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A Third Year of Breastfeeding and Atopic Dermatitis Development: Data from a General Population Cohort of Full-Term Newborns

Treneva M[1,2*], Varlamov E[1] and Pampura A[1,2]

Abstract

Background: breastfeeding may have some protective effect on atopic dermatitis (AD) development in children, but existing evidence is unclear. Studies on breastfeeding duration effect were inconclusive and data is limited to longitudinal data and population cohort recruitment in healthy full-term newborns.

Objective: To evaluate an effect of prolonged breastfeeding on AD development in early childhood.

Methods: 393 mothers and their healthy full-term newborns were enrolled into general population-based prospective three-year cohort study. Breastfeeding duration and AD diagnostic criteria were evaluated in children at the age of 1, 2 and 3 years. Logistic regression model was used to evaluate association between AD in children and breastfeeding duration.

Results: Breastfeeding duration in the first two years of life had no influence on AD development. Breastfeeding during the third year of life was associated with a higher incidence of AD. There was no reverse causation found. Adjustment for maternal allergy history, maternal sensitisation, maternal age, parity, mode of delivery, maternal exposure to smoke during pregnancy and sex of a newborn did not influence analysis outcomes.

Conclusion: There is some evidence that prolonged breastfeeding, up to 25-36 months of life, is associated with a higher risk of AD in healthy full-term newborns regardless of maternal sensitisation and/or maternal allergy history. These results provide a reason to further research of prolonged breastfeeding influence on the risk of AD and other allergic diseases development.

Keywords

Atopic dermatitis; Breastfeeding duration; Cohort; Early childhood; General population, Infants; Full-term newborns

Abbreviations: AD: Atopic Dermatitis; OR: Odds Ratio; 95% CI: 95% Confidence Interval

Background

The World Health Organization (WHO) currently recommends breastfeeding for at least 6 months with continuing to breastfeed up to 2 years of age alongside with other foods introduction [1,2]. Breastfeeding may have a protective effect on the risk of atopic dermatitis (AD) development in children [3]. AD, also often called eczema, is a multifactorial chronic inflammatory skin disease and affects an estimate of 10-20% children in developed countries [4,5].

Preventative effect of breastfeeding on AD development was first described by Grulee and Sanford in 1936 [6] in a large population study. Since then a number of publications attempted to find an association between AD and breastfeeding. Some authors reported a strong protective effect [7], while others did not find any evidence of it [8]. Meta-analysis of eighteen prospective studies was performed by Gdalevich and Mimouni fifteen years ago [9]. AD incidence was lower in breastfed children, especially those at high risk of allergy development [9]. Several large prospective studies performed later provided conflicting results, from protective or neutral effect, to increased risk of AD development associated with breastfeeding [10-14]. None of the studies mentioned above were randomized. The only randomized study done by Kramer et al. demonstrated protective effect of breastfeeding during the first 12 months of life [15].

However, studies on breastfeeding duration effect have been inconclusive and often have methodological issues, e.g. data on total breastfeeding duration and/or the recruitment bias of children's in families with allergy. There is still no clear answer on the best time to cease breastfeeding and on ability of breastfeeding and its' duration on AD prevention in general population.

The aims of this study were: 1) to prospectively assess breastfeeding duration practices in a general population cohort of full-term newborns delivered in Moscow; 2) to evaluate AD incidence in these children; 3) to investigate associations between AD incidence and breastfeeding duration within the first three years of life.

Methods

Study setting

This study is a three-year prospective population observation of a birth cohort. Recruitment took place at postnatal unit of Maternity Hospital No.1, Moscow, Russia, between 15 October and 16 December 2011. All mothers resided in Moscow metropolitan area and were supervised in female centers. Inclusion criteria for the study were: healthy term infants and their mothers willing to comply with the study procedures. Exclusion criteria were: maternal immunosuppressive treatment during lactation, or severe illness; infants with a major birth defect, admitted to neonatal intensive care, other severe illness, born prematurely (<37 weeks gestation) or with low birth weight, defined as weight for gestation less than 10th percentile.

Participation involved a questionnaire during women stay at postnatal unit, three telephone interviews 1, 2 and 3 years postpartum, follow-up in person assessment at the allergy department at 1 and 3 years of age, allergy skin prick testing (SPT) of the mothers one year postpartum.

***Corresponding author:** Treneva M, MD, PhD, Allergy Department, Veltischev Clinical Pediatric Research Institute of Pirogov Russian National Research Medical University, Taldomskaya Street 2, Moscow 125412, Russia, Tel: +7 916 226 64 63; E-mail: trenevamarina@mail.ru

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Comprehensive data collection and further analysis was conducted by a trained interviewer. A clinical allergist researcher enrolled women into the study, performed annual examination, SPT and phone interviews.

Potential source of bias was revealed before the cohort enrollment, in a pilot pre-cohort recruitment of 77 mother-child pairs admitted to the postnatal unit in September 2011. Women with family history of allergy were more prone to contact since annual visits to an allergist and free skin prick-tests were announced in an information paper [16]. So, data on this pilot group were not included in the cohort and used later on in a Extra nimber cases analysis.

To minimize the specified bias, a cohort contained data on all women admitted in a postnatal unit between 15 October and 16 December 2011. Those who did not want to visit outpatient department once a year or to have allergy SPT, were interviewed by phone every year by a specially trained allergist.

Breastfeeding and AD definitions

AD was the outcome in the study. For the purpose of this study AD was defined according to UK Working Party's Diagnostic Criteria for Atopic Dermatitis [17] - one of the most consistently validated tools in children [18]. Child was considered to have AD, if itch or pruritic skin was combined with 3 or more of the following: 1) history of atopic disease in first degree relative; 2) generally dry skin in the last 12 months; 3) history of a flexural involvement (cheeks and/or extensor involvement for children <18 months of age); 4) visible flexural involvement (cheeks and/or extensor involvement for children <18 months of age). Diagnostic sensitivity of this criteria is 85%, specificity 97%; in a phone interview – 85% and 91% respectively [19].

Over three years AD positive outcome was defined as a number of children diagnosed with AD at least once during a three-year observation period.

Breastfeeding duration was defined as any or total breastfeeding (age when the child was breastfed for the last time).

At the age of 6 months, duration of exclusive breastfeeding was defined as that the infant received only breast milk. No other liquids or solids are given – not even water – besides of oral rehydration solution, or drops/syrups of vitamins, minerals or medicines [20].

Maternal sensitisation assessment

Maternal sensitisation was determined using SPT at 1 year postpartum during follow-up visit at Veltischev Clinical Pediatric Research Institute. SPT was undertaken using the following solutions: Histamine 1% Positive Control, Glycerol Negative Control, House Dust Mite (*Dermatophagoides pteronyssinus*), Cat (*Felix domesticus*), Birch pollen, Grass pollen, Ryegrass, Peanut, Hazelnut, Egg (all from Stallergenes, SA 92160 Anthony, France) and Cow's milk (ALK-Abello, HØrsholm, Denmark), and were read at 15 minutes. Allergic sensitisation was defined as a wheal ≥ 3 mm at least to one allergen, in the context of a wheal ≥ 3 mm to histamine and no wheal to the negative control.

Statistical methods

Power calculation revealed that sample size of 393 newborns gives 99.1% power at alpha 0.01 in a two-sided test to detect a difference in the rate of AD incidence 2% compared to 6.9% in children under 5 years published by Hamada [21].

Children were excluded from the statistical analysis if information on AD and/or breastfeeding duration was missing. Missing data at the age of 1, 2 and 3 years were 46 (11.7%), 41 (10.4%) and 50 (12.7%) of 393 (100%) respectively.

A normality of breastfeeding duration data distribution was evaluated by Kolmogorov-Smirnov test. Normal distribution point was set at p=0.2.

Mann-Whitney nonparametric U-test was used to compare breastfeeding duration between the groups.

We provided adjustment for the following potential confounding factors: maternal age, smoking, parity, sex of a newborn, maternal allergy [22,23] and type of birth [24]. Associations were tested using ANOVA or chi-square test.

Logistic regression models were performed to determine the association between breastfeeding duration and AD. Extended models with variables identified in the literature as associated with AD were also performed. Extra number of cases analysis was performed by including 77 mother-newborn pairs enrolled a month prior to the cohort recruitment in the same department. Odds ratio (OR) of AD associated with breastfeeding duration was calculated with 95% confidence interval (95% CI).

Spearman's correlation nonparametric test was used prior to logistic regression to investigate correlations between: 1) breastfeeding duration and AD positive criteria; 2) breastfeeding duration and maternal sensitisation and 3) AD positive criteria and maternal sensitisation.

Data were analyzed in «IBM SPSS Statistics Version 20». Results were considered significant when p-values were reported at a level less than 0.05.

Results

Demographic data of the participants is presented in Table 1. Breastfeeding duration data was obtained in 364 women (92.6 % of 393).

Data on breastfeeding duration is shown in Figure 1. The incidence of breastfeeding duration was not normally distributed (p<0.0001).

The annual response concerning AD criteria was 92.4%, 89.8% and 89.3% of the cohort at the age of children 1, 2 and 3 years respectively. Over all three-year period, a follow-up was complete for 329 children of 393 (83.7%). Number of outcome events (positive AD) over a three-year follow-up was 39 of 329 children (cumulative incidence 11.9%).

SPT has been performed in 130 women, who were agreed to this diagnostic procedure. A wheal of 3 mm or more in a diameter to at least one allergen was detected in 19 of them (14.6%).

We did not find any significant correlation between AD and maternal sensitisation. Breastfeeding duration also did not correlate with maternal sensitisation. We found a very weak correlation between AD and breastfeeding duration: 0.125 95%CI [0.013…0.232] (p=0.023). In AD children (n=39) a breastfeeding duration (median, [Q1; Q3]) was significantly longer (13.0 months [9.5; 22.0]), when compared with 290 children with no AD (11.5 months [4.5; 17.0]) (p<0.0001). Breastfeeding duration in children with AD and healthy ones at the age 1, 2 and 3 years is shown in a Table 2.

Table 1: Characteristics of women participating in a study.

Characteristic	Data on study participants
Age	29.6 ± 4.8 years (Mean ± Standard Deviation)
Gravidity	first - in 35.5% of women, second – in 27%, third – in 13.5%, fourth in 9.5%, fifth in 7.5%, sixth in 5.5%
Parity	primiparous – 46.5%, second childbirth – 32.5%, third – 14.5%, fourth – 3.5%, fifth or more – 1.0%
Normal delivery type	83% of woman; cesarean section 17%
Gestation at birth	39.5 ± 1.2 weeks (Mean ± Standard Deviation)
Newborns weight	3509 ± 447 g (Mean ± Standard Deviation)
Male gender	53.5% of newborns
Breastfeeding duration (months)	Median 11.5 [interquartile range Q1=4.5; Q3=17.0]; Mode 12;
	Mean 11.67 ± 8.34
Allergy history reported by women	98 of 393 (25%) women, including asthma in 1 of 200 (0.5%), allergic rhinitis in 30 of 199 (15%), eczema in 1 of 199 (0.5%), food allergy in 17 of 200 (8.5%), other allergic manifestations in 31 of 199 (15.6%)
Smoking	187 of 195 (95.8%) women were not smokers; 1-10 cigarettes per day – 3.6% of women, 11-20 cigarettes – 0.5 %
Second-hand smoking exposure	89 of 195 (45.6%) women
Other household members smoking	1-10 cigarettes per day in 41 of 195 (21%) of women families, 11-20 cigarettes – in 35 (18%), 21-30 in 6 (3%), 31-40 in 5 (2.5%), more than 40 cigarettes – in 2 (1%)

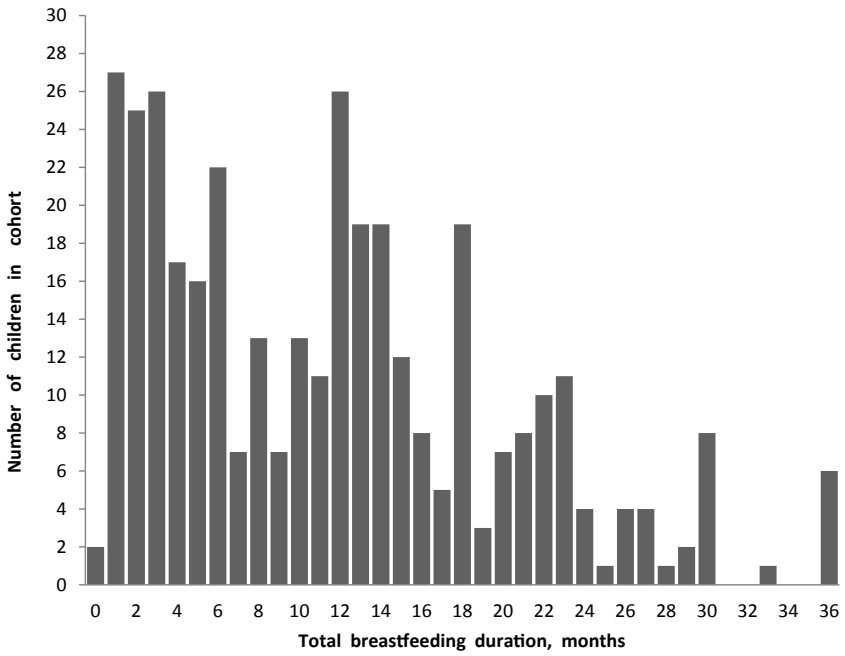

Figure 1: Breastfeeding Duration Distribution in Cohort Children.

Total breastfeeding duration in Moscow children is rather extended. 135 children were breastfed up to 6 months of life, 77 – 7-12 months, 82 – 13-18 months, 43 – 19-24 months, 20 – 25-30 and 7 children – 31-36 months

There was a significant difference in breastfeeding duration, with longer breastfeeding patterns seen in those children, who had AD at three years of age as well as throughout three years of life. No significant difference was found in other characteristics at 3 years of age between children developed AD (Table 3), except for gravidity (p=0.049).

Breastfeeding duration was significantly associated with increased risk of AD at the age of 3 (Table 4). Significant association of breastfeeding duration with increased risk of AD remained upon adjustment for gravidity. Adjustment for other potential confounding factors: maternal allergy history, maternal sensitisation, maternal age, parity, type of birth, exposure to smoke during pregnancy and sex of a newborn did not change the results.

An enlarged number of observations did not change the results (Table 5). 77 mother-newborn pairs were admitted in the same department a month prior to the cohort recruitment. Their data were not used in a cohort to escape a potential bias, since these newborns had a significantly higher number of relatives with positive allergy history [16].

Breastfeeding with some plain water only was gained in 164 of 191 children. Duration of such a breastfeeding was ≥ 180 days in 24 children; 164-174 days in 21; 150 in 18; 120-134 in 25; 90 in 12; 60 in 12; 42-44 in 9; 30 in 16; 10-21 in 19 and ≤ 7 days in 8 children. Exclusively breastfed infants were a rare exception, since most of the mothers gave a small volume of water daily. We found no association between AD at any year of life and in all three-year period with breastfeeding with plain water only duration.

Table 2: Breastfeeding duration in children with atopic dermatitis at age 1, 2 and 3 years.

Variable		Overall	Atopic dermatitis		p*
			positive	negative	
Atopic dermatitis at age 1 mean [CI 95%] (n/N)	Months being breastfed,	11.79 [10.90…12.69] (347/393)	13.63 [4.02...23.25] (8/347)	11.74 [10.85...12.63] (339/347)	0.534
Atopic dermatitis at age 2 mean [CI 95%] (n/N)	Months being breastfed,	11.83 [10.96...12.72] (352/393)	13.10 [9.04...17.16] (15/352)	11.78 [10.87...12.69] (337/352)	0.553
Atopic dermatitis at age 3 mean [CI 95%] (n/N)	Months being breastfed,	11.82 [10.93...12.72] (343/393)	16.71 [13.58...19.85] (26/343)	11.42 [10.50...12.35] (317/343)	**0.002**
Atopic dermatitis at age 1-3 mean [CI 95%] (n/N)	Months being breastfed,	12.03 [11.11...12.95] (329/393)	14.86 [12.15...17.57] (39/329)	11.65 [10.68...12.62] (290/329)	**0.026**
* means compared by ANOVA					

Table 3: Cohort characteristics by atopic dermatitis at age 3.

Variable	Overall	Atopic dermatitis		p*
		positive	negative	
Age of mother at the childbirth, Mean [95%CI] (n/N)	29.68 [28.98…30.37] (183/393)	31.00 [29.13…32.87] (19/183)	31.00 [29.13…32.87] (164/183)	0.201
Gravidity (number of previous pregnancies)				**0.049**
0, % (n/N)	36.1 (65/180)	22.2 (4/18)	37.7 (61/162)	
1, % (n/N)	26.7 (48/180)	22.2 (4/18)	27.2 (44/162)	
2, % (n/N)	14.4 (26/180)	38.9 (7/18)	11.7 (19/162)	
3, % (n/N)	10.6 (19/180)	11.1 (2/18)	10.5 (17/162)	
4, % (n/N)	7.8 (14/180)	0	8.6 (14/162)	
≥ 5, % (n/N)	4.4 (8/180)	5.6 (1/18)	4.3 (7/162)	
Parity (number of previous live deliveries)				0.652
0, % (n/N)	48.0 (86/179)	33.3 (6/18)	49.7 (80/161)	
1, % (n/N)	32.4 (58/179)	44.4 (8/18)	31.1 (50/161)	
2, % (n/N)	16.2 (29/179)	16.7 (3/18)	16.1 (26/161)	
3, % (n/N)	2.8 (5/179)	5.6 (1/18)	2.5 (4/161)	
≥ 4, % (n/N)	0.6 (1/179)	0	0.6 (1/161)	
Maternal smoking during pregnancy (number of cigarettes per day), Mean [CI 95%] (n/N)	0,04 [0,01…0,08] (178/393)	0.06 [0…0.17] (18/178)	0.04 [0.01…0.08] (160/178)	0.839
Maternal second-hand smoking during pregnancy, % (n/N)	54,2 (97/179)	66,7 (12/18)	52,8 (85/161)	0.263
Labor type, %				0.979
normal	82.9 (150/181)	83.3 (15/18)	82.8 (135/163)	
cesarean with labour	10.5 (19/181)	11.1 (2/18)	10.4 (17/163)	
elective cesarean	6.6 (12/181)	5.6 (1/18)	6.7 (11/163)	
Gestation at birth (weeks), Mean ± SD (n/N)	39.49 ± 1.15 (166/393)	39.25 ± 1.29 (17/166)	39.49 ± 1.10 (149/166)	0.346
Newborns weight (g), Mean ± SD (n/N)	3502 ± 447 (182/393)	3561 ± 398 (18/182)	3495 ± 469 (164/182)	0.527
Sex, boys, % (n/N)	53.0 (96/181)	72.2 (13/18)	50.9 (83/163)	0.086
Positive allergy history from Mother, % (n/N)	32.2 (59/183)	36.8 (7/59)	63.2 (12/124)	0.65
Maternal skin prick-tests positive				
≥ 3 mm, % (n/N)	14.4 (18/125)	18.8 (3/16)	13.8 (15/109)	0.596
≥ 1 mm, % (n/N)	18.4 (23/125)	18.8 (3/16)	18.3 (20/109)	0.969
Vitamins or any other medical supply during pregnancy, % (n/N)	66.7 (118/177)	52.9 (9/17)	68.1 (109/160)	0.207
Infections during the pregnancy				0.96
0, % (n/N)	75.8 (135/178)	72.2 (13/18)	76.2 (122/160)	
1, % (n/N)	18.0 (32/178)	22.2 (4/18)	17.5 (28/160)	
2, % (n/N)	4.5 (8/178)	5.6 (1/18)	4.4 (7/160)	

3, % (n/N)	0.6 (1/178)	0	0.6 (1/160)	
≥ 4, % (n/N)	1.1 (2/178)	0	1.2 (2/160)	
Antibiotics during the pregnancy				0.343
0, % (n/N)	89.2 (157/176)	82.4 (14/17)	89.9 (143/159)	
1, % (n/N)	8.0 (14/176)	11.8 (2/17)	7.5 (12/159)	
2, % (n/N)	1.1 (2/176)	0	1.3 (2/159)	
3, % (n/N)	0	0	0	
4, % (n/N)	1.1 (2/176)	5.9 (1/17)	0.6 (1/159)	
≥ 5, % (n/N)	0.6 (1/176)	0	0.6 (1/159)	
Months of breastfeeding, Mean [CI 95%] (n/N)	11.82 [10.93...12.72] (343/393)	16.71 [13.56...19.85] (26/343)	11.43 [10.50...12.36] (317/343)	0.002
*Continuous variables were tested using ANOVA and categorical variables were tested using chi-square test				

Table 4: OR for atopic dermatitis at ages 1, 2 and 3 years associated with breastfeeding duration.

Variable	Unadjusted			Adjustment for variable associated to atopic dermatitis *			Adjustment for potential variables associated to allergy **			Adjustment for additional potential confounders ***		
	N	OR (95% CI)	p	N	OR (95% I)	p	N	OR (95% CI)	p	N	OR (95% CI)	p
Age 1 Atopic dermatitis	347	1.025 (0.948…1.109)	0.543	179	1.005 (0.930...1.085)	0.905	120	1.048 (0.959...1.144)	0.302	174	1.020 (0.939...1.108)	0.634
Age 2 Atopic dermatitis	352	1.018 (0.960...1.080)	0.553	181	1.038 (0.967...1.115)	0.299	126	1.029 (0.948...1.117)	0.497	175	1.035 (0.960...1.116)	0.367
Age 3 Atopic dermatitis	343	1.069 (1.023...1.116)	**0.003**	178	1.077 (1.014...1.145)	**0.016**	124	1.102 (1.033...1.176)	**0.003**	172	1.072 (1.010…1.138)	**0.023**
Age 1-3 Atopic dermatitis	329	1.043 (1.005...1.082)	**0.028**	167	1.037 (0.990...1.087)	0.125	117	1.074 (1.015...1.137)	**0.013**	162	1.036 (0.985...1.088)	0.168
*Adjusted for gravidity												
**Adjusted for allergy history from mother and maternal skin prick-tests papule diameter												
***Adjustment for maternal age, parity, type of birth, maternal smoking during pregnancy, maternal second-hand smoking during pregnancy and sex of a newborn												

Table 5: Extra number of cases analyses.

Variable	Unadjusted			Adjustment for variable associated to atopic dermatitis *			Adjustment for potential variables associated to allergy **			Adjustment for additional potential confounders ***		
	N	OR (95% CI)	p	N	OR (95% CI)	p	N	OR (95% CI)	p	N	OR (95% CI)	p
Age 1 Atopic dermatitis	416	1.007 (0.941...1.078)	0.832	246	0.994 (0.928...1.064)	0.859	166	1.015 (0.944...1.092)	0.690	233	0.995 (0.928...1.068)	0.897
Age 2 Atopic dermatitis	419	1.016 (0.965...1.069)	0.545	246	1.030 (0.971...1.092)	0.333	167	1.029 (0.961...1.102)	0.411	232	1.014 (0.955...1.076)	0.653
Age 3 Atopic dermatitis	408	1.058 (1.016...1.102)	**0.006**	241	1.055 (1.003...1.110)	**0.037**	165	1.081 (1.021...1.144)	**0.007**	228	1.054 (1.001...1.108)	**0.044**
Overall age 1-3 Atopic dermatitis	388	1.027 (0.993...1.063)	0.119	224	1.016 (0.967...1.058)	0.436	155	1.042 (0.995...1.092)	0.083	212	1.011 (0.968...1.055)	0.632
*Adjusted for gravidity												
**Adjusted for allergy history from mother and maternal skin prick-tests papule diameter												
***Adjustment for maternal age, parity, type of birth, maternal smoking during pregnancy, maternal second-hand smoking during pregnancy and sex of a newborn												

Discussion

This research was aimed to provide a quantitative assessment of breastfeeding duration in relation to AD throughout early childhood. Mothers and their healthy full-term newborns were followed for three years to reveal if breastfeeding duration has any influence on AD incidence in a general population. Total breastfeeding duration in Moscow children is rather extended. Breastfeeding duration was not associated with AD risk reduction in one- or two-year old children. Breastfeeding prolonged on the third year of life was associated with a higher incidence of AD and risk of AD development, regardless of maternal sensitisation, maternal allergy history, age, parity, mode of delivery, exposure to smoke during pregnancy and sex of a newborn. The effect of prolonged breastfeeding duration on AD incidence was not associated with maternal sensitisation. We believe that higher incidence of AD in those infants who were breastfed for a longer period was not influenced by a reverse causation.

A wide spectrum of traditional risk factors, analyzed by Carson and co-authors in 2013 [25], demonstrated that adjustment for demographics, filaggrin variants R501X and 2282del4 status, parent's AD and pets at home remains increased risk of AD until age 2 years depended on duration of breastfeeding (RR 2.09, 95% CI 1.15-3.80, p=0.016). Results of Carson were obtained in high-risk children based on COPSAC cohort data of children born to mothers with asthma. Hong and co-authors [22] reported increased the risk of AD in Korean children breastfed for a longer time, regardless of other factors of parental allergic history. Our results support Carson et al. [25] and Hong et al. [22] researches and suggesting that extended breastfeeding duration may be a risk factor for AD development in healthy full-term infants.

A restricted to 6 months of observation breastfeeding duration period [26] didn't demonstrate any influence of breastfeeding duration on long-term risk of AD in children of SEATON birth cohort at 1, 2, 5 and 10 years. In 18-month timeframe the Danish National Birth Cohort (children with and without parental history of allergy researched in a telephone interview) demonstrated that current breastfeeding was not associated with AD as well [23]. The authors found no overall effects of exclusive or partial breastfeeding on the risk of AD. A prolonged for 36 months' period of observation in our study confirms absence of AD risk increase in relation to 24 months of breastfeeding, and found positive association with breastfeeding during 24-36 months of life.

We hypothesize that breast milk obtained so far as the third year of life, and thus remote from 'critical early window' of development, which is defined to be between the 4-th and the 6-th months of life [27], could be in some relation to further conditions associated with allergic inflammation, appeared in AD in early childhood, and with following non-communicable inflammation diseases later in life.

Furthermore, the protective effect of a type of breastfeeding with plain water only was not obvious. Negative results in children breastfed this way for less than six months, in parallel with our results obtained for the total breastfeeding, may give an assumption that the duration of breastfeeding itself, rather than the potential exclusiveness, may influence some AD incidence increase. The latter nevertheless is not so clear with the results obtained for the type of breastfeeding with plain water only. The observation period for this breastfeeding type was rather short in our study, for six months only.

Results obtained in this study should not be considered as a guide to short breastfeeding duration in any way. It would not be correct to use results of logistic regression in other children, then full-term infants being breastfed during a third year of life. Overall results of a three-year period are seemed to be under a power impact of the third year of breastfeeding, which modulates the whole model.

Only healthy full-term newborns were recruited and results of this study can't be directly transferred on to general population. Although they are more close to general population children in a context of general population cohort recruitment, in compare to high risk children.

Further studies are needed to understand prolonged breastfeeding influence on the risk of AD development as well as other allergic diseases development in later life.

Strengths and limitations of the research

This prospective birth-cohort study is one of a very few to assess association of AD with breastfeeding duration in general population of full-term newborns.

Breastfeeding duration in Moscow is prolonged in many newborns and provides an opportunity for the analysis of its impact on AD development throughout tree years of breastfeeding.

A selection bias is unlikely due to the type of inclusion criterion and the high participation rate in this study.

In addition, potential confounders were collected at several points.

Limitations, however, should be considered. The exact amount of breast milk for breastfed infants was not measured. Not all women provided us with data on potential confounders. So, observations in adjusted analyses were less than in an unadjusted one. To overcome this data limits, adjustment was divided into parts.

Although SPT in mothers were not a major income variable, few women who breastfed over 2 years, were tested positive on SPT (3 positive vs 9 negative). We didn't evaluate any correlation between the results of SPT in mothers and the clinical manifestations of allergic disease due to exposure or natural exposure to the allergens. To assess clinical level of allergy we estimated maternal allergy history, which was in a list of confounders.

A related question on the extent of AD in individual infants was not in a focus of the research. Whether that was or was not related to the duration of breastfeeding should be covered in future researches. There were certain transitions in AD in individual infants, which are planned to be submitted in a special paper.

Conclusion

Results of this population cohort prospective three-year study provide some evidence that breastfeeding during 25-36 months of life may have a positive association with AD incidence in healthy full-term newborns regardless of maternal sensitisation, maternal allergy history and other factors. There is much more work to be done to establish if breastfeeding for 25-36 months should be considered as a primary prevention of AD. Further study is required to be clarified reasonable period for breastfeeding and high-risk population of AD not recommended for long-term breastfeeding. Data from a large international cohort is needed to reveal other factors and make a proper evaluation.

Ethics Approval and Consent to Participate

Participation in this study was voluntary and informed consent was obtained from each participant. The study was approved by the medical ethics committee of Veltischev Clinical Pediatric Research Institute of Pirogov Russian National Research Medical University, Moscow, Russia (protocols № 1 MS/11 18.01.2011 and №14/14 29.09.2014)

Competing Interests

The authors declare that they have no competing interests.

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Author Affiliations

Top

[1]*Allergy Department, Veltischev Clinical Pediatric Research Institute of Pirogov Russian National Research Medical University, Moscow, Russia*

[2]*International Inflammation Network (in-FLAME), World Universities Network, UK*