

# Effect of Breastfeeding, Timing of Introduction of Complementary Foods, and other Confounders on the Development of Childhood Atopic Dermatitis

Suhair Aboud Essa, M.B.Ch.B., F.I.C.M.S./FM,\*

Ahmed Khairi Mishari, M.B.Ch.B., F.I.C.M.S./FM,\*\*

Najla'a Turki, M.B.Ch.B.,\*\*\*

## Abstract:

**Background:** Atopic dermatitis is a chronic skin disease. Its incidence around the world has increased dramatically over the past several decades. A multi-factorial etiology is postulated, with genetic, immunological and environmental factors all thought to be relevant to the pathogenesis.

**Objective:** To assess the effect of breastfeeding, solid food introduction to the infant's diet, and other confounders on the development of atopic dermatitis.

**Methods:** Two hundred and forty children between 2 to 6 years were enrolled in this case control study in Baghdad, comprised of 60 children with atopic dermatitis and 180 children free from atopic dermatitis of the same age, sex and ethnicity as a control. Data collection had been done by an interview using a questionnaire form designed by the investigators. Diagnosis of atopic dermatitis was made according to the Haninfin and Rajka's diagnostic criteria.

**Results:** This study showed a significant difference between case and control groups regarding the presence of family history of atopy among child's parents. The frequency of children with positive history of animal contact differs significantly between patients and control groups. No significant association was detected between atopic dermatitis and positive breastfeeding history. However, the relation between atopic dermatitis and breastfeeding is duration dependent, the percentage of infants with short exclusive breastfeeding was higher among control group (85.3%) as compared to (58.1%) in the case group. While, with prolong breastfeeding more than 6 months the reverse was found. Early supplement feeding increased the rate of atopic dermatitis, there was more infants with atopic dermatitis when solid food introduced at the age of 4 months, this was statistically significant ( $P=0.023$ ).

**Conclusion:** Exclusive breastfeeding for 6 months is effective in reducing atopic dermatitis. On the other hand, prolonging exclusive breastfeeding and postponing the introduction of solid foods for over 6 months is not helpful in prevention of atopic dermatitis.

**Key words:** Atopic dermatitis, breastfeeding, solid food, Haninfin and Rajka's diagnostic criteria.

## Introduction:

Atopic dermatitis (AD) is a chronic inflammatory skin disease that nearly always begins in childhood and follows a remitting flaring course that may continue throughout life, it is characterized by poorly defined erythema with odema, vesicles and weeping in the acute stage, skin thickening (lichenification) in the chronic stage. AD is type 1 IgE-mediated hyper sensitivity reaction, but the exact etiology is unknown, it may be the result of interaction between hereditary, immunological and environmental factors.<sup>1</sup>

The prevalence of AD has doubled or tripled in industrialized countries during the past three decades; 15 to 30% of children and 2 to 10% of adults are affected.<sup>2</sup>

AD may occur in people at any age but often starts in infants aged 2-6 months. 90% of patients with AD experience the onset of disease prior to age of 5 years.<sup>3</sup> Males and females are affected with equal incidence and severity.<sup>4</sup>

There are no specific cutaneous signs, no known distinctive histological features, and no characteristic laboratory findings for AD. There are varieties of characteristics which indicate that the patient has AD, they include major and minor features; the diagnosis of AD is made when the patient has three or more of the major features and three or more of the minor features. Each patient is different, with a unique combination of major and minor features. These major and minor diagnostic features were proposed by Haninfin and Rajka<sup>5</sup> in

1980 and adopted by the American Academy Of Allergy, Asthma and Immunology.

The relationship between breastfeeding (BF) and the development of AD is a controversial issue. Although most studies agree on the protective effects of BF.<sup>6</sup> In a study on the association between AD and BF, exclusive breastfeeding (EBF) during the first 3 months of life was observed to decrease the risk of AD just in children with positive family history of atopy.<sup>7</sup>

Some studies found reverse relationship between AD and BF. A cohort study showed that each month of BF increased the risk of AD.<sup>8</sup> These different outcomes may be due to the effect of confounding factors, like; contact with pet, cigarette smoking, birth weight, and maternal delivery age. Other factors which may cause this controversy to occur are duration of BF, different definition of EBF, study design, sample size and different criteria used for diagnosis of AD.

Many studies have examined the duration of BF and its effect on AD. However, few studies have examined the timing of the introduction of complementary foods as an independent risk factor for AD in breastfed or formula-fed infants.

Until now, there is no published data on the assessment of the factors that might be related to the development of AD in Baghdad city.

This study was carried out to fill this gap and evaluate some factors suggested to be associated with the development of AD in children.

## Patients and Methods:

This study is a case control study which was performed between 22<sup>nd</sup> December 2011 and 30<sup>th</sup> May 2012.

The study population was comprised of cases (with AD) and controls (free from AD). Cases were selected from outpatient clinics of dermatology of three hospitals in Baghdad; Baghdad teaching hospital, Al-Kadhmia teaching hospital, and Central child hospital. Controls were AD-free outpatients from other clinics in the same hospitals during the same period when the cases were recruited. We had matched case and control groups for age, sex, and ethnicity.

AD was diagnosed according to the Haninfin and Rajka's diagnostic criteria, and confirmed by dermatologists in the above mentioned centers.

Data collection had been done by an interview using a questionnaire form designed by the investigators. The questionnaire includes questions about the socio-demographic characteristics of the study people, and questions concerning child's feeding regimen; The child's parents were asked: "What kind of milk did your child drink during (each of) the first 6 months of life?". The child was defined as "exclusively breastfed" if parents selected "exclusively human milk" for all of months 1 to 6. Otherwise the child was labeled "partly breastfed" if BF combined with formula feeding. Child was further defined to be "conventional cow's milk formula fed" if he/she had been fed conventional cow's milk formula during the first year of life.

The child's parents were also asked about time and type of new solid foods that were introduced, especially potentially allergenic foods such as; cow's milk, eggs, fish, nuts, and citrus fruits.

In order to understand the effect of BF on AD occurrence, all the study groups (cases and controls) were divided into two groups; First group represented those with a history of BF irrespective to the duration of BF, and the second group represented those with no such history. Moreover, in order to study the effect of the duration of BF on AD occurrence, all participants with positive history of BF were sub-divided into two sub groups; the first group represented those with short EBF ( $\leq 6$  months), and the second group was those with long EBF ( $> 6$  months).

All data were analyzed using the SPSS version 20.0 statistical package for the social sciences. The significance of difference of different percentages was tested using Pearson Chi-square ( $\chi^2$ ) test, level of significance was denoted as P value of  $< 0.05$ .

## Results:

### Socio-demographic characteristics

The study population was 240, 60 suffered from AD and 180 were AD-free children, with age of 2-6 years. The mean age of children with AD and

control were  $3.9 \pm 1.3$  and  $3.6 \pm 1.3$  years respectively.

33 children with AD (55%) and 97 AD-free children (53.9%) were males, whereas 27 children with AD (45%) and 83 AD-free children (46.1%) were females.

More than half (55%) of patients were males and (45%) were females. This difference was statistically not significant ( $P=0.881$ ).

There was no significant association between educational level of child's mothers and occurrence of AD ( $P=0.232$ ) (table 1).

### Family history of smoking

The presence of family history of smoking was higher among patients group than control group (73.3% vs. 67.2%, respectively). However, no statistically significant difference was observed between these two groups regarding this factor ( $P=0.376$ ).

### History of animal contact

The frequency of children with history of animal contact differs significantly ( $P=0.0001$ ) between case and control groups (88.3% vs. 32.8%, respectively).

### Family history of atopy

This study showed a significant difference between case and control groups regarding the presence of family history of atopy (AD, asthma, and allergic rhinitis) among child's parents ( $P=0.0001$ ).

AD rate was 38.4% in patients with one affected parent, and this rate rises to 48.3% for patients of two affected parents (table 2).

### Breastfeeding and AD occurrence

Mean duration of BF in AD and AD-free infants was ( $5.2 \pm 2.9$  and  $8.0 \pm 4.4$  months, respectively). No significant association ( $P=0.882$ ) was detected between AD and positive BF history ( $OR=0.69$ ) (table 3). Moreover, in order to study the effect of duration of BF on AD development; the percentage of infants with short EBF ( $\leq 6$  months) was higher among control group (85.3%) as compared to (58.1%) in AD group. While with prolong BF more than 6 months the reverse was found; the percentage of infants was higher in AD group (41.9%) as compared to (14.7%) in the controls. The risk of AD increased when EBF have been prolonged to more than 6 months duration ( $OR=4.18$ ), this was statistically significant ( $P=0.001$ ) (table 4).

### Timing of solid food introduction and AD development

Table 5 shows that there was more infants with AD when solid food introduced at the age of 4 months 43.4% as compared to 23.3% among the control group. While, the rate at 6 months of age

was (18.3% vs. 31.1%) in the cases and controls respectively. After 6 months of age, the rate elevated again among AD group to be nearer to that of the

controls (20% vs. 25%, respectively). This was statistically significant ( $P=0.023$ ).

**Table 1. Association between educational level of child's mothers and AD occurrence**

Educational level of child's mothers	Case		Control		P value
	No.	%	No.	%	
Illiterate	12	20.0	21	11.7	0.232
Primary	25	41.7	82	45.6	
Secondary	17	28.3	66	36.7	
Higher	6	10.0	11	6.0	
Total	60	100.0	180	100.0	

**Table 2. Association between family history of atopy and AD occurrence**

Number of parents with atopic disease	Case		Control		P value
	No.	%	No.	%	
No	8	13.3	72	40.0	0.0001
One	23	38.4	69	38.3	
Both	29	48.3	39	21.7	
Total	60	100.0	180	100.0	

**Table 3. Relationship between BF and AD occurrence**

Breastfeeding	Case		Control		P value
	No.	%	No.	%	
Yes	31	51.7	95	52.8	0.882
No	29	48.3	85	47.2	
Total	60	100.0	180	100.0	

**Table 4. Relationship between duration of BF and AD occurrence**

Breast feeding duration	Case		Control		P value
	No.	%	No.	%	
≤6 months	18	58.1	81	85.3	0.001
>6 months	13	41.9	14	14.7	
Total	31	100.0	95	100.0	

**Table 5. Relationship between time of solid food introduction and AD occurrence**

Time of solid food introduction	Case		Control		P value
	No.	%	No.	%	
4 months	26	43.4	42	23.3	0.023
5 months	11	18.3	37	20.6	
6 months	11	18.3	56	31.1	
≥7 months	12	20.0	45	25.0	
Total	60	100.0	180	100.0	

#### Discussion:

The current study showed that the rate of AD in children belonged to mothers with low educational level is high as compared to the control, while the percentage of child's mothers with higher education is low within AD group as compared to control group, but this was statistically not significant.

These findings are in agreement with a study carried out in Copenhagen,<sup>9</sup> which revealed that social status in term of household income, mother's educational level and work didn't demonstrate any significant differences on the development of atopic disease.

Although the current study showed that smoking was more prevalent among AD group as compared to AD-free group, this difference was statistically not significant. The role of passive/active maternal smoking in the past and during pregnancy was evaluated in some studies; An animal study demonstrated that "second-hand smoke" increases the incidence and severity of allergies in children residing in households with smokers.<sup>10</sup>

Regarding animal contact, this study illustrated a significant association between AD and living with animals. This conforms to the data obtained in a study done by Solomon in Michigan,<sup>11</sup> who illustrated that domestic animals' hair and dander are well known allergens contribute to AD.

This study stated a significant effect of positive family history of atopy on the development of the AD in the children in the future. Family studies support a genetic basis for AD. When both parents are atopic, their offspring have a 70% risk for AD,<sup>12</sup> with a higher risk of inheritance if the mother is atopic. The mode of inheritance appears to be complex and likely involves several genes. To date, no specific single gene has been identified as a unique marker for AD or atopy.<sup>13</sup>

BF is the preferred method of infant nutrition for numerous reasons. However, its role in the prevention of allergic diseases remains controversial.<sup>14</sup> Reasons for this controversy include methodological differences and flaws in the studies performed to date, the immunologic complexity of breast milk itself and, possibly, genetic differences among patients that would affect whether BF was protective against the development of allergies or is in fact sensitizing.

The current study tried to investigate the impact of BF on the development of AD. Although, a little protective effect was noticed (51.7%) in the case group as compared to (52.8%) in the control group, this was statistically not significant, and it may be either due to the over estimating of breastfed children with AD or due to memory bias. This finding supported by Girolomoni *et al.*<sup>15</sup> who reported that there was no association between AD and BF. Moreover, in order to study the effect of duration of BF on AD occurrence; the percentage of infants with short EBF ( $\leq 6$  months) was higher among healthy group as compared to AD group. While, with prolong BF more than 6 months the reverse was found.

The protective effect against the development of AD seems to be directed towards short EBF, while if we take short EBF as a reference, so the risk of AD increase to 4.18 times with prolongation of BF more than six months. This makes prolong EBF acts as a risk factor for the development of AD. Labeta *et al.*<sup>16</sup> explained this protective effect of BF against development of AD, as children on BF are less exposed to infections, because breast milk contains a wide variety of immuno-modulating agents,

including both anti-inflammatory and a pro-inflammatory mediators.

The other factor which is considered in this study is the role of timing of solid food introduction to the infant's diet on the development of AD. The study groups differed considerably in regard to the age of the infant when solid food was first introduced.

This study showed that there was more infants with AD when solid food introduced at the age of 4 months. Notably, the rate of AD in the 4th months (43.4%) was double than that seen with later administration of solids at 6th months of age (18.3%). Moreover, the protective effect decreased when the introduction of solids was postponed to later than 6 months. This may be attributed to the development of gut integrity and intestinal mucosal barrier function, that would enhance the immune system function, as the age of the infant increases. So, delay in initiating supplements may associates with lower risk of AD.<sup>17</sup>

These findings are similar to that reported in some other studies, such as; A longitudinal study in New-Zeland,<sup>18</sup> stated that early introduction of solid diet during the first 4 months of life roughly doubled the risk of developing AD in children followed for 10 years. Another study carried out in Germany, concluded that delaying the introduction of solids for the first 4 months of life might offer some protection, while no evidence supporting a delayed introduction of solids beyond the sixth month of life for the prevention of AD and atopic sensitization.<sup>19</sup>

High rate of AD were found in families with history of atopy, and in families keeping domestics. Although, our study did not observe a strong protective effect of BF against AD, EBF for six months may be effective in reducing AD in subgroup of children with atopic heredity. Moreover, prolonging EBF and postponing the introduction of solid foods for over six months of age is not helpful in prevention of atopy. Instead, it may be associated with an increased risk of subsequent AD in children with a family history of atopy.

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\* Al-Salam primary health care centre, Baghdad/ Iraq.  
Email: dr\_suhair29@yahoo.com

\*\* Al-Salam primary health care centre, Baghdad/ Iraq.

\*\*\* Al-Salam primary health care centre, Baghdad/ Iraq.