

**PRIMARY ALLERGY AND ASTHMA PREVENTION: A REVIEW ARTICLE**Andry Sultana<sup>1</sup>\*Corresponding author email: [andrysultanamd@yahoo.co.id](mailto:andrysultanamd@yahoo.co.id)DOI: <https://doi.org/10.33508/jwmj.v6i3.5766>**ABSTRACT**

The prevalence of asthma and other allergic diseases has been increasing over the last few decades in both industrialized and developing countries. It is generally recognized that asthma is disease caused by exposure of genetically predisposed individuals to environmental risk factor. Environmental variables might raise or reduce the likelihood of becoming asthma and allergies. These environmental factors can be managed as primary preventive actions by removing risk factors for asthma and allergies

**INTRODUCTION**

Asthma and allergies are now important problems in public health.<sup>1</sup> Reducing the morbidity and mortality of asthma and allergy is crucial since these diseases have negatively impacted the quality of life for millions of adults and children. This can be accomplished using either primary or secondary preventive strategies.<sup>2,3</sup> Primary preventative strategies are intended to avoid the development of allergic manifestations such as asthma, allergic rhinitis, atopic dermatitis, and so on, while secondary preventive strategies aim to avoid symptoms related to allergies, flare-ups, or worsening of pulmonary function among people with already existing preceding allergic disease.<sup>2</sup>

The prevalence of asthma and allergies has increased rapidly in recent decades in both developed and developing countries.<sup>4-7</sup> It is

estimated that more than 20% of the world's population has asthma and allergies. In the United States, 4-5% of the population has asthma. Asthma can be seen at any age, but especially at an early age. As many as half of asthma cases occur before the age of 10 years and a third before the age of 40 years.<sup>8</sup> The concept of allergy pathogenesis is that allergic disorders develop in atopy predisposed individuals when they are exposed to allergens.<sup>2,6</sup> However, atopy is simply one of several variables that contribute to the etiology of these diseases. For example, atopy plays a major role in IgE-mediated food allergies, such as peanut allergy; nevertheless, other immunological pathways, directed directly by T cells, have important roles in disorders such as non-atopic asthma.<sup>2</sup> Atopy refers to a hereditary tendency for allergies to develop as a result

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of an overabundance of Ig E antibodies.<sup>2,9</sup> An allergic condition has a 25% probability of striking a kid of one atopic parent, and a 50% chance if both parents are atopic.<sup>6, 10,</sup>

<sup>11</sup> Multiple genes on distinct chromosomes contribute to the development of allergic illnesses, which are polygenic. Nevertheless, for the disease to exhibit clinical symptoms, a combination of genetic and environmental variables must act.<sup>2,12,13</sup> Environmental variables might raise or reduce the likelihood of becoming asthma and allergies. These environmental factors can be managed as primary preventive actions by removing risk factors for asthma and allergies through exclusive breastfeeding and limiting exposure to allergens, cigarette smoke, endotoxins, and other substances.<sup>2,14-16</sup> In order to avoid the development of asthma and other allergy disorders, this paper will address the primary protective strategies against environmental risk factors.

## **MECHANISM OF ALLERGIC REACTION**

Symptoms of allergies typically start in early childhood. Therefore, during pregnancy or as soon as the infant is born, primary preventative actions should be undertaken.<sup>2,15</sup> Allergic reactions are essentially a person's immunological response to certain antigens known as

allergens. Allergic reactions can occur when an individual has an allergic talent (atopy) combined with congenital factors (heredity / genetics) following exposure to numerous environmental factors. Environmental factors can facilitate and strengthen the body's reaction to the allergen. Atopy arises when a person with a genetic susceptibility is exposed to a variety of allergens.<sup>6,10</sup> There is evidence that early childhood exposure to aeroallergens, specifically house dust mites, is associated with the development of asthma later in life.<sup>16-18</sup>

During pregnancy, there is a TH<sub>1</sub>-TH<sub>2</sub> imbalance, with TH<sub>2</sub> having the edge. After birth, a mature immune system strikes a balance between TH<sub>1</sub> and TH<sub>2</sub> cytokine responses. However, in children with a history of atopy, this balance is never achieved, since TH<sub>2</sub> is constantly dominant, resulting in sensitization and allergic illness. So, if environmental manipulation occurs early in life (in during pregnancy and early infancy), before the immune system matures and is not exposed to allergens that produce sensitization, it is expected to enhance the balance of TH<sub>1</sub> and TH<sub>2</sub>.<sup>2,5,19</sup>

## **ALLERGIC DISEASE COURSE**

Allergic disorders typically affect multiple organs at the same time, though they may

affect only one. The symptoms vary depending on the organs affected, including those in the gastrointestinal tract (vomiting, diarrhea, stomach discomfort), respiratory tract (asthma, rhinitis), and skin (urticaria, atopic dermatitis).<sup>6,11</sup>

Typically, allergy symptoms appear in the gastrointestinal tract first (during infancy), followed by skin symptoms in older infants or children aged 1 - 2 years, and ultimately respiratory tract complaints in later children.<sup>6</sup> Aeroallergens have been linked to the development of airway allergies. The types of aeroallergens vary depending on the socioeconomic circumstance. House dust mites, for example, are the most prevalent allergen in humid (tropical) regions; allergies to pets such as dogs and cats are common in cold climate countries; and cockroaches are common in inner-city areas among low-income people.<sup>2,14</sup>

According to the Hygiene Hypothesis, reduced exposure to bacterial infections, gut microbiota, and parasites during early life may increase vulnerability to allergy disorders. This idea proposes that infection will protect against allergy.<sup>20,21</sup> Specific infections and immunizations can change the direction of the immune response, preventing atopy. However, not all infections offer protection. Recurrent lower respiratory tract infections in newborns

have been linked to a higher risk of childhood asthma.<sup>2,22</sup> The respiratory syncytial virus (RSV) is the most prevalent cause of airway infection in infants, while rhinovirus and influenza virus are responsible in older children and adults. These infections can cause wheezing, asthma, and airway blockage.<sup>2,8,16,23</sup> Smoking by mothers and/or fathers during pregnancy and after childbirth harms newborn lung development and promotes childhood asthma.<sup>12,24-26</sup>

## **PRIMARY PREVENTION STRATEGIES**

The identification of the causes of asthma and allergies has resulted in a variety of primary prevention strategies. Primary preventive measures include avoiding allergens (food, dust, house mites, animal dander, cockroaches, cigarette smoke), administering vaccines, probiotics, omega-3, immunotherapy, and preventing occupational asthma.<sup>2</sup>

### **I. Avoidance of food allergens**

For babies at high allergy risk, avoiding cow's milk protein through exclusive breastfeeding or hydrolyzed formula is advised. Breastfeeding for 4 to 6 months protects against allergies; this effect may be attributed to the immunomodulatory effect of breast milk, the avoidance of cow's milk

protein allergens, or both. Breastfeeding for less than 4 months is linked to an increased risk of allergic disease, including atopic dermatitis, allergic rhinitis, and wheezing.<sup>2,3,12,19</sup> Breastfeeding is advised for all newborns throughout the first 4 to 6 months of life. The American Academy of Allergy, Asthma, & Immunology and the European Academy of Allergy & Clinical Immunology both advocate exclusive breastfeeding for at least 4 to 6 months as a major preventive measure for allergic disorders. If breastfeeding is insufficient or not possible, high-risk infants may be given a hypoallergenic formula with proven preventative effects for the first four months.<sup>26</sup> There is a substantial inverse correlation between breastfeeding duration and allergy illness in children with non-allergic parents, hence breastfeeding should be provided for 6 months in newborns at high risk of atopy.<sup>27-29</sup> Ahmadizar et al reported that in a population of asthmatic children (4-12 years old), those who were breastfed had a statistically significantly decreased risk of asthma exacerbations later in life than those who were not breastfed.<sup>28</sup> Wilson et al found that duration of exclusive breastfeeding in children aged 4-6 years longer than 6 months had a protective relationship with the incidence of childhood asthma.<sup>29</sup> In contrast, a study by Sears MR et al reported that breastfeeding

does not protect children from atopy and asthma and may even increase the risk. This study needs to be scrutinized because breastfeeding was not exclusive and there was additional formula feeding.<sup>30</sup>

Giving hydrolyzed milk (hypoallergenic infant formulas) either as a milk substitute or in addition to exclusive breastfeeding can be done to avoid proteins from cow's milk. The German Infant Nutritional Intervention Study compared the effects of hydrolyzed milk and cow's milk and found that the incidence of allergies such as atopic dermatitis was significantly reduced in those using hydrolyzed milk.<sup>31</sup>

Several studies have demonstrated that avoiding highly allergic foods such as eggs, nuts, cow's milk, and fish during pregnancy and nursing reduces food sensitization on the Prick test as well as atopic dermatitis at two years of age. However, this study found no long-term benefit effects, therefore avoiding particular meals during pregnancy and breastfeeding is not suggested because it may harm the mother and baby (nutritional deficiency).<sup>2,3,12</sup>

## II. **Avoidance of exposure to house dust mites, cat, dog and cockroach allergens**

House dust contains numerous allergens, but house dust mites (HDM) are the most prevalent source of indoor allergens.

Exposure to house dust mites has been reported to cause asthma.<sup>14,32</sup> The most common mites are *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*.<sup>32</sup> The Manchester Asthma and Allergy Study (MAAS) found that lower levels of house dust mites in pregnant women and the postnatal period were related with fewer respiratory symptoms and improved lung function in 3-year-old children, but substantially raised the likelihood of HDM sensitization.<sup>12,33</sup> Dust mites can be avoided by using impermeable bed covers, washing bedding with hot water, not using carpets, lowering room humidity, and using benzyl benzoate as a mite repellent.<sup>2,26</sup>

Allergies to cat and dog proteins can induce asthma, rhinoconyngitis, and eczema. Cat allergies are mostly formed in salivary glands and skin flakes, whereas dog allergens are primarily found in saliva, skin flakes, and urine.<sup>14,34,35</sup> Although contact to cats and dogs can induce asthma, rhinoconjunctivitis, and eczema, the study discovered a protective effect against allergy development. It is believed that exposure to endotoxins produces this protective effect. Endotoxins are cell wall components present in gram-negative bacteria, particularly in the feces of cats and dogs.<sup>36,37</sup> Exposure to these endotoxins will enhance the production of TH<sub>1</sub> cytokines

while decreasing the production of TH<sub>2</sub> cytokines (which play a role in the pathogenesis of allergies).<sup>37-39</sup> Because there is no clear evidence that exposure / avoidance of cat / dog allergens will have a protective effect on allergies, patients with a predisposition to atopy should not keep dogs / cats.<sup>40</sup>

In communities with low incomes, cockroaches are a common allergy. Cockroach exposure and sensitization are linked to a greatly higher risk of asthma.<sup>41-43</sup> To prevent cockroach exposure, limit their entry into the home, eliminate sources of food, water, and shelter, use traps and insecticides, remove reservoirs with High-Efficiency Particulate Air (HEPA) vacuum cleaners, and wear impermeable bed covers.<sup>42</sup>

### **III. Prevention of exposure to cigarette smoke**

Maternal smoking during pregnancy and after childbirth causes sensitization and the development of asthma. A number of studies have found a link between exposing newborns in utero to smoke tobacco environments and the development of asthma in childhood and adults.<sup>12,25,26</sup>

### **IV. Endotoxin exposure/vaccination and probiotics**

Enhancing the TH<sub>1</sub>/TH<sub>2</sub> balance through TH<sub>1</sub> cytokine stimulation from infection, immunization, or endotoxin will avoid atopy and allergic symptoms.<sup>2,12,15</sup>

Childhood vaccinations are frequently used to avoid viral and bacterial illnesses. Clinical evidence indicates that vaccination may have an impact on the onset of allergic reactions. For instance, immunization with Bacille Calmette Guerin (BCG) will alter the TH<sub>1</sub>/TH<sub>2</sub> balance and boost the TH<sub>1</sub> immune response. This vaccine will lessen the onset of allergic sensitization.<sup>2,20</sup> Aaby P et al. found that BCG immunization in babies can minimize the development of atopy.<sup>44</sup> Surachmanto EE and Datau EA reported that administering BCG immunization three times significantly decreased clinical symptoms in adult atopic asthma patients.<sup>45</sup>

The significance of the interaction between the microbiota and the human immune system promotes efforts to balance the development of the immune system by supplying favorable living microorganisms (bacteria), namely probiotics.<sup>46</sup>

Probiotics are defined by the Food and Agriculture Organisation (FAO) and the World Health Organization (WHO) as 'living microorganisms' that provide health advantages to their hosts when provided in sufficient quantities.<sup>47</sup> Probiotics have been shown in research to benefit the

prevention/reduction of allergy symptoms such as atopic dermatitis, allergic rhinitis, asthma, and food allergies; however, because other studies have found no substantial benefits, further research is needed to determine the benefits of probiotics.<sup>48-49</sup>

## V. Diet

Antioxidants such as vitamins C, E, A, and selenium are suggested to help prevent atopic disease and asthma. Several trials, however, demonstrated no benefit for people with asthma.<sup>2,50</sup>

The administration of omega-3 polyunsaturated fatty acids (omega-3 PUFAs) is suggested to help avoid allergy disorders. Using fish oil rich in omega-3 PUFAs in pregnant women's diets will minimize cytokine responses and allergy symptoms in infants (atopic dermatitis and rhinitis allergic).<sup>2,51</sup> Cumin (*Nigella sativa*) contains omega-3 PUFAs, which are beneficial to people who are allergic to fish.<sup>52</sup>

## VI. Immunotherapy

Immunotherapy against specific allergens in children with airway symptoms and monosensitization (sensitization to a single allergen) reduces the development of new sensitizations when compared to treatment alone. Patients with allergic rhinitis are at a

considerable risk for getting asthma. Immunotherapy prevents allergic rhinitis from progressing to asthma.<sup>2,53</sup>

## VII. Prevention of Occupational Asthma

Sensitizing chemicals inhaled at work are the cause of occupational asthma. Occupational asthma is best managed by primary prevention, which involves limiting exposure to occupational allergens.<sup>16,54,55</sup>

## CONCLUSION

Asthma and allergies have emerged as serious public health issues, affecting the quality of life for millions of children and adults. Primary and secondary preventative interventions can be employed to lower morbidity and mortality rates. Environmental variables can either raise or reduce the likelihood of acquiring asthma and allergies. These environmental factors can be manipulated as primary preventive measures by removing risk factors for asthma and allergies through exclusive breastfeeding, avoiding allergens, cigarette smoke, endotoxins/vaccination, probiotics, omega 3, and occupational asthma prevention, with variable results (benefit or unclear benefit). Individuals with varied risk profiles may require distinct preventative techniques It is intended that a

child would be evaluated to determine his or her risk profile (genetic and maybe environmental factors), allowing appropriate preventative interventions to be offered.

## REFERENCES

1. Kim Ki-Hyun, Jahan SA, Kabi E. A review on human health perspective of air pollution with respect to allergies and asthma. *Environment International* 2013;59:41–52.
2. Arshad SH. Primary prevention of asthma and allergy. *J Allergy Clin Immunol* 2005;116:3–14.
3. Johanson SGO, Heahtela T. World allergy organization guidelines for prevention of allergy and allergic asthma. *Allergy Clin Immunol Int – J World Allergy Org* 2004;16:176-85.
4. Konthen SH. Allergy is a global disease. In: Soegiarto S, Baskoro A, Endaryanto A, eds. *National immunology week 2004*. 2<sup>nd</sup> edition. Surabaya; 2004. pp. 34-37.
5. Arshad SH, Bateman B, Matthews SM. Primary prevention of asthma and atopy during childhood by allergen avoidance in infancy; a randomized controlled study. *Thorax* 2003;58: 489-93.
6. Akib A. Pengobatan dini pada anak atopik. In: Sundanu H, Djauzi S, eds. *Allergy & clinical immunology up date–*

current treatment in daily practice. Tangerang; 2001. pp. 49 – 54.

7. Baldacci S, Maio S, Cerrai S, Sarno G, Baiz N, Simoni Met al. Allergy and asthma: Effects of the exposure to particulate matter and biological allergens. *Respiratory Medicine* 2015;109(9): 1089-1104.

8. Mc Fadden ER. Asthma. In: Kasper DL, Fauci AS, Longo DL et al, eds. *Harrison's principles of internal medicine*. 16<sup>th</sup> ed. Vol II. New York : McGraw Hill; 2005. p.1508 - 16.

9. Matidi DSA. Prinsip diagnosa penyakit alergi. In: Djauzi S, eds. *Penatalaksanaan penyakit alergi*. Jakarta: Balai penerbit FKUI; 2003. pp.1 – 6.

10. Roitt JM, Brostoff J, Male DK. Hypersensitivity – type I. In: *Immunology*. London: The CV Mosby Company; 1987. pp. 19.1 – 17.

11. Subowo. Reaksi anafilaktik. In: *Imunologi Klinik*. Bandung: Angkasa; 1993. pp. 9 – 35.

12. Prescott SL, Tang M. Position statements: Allergy prevention in children school of pediatrics and child health research. Department of Immunology Royal Children's Hospital. University of Western Australia; 2004.

13. Martinez FD. Toward asthma prevention – does all that really mothers

happen before we learn to read ? *N Engl J. Med* 2003;349(15):1473-5.

14. Mygin N, Dahl R, Pederson S. Allergy an increasing problem. In: *Instant allergy*. Australia: Blackwell science Ltd; 1997. pp.16-35.

15. Global initiative for asthma. [serial on line] 2024 [Cited 2024 Mei 21]. Available from URL : [https://ginasthma.org/wp-content/uploads/2024/05/GINA-2024-Strategy-Report-24\\_05\\_22\\_WMS.pdf](https://ginasthma.org/wp-content/uploads/2024/05/GINA-2024-Strategy-Report-24_05_22_WMS.pdf).

16. Burney PGJ. Epidemiology of asthma. In: Clark TJH, Godfrey S, Lee TH et al. eds. *Asthma*. 4<sup>th</sup> ed. London: Oxford University Press Inc; 2000. p. 197 – 223.

17. Baxi SAN, Phipatanakul W. The Role of Allergen Exposure and Avoidance in asthma. *Adolesc Med State Art Rev*. 2010;21(1):1-14.

18. The Klain A, Senatore AA, Licari A, Galletta F, Bettini I, Tomei L et al. Prevention of house dust mite allergies in pediatric asthma. *Children* 2024;11(469):1-15.

19. Wickman M, Kull I, Nordvall SL. Breast feeding and allergic disease in infants a prospective birth cohort study. *Arch Dis Child* 2002;87:478 – 81.

20. Strachan DP. Family site, infection and atopy: The first decade of the “Hygiene Hypothesis.” *J Allergy Clin Immunol* 1999;104:554–8



21. Ball TM, Castro-Rodriguez JA, Griffith KA, Holberg CJ, Martinez FD, Wright AL. Siblings, day-care attendance, and the risk of asthma and wheezing during childhood. *N Engl J Med* 2000;343:538-43
22. Arshad SH, Fenn N, Matthews S. Early life risk factors for current wheeze, asthma, and bronchial hyperresponsiveness at 10 years of age. *Chest* 2005;127:502– 8.
23. Rakes GP, Arruda E, Ingram JM . Rhinovirus and respiratory syncytial virus in wheezing children requiring emergency care. *Am J Respir Crit Care Med* 1999;159:785-90.
24. Gilliland FD, Berhane K, Rappaport EB et al. Effects of early onset asthma and in utero exposure to maternal smoking on childhood lung function. *Am J Respir Crit Care Med* 2003; 167:217-24.
25. Cook DG, Strachman DP. Health effects of passive smoking. *Thorax* 1997;52:1081-94.
26. Muraro A1, Halken S, Arshad SH, Beyer K , Dubois AEJ , Du Toit G et. EAACI Food Allergy and Anaphylaxis Guidelines. Primary prevention of food allergy. *Allergy* 2014;69:590-601
27. Obihara CC, Marais BJ, Gie RP, Potter P, Bateman ED, Lombard CJ et al. The association of prolonged breastfeeding and allergic disease in poor urban children. *Eur Respir J* 2005; 25: 970-77.
28. Ahmadizar F, Vijverberg SJH, Arets HGM, de Boer A, Garssen J, Kraneveld AD et al. Breastfeeding is associated with a decreased risk of childhood asthma exacerbations later in life. *Pediatr Allergy Immunol* 2017;28(7):649-54.
29. Wilson K, Gebretsadik T, Adgent MA, Loftus C, Karr C, Moore PE, et al. The association between duration of breastfeeding and childhood asthma outcomes. *Ann Allergy Asthma Immunol* 2022;129(2):205-11.
30. Sears MR, Greene JM, Willan AR, Taylor DR, Flannery EM, Cowan JO, et al. Long-term relation between breastfeeding and development of atopy and asthma in children and young adults: a longitudinal study. *Lancet* 2002;360:901-7
31. Von Berg A, Pittroff AB, U. Krämer , Link E, Heinrich J, Koletzko S et al. The German Infant Nutritional Intervention Study (GINI) for the preventive effect of hydrolyzed infant formulas in infants at high risk for allergic diseases. Design and selected results. *Allergologie select* 2017;1(1):28-38.
32. Gøtzsche1 PC, Johansen HK. House dust mite control measures for asthma. *Cochrane Database of Systematic Reviews* 2008;2:1-61.
33. Woodcock A, Lowe LA, Murray CS, Simpson BM, Pipis SD, Kissen P. Early

Life Environmental Control: effect on symptoms, sensitization, and lung function at age 3 years. *Am J Respir Crit Care Med* 2004;170:433–39.

34. Brunekreef B, Von Mutius E, Wong G, Odhiambo J, García-Marcos L, Foliak S. Exposure to Cats and Dogs, and Symptoms of Asthma, Rhinoconjunctivitis, and Eczema. *Epidemiology* 2012;23:742–750.

35. Chan SK, Leung DYM. Dog and Cat Allergies: Current State of Diagnostic Approaches and Challenges. *Allergy Asthma Immunol Res.* 2018;10(2):97-105.

36. Ownby DR, Peterson EL, Wegienka G, Woodcroft KJ, Nicholas C, Edward Zoratti E et al. Are Cats and Dogs the Major Source of Endotoxin in Homes? *Indoor Air* 2013; 23(3): 219–226.

37. Indolfi C, D’Addio E, Bencivenga CL, Rivetti GI, Bettini I, Licari A, Manti S. The Primary Prevention of Atopy: Does Early Exposure to Cats and Dogs Prevent the Development of Allergy and Asthma in Children? *Life* 2023; 13(1859):1-16.

38. Mandhane PJ, Sears MR, Poulton R, Greene JM, Lou WYW, D. Robin Taylor DR et al. Cats and dogs and the risk of atopy in childhood and adulthood. *J Allergy Clin Immunol* 2009;124:745-50.

39. Salo PM, Zeldin DC. Does exposure to cats and dogs decrease the risk of developing allergic sensitization and

disease? *J Allergy Clin Immunol.* 2009; 124(4):751–52.

40. Lau S, Wahn U. Pets—good or bad for individuals with atopic predisposition. *J Allergy Clin Immunol* 2003;112:263-4.

41. Wang C, El-Nour MMA, Bennett GW. Survey of Pest Infestation, Asthma, and Allergy in Low-income Housing. *J Community Health* 2008; 33:31–39.

42. Kalayci O, Miligkos M, Beltrán CFP, El-Sayed ZA, Gómez RM, Hossny E et al. The role of environmental allergen control in the management of asthma. *World Allergy Organization Journal* 2022;15:1-16.

43. Do DC, Zhao Y, Gao P. Cockroach allergen exposure and risk of asthma. *Allergy* 2016;71:463–74.

44. Aaby P, Shaheen SO, Heyes CB et al. Early BCG vaccination and reduction in atopy in Geine – Bissau. *Clinical and Experimental Allergy* 1999;30:644-50.

45. Surachmanto EE, Datau EA. Studi kohor efikasi vaksinasi BCG terhadap gejala klinis, kadar IL – 4 dan IFN –  $\gamma$  serum pada asma ekstrinsik atopi dewasa. Tesis Program Studi Ilmu Penyakit dalam PPDS – 1 FK Unsrat Manado 2005.

46. Spacova I, Ceuppens JL, Seys SF, Petrova MI, Lebeer S. Probiotics against airway allergy: host factors to consider. *Disease Models & Mechanisms* 2018;11:1-13 .

47. Food and Agricultural Organization of the United Nations and World Health Organization. Health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria. World Health Organization [online], [http://www.who.int/foodsafety/publication/fs\\_management/en/probiotics.pdf](http://www.who.int/foodsafety/publication/fs_management/en/probiotics.pdf) (2001).
48. Michail S. The role of Probiotics in allergic diseases. *Allergy, Asthma & Clinical Immunology* 2009;5(5):1-7.
49. Taylor AL, Dunstan JA, Prescott SL. Probiotic supplementation for the first 6 months of life fails to reduce the risk of atopic dermatitis and increases the risk of allergen sensitization in high-risk children: A randomized controlled trial. *Journal of Allergy and Clinical Immunology* 2007;119(1):184-91.
50. Mc Keever TM, Britton J. Diet and asthma. *Am J Respir Crit Care Med* 2004;170:725-9.
51. Dunston JA, Mori TA, Barden A et al. Fish oil supplementation in pregnancy modifies neonatal allergen specific immune response and clinical outcome in infant at high risk of atopy. *J Allergy Clin Immunol* 2003;112:1170-84.
52. Al Jassir, Saleh M. Chemical composition and microflora of black umin (*Nigella sativa*) seeds growing in Saudi Arabia. *Food chemistry* 1992;45:39-42.
53. Dinakar C, Portnoy JM. Allergen immunotherapy in the prevention of asthma. *Curr opin Allergy Clin Immunol* 2004;4:131-6.
54. Gradman J, Halcken S. Preventive effect of allergen immunotherapy on asthma and new sensitizations. *The Journal of Allergy and Clinical Immunology* 2021;9(5):1813-7.
55. Rui1 F, Otelea MR, Fell AKM, Stoleski S , Mijakoski D, Holm M et al. Occupational Asthma: The knowledge needs for a better management. *Annals of Work Exposures and Health* 2022; 66(3):287-90.