Immunological Mediators of Breast Feeding to Protect against Celiac Disease

Haniye Ghasiyari¹, Mohammad Rostami Nejad²*, Mohammad Reza Zali²

1Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
*Corresponding author: m.rostamii@gmail.com


1. Introduction

Celiac disease (CD) as an immune mediated systemic disorder is caused by a permanent sensitivity to gluten [1,2] in genetically susceptible individuals who are carrying the HLA-DQ2 and/or HLA-DQ8 haplotypes and characterized by a the wide range of clinical manifestations [3,4]. Current knowledge indicates that intestinal immune responses to gluten can damage the small intestine [4].

While both genetic and environmental factors are involved in the etiology of celiac disease, the genetic factors are a key actors in the development of the disease. On the other hand some environmental risk factors such as dysbiosis of gut microbiota plays an important role for the subsequent development of CD [5].

Recent epidemiological studies suggest that breast feeding (BF) at the time of dietary gluten introduction has protective value to delays the onset of symptoms CD in infants [6,7]. In this regard, studies have shown that the prevalence of the celiac disease in developing countries like India with low rates of breast feeding is more than developed countries [8].

Recently Szajewska et al. [9] proposed the primary prevention of CD via breast feeding in infants and children. They demonstrated that BF is reduce the risk of CD development and reprieve the introduction of gluten in infants’ diet can delays onset of symptoms CD [9].

Meta-analysis study by Akobeng et al. [10] also showed that there is an association between increasing duration of BF and decreased risk of developing CD. Accordingly the risk of development of CD in children being BF at the time of gluten introduction was 52% decreased compare with their peers who were not.

These studies also confirmed that longer breastfeeding is expressively degraded the possibility of development of CD [9,10]. It is, however, not clear whether it merely delays the onset of symptoms or provides constant protection.

Now this question may raised, how breastfeeding could protective against celiac disease development? At birth, the immune system of infants are very weak and some part of their defense provides via breast milk [11]. In that time, IgA antibodies transferred from the maternal milk can provide passive immunity against gut infections such as enterotoxigenic Escherichia coli (ETEC) [12], Shigella [13], Campylobacter [14] and Vibrio cholera [15]. On the other hand, it may decrease immune response to ingested gluten peptides by mechanisms such as agglutination of the antigen to immune complexes on the mucosal surface and prevention of antigen uptake and thus lead to reduce the risk of CD (Figure 1) [16].

Another protective factors of human milk are including Lactoferrin and oligosaccharides. Human Lactoferrin has anti-inflammatory capacity that it blocking the production of IL-1β, TNF, IL-6 and IL-8 and result in protection against microbial infections [17]. Also substantial fraction of oligosaccharides as analogues for microbial receptors can prevent from attachment of mucosal infections to epithelium (Figure 1) [11,18]. This issue is very important because in the early life of infant that the immune system is weak and in a few percent of adults, infections of the gastrointestinal tract with increased permeability of the intestinal mucosa and tissue transglutaminase expression leading to triggering CD in susceptible individuals [11,16].

In contrast some studies showed that in infants who were breast feeding at the time of gluten introduction, the risk of CD was significantly reduced compared with those who were not breast feeding during this period [9,10]. In addition to the mentioned factors, human milk contain many bioactive factors such as hormones, enzymes and growth factors which can help development of the infant’s innate and acquired immunities (Figure 1) [19,20]. On the other side the BF effect on preliminary intestinal microbiota and therefore prevents induction of immune-mediated diseases. Its possible mechanism is that BF motivate the production of a proportionate and diverse microbiota (Bifidobacteria, Lactobacillus, and Bacteroides), by activation of T-regulatory cells which primarily effects a switch from Th2 predominant to a Th1/Th2 balanced response.

In conclusion available evidences suggests that according to the important role of BF in the development of different disorders, such as CD, long term prospective...
cohort studies are required to investigate different aspects of relationship between breast feeding and CD.

Figure 1: Protective effects of breast feeding against development of celiac disease

Passive immunity by the IgA antibodies
- Protection against infections
- Reduce the risk of CD

Regulation of gut permeability
- Reduce of gastrointestinal infections
- Prevent of tissue transglutaminase expression

Bioactive antimicrobial factors
- Maturation of gut
- Development of the infant’s innate and acquired immunities

Exerted of immunoregulatory
- Via suppression of autoimmunogenic T-cell

Antimicrobial and anti-inflammatory agents
- Blocking of the inflammatory cytokines production by lactoferrin
- Protection against infections via oligosaccharides

References