

## Role of Breast-feeding in the Development of Atopic Dermatitis in Early Childhood

Jeong Hee Kim<sup>1,2</sup>

<sup>1</sup>Department of Pediatrics, School of Medicine, Inha University Hospital, Incheon, Korea <sup>2</sup>Environmental Health Center for Allergic Rhinitis, Inha University Hospital, Ministry of Environment, Incheon, Korea

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

For all infants, breast-feeding is recommended for at least first 4 to 6 months of life.<sup>1-4</sup> Breast-feeding has many physiological and psychological benefits in both mothers and infants, and the World Health Organization recommends that infants be exclusively breast-fed for the first 6 months of life to achieve optimal growth development and health.<sup>4</sup>

The American Academy of Allergy, Asthma & immunology and the European Academy of Allergy and Clinical Immunology recommended exclusive breast-feeding for at least 4 and up to 6 months for primary prevention of allergic disease.<sup>1,5</sup> Allergy prevention through breast-feeding has been issued for more than 70 years. Many studies have investigated the role of breastfeeding in the development of allergic disease, including atopic dermatitis (AD), with inconsistent findings.

Some studies showed that breast-feeding reduces the risk for childhood AD. In a birth cohort of 4,089 children, breast-feeding for 4 months or more reduces the risk for AD and delays the onset of allergy march to age 4.6 A cross-sectional survey in developing countries found that prolonged breast-feeding reduces the risk of developing allergic diseases including AD even in the presence of maternal allergy.<sup>7</sup> A prospective, interventional study in Belarus, 17,046 healthy mothers of full-term infants were randomly assigned to receive assistance with initiating and maintaining breast-feeding or routine postnatal follow-up. The occurrence of AD was reduced by 46 percent in infants whose mothers received breast-feeding support compared with those whose mothers did not, although the findings just reached statistical significance.8 A Taiwanese birth cohort study with 186 subjects reported that exclusive or partial breast-feeding for at least 6 months appears to be associated with a reduced risk of developing AD in early childhood.<sup>9</sup> A systematic review with meta-analysis of 18 prospective studies evaluating the association between exclusive breast-feeding during the first 3 months after birth and AD demonstrated that exclusive breast-feeding is associated with a lower incidence of AD during childhood in children with a family history of atopy. This effect is lessened in the general population and negligible in children without first-order atopic relatives.<sup>10</sup> In a prospective cohort of healthy term newborns at risk of atopy, 865 infants exclusively breast-fed and 256 infants partially or exclusively formula-fed were followed up until the end of the first year, and it was found that in infants at high risk of atopy, exclusive breast-feeding for at least 4 months is effective in preventing AD in the first year of life.<sup>11</sup>

In contrast, other studies did not find protective effects of breast-feeding against AD. The current issue of the AAIR, Lee *et al.*<sup>12</sup> investigated the association between breast-feeding and AD in young children. They analyzed 2,015 children aged 1 to 3 years from the Korea National Health and Nutrition Examination Survey. They stated that there was no association between breast-feeding and AD. They also reported that parents with allergic disease favored breast-feeding and tended to prolong breast-feeding, which is consistent with the result of other studies.<sup>13</sup>

An earlier study on breast-feeding and atopy in infants has yielded similar results. In a cohort of infants in south-east Sweden, the risk of AD during the first year of life was evaluated in relation to the duration of exclusive breast-feeding <4 months. This study indicates that exclusive breast-feeding does not influence the risk of AD during the first year of life.<sup>14</sup> A 2007 cluster randomized trial results, in which avoids the ethical issues of interfering directly with maternal choices about infant feeding, do not support a protective effect of prolonged and exclusive breast-feeding on asthma or allergy.<sup>15</sup> A 2009 systematic re-

Correspondence to: Jeong Hee Kim, MD, PhD, Department of Pediatrics, Inha University Hospital, 27 Inhang-ro, Incheon 22332, Korea. Tel: +82-32-890-3618; Fax: +82-32-890-2844; Email: kimjhmd@inha.ac.kr Received: April 12, 2017; Accepted: April 13, 2017

• There are no financial or other issues that might lead to conflict of interest.

view and meta-analysis of prospective cohort studies in developed countries compared breast-feeding with conventional infant formula feeding or partial breast-feeding in the development of AD, and revealed that exclusive breast-feeding for at least 3 months was not significantly protective against the development of AD compared with partial breast-feeding or conventional formula.<sup>16</sup> A birth cohort study with infants born to mothers with a history of asthma reported that no significant association between the duration of exclusive breast-feeding and the development of sensitization in the first 6 years of life. The results were adjusted for reverse causation.<sup>17</sup>

Furthermore, there have been several reports that prolonged exclusive breast-feeding may increase the risk for AD. The prevalence of AD in the first 7 years increased with each additional month of breast-feeding in an observational birth cohort study with 1,314 infants.<sup>13</sup> The Auckland Birthweight Collaborative case-control study investigated risk factors for AD in babies with small for gestational age and concluded that duration of breast-feeding was associated with an increased risk of AD at the age of 3.5 years.<sup>18</sup> A prospective 20-year follow-up study reported that exclusive breast-feeding for 9 months was associated with AD and symptoms of food hypersensitivity at the age of 5 years, and with symptoms of food hypersensitivity at the age of 11 years, in children with a family history of allergy.<sup>19</sup> A Copenhagen birth cohort with infants who were born to mothers with a history of asthma found that breast-feeding significantly increased the risk of AD, but reduced the risk of wheezy episodes and severe wheezy exacerbation.<sup>20</sup> A Japanese study also showed that exclusively breast-fed infants were more likely to have AD than those fed formula alone. In addition, children with longer breast-feeding duration were significantly more likely to have AD.<sup>21</sup> Similarly, a Korean cross-sectional study with 10,383 children aged 0-13 years reported that prolonged breast-feeding increased the risk of AD in children <5 years of age, regardless of parental history of atopic diseases.<sup>22</sup>

Different study designs and methods may account for these discrepancies, and there should be various uncontrollable confounding factors which could not be adjusted for.<sup>23-25</sup>

It is important to exclude 'reverse causation,' as families with a history of allergic disease are also more likely to have breast-feeding in observational studies.<sup>13</sup> Although reverse causation has been taken into account by adjusting for parental history of allergic disease, the influence of reverse causation can only be eliminated with a prospective double-blind randomized controlled trial (RCT) design. However, it is not ethically accepted to randomly divide the infants into the breast-fed and formula-fed groups. In addition, it is almost impossible to control for other various confounding factors, such as maternal immunity, maternal diet during pregnancy and lactation, breast milk composition, environment, and other lifestyles.

In summary, many studies have been conducted to evaluate the relationship between breast-feeding and allergy. The results are inconsistent: protection against allergy, no effects, and even increased risk for allergy. The immune system in early life is greatly influenced by maternal immunity during pregnancy and lactation. Thus, further studies focusing on breast milk characteristics with well-designed RCT are needed to clarify these issues.

## ORCID

Jeong Hee Kim http://orcid.org/0000-0002-7054-8552

## REFERENCES

- 1. Muraro A, Halken S, Arshad SH, Beyer K, Dubois AE, Du Toit G, et al. EAACI food allergy and anaphylaxis guidelines. Primary prevention of food allergy. Allergy 2014;69:590-601.
- 2. Section on Breastfeeding. Breastfeeding and the use of human milk. Pediatrics 2012;129:e827-41.
- Chan ES, Cummings C; Canadian Paediatric Society, Community Paediatrics Committee and Allergy Section. Dietary exposures and allergy prevention in high-risk infants: a joint statement with the Canadian Society of Allergy and Clinical Immunology. Paediatr Child Health 2013;18:545-54.
- Vandenplas Y, Abuabat A, Al-Hammadi S, Aly GS, Miqdady MS, Shaaban SY, et al. Middle east consensus statement on the prevention, diagnosis, and management of cow's milk protein allergy. Pediatr Gastroenterol Hepatol Nutr 2014;17:61-73.
- Fleischer DM, Spergel JM, Assa'ad AH, Pongracic JA. Primary prevention of allergic disease through nutritional interventions. J Allergy Clin Immunol Pract 2013;1:29-36.
- Kull I, Böhme M, Wahlgren CF, Nordvall L, Pershagen G, Wickman M. Breast-feeding reduces the risk for childhood eczema. J Allergy Clin Immunol 2005;116:657-61.
- Ehlayel MS, Bener A. Duration of breast-feeding and the risk of childhood allergic diseases in a developing country. Allergy Asthma Proc 2008;29:386-91.
- Flohr C, Nagel G, Weinmayr G, Kleiner A, Strachan DP, Williams HC; ISAAC Phase Two Study Group. Lack of evidence for a protective effect of prolonged breastfeeding on childhood eczema: lessons from the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Two. Br J Dermatol 2011;165:1280-9.
- Chiu CY, Liao SL, Su KW, Tsai MH, Hua MC, Lai SH, et al. Exclusive or partial breastfeeding for 6 months is associated with reduced milk sensitization and risk of eczema in early childhood: the PATCH Birth Cohort Study. Medicine (Baltimore) 2016;95:e3391.
- Gdalevich M, Mimouni D, David M, Mimouni M. Breast-feeding and the onset of atopic dermatitis in childhood: a systematic review and meta-analysis of prospective studies. J Am Acad Dermatol 2001;45:520-7.
- Schoetzau A, Filipiak-Pittroff B, Franke K, Koletzko S, Von Berg A, Gruebl A, et al. Effect of exclusive breast-feeding and early solid food avoidance on the incidence of atopic dermatitis in high-risk infants at 1 year of age. Pediatr Allergy Immunol 2002;13:234-42.
- 12. Lee KS, Rha YH, Oh IH, Choi YS, Kim YE, Choi SH. Does breastfeeding relate to development of atopic dermatitis in young Korean children?: based on the Fourth and Fifth Korea National Health and Nutrition Examination Survey 2007–2012. Allergy Asthma Im-

## **Breast-Feeding and Atopic Dermatitis**

munol Res 2017;9:307-13.

- 13. Bergmann RL, Diepgen TL, Kuss O, Bergmann KE, Kujat J, Dudenhausen JW, et al. Breastfeeding duration is a risk factor for atopic eczema. Clin Exp Allergy 2002;32:205-9.
- 14. Ludvigsson JF, Mostrom M, Ludvigsson J, Duchen K. Exclusive breastfeeding and risk of atopic dermatitis in some 8300 infants. Pediatr Allergy Immunol 2005;16:201-8.
- Kramer MS, Matush L, Vanilovich I, Platt R, Bogdanovich N, Sevkovskaya Z, et al. Effect of prolonged and exclusive breast feeding on risk of allergy and asthma: cluster randomised trial. BMJ 2007;335:815.
- Yang YW, Tsai CL, Lu CY. Exclusive breastfeeding and incident atopic dermatitis in childhood: a systematic review and meta-analysis of prospective cohort studies. Br J Dermatol 2009;161:373-83.
- 17. Lodge CJ, Tan DJ, Lau MX, Dai X, Tham R, Lowe AJ, et al. Breast-feeding and asthma and allergies: a systematic review and metaanalysis. Acta Paediatr 2015;104:38-53.
- Purvis DJ, Thompson JM, Clark PM, Robinson E, Black PN, Wild CJ, et al. Risk factors for atopic dermatitis in New Zealand children at 3.5 years of age. Br J Dermatol 2005;152:742-9.
- 19. Pesonen M, Kallio MJ, Ranki A, Siimes MA. Prolonged exclusive breastfeeding is associated with increased atopic dermatitis: a pro-

spective follow-up study of unselected healthy newborns from birth to age 20 years. Clin Exp Allergy 2006;36:1011-8.

- 20. Giwercman C, Halkjaer LB, Jensen SM, Bønnelykke K, Lauritzen L, Bisgaard H. Increased risk of eczema but reduced risk of early wheezy disorder from exclusive breast-feeding in high-risk infants. J Allergy Clin Immunol 2010;125:866-71.
- 21. Ito J, Fujiwara T. Breastfeeding and risk of atopic dermatitis up to the age 42 months: a birth cohort study in Japan. Ann Epidemiol 2014;24:267-72.
- 22. Hong S, Choi WJ, Kwon HJ, Cho YH, Yum HY, Son DK. Effect of prolonged breast-feeding on risk of atopic dermatitis in early childhood. Allergy Asthma Proc 2014;35:66-70.
- 23. Nickerson K. Environmental contaminants in breast milk. J Midwifery Womens Health 2006;51:26-34.
- 24. Nagayama J, Tsuji H, Iida T, Nakagawa R, Matsueda T, Hirakawa H, et al. Immunologic effects of perinatal exposure to dioxins, PCBs and organochlorine pesticides in Japanese infants. Chemosphere 2007;67:S393-8.
- 25. Grandjean P, Poulsen LK, Heilmann C, Steuerwald U, Weihe P. Allergy and sensitization during childhood associated with prenatal and lactational exposure to marine pollutants. Environ Health Perspect 2010;118:1429-33.