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Research Article

EXCLUSIVE BREASTFEEDING ABLE TO REDUCE THE DEVELOPMENT OF CHILDHOOD ASTHMA

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ABSTRACT

Objective: To determine the association between maternal characteristics, maternal obstetrics history, fetal chacteristics and development of childhood asthma in offspring.

Methods: This was a case control study that enrolled children visiting the pediatric polyclinic of Rumah Sakit TNI-AD Padangsidimpuan, Indonesia starting from June to December 2015. Childhood asthma was diagnosed by spirometry. Breastfeeding history were taken by history taking. Data were analyzed by SPSS with $p<0.05$ as significant value.

Results: A total of 130 children were included in this study. The children analyzed in both groups had similar age ($p=0.232$), 20.5±12.2 months and 25.4±13.9 months. No differences were found in maternal characteristics, maternal obstetrics history, and fetal characteristics between both groups, except the history of breastfeeding ($p=0.002$).

Conclusion: Of all maternal characteristics, maternal obstetrics history, and fetal characteristics, only exclusive breastfeeding was associated for development of childhood asthma in offspring.

Keywords: Breastfeeding, Childhood asthma, Allergy, Exclusive, Children.

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INTRODUCTION

The prevalence of childhood asthma was consistently rising in worldwide. Asthma is the most chronic disease of childhood and the leading cause of morbidity with the high inpatient care, emergency department visit, and days of missed school [1]. Asthma is a heterogeneous disease of the airways that is characterized by increased responsiveness of the tracheobronchial tree to a variety of stimuli and airway obstruction that is partially or completely reversible [2]. Asthma could also be defined as at least one attack of wheeze and/or dyspnea and/or prescription of inhalation steroids in the last year [3]. Many studies used symptoms such as wheezing and shortness of breath, as main indicator of asthma in children [4].

Although the development of asthma and allergic diseases has a strong genetic component, the rise in the prevalence of these diseases indicates that environmental factors play an important role as well. Barker hypothesized that pre-natal maternal-fetal interactions might influence disease later in life in fetal. Therefore, this early life programming during intrauterine life could be associated to the development asthma in later life [5]. Many risk factors of asthma have been proposed including age, gender (male), low birth weight, maternal asthma, parental smoking, and family history of asthma. Another risk factors such as risk factors in early life for asthma-related symptoms include gestational age, parental socioeconomic status, and ethnicity [6].

The aim of the present study was to assess whether maternal characteristics, maternal obstetric history, and fetal characteristics were associated with the development of childhood asthma in offspring. In this study, we did not analyzed how family history contributed to asthmatic children. However, Subbarao *et al.* (2009) showed that nearly 100 genes have been found to be associated with asthma or asthma-related phenotypes [7]. We did want to know the results of asthma development in offspring induced by mother and fetal characteristics regardless of knowing the family history of asthma. This was because the high recall bias that could be occurred.

METHODS

This was an analytical, case-control study that analyzed how maternal characteristics, obstetric history, and fetal characteristics predicting offspring childhood asthma. This study was conducted at Rumah Sakit TNI-AD Padangsidimpuan, Indonesia. This hospital was geographically located at the cross section between highway roads of Sumatera-Java. This place represented the portrait of underserved area in Indonesia. This study has been approved by the Ethical Committee of University of Sumatera Utara.

This study enrolled consecutive children visiting the pediatric polyclinic starting from June to December 2015. We only included children who born in this hospital, no other pulmonary diseases, no congenital malformation, no malignancy, and no endocrine disorder. Exclusion criteria were children whose parents had psychiatric disorders, not complete data, and obese mother. In this study, we also excluded obese maternal. Many studies had positively showed the associated of obesity with asthma, due to elevated levels of pro-inflammatory cytokines (tumor necrosis factor-alpha, interleukin [IL]-6, and transforming growth factor [TGF]-beta1). Children were divided into two groups, children with childhood asthma, and children without childhood asthma. We restricted the samples to children aged below 5 years old [8].

Written informed consents were taken from all parents. Mother characteristics such as maternal age at the time of delivery, maternal ethnicity, maternal education, and maternal education were taken by history taking. We also asked their obstetric history such as parity, mode of delivery, and the presence of preterm labor, pre-eclampsia, or premature rupture of membrane in the time they delivered the children that included in this study. The information given were being cross-check with the medical records. Any discordance was found, did we ask the mother again for confirmation. If conclusion could not be reached, we excluded the participant from this study. Fetal characteristics such as fetal age, birth weight, and history of breastfeeding were taken from the medical records.

Diagnosis of asthma in children is often difficult. Spycher *et al.* defined asthma as the presence of wheezing, included viral or multiple trigger wheeze, and presence of allergic sensitization. Asthma can be diagnosed above 6 years old after the airway had been matured [9]. In this study, spirometry was also performed to diagnosis of asthma.

Data were analyzed by SPSS (Statistical Product and Service Solutions, Chicago, IL, USA) 22.0 for Windows. Categorical data were expressed as number and continuous data as mean±standard deviation. Chi-square test (Fisher's exact test) was used to examine the relation between qualitative variables. T-independent was used to evaluate quantitative variables. Significant value was take 95% and $p<0.05$ was considered significant.

RESULTS

From June to December 2015, there were 1197 children visiting pediatric polyclinic in our institution. As many as 130 children eligible for this study, 50 children with childhood asthma and 50 children without childhood asthma. Maternal characteristics, obstetric history, and fetal characteristics in childhood asthma were shown in Table 1.

The children analyzed in both groups had similar age (p=0.232), 20.5±12.2 and 25.4±13.9 months. In children both suffered or not from childhood asthma, mostly mothers were 20-35 years old while giving birth (66% and 71.3%), Bataknese (56% and 50%), educated until senior high school (38% and 38.8%), and housewives (46% and 46.3%). No differences were found in maternal characteristics between both groups.

Regarding of obstetric history, no differences were found in maternal obstetric history between both groups. In both groups' mothers, mostly were nulligravida (40% and 36.3%), had spontaneous delivery (54% and 50%), no preterm labor (80% and 93.7%), no pre-eclampsia 18% and 26.3%), and no premature rupture of membrane (88% and 93.7%).

Child characteristics were also not associated with the development of childhood asthma, except exclusive breastfeeding. Both groups had dominance of male gender (58% and 63.8%). Birth weight was found lower in asthmatic group, but the proportion was slightly similar between all samples. As mentioned, only exclusive breastfeeding differed in both groups. Children that were breastfed exclusively were more likely to develop childhood asthma (p=0.002).

Table 1: Maternal characteristics, obstetric history, and fetal characteristics in childhood asthma

Characteristics	Childhood asthma (n=65)		No childhood asthma (n=65)		p value*
Children age	20.5	12.2	25.4	13.9	0.232
Maternal characteristics					
Maternal age					
<20 years old	6	12.0	11	13.8	0.593
20-35 years old	33	66.0	57	71.3	
>35 years old	11	22.0	12	15.0	
Ethnicity					
Javanese	12	24.0	23	28.8	0.782
Bataknese	28	56.0	40	50.0	
Others	10	20.0	17	21.3	
Maternal education					
Secondary school	5	10.0	8	10	1.000
Junior high school	16	32.0	25	31.3	
Senior high school	19	38.0	31	38.8	
Diploma/University	10	20.0	16	20.0	
Maternal employment					
Housewife	23	46.0	37	46.3	0.287
Employee	11	22.0	11	13.8	
Businesswoman	12	24.0	17	21.3	
Honorary worker	4	8.0	15	18.8	
Maternal obstetric history					
Parity					
Nulligravida	20	40.0	29	36.3	0.714
Secundigravida	10	20.0	14	17.5	
Multigravida	14	28.0	30	37.5	
Grand multigravida	6	12.0	7	8.8	
Mode of delivery					
Spontaneous delivery	27	54.0	40	50.0	0.886
Assisted delivery	8	16.0	15	18.8	
Vaginal delivery	15	30.0	25	31.3	
Preterm labor					
Yes	10	20.0	7	8.8	0.036
No	40	80.0	73	91.2	
Pre-eclampsia					
Yes	9	18.0	21	26.2	0.277
No	41	82.0	59	73.8	
Premature rupture of membrane					
Yes	6	12.0	5	6.3	0.252
No	44	88.0	75	93.7	
Child characteristics					
Fetal sex					
Male	21	42.0	29	36.3	0.512
Female	29	58.0	51	63.8	
Birth weight (g)					

(Contd...)

Table 1: (Continued)

Characteristics	Childhood asthma (n=65)		No childhood asthma (n=65)		p value*
≤2500	22	44.0	44	55.0	0.222
>2500	28	56.0	36	45.0	
Exclusive breastfeeding					
Yes	33	66.0	31	38.8	0.002*
No	17	34.0	49	61.3	

*Chi-square, **(p<0.05 is considered significant)

DISCUSSION

Theory of perinatal programming had been proposed that intrauterine environmental stimuli influenced the fetal development both in pre-natal and post-natal. It induced permanent changes in gene expression and body metabolism function [10].

In previous study, maternal age at delivery was inversely associated with the risk of asthma [11]. McKeever *et al.* (2001) found the same results, but this association attenuated in children diagnosed at older ages [12]. Ethnicity brought out variation of innate immune response, but no association was found in this study [13]. In another study by Victorino *et al.*, they found that children in families with a higher education were more likely to have allergies [14]. In this study, no differences were found in maternal age (p=0.593), ethnicity (p=0.782), senior high school (p=1.000), and housewife (p=0.287) in children with and without childhood asthma. These findings were contradicted to those of previous studies.

The number of maternal previous deliveries was also inversely associated with childhood asthma, especially in grand multigravida [15]. Meta-analysis by Bager *et al.* (2008) reports that delivery by cesarean section was associated with an increase in the childhood asthma development. Preterm birth might lead to unmatured airways and impaired lung function, which predispose the participant to asthma and chronic obstructive pulmonary disease in childhood and adulthood [16]. Voort *et al.* showed that preterm birth was associated with higher risks of preschool-age asthma (odds ratio [OR]=4.47; p<0.05) [17]. Meta-analysis by Voort *et al.* (2012) even showed the increased risk of asthma development until 24 years of age [18]. Pre-eclampsia has remained a bad contributor to maternal and perinatal morbidity and mortality globally [19]. Pre-eclampsia is associated with unbalance of Th1/Th2 balance [20] which could potentially skew the child's cytokine balance after birth in the same direction and thereby protect against the development of atopic disease, including asthma [21]. Pro-inflammatory cytokines, chemokines, and adhesion molecules that increase during pre-eclampsia could contribute for asthma development in offspring [22]. Byberg *et al.* showed that severe maternal pre-eclampsia was associated with high-level allergic sensitization but not associated with atopic dermatitis, asthma, or altered lung function in late childhood [23]. Liu *et al.* showed positive association between maternal pre-eclampsia and asthma. The incidence rate ratios for asthma according to early- and late-onset pre-eclampsia were 1.88 (95% confidence interval [CI]=1.67-2.11) and 1.14 (95% CI=1.10-1.19) [24]. Getahun *et al.* (2010) showed that premature rupture of membranes with infection 1.66 times increased risk of asthma [25]. However, regarding of obstetric history, no differences were also found in maternal obstetric history such as parity (p=0.714), mode of delivery (p=0.886), history of preterm labor (p=0.064), pre-eclampsia (p=0.277), and premature rupture of membrane (p=0.252) between both groups in this study.

Child characteristics were also not associated with the development of childhood asthma, except exclusive breastfeeding (p=0.002). Voort *et al.* (2012) showed that preschoolchildren who were not breastfed for 6 months or non-receiving breastfed had increased risk of asthma. This happened the same for the presence of shortness of breath, dry cough, and persistent phlegm during the first 4 years (OR=1.44 (95% CI=1.24-1.66), 1.26 (1.07–1.48), 1.25 (1.08–1.44), and 1.57 (1.29–1.91), respectively) [26]. Oddy *et al.* showed that exclusive breastfeeding for at least 4 months was associated with a decreased risk of asthma at age 6 years, regardless of maternal history of asthma [27]. Scholtens *et al.* showed that breastfeeding for >3 months had been showed reduced risk of developing asthma in children 3-8 years old. However, the result was not significant, and there was no association observed for bronchial hyper-responsiveness [28]. In a large-scale study, Takemura *et al.* (2000) showed that breastfeeding was related to the higher prevalence of asthma during pre-adolescence (OR=1.198; p<0.01) after adjustment for age, gender, parental smoking status, and parental history of asthma [28]. However, Bjorksten *et al.* (2011) in 206, 453 children from 32 countries report a lack of association between breastfeeding and mild-moderate allergic disease, but there was inverse association between in severe allergic disease [29].

Many studies have claimed that breastfeeding is highly protective against asthma regardless of family history of asthma. Breast milk had bioactive enzymes, hormones, growth factors, cytokines and immunological agents, that played important role in the allergy development [30,31]. The most important component was the presence of TGF-beta in breast milk. TGF-beta was induced by regulatory CD4+ T lymphocytes and could be transferred to children. TGF-beta played important role as antigen-specific protection from allergic airway disease [32,33]. Guilbert *et al.* also found that a longer duration of breastfeeding favorably influenced lung growth in children [34]. Other clinicians hypothesized the contrast effect. Fat-soluble chemicals and foreign protein antigens in breast milk might provoke hypersensitivity. However, some clinicians proved that glycans in breast milk might induce innate immune system of anti-inflammatory mechanism [35].

CONCLUSION

Of all maternal characteristics, maternal obstetric history, and fetal characteristics, only exclusive breastfeeding was associated for the development of asthma in offspring.

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