Review Article:
Maternal Serum IgE, Cord Blood IgE, and Children's Allergy: A Narrative Review

Zeinab Nazari[1], Abbas Dabbaghzadeh[2*], Negar Ghaffari[1]

1. Department of Obsobstetrics & Gynecology, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
2. Department of Immunology, School of Medicine, Pediatric Infectious Diseases Research Center, Mazandaran University of Medical Sciences, Sari, Iran.

Use your device to scan and read the article online

Citation Nazari Z, Dabbaghzadeh A, Ghaffari N. Maternal Serum IgE, Cord Blood IgE, and Children's Allergy: A Narrative Review. Journal of Pediatrics Review. 2019; 7(4):211-216. https://doi.org/10.32598/jpr.7.4.211

https://doi.org/10.32598/jpr.7.4.211

Article info:
Received: 2018 Septemer 26
First Revision: 2018 November 18
Accepted: 2018 November 21
Published: 01 October 2019

Key Words:
Cord blood IgE,
Children's asthma,
Maternal serum IgE

ABSTRACT

Context: Asthma is a chronic inflammatory disorder of the respiratory system in children. Immunoglobulin E (IgE) has an important role in allergic disorders like asthma. This study aimed to review the association between maternal serum IgE and the incidence of childhood asthma.

Evidence Acquisition: Three researchers searched all articles in PubMed, Scopus, Google, and Embase databases related to maternal serum IgE, cord blood IgE, childhood asthma, and its incidence. We used keywords such as "maternal IgE, cord blood IgE, relation, association, childhood asthma, and child allergy".

Results: We found a few related articles on maternal IgE, cord blood IgE, and childhood asthma. In total, we reviewed 11 articles. Parental atopy and allergy are the most important predictive factors for children's allergies, like asthma. IgE levels were higher in children whose mothers had higher IgE levels. Total IgE level was significantly higher in boys, compared to girls.

Conclusions: Increased maternal and cord blood IgE may be a predictive factor for the development of childhood asthma. More data are required to clarify this relationship.

1. Context

Asthma is a chronic inflammatory disorder of the respiratory system in children. The worldwide incidence of asthma in children has been increasing over the last decades (1). Cough, wheezing, and dyspnea are the most common clinical manifestations of asthmatic patients. Etiology of asthma is unclear; however, genetic and environmental factors are involved. Reversible airflow obstruction, bronchial hyper-responsiveness, mucus hypersecretion, inflammatory cell migration into the airways, and structural airway remodeling due to cytokines and chemokines are the characteristics of asthma. Some of the cytokines and chemokines are related to the severity and prediction of asthma (2, 3). There is an association between parents' anxiety and their child's asthma severity (4). Asthma imposes a high financial burden to the patient, family, and society (5). Immunoglobulin E (IgE) is synthesized by plasma cells that are transformed from B cells.

** Corresponding Author:*
Abbas Dabbaghzadeh, MD.
Address: *Department of Immunology, Schoole of Medicine, Pediatric Infectious Diseases Research Center, Mazandaran University of Medical Sciences, Sari, Iran.*
Tel: *+98 (11) 33344506*
E-mail: *siamakdabbaghzade@yahoo.com*

For this process, T helper cells have an essential role in the synthesis of cytokines like IL4 and IL13. IgE has a vital role in allergic disorders such as asthma, allergic rhinitis, atopic dermatitis, urticaria, and anaphylaxis. In addition, IgE has a defensive role against parasite infections. An atopic person is defined by an increased level of allergen-specific IgE. Approximately 50% of IgE positive individuals (by skin prick test or serum assay) suffer from an allergic disorder. Studies revealed that males have higher total and allergen-specific IgE levels than females. The IgE levels generally appear to decrease in adulthood (6).

There is evidence that factors associated with early life, such as cord serum and maternal IgE level affect the later development of allergic disorders. Serum IgE might be a predictive factor for allergic diseases. There is a strong relationship between specific IgE antibodies, or total IgE and asthma (7). This study aimed to review the literature on the association between maternal serum IgE, cord blood IgE, and the incidence of childhood asthma.

2. Evidence Acquisition

In this narrative review, PubMed, Scopus, Google Scholar, and Embase databases were searched using the following keywords: "maternal IgE, cord blood IgE, children asthma, prevalence and incidence, and relation or association". Three researchers searched all articles related to maternal serum IgE, cord blood IgE, and the incidence of childhood asthma up to September 2018. There was no time limitation to this search. All of the articles in English; abstracts, brief reports, and full-texts were included. Irrelevant studies were excluded from the review process. We found a few relative articles, and the extracted data included maternal serum IgE, cord blood IgE, and allergy, which are discussed here.

3. Results

We found 11 articles related to the association between maternal IgE, cord blood IgE, and childhood asthma. Tables 1 and 2 present the data extracted from the reviewed articles. Allergic disorders usually appear in early life. Allergy sensitization may be possible in fetal life. The relevant predictive factors are more diverse and heterogeneous. The primary criteria for the prevalence and persistence of asthma are parental asthma or atopy, sensitization to aeroallergens, and personal eczema. The atopic or allergic history of parents has been used as an essential predictor for infant disorders. The minor criteria for the prevalence and persistence of asthma are sensitization to food, wheezing apart from cold, allergic rhinitis, and eosinophilia (more than 4%) (19).

IgE levels were higher in children whose mothers had higher IgE levels, whereas IgE levels were lower in children whose mothers' IgE levels were lower; both groups of children were breastfed. There was no significant association between feeding and IgE levels in the studied children. Inheritance and environmental factors have essential roles in IgE production. The relationship between breastfeeding and IgE levels is unclear (13).

Table 1. Quantities of cord serum and maternal IgE, association with allergy

Author	CS[a] IgE	Maternal IgE	Allergy	PV
Shah (8)	0.55 IU/mL	280 IU/mL	AR[b], AD[c], wheezing at 1 y	<0.001
Canfield (9)	>150 IU/mL	>150 IU/mL	Various	0.04
Nabavi (10)	Male 1.70 IU/mL Female 1.80	<30y 1.80 IU/mL >30y 1.50 //	-	0.001
Liu (11)	>0.5 KU/L	>150 //	Eczema	0.000
Scirica (12)	5.1 IU/mL	>115 //	Eczema	0.05
Wright (13)	0.10-0.12 IU/mL	113.5-118.3 //	-	
Croner (14)	≥0.9 kU/L	-	5.3% asthma	
Bønnelykke (15)	0.26 (<0.1-0.71) IU/mL	47 (17-140) Iu/mL	-	P <0.001
Shirakawa (16)	0.286 kU/L	66.25 kU/L	-	0.07
Hicks (17)	0.38 (0.27–0.53) IU/mL	52.7 (40.9-68.0)IU/mL	Eczema at 2 y	(OR 2.6; 95% CI 1.2-5.7)

a. CS: Cord Serum; b. AR: Allergic Rhinitis; c. Allergic Dermatitis

Table 2. The relation between cord blood IgE and multiple factors

Author	CB[a] IgE Positive Relation Factors	CB IgE No Relation Factors	CB IgE Negative Relation Factors	Publishing Year
Scirica (12)	Maternal history of asthma or atopy, maternal total serum IgE level of greater than 36.0 IU/mL, and maternal allergen sensitization, black and Hispanic race/ethnicity, smoking during pregnancy, male gender, residence in areas	Maternal parity, mode of delivery, gestational age, and season of birth	Maternal age greater than 27.3 years	2007
Nabavi (10)	delivery season, type of delivery, history of allergy during pregnancy, the number of previous pregnancies, maternal age	allergic disease and history of allergic disease before pregnancy, neonatal gender, family history,		2103
Kaan (18)	Increase maternal age,	-	-	2000
Shah (8)	Allergic Mothers, γIFN[a] and HDM[b] allergens (CS Der p1 and CS Blo t5)	-	-	2009
Wright (13)	Higher maternal IgE	feeding status	Lower maternal IgE	1999
Liu (11)	Maternal IgE levels (>150 KU/L)	Paternal IgE	-	2003
Bønnelykke (15)	Maternal IgE, cord blood IgA	Paternal IgE	-	2010
Shirakawa (16)	Mother (positive allergic history and IgE of more than 400 IU/mL, siblings. Frequency of parity, the gender of baby and mother's age at the deli	Hereditary effects of fathers and grandparents	-	1997

[a]. IFN: Interferon; [b]. HDM: House Dust Mite.

Journal of Pediatrics Review

Total IgE level was significantly higher in boys, compared to girls. Boys' total IgE levels were highly correlated with both mothers' and fathers' total IgE levels; however, no such correlation was found in girls. Higher IgE in male cord blood may have a more gender-related effect (9). Because IgE does not cross the placenta, the cord blood IgE is produced by fetus itself. Bønnelykke et al. believed that the transfer of IgE from maternal to fetal blood might be a common cause of high cord blood IgE levels (15).

There was an association between maternal IgE and cord blood IgE levels. This association is related to many factors such as maternal sensitization, socioeconomic class, smoking, maternal age, the season of birth, race/ethnicity, neonatal gender and delivery type (10, 12).

Antenatal sensitization, the elevation of Cord Blood IgE (CBIgE), as a predictor of asthma and other allergic diseases have been studied; however, the obtained results are controversial. There are a few studies that confirmed a relationship between cord blood IgE and asthma in children. Sadeghnejad et al. argued that increased cord serum IgE is a risk factor for asthma at ages 4 and 10 years (15.2% and 12.8%, respectively) and increased aeroallergen sensitizations. Childhood asthma was more common (5-fold) in children with high cord blood IgE (more than 0.9 kU/L) (7, 14).

Maternal total IgE level (>150 KU/L) correlates with elevated cord blood IgE levels (IgE >0.5 KU/L), infant IgE levels (>40 KU/L; 80th percentile) and infant atopy. Specificity and sensitivity for the prediction of infant atopy were 83% and 34%, respectively. Fetal allergic sensitization and increased infantile eczema were more commonly associated with higher maternal IgE level (specificity: 83%, sensitivity: 34%) (14). Cord serum IgE level (IgE >0.55 IU/mL), fails to predict the infants at-risk of allergies. However, children with sensitization to mite allergens are more at risk of developing asthma (8). Aeroallergen sensitization is more prevalent in infants with a history of higher cord blood IgE level (20). Two studies reported that recurrent wheezing and asthma are more frequent in children with higher cord blood IgE (7, 21).

Increased maternal total IgE level, maternal allergen sensitization, and residence in low-income areas were associated with detectable or increased cord blood IgE levels. However, this study suggested that maternal atopy or asthma were not significantly associated with detectable cord blood IgE (12). Kaan et al. demonstrated that higher cord blood IgE is a significant risk factor for the development of urticaria at 12 months, but not for other allergic disorders (18).

Other studies indicated that allergic disorders in childhood were not related to increased cord blood IgE (22-24). Croner et al. believed that bronchial asthma was developing 5-fold in infant and children with a higher cord blood IgE (≥0.9 kU/L). The sensitivity of cord blood IgE with a cut-off point of 0.9 kU/L was only 26%. Therefore, cord blood IgE cannot be recommended as a single screening test (14). Types of evaluation of serum total IgE and specific IgE were different in the reviewed studies. Both quantities and cut-off points of IgE were different. It is not possible to conduct a meta-analysis with this data, because the studies were heterogeneous, and the results were different. Nasal eosinophilia and increased serum IgE levels are associated with an increased risk of children developing allergic disorders (25).

4. Conclusion

Parental atopy and allergy are the most important predictive factors for childhood allergies like asthma. Most researchers believed that IgE production and allergic sensitization begin at the fetal period. Cord blood IgE levels depend on many factors, such as parental atopy, parental IgE, smoking, and aeroallergen sensitization. A great body of studies believe that higher maternal IgE could increase cord blood IgE level. Increasing maternal and cord blood IgE may be a predictive factor for the development of children's asthma. Further data are required to clarify such relation.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles were considered in this article. The participants were informed about the purpose of the research and its implementation stages; they were also assured about the confidentiality of their information; Moreover, They were allowed to leave the study whenever they wish, and if desired, the results of the research would be available to them.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

Author's contributions

Read and approve the final manuscript: Zeinab Nazari, Abbas Dabbaghzadeh; Performed editing the final version: Negar Ghafari.

Conflict of interest

All authors certify that this manuscript has neither been published in whole nor part nor being considered for publication elsewhere. The authors declare no conflict of interest.

References

1. Ghaffari J, Aarabi M. The prevalence of pediatric asthma in the Islamic Republic of Iran: A systematic review and meta-analysis. Journal of Pediatrics Review. 2013; 1(1):2-11.

2. Hatami H, Ghaffari N, Ghaffari J, Rafatpanah H. Role of Cytokines and chemokines in the outcome of children with severe asthma. Journal of Pediatrics Review. 2019; 7(1):17-28. [DOI:10.32598/jpr.7.1.17]

3. Ghaffari J, Rafiei AR, Ajami A, Mahdavi M, Hoshiar B. Serum interleukins 6 and 8 in mild and severe asthmatic patients, is it difference? Caspian Journal of Internal Medicine. 2011; 2(2):226-8. [PMID] [PMCID]

4. Ghaffari J, Shafaat A, Yazdani Charati J, Kheradmand A. The relationship between intensity of parental anxiety and severity of asthma in 5-to 15-year-old children. Iranian Journal of Psychiatry and Behavioral Sciences. 2018; 12(1):e9361. [DOI:10.5812/ijpbs.9361]

5. Ghaffari J, Hadian A, Daneshpoor SM, Khademloo M. [Asthma burden in the hospitalized patients in North of Iran (Persian)]. International Journal of Pediatrics. 2014; 2(4.1):257-66.

6. Leffler J, Stumbles P, Strickland D. Immunological processes driving IgE sensitisation and disease development in males and females. International Journal of Molecular Sciences. 2018; 19(6):1554. [DOI:10.3390/ijms19061554] [PMID] [PMCID]

7. Sadeghnejad A, Karmaus W, Davis S, Kurukulaaratchy R, Matthews S, Arshad S. Raised cord serum immunoglobulin E increases the risk of allergic sensitisation at ages 4 and

10 and asthma at age 10. Thorax. 2004; 59(11):936-42. [DOI:10.1136/thx.2004.024224] [PMID] [PMCID]

8. Shah S, Bapat M. Cord serum screening test and the newborn's allergic status. Indian Pediatrics. 2009; 46(4):295-9. [PMID]

9. Canfield SM, Jacobson JS, Perzanowski MS, Mellins RB, Zemble RM, Chew GL, et al. Total and specific IgE associations between New York City head start children and their parents. Journal of Allergy and Clinical Immunology. 2008; 121(6):1422-7. [DOI:10.1016/j.jaci.2008.03.011] [PMID]

10. Nabavi M, Ghorbani R, Asadi AM, Faranoush M. Factors associated with cord blood IgE levels. Asian Pacific Journal of Allergy and Immunology. 2013; 31(2):157-62. [DOI:10.12932/AP0234.31.2.2013] [PMID]

11. Liu CA, Wang CL, Chuang H, Ou CY, Hsu TY, Yang KD. Prenatal prediction of infant atopy by maternal but not paternal total IgE levels. Journal of Allergy and Clinical Immunology. 2003; 112(5):899-904. [DOI:10.1016/j.jaci.2003.08.030] [PMID]

12. Scirica CV, Gold DR, Ryan L, Abulkerim H, Celedón JC, Platts-Mills TA, et al. Predictors of cord blood IgE levels in children at risk for asthma and atopy. The Journal of Allergy and Clinical Immunology. 2007; 119(1):81-8. [DOI:10.1016/j.jaci.2006.09.002] [PMID]

13. Wright AL, Sherrill D, Holberg CJ, Halonen M, Martinez FD. Breast-feeding, maternal IgE, and total serum IgE in childhood. Journal of Allergy and Clinical Immunology. 1999; 104(3):589-94. [DOI:10.1016/S0091-6749(99)70328-3]

14. Croner S, Kjetlman NI. Development of atopic disease in relation to family history and cord blood IgE levels: Eleven-year follow-up in 1654 children. Pediatric Allergy and Immunology. 1990; 1(1):14-20. [DOI:10.1111/j.1399-3038.1990.tb00003.x]

15. Bønnelykke K, Pipper CB, Bisgaard H. Transfer of maternal IgE can be a common cause of increased IgE levels in cord blood. The Journal of Allergy and Clinical Immunology. 2010; 126(3):657-63. [DOI:10.1016/j.jaci.2010.06.027] [PMID]

16. Shirakawa T, Morimoto K, Sasaki S, Taniguchi K, Motonaga M, Akahori W, et al. Effect of maternal lifestyle on cord blood IgE factor. European Journal of Epidemiology. 1997; 13(4):395-402. [DOI:10.1023/A:1007361013917] [PMID]

17. Hicks WB, Nageotte CG, Wegienka G, Havstad S, Johnson CC, Ownby DR, et al. The association of maternal prenatal IgE and eczema in offspring is restricted to non-atopic mothers. Pediatric Allergy and Immunology. 2011; 22(7):684-7. [DOI:10.1111/j.1399-3038.2011.01160.x] [PMID] [PMCID]

18. Kaan A, Dimich-Ward H, Manfreda J, Becker A, Watson W, Ferguson A, et al. Cord blood IgE: Its determinants and prediction of development of asthma and other allergic disorders at 12 months. Annals of Allergy, Asthma & Immunology. 2000; 84(1):37-42. [DOI:10.1016/S1081-1206(10)62738-X]

19. Liu AH, Covar RA, Spahn JD, Sichere SH. Childhood asthma. In: Kliegman RM, Stanton B, Geme JS, Schor NF, Behrman RE, editors. Nelson Textbook of Pediatrics. 20th edition. Philadelphia: Elsevier; 2016.

20. Wu CC, Chen RF, Kuo HC. Different implications of paternal and maternal atopy for perinatal IgE production and asthma development. Clinical and Developmental Immunology. 2012; 2012(132142):1-10. [DOI:10.1155/2012/132142] [PMID] [PMCID]

21. Ferguson A, Dimich-Ward H, Becker A, Watson W, DyBuncio A, Carlsten C, et al. Elevated cord blood IgE is associated with recurrent wheeze and atopy at 7 yrs in a high risk cohort. Pediatric Allergy and Immunology. 2009; 20(8):710-3. [DOI:10.1111/j.1399-3038.2009.00869.x] [PMID]

22. Hansen LG, Høst A, Halken S, Holmskov A, Husby S, Lassen LB, et al. Cord blood IgE. II. Prediction of atopic disease: A follow-up at the age of 18 months. Allergy. 1992; 47(4):397-403. [DOI:10.1111/j.1398-9995.1992.tb02079.x] [PMID]

23. Edenharter G, Bergmann RL, Bergmann KE, Wahn V, Forster J, Zepp F, et al. Cord blood-IgE as risk factor and predictor for atopic diseases. Clinical and experimental allergy. 1998; 28(6):671-8. [DOI:10.1046/j.1365-2222.1998.00241.x] [PMID]

24. Hide DW, Arshad SH, Twiselton R, Stevens M. Cord serum IgE: An insensitive method for prediction of Atopy. Clinical and Experimental Allergy. 1991; 21(6):739-43. [DOI:10.1111/j.1365-2222.1991.tb03204.x] [PMID]

25. Wang QP ,Wu KM , Li ZQ , Xue F, Chen W, Ji H, et al. Association between maternal allergic rhinitis and asthma on the prevalence of atopic disease in offspring. International Archives of Allergy and Immunology. 2011; 157(4):379-86. [DOI:10.1159/000328789] [PMID]

This Page Intentionally Left Blank