Bifidogenic Effect and the Immunity Power of Human Breast Milk

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Abstract

Bifidobacteria finds optimal living conditions for growth and overgrowth in the colonized part of the bowel when the chyme is rich in malabsorbed carbohydrate and poor in protein. Such condition is fulfilled with breastfeeding. Though the bifidogenic principle of human milk is attributed to the protein free fraction, the quality and quantity of its protein play an important role in the origination and maintenance of microflora .The low concentration of protein in human milk, the properties of this protein and the presence of specific proteins that inhibit competing microbes in the intestinal microflora are essential components of the bifidogenic principle of human milk. Due to the presence of immunological factors in breast milk like antimicrobial agents, anti-inflammatory agents, and immunomodulatory agents, human milk plays vital protective and defensive role when the infant's immune apparatus is immature. It also contributes early childhood growth and development when the infant is absolutely dependent on his/her caregivers for provision of nutrition.

Keywords: *Bifidogenic effect, immunity power, breast milk.*

Delta Med Col J.Jan 2013;1(1):20-24

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Introduction

Breast feeding is going on from time immemorial. Nothing is substitute for, or equal to, or superior to breast milk. Most of the paediatricians are knowledgeable about the advantages of breast feeding especially exclusive breast feeding for the first six months of an infant's life which includes provision of optimum nutrition that sustains adequate growth and development, hydration, prevention of allergy and diseases, improved child spacing, bonding between baby and mother, as well as economic, emotional, and psycho-social benefits.[1-4] Despite our understanding of the numerous benefits of breast milk, the more research is going on, the more and more new properties of human milk are being identified each year. Human has the capability to develop and maintain a predominance of bifidobacteria in the large bowel of infants by enteromammary circulation. Bifidobacteria and immuno-nutrients stimulate an infant's natural defense system to provide the power of immunity by anti-inflammatory and immune-modulatory agents present in breast milk.[2-5]

Phases of gut colonization:

At birth - Sterile.

Phase 1 - Aerobic/optionally aerobic bacteria (*E. coli,* streptococcus).
- Creates O_2 free environment.
- Colonizes anaerobic bacteria (bacteroides, bifidobacteria, clostridia).

Phase 2 - Breastfeeding - bifidobacteria.
- Formula - mixed flora.

Phase 3 - Weaning - mixed flora, increasing diversity of species.

Phase 4 - Post-weaning - adult like intestinal flora.

Bifidobacteria was first described and named by Tisser in 1900. It is a gram-positive, strictly anaerobic fermentative rod, often Y- shaped acid-tolerant bacteria. It accounts for 99% of total gut flora of breastfed infants and is also present in the lactiferous sinuses of the breast. Some species of bifidobacteria are - *B. bifidum, B. longum* and *B. infantis.*[6-8]

Functions of bifidobacteria:[8]

- It produces antibodies and inhibits pathogenic growth in the GIT.
- It produces organic acids and inhibits non-friendly bacterial growth.
- It competes with other bacteria for nutrients.
- It can also prevent proliferation of cancer cells.

Harmful bacteria of GIT are - *Ps. aeruginosa,* proteus, staphylococci, clostridia, veillonellae, etc. Bacteria having both gram positive and gram negative effects are enterococci, *E. coli,* streptococci, bacteroides and health promoting bacteria includes bifidobacteria, eubacteria and lactobacilli. The intestinal bacteria flora of breast fed infants found in different studies are; bifidobacteria $6x10^{10}$, *E. coli* $3x10^{8}$, streptococci $1x10^{8}$ (Mitsuoka[9]), bifidobacteria $7x10^{9}$, enterobacteria $5x10^{7}$ (Roberts[10]) and bifidobacteria $1.1x10^{8}$ (Nagendra[11]).

Nutrition affects the composition of the intestinal flora. Higher whey content and alpha- lactalbumin in breast milk promotes the growth of bifidobacteria. Lactose being a slowly digested carbohydrate, acts as the preferential substrate for the growth of bifidobacteria in the intestine. Low intestinal phosphorus results in a predominance of bifidobacteria over *E. coli* .[4,7]

Bifidogenic effect in breast milk:[8,9,11]

Bifidogenic effect is to provide an environmental conducive to the growth of bifidobacteria. Nutritional factors contributing to bifidogenic effect of breast milk are quantitatively and qualitatively different in protein and overall low content of it, low phosphorus content and high lactose of breast milk. This encourages the maintenance of acid tolerant bifidobacteria, simultaneously inhibiting the growth of harmful bacteria, promoting the bifidogenic effect. The fermentable carbohydrate lactose and the bifidus factor in breast milk play significant role in promoting the growth of bifidobacteria. Different characteristics of breast milk and non-breast milk are shown below.

Table I: Difference between breast milk and non-breast milk (formula)

Parameters	Breast milk	Non-breast milk
Lactose & acid production	More	Less
Protein - quantity & quality	Optimum	Quantity more & not sure about quality
pH & buffering capacity	Low	High
Infant's gastrointestinal tract	Bifidobacteria predominates	*E. coli* predominates

Immuno-nutrients:[12-16]

Zinc: Plays a central role in the immune system. It increases the neutrophil chemotaxis and is important for the growth and function of the thymus.

Vitamin A: Important in cell differentiation and for the growth and function of the thymus gland. It also has a role in the migration of lymphocytes to the intestinal villi and maintains the integrity of surface epithelium.

Selenium: Helps in lymphocyte proliferation and also protects the body against oxidative stress.

L-arginine: Increases the size and activity of the thymus gland which is responsible for the synthesis of T-lymphocytes.

Other important immuno-nutrients: Vitamin B_6, vitamin E, vitamin C and copper which play very important role in the defense mechanism of the body.

The immunity power of breast milk:

Bifidogenic effect coupled with immunomodulating nutrients build up immunity. Some of the immuno-nutrients present in breast milk are zinc, copper, selenium, vitamin A, vitamin E, vitamin B_6, vitamin C and L-arginine.[14-16] Studies of the immune system of human milk provide indisputable evidence

that it is the optimal food for the infant and that there is really no such thing as a substitute. Dr. Armond Goldman so nicely describes the immune system of human milk for a continuum of the maternal immune protection that extends from transplacental transfer of IgG in utero until the second year of life.[17] Human milk furnishes the necessary immunologic protection while the infant's immune system is maturing and production of the full antibody repertoire is not fully mature until about 24 months of age.[2,4,8,12]

Table II: Representative immune factors in human milk[1,2]

Agents	Time of maturation
Secretory Ig A (S IgA)	4-12 months
Full antibody repertoire	24 months
Lysozyme	1-2 years
Lactoferrin	? (uncertain)
Interleukin-6	? (uncertain)
Platelet activating factor-acetyl hydrolase	? (uncertain)
Memory T-cells	2 years

Human milk contains three major categories of immunologic factors: anti-microbial agents, anti-inflammatory agents, and immunomodulating agents. The list of factors in each category grows longer each year as more and more properties of human milk are identified by research.[1,2]

The anti-microbial agents:

The anti-microbial agents in human milk illustrate the unique interaction between infant and mother in responding to environmental challenges. For example, within a few days of maternal exposure to pathogen such as shigella, antibodies to this bacterium are noted in the mother's milk, which confers protection to the breastfeeding infant. This is due to the enteromammary circulaton pathway, which is triggered by antigen exposure to B-cells (IgM+) from the payer's patches of the lower intestinal tract and the consequent migration of those isotopes switched B-cells (IgA+) to the lamina propria of the mammary gland with help of cytokines. At the mammary gland, the transported B-cells differentiate into the IgA producing secretory plasma cells and through a number of steps within the mammary gland, secretory IgA (S IgA) is formed and secreted.[5] S IgA and other antimicrobial agents present in human milk are resistant to digestive enzymes, confer protection without triggering the inflammatory reactions, compensate for the infant's inability to process antimicrobial agents, kill certain bacterial pathogens synergistically, and are common to mucosal sites.[2,17]

Table III: Common pathogens against which S Ig A antibodies are present in human milk[17]

Bacteria & toxins	Viruses	Others
E. coli	Rota virus	Giardia
Shigella	Respiratory syncytial virus	*Candida albicans*
Salmonella	Polio virus	
Campylobacter	Influenza virus	
H. Influenza	Cytomegalo virus	
Strep. pneumonia	HIV	
Cl. difficle		
Cl. botulinum		
Vibrio cholera		

Following table shows functions of different antimicrobial agents present in human milk.[2]

Table IV: Functions of antimicrobial agents in human milk

Agents	Primary function
Lactoferrin	Iron chelation
Lysozyme	Peptidoglycan degradation
Fibronectin	Opsonization
Secretory Ig A	Antigen binding
Complement C_3	Fragments are opsonins
Mucin	Antivirus, receptor analogues
Oligosaccharides	Receptor analogues
Lipids	Disrupts enveloped viruses

Anti-inflammatory agents / factors:[2]

The anti-inflammatory agents present in breast milk represent a complex group of immune factors. Acetylhydrase, an enzyme that degrades platelet activating factor, is present in breast milk and may play a role in the decreased risk of necrotizing enterocolitis in the breast fed preterm infant and epithelial growth factor hastens recovery from diarrhea sooner. Dr. Anne Wright and co-workers from Arizona found that 11% of recurrent wheezing among non-atopic children studied was attributed to not breastfeeding.

Now some allergists recommend avoidance of all cow's milk based products in the maternal diet for the last trimester of pregnancy and during lactatation.[2,5,17-21]

Anti-inflammatory agents in breast milk are:[17]

- Cytoprotective.
- Epithelial growth factor.
- Insulin like growth factor (IGF).
- Maturational factor.
- Enzymes that degrade mediators.
- Binders of enzymes.
- Modulators of leukocytes - cytokines, alpha-tocopherol, β-casomorphine, prolactin, etc.
- Antioxidants - β carotene, inositol, vitamin A, E, C.

Immunomodulatory factors:

The complex role of human milk in maintaining the health of infant is well represented by the immunomodulating factors, including cytokines α-tocopherol, β-casomorphines and prolactin. These agents may play a role in the prevention of disease after infancy and be factors in the decreased risk for breastfed infants to develop Crohn's disease, insulin-dependent diabetes and lymphoma. The immunomodulating role of cytokines has been documented to include the possible functions of activating T-cells, enhancing Ig A and secretory components production, and participating in the enteromammary and bronchomammary circulation. All of these processes potentiate the infant's infection fighting response.[2, 17]

Table V: Cytokines with their potential functions in human milk[17]

Cytokines	Possible functions
Interleukin-1 β	Activates T cells
Interleukin- 6	Enhances Ig A production
TNF-α	Enhances secretory component secretion
TGF-β	Enhances isotope switching to IgA, +B cells

Human milk has the unique capability to originate and maintain a predominance of bifidobacteria in the large gut of infants, which helps in resistance against gastrointestinal infections as well as on a symbiotic utilization of some milk components. Besides, it has other protective factors those fight against the common pathogenic microbes. These aspects can be looked upon as a challenge for further research on mother's milk composition and on the metabolic effects of its constituents in future.

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