence of immune mediated diseases, like celiac disease, inflammatory bowel disease, type 1 diabetes, rheumatoid arthritis, asthma, eczema, NEC and multiple sclerosis.

Maternal immune system: Depending on the stage of lactation, a variety of leukocytes is present in colostrums and mature milk,that could play a significant role in promoting the development of the infant's immune response. Macrophages (55–60%) and neutrophil (30–40%) dominate over lymphocytes (5–10%) .[5]

Viable leukocytes, have been isolated in feces from infants fed human milk, it is also possible that key surface molecules on these viable cells can remain antigenetically intact in the gut.

Antimicrobial Properties of Human Milk: Breast milk contains a variety of antimicrobial substances which are relatively resistant against intestinal proteolysis, that provide both, protection to the lactating mammary gland and to the suckling infant at a time when its immune system is still immature.

- **Macrophages:** Macrophages likely affects infant T cell and B cell function because they have been noted to express activation markers, demonstrate phagocyte activity, and also

secrete immune regulatory factors. Also, milk macrophages have been observed to contain engulfed sIgA, which can be release on contact with micro organism in the gut.

- **Neutrophil:** They demonstrate decreased in adherence, polarity, and motility and express high levels of CD11b and low levels of L- selectin , all these indicates prior activation. Little is known about the impact of these neutrophil on immune development in new born, but most researchers suggest that their main role is to protect mothers, as they have limited functional capacity once they are secreted in the milk capacity once they are secreted in the milk.
- **Lymphocyte:** The predominant lymphocytes in milk are T cells. The presence of higher proportion of CD8 and lymphocytes, in comparison to that of blood, suggests that these CD8 cells are selectively transferred from the mucosal immune system to the mammary gland. Human milk CD4 cells are also present in activated state, and express CD45RO, a surface protein associated with immunological memory. Recent studies have shown that immune phenotypic differences in systemic lymphocyte populations occur following exposure to breast milk. These include a decrease in CD4: CD8 cells and an increase in natural killer cells.
- **Cytokines:** Human milk contains an array of cytokines and chemokine, TNF[6], TGF[7], INF, granulocyte colony stimulating factor, monocytes chemo tactic protein 1, and RANTES. The primary source of these cytokines is mammary gland. Although, particular cytokines can be in high concentrations in some women's milk. Generally the concentrations of cytokines vary widely; it is difficult to assess their roles in the development of the infant's immune system. But the intake of cytokines through breast milk has the high potential to influence the maturation and development of immune cells in infants.

Breast milk Nutrients helping innate immunity: There are many components of breast milk which not only serve as a major source of nutrients, but in its native form or partially digested form, functions to protect the infant. They are multifunctional agents that we classify as part of an innate immune system of Breast milk.

- **Lactoferrin:** It is present at the range of 1–3 g/L. It is a major protein of human milk that binds free iron, assisting iron absorption by the infant. It's a well known fact that unbound iron is an essential nutrient for many pathogens. Thus presence of lactoferrin and resultant absence of free iron, would have broad bacteriostatic effect. It also inhibits growth of several bacteria[8,9], enhances phagocyte activity of macrophage, and inhibits

HIV, CMV, and herpes virus.[10,11] It is also noted that, partial digestion of lactoferrin produces lactoferricin B, a positively charged peptide loop of 18 amino acids with potent broad spectrum antibacterial activity for both Gram positive and Gram negative pathogens.

- **Lysozyme**: It is an enzyme that breaks 1,4 bonds between N acetyl muramic acid and N acetyl glucosamine, a critical link in the peptido glycan of bacterial cell walls. The amount in human milk varies, but is often approximately 100 g/L, is found in the feces of breast fed infant[4] which indicates that it survives intestinal digestion, and potentially break down the cell walls of Gram negative pathogens.
- **Haptocorrin:** Breast milk protein that chalets vitamin B12 is resistant to digestive juices and it inhibits entero toxic, E. coli.
- **Vitamins**: It is also rich in vitamin and minerals, helping immune system to function adequately and protect the infant from infective pathogens.

Hormones and growth factors: In Breast Milk one can find, many hormones, like cortisol, estrogen, pregnenadiol, progesterone, thyroid hormones, erythropoietin, gonadotropin, human chorionic gonadotropin, insulin, leptin, prolactin and pro calcitonin. Other than above, epidermal growth factor, insulin like growth factors and binding proteins, nucleotides, lacto albumin, lacto globulin, and lactoferrin are also found in Human milk.[6, 12]

Long chain PUFA (LCP): It is reported that those infants who were fed with Long Chain PUFA supplemented formula milk had lymphocyte populations and cytokines more similar to that of human milk fed infants, than infants who received unsupplemented formula milk. Conjugated linoleic acid, found in variable amounts in breast milk, also suggested contributing to immune development in infant.[13]

The presence of 4% fat in human milk is a major caloric source for the infant. It is also a multifunctional component. As milk mixes with lingual and gastric lipases, triglycerides are digested into Free Fatty Acid and mono glycerides; these strongly inhibit enveloped viruses, some bacteria, and protozoa.[14] The strongest inhibition is seen by mono glycerides, which act as detergents on pathogen membranes.

Nucleotides: It is a well known fact that, Nucleotides are beneficial in the systemic immune system by enhancing lymphocyte proliferation, NK activity, and macrophage activation and producing a variety of other immuno modulatory factors. Nucleotide supplemented formula

when fed to full term and a preterm infant improves, their responses to immunization, promote T cell maturation, and reduced the risk of diarrheal disease.[15]

Immune modulator/Anti Inflammatory Components in Human Milk: Although inflammation is a beneficial defense to the infant, an exaggerated inflammatory response will result in reduced intake, illness, and gut damage. It is not exactly known whether the exaggerated or unchecked inflammatory response to an infection occurs only in the gut or it is extends to the infant's systemic immune system. Over all breast milk appears to dampen the inflammatory response. A potent immune suppressive cytokine, IL-10, is found in breast milk [7,16]. It is a anti inflammatory agent and produced by mammary cells[16], it is present in lymphocytes and macrophages. This IL-10 dampens the Th1 response, thus inhibiting pro inflammatory cytokine release. TGF regulates immune system, and down regulate inflammation. It promote healing of intestinal cells damaged by cytokines or infection.[17]

CONCLUSION

It is summarize from the above discussion that, incomplete evidence suggesting, inter dependent links among multiple factors like, human milk components, ontogeny of intestinal function, mucosal immune system development, intestinal micro biota colonization, and protection against pathogens. Timely coordination of all these interacting components seems to optimize the health potential of neonates.

Normal regulation of these systems helps in minimizing acute conditions such as diarrhea, otitis media, and respiratory disease, and chronic conditions such as inflammatory bowel disease, allergy, obesity, cancer, and other manifestations of autoimmune dysfunction.

Better understanding of these factors, primarily may provide further evidence supporting active promotion of breast feeding for all infants. It can also help to improve the composition of formulas for premature and term infants.

Recommendations

Breastfeeding is one of the most effective ways to ensure child health and survival. If every child was breast fed within an hour of birth, given only breast milk for their first six months of life, and continued breastfeeding up to the age of two years, about 800 000 child lives would be saved every year. Globally, less than 40% of infants fewer than six months of age are exclusively breastfed. Adequate breastfeeding counselling and support are essential for mothers and families to initiate and maintain optimal breastfeeding practices.

The role of Pediatrician and health care workers should be one of promoting, protecting and facilitating the practice of breast feeding. The health care workers should be trained in practice of breast feeding. Social and legal law should be framed to facilitate the practise of breast feeding, by protecting the nursing mothers and granting minimum six month Maternity leave. Colostrum, the yellowish, sticky breast milk produced at the end of pregnancy, is recommended by WHO as the perfect food for the newborn, and feeding should be initiated within the first hour after birth. Exclusive breastfeeding is recommended up to 6 months of age, with continued breastfeeding along with appropriate complementary foods up to two years of age or beyond.

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