Research Article

Post Term Gestational Age and Non Exclusive Breastfeeding are Risk Factors for Atopic Dermatitis in The First 3 Months of Life. A Study From Bali Province-Indonesia

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ABSTRACT

Background: Studies reported that Atopic Dermatitis (AD) start to occur during the first 3 months of life. Our preliminary study showed that post term birth giving high risk for the development of AD. Hence we did the study to cover post term birth together with other known factors for the development of AD.

Methods: A hospital-based prospective observational study was done to mothers giving birth in Sanglah Hospital Denpasar and Tabanan Hospital in Bali-Indonesia. Infants were followed by phone at 1 month interval until 3 months, otherwise parents called researcher once symptom appeared. Study was terminated once AD was diagnosed, subject died, or lost to follow up (cannot be reach by phone within 3 months of study). Diagnose of AD was done by independent physician based on William criteria through text message or photo sent by parent.

Results: Between May 1st 2017 until July 31th 2017 there were 110 live births, of which 10 of them was failed to be contacted during follow up. Incidence of AD was 11%. Post term gestational age giving Relative Risk (RR) 7.73 for AD with 95% CI 2.23-26.76, p value 0.001. Non-exclusive breastfeeding giving RR 5.79 for AD with 95% CI 1.23-27.27, p value 0.02.

Conclusions: During 3 months of life we found AD incidence as much as 11%. Post term and non-exclusive breastfeeding are independent factors for development of AD. Post term contributes 7.73 risk for development of AD. Non-exclusive breastfeeding contributes 5.79 risk for development of AD.

Keywords: atopic dermatitis, gestational age, non-exclusive breastfeeding, infant

INTRODUCTION

Atopic dermatitis (AD) is a chronic, relapsing, and highly pruritic dermatitis, which generally develops in infancy and early childhood, has a characteristic age-dependent distribution with the peak age of onset before 3 months.[1-3] Atopic dermatitis has become a significant public health problem because of increasing prevalence, and become a significant clinical problem particularly in infants and young children.[4,5] The AD starts in the first few years of life6-8, and it's incidence has increased dramatically over the past several decades.[6-9]

Atopic dermatitis (AD) has become a significant public health problem because of increasing prevalence, together with increasing evidence that it may progress to other allergic phenotypes. Atopic dermatitis (AD) has become a significant public health problem because of increasing prevalence, together with increasing evidence that it may progress to other allergic phenotypes.

The International Study of Asthma and Allergies in Childhood (ISAAC) suggests that the prevalence of atopic dermatitis varies between 0.3% and 20.5% worldwide.[10] The incidence of AD in infancy at Sanglah Hospital in 2012 was generally 10.98% which would be increased to 45.7% in infants with either one or both parents had a history of atopy.[11]

There were various risk factor play a role in the occurrence of atopic dermatitis such as genetic, sex, gestational

age (≥37 weeks), birth weight (≥2500 grams), maternal allergic disease, paternal allergic disease, nutritional selection, and environmental factors.[12-15]

Previous diagnostic criteria for AD, such as Hanifin Rajka criteria has prevent many researchers to establish diagnosis in shorter duration of research. Hence newer criteria has been developed, such as Williams[16] and NICE[17] criteria. These consensus criteria for the main clinical features of atopic dermatitis have led to a short list of reliable and valid discriminators that are used worldwide.[14] Williams criteria has advantages that it is allows parental report which will ease researcher to efficiently assess clinical condition without meet the subjects in person. This criteria is the most common validated.[16]

Our previous research held in Sanglah Hospital documented incidence of AD 13%.[12] In the era of national health insurance (Jaminan Kesehatan Nasional), Sanglah Hospital only accept non simple delivery, hence, we need to adapt subject recruitment toward wider population to get more reliable data. We sought to see current incidence of AD and see the risk factors associated with AD. In particular we want to see whether gestational age influence the development of AD.

METHODS

This was a hospital and community-based observational study. This research was conducted in Sanglah and Tabanan Hospital. As previously mentioned, Sanglah Hospital is a tertiary level hospital in Bali which has less patient for normal delivery, hence Tabanan Hospital which is a secondary hospital is involved in the study to allow time efficiency. Tabanan hospital is situated in 21 km distance to Denpasar. Daily living and allowance is nearly the same to Denpasar. Many Denpasar employees stay in Tabanan and vice versa. Current number of non-complicating delivery in Tabanan Hospital as near as 3 times of Sanglah Hospital. Data was collected in May 2017 until sample size was met.

Target population was all infants born in the delivery room and operating room Sanglah Hospital and Tabanan Hospital from May 2017. Inclusion criteria were vigorous baby, birth weight between 2500-4000 gram, subjects living in Bali and not planning to leave the area for at least 3 months ahead of study start, parents consent to their baby participating in this study by signing informed consent form, has mobile phone (preferably with photo chat features), especially during the validation period. Exclusion criteria were infants with major congenital anomaly, infants with long term antibiotics needing hospitalization, infants with ventilator support, mothers with known immunologic disorders, autoimmune disorders, and those who received long-term corticosteroid therapy.

Sampling was done by consecutive random sampling until the number of samples was fulfilled.

Parent of babies born Sanglah and Tabanan Hospital from May 2017, who fulfilled the eligibility criteria were given complete information regarding this study and asked for willingness to participate in the study by signing the form after understand the information. The preferential of contact either by phone, or chat (SMS/WA/LINE/telegram) was obtained.

Subjects were followed up monthly for 3 months or once diagnosis of atopic dermatitis was confirmed by Allergy consultant in Sanglah Hospital. Researcher's team contacted subjects by phone or short messages/chat service on monthly basis or parents might contacted the researcher's team earlier when any suspected symptoms for AD were appeared prior to contact schedules. During communication, symptoms and condition related to AD based on Williams criteria of atopic dermatitis was assessed and parents also send photos of subjects exposing area of body predilection of AD or whole body when needed. Researchers give information for certain angle and lighting exposure needed for subjects picture to enable the counsultant get better impression for AD. When in doubt, consultant advised parent to bring the child to seek further evaluation in Sanglah Hospital, either for better diagnosis conformation or if more severe manifestation appeared, or better management needed. Consultant in charge were blinded for gestational age and other factors also age of the subject, but they were informed that the subjects in the photo and chats were participated in the study. If diagnosis of AD was confirmed, subject was considered to have fulfilled the study outcome and terminated for observation. Time for

study completion was recorded and subject was referred for standard management. The time of AD diagnosis confirmation were recorded.

The data was analyzed with statistic programme, which include:

- Descriptive analysis to describe the characteristics of the research subjects.
- Association analysis was used to assess the association between risk factors and atopic dermatitis in bivariate analysis. Associated factors with p value <0.25 were included in multivariate analysis.
- Factors associated with AD in multivariate analysis were reported with relative risk (RR) and 95% confidence interval (95% CI) and p value.
- Multivariate cox-regression analysis was used to assess factors associated with AD while controlling confounders. Associated factors in multivariate analysis were reported with relative risk (RR) and 95% confidence interval (95% CI) and p value.

The Research Ethics Committee at School of Medicine, Udayana University/ Sanglah Hospital, Denpasar approved this study under approval number 1801/UN.14.2/KEP/2017.

RESULTS

There were 110 vigorous baby born from May 2017-July 2017 in Sanglah and Tabanan hospital and agree to participate. Ten out from this number were failed to be contacted during follow up period. In this study, incidence of AD was 11%. Flowchart of study subjects recruitment and follow up was shown in Figure 1. Characteristic of study subjects was shown in Table 1.

Bivariate analysis was used to assess the association between risk factors and atopic dermatitis as shown in Table 2.

Multivariate analysis showed post term birth and non exclusive breastfeeding was independent risk factor for atopic dermatitis with RR 7.73; 95% CI 2.23-26.76; P value 0.001, and RR 5.79; 95% CI 1.23-27.27; P value 0.02 as shown in Table 3.

Figure 1. Flowchart of the study

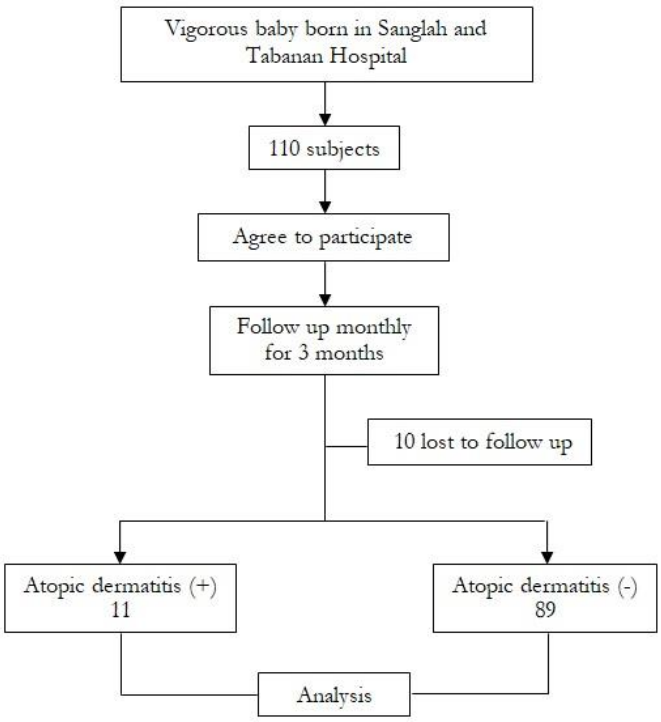

Table 1. Subjects Characteristic

Variable	n = 100
Sex, n (%)	
Male	49 (49)
Female	51 (51
Mode of delivery, n (%)	
Vaginal	43 (43)
Vacuum extraction	1 (1)
Forceps	4 (4)
Caesarean section	52 (52)
Indication of labor, n (%)	
In partu	58 (58)
Preeclampsia	14 (14)
Eclampsia	1 (1)
Prolong labor	3 (3)
Fetal distress	7 (7)
Breech position	2 (2)
Antepartum haemorrhage	1 (1)
Heart disease	1 (1)
Premature rupture of membranes	11 (11)
Low weight mother	2 (2)
NBS, n (%)	
Post term	9 (9)
Non post term	91 (91)
Birth weight, n (%)	
2500-4000 grams	95 (95)
>4000 grams	5 (5)
History of mother's allergy, n (%)	
Yes	19 (19)
No	81 (81)
History of father's allergy, n (%)	
Yes	11 (11)
No	81 (81)
History of siblings allergy, n (%)	
Yes	7 (7)
No	93 (93)
Chemical environmental factors, n (%)	
Yes	20 (20)
No	80 (80)
Laundry, n (%)	
Yes	8 (8)
No	92 (92)
Air freshener, n (%)	
Yes	10 (10)
No	90 (90)
Perfume, n (%)	
Yes	10 (10)
No	90 (90)
Physical environmental factors, n (%)	
Yes	14 (14)
No	86 (86)
Cloth covered sofa, n (%)	
Yes	13 (13)
No	87 (87)
High humidity wall, n (%)	
Yes	6 (6)
No	94 (94)
Exposure to pets, n (%)	
Yes	46 (46)
No	54 (54)
Nutritional selection, n (%)	
Exclusive breastfeeding	50 (50)
Non-exclusive breastfeeding	50 (50)

Table 2. Bivariate analysis of predictors for atopic dermatitis in infants in the first 3 months of life

Variable	Atopic dermatitis		RR	95% CI	p value
	Yes	No			
Post term, n (%)					
Yes	4 (44.4)	5 (55.6)	5.78	2.1-16.02	0.001
No	7 (7.7)	84 (92.3)			
Birth weight, n (%)					
>4000 grams	1 (20)	4 (80)	1.9	0.29-12.06	0.51
2500-4000 grams	10 (10.5)	85 (89.5)			
History of mother's allergy, n (%)					
Yes	4 (21.1)	15 (78.9)	2.43	0.79-7.48	0.12
No	7 (8.6)	74 (91.4)			
History of father's allergy, n (%)					
Yes	1 (9.1)	10 (90.9)	0.81	0.11-5.73	0.83
No	10 (11.2)	79 (88.8)			
History of siblings's allergy, n (%)					
Yes	1 (14.3)	6 (85.7)	1.32	0.19-8.94	0.77
No	10 (10.8)	83 (89.2)			
Chemical environmental factors, n (%)					
Yes	5 (25)	15 (75)	3.33	1.13-9.82	0.025
No	6 (7.5)	74 (92.5)			
Laundry, n (%)					
Yes	3 (37.5)	5 (62.5)	4.3	1.41-13.12	0.01
No	8 (8.7)	84 (91.3)			
Air freshener, n (%)					
Yes	1 (9.1)	10 (90.9)	0.8	0.11-5.73	0.83
No	10 (11.2)	79 (88.8)			
Perfume, n (%)					
Yes	2 (20)	8 (20)	2	0.50-7.99	0.34
No	9 (10)	81 (90)			
Physical environmental factors, n (%)					
Yes	2 (14.3)	12 (85.7)	1.36	0.32-5.67	0.67
No	9 (10.5)	77 (89.5)			
Upholstered sofa, n (%)					
Yes	2 (15.4)	11 (84.6)	1.48	0.36-6.13	0.58
No	9 (10.3)	78 (89.7)			
High humidity wall,n (%)					
Yes	2 (33.3)	4 (66.7)	3.48	0.95-12.65	0.07
No	9 (9.6)	85 (90.4)			
Exposure to pets, n (%)					
Yes	2 (4.3)	44 (95.7)	0.26	0.05-1.14	0.05
No	9 (16.7)	45 (83.3)			
Nutritional selection, n (%)					
Non-exclusive breastfeeding	9 (18)	41 (82)	4.5	1.02-19.79	0.025
Exclusive breastfeeding	2 (4)	48 (96)			

Table 3. Multivarite analysis of predictors for atopic dermatitis in infants in the first 3 month of life

Covariate	RR	CI	p value
Post term	7.73	2.23-26.76	0.001
Non exclusive breastfeeding	5.79	1.23-27.27	0.02
History of mother's allergy	2.42	0.61-9.51	0.20
Chemical environmental factors	1.83	0.34-9.74	0.47
Laundry	1.51	0.22-10.26	0.67
High humidity wall	2.00	0.38-10.46	0.41
Exposure to pets	0.38	0.07-1.92	0.24

DISCUSSION

Along with the previous findings, our study portrayed the incidence of AD in a specific early period of life.; which is the first 3 months of life. We noticed that in our setting in Bali, AD developed in 11% of study subjects. This number was in agreement to Widyanti, et.al. who found incidence of AD in the specific 3 months of life was 13% in the year 2012.[12] The small different of the number probably contributed by the study setting which was done in tertiary and secondary hospital, while Widyanti did the study only in tertiary level in Bali. Munasir, et.al. found incidence of AD in Jakarta was 16.4% in the first 6 months of life in the year 2009 which was done in tertiary level of hospital.[18] Moore, et.al. found incidence of AD in the first 6 months of life was 17.1%.[6] Kabondo, et.al. found incidence risks of AD was 21.0%, at 0-6months.[19] Kamer, et.al. found AD highly prevailing infants in the first three months of life.[20]

While there are common agreement for post natal environmental role in allergy development, there might be a potential neglect for the role of prenatal environment, in especially intra uterine prolong exposure. Our study documented that post term infant would be 7.73 times as likely as non post term infant to develop AD. This finding was supported by previous studies, which have shown that post term gestational age giving risk for AD. Longer intrauterine life exposes the infant to prolong dominancy of Th2 activity during gestation. This in turn induce persistency of predominantly Th2 over Th1 after delivery or longer reolustion to downwarding level of IL-4 into a balance with IFN gamma.[21-23] The risk noticed in our study was far higher than Moore, et.al. findings, who reported that the increasing length of gestation up to 40 weeks predicted atopic dermatitis (OR 1.14; 95% CI: 1.02-1.27).[6] This higher risk possibly explained by definition of variable in which we used gestational age to more than 41 weeks enabled more subjects captured. Tronnes, et.al. found prevalence atopic dermatitis increasing in the post term birth with OR 1.07; 95% CI: 1.00-1.15.[24] Korhonen, et.al. also found post term birth predicted atopic dermatitis with OR 1.06; 95% CI 1.01-1.1.[25]

While the superiority of breastfeeding to prevent the development of AD is accepted,14,[26-29] there were lots of mothers fail to keep their babies exclusively breastfed. Our data showed that non-exclusive breastfeeding independently gave significant impact for the development of AD to subjects with exclusive breastfeeding (RR 5.57 with 95% CI 1.23-27.27; P value 0.026). Similarly, Budiastuti, et.al. found that not receiving exclusive breastfeeding was a significant risk factor to AD in high risk infant (OR 3.72; 95% CI: 1.40-9.90, P value 0.01).[30] Kerkhof, et.al. found that exclusive breastfeeding in the first 3 months was negatively associated with AD (OR 0.6; 95% CI 0.3-1.2).[2] Our findings supporting the role of breast milk against allergy development, either from it's content of immunomodulatory factors such as IgA that promote the development of an infant immune system, also promotion the establishment of the predominantly bifidobacteria intestinal flora, including provision of oligosaccharides that promotes the environment for bifdobacteria.31

The strength of our study including the prospective nature of the study, also discovery the potential role of post term birth in the development of AD in the early phase of life. This will give impact to leverage the practice of better gestational age control and full term termination, instead of unintentionally withhold the pregnancy which is still exist recently. Our study has a potential to be a tool for education in parenting on how the less exclusive breastfeeding contributes for development of allergy. This is especially important as it is discover the challenges about breastfeeding practice while at the same time allow an alternative to reach parents to be more keen in successfully giving exclusive breastfeed if no contraindication found.

Study limitation in term of the study duration, our design probably can be extended to get to know more incidence in broader age range, so it considered Limitation of this study. includes not involving family type of allergy.

CONCLUSIONS

Incidence of AD in the first 3 months of life was 11%. Post term birth and non exclusive breastfeeding predict development of AD in this period. Post term birth independently contributes 7.73 risk for development of AD while non exclusive breastfeeding independently contributes 5.79 risk for development of AD.

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