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LITERATURE REVIEW

The role of obstetrician in reducing the risks of childhood allergy related to Caesarean birth: A literature review

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Abstract

Women's decision on birth mode should consider its risks and benefits, including long-term risks of Caesarean section among children. This study aims to present the current available evidences on the risks of Caesarean towards childhood allergy and how an obstetrician could prevent this outcome through nutrition and education. We searched articles from several online databases about the link between Caesarean, childhood allergy, and prenatal intervention. There were significant risks of childhood asthma and food allergy, but it was still unclear for allergic rhinitis and atopic dermatitis. Nutritional intervention could be done for pregnant women with consumption of probiotics and vitamin D supplementation. In addition, prenatal education is necessary to prepare better childhood outcomes.

Keywords: Caesarean section, prenatal education, children, obstetrician

Introduction

There is an increasing number of Caesarean deliveries throughout the world, including in Indonesia. In 2018, the rate of Caesarean delivery in Indonesia was 17.6%,[1] slightly higher than World Health Organization (WHO) recommendation rate which was around 10–15%.[2] Initially, Caesarean section (C-section) is performed due to life-threatening conditions towards mother and/or fetus. However, in present times, women have options to request for C-section, not necessarily related to medical indications. It is assumed that Caesarean delivery on maternal request (CDMR) is rising and contributes to the high rate of C-section. In US, the CDMR is estimated at 2.5% of all births.[3] In Indonesia, there had not been any studies which estimated the nation-based CDMR rate. Nevertheless, a study conducted in tertiary hospitals in Indonesia found that approximately 3.7% were performed on maternal request.[4]

The potential health risks of C-section in the short- and long-term, for mother, child, and subsequent pregnancies, have been widely discussed. Women who birth by C-section have higher risk for post-partum infection, thromboembolism, and even death, as short-term risk.[5] While in the long run, there are increasing risks of subfertility, ectopic pregnancy, placenta previa, placenta accreta, placental abruption, uterine rupture, and stillbirth, in subsequent pregnancy.[6]

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Additionally, children born by C-section have higher risk for asthma, overweight, obesity, and type 1 diabetes.[6] Nevertheless, C-section is not the only factor that contributes to child's allergy. Maternal factors, such as maternal obesity, gestational weight gain, maternal allergy, antibiotic use, and type of food consumption by the child, also modulate the risk of allergy in offspring.[7]

These health risks must be effectively delivered to mothers before deciding on the birth delivery mode. Prenatal care holds important role in preparing childbearing women for birth and to teach them about risks and benefits of C-section. Obstetricians play a key role in prenatal care, in giving advice and intervention to prevent unnecessary childhood outcomes in women choosing C-section method.

This article is part of Series on Caesarean Section. We aimed to describe the potential health risks of C-section on childhood allergy and the role of obstetrician in preventing this poor outcome by doing nutrition and education interventions.

Methods

We identified articles through various channels, e.g. international surveys and reports, national database, along with articles from electronic search engine. We searched for the frequency and trends of childhood allergy among those delivered via C-section, and also prenatal intervention to prevent it. Given the possibility of limited data, we include all type of articles and did not limit the publication year in our searching.

Results and Discussion

This review is classified into three main topics: 1) Risks of C-section towards childhood allergy; 2) Nutritional intervention; and 3) Prenatal education to prevent childhood allergy in infants born through C-section.

Risks of C-section on childhood allergy

Allergic disorders affect more than 30% of the children, and the prevalence of these diseases has been on the rise in recent years.[8] Major allergic diseases include asthma, rhinitis, atopic eczema, food allergy, and acute urticaria. These allergic diseases are complex multifactorial disorders, resulting from the combination of genetic and environmental factors.[9] Positive family history is one of the major risk factors for childhood allergic disorders. A child with maternal asthma has an odd risk of 2.26 (95% CI: 1.24–3.73) to develop childhood asthma, and higher risk (OR: 2.30; 95% CI: 1.17–4.52) if both parents had asthma.[10] Similar with other allergic diseases, if only father or mother had atopic dermatitis, the prevalence rate ratio was 1.9 (95% CI:0.3–11.8) and 1.5 (95% CI:0.4–5.5). The risk would increase to 2.3 (95% CI:0.4–13.7) if both parents affected.[11]

There is a hypothesis that the composition of gut flora in babies delivered through Caesarean are different than those through vaginal deliveries.[12,13] This could affect the initial colonizing events in infant's intestine, which could prolong immunological immaturity and potentially increase the risk of childhood allergic disorders. Caesarean babies undergo different procedure from babies born through vaginal deliveries. They are not directly exposed to maternal flora, therefore there is reduction of colonization in some bacteria, such as *Bacteroides fragilis* and *Bifidobacteria*, and increase in *Clostridia* and *Firmicutes*.[13]

Colonization rate of *Bifidobacterium*-like bacteria and *Lactobacillus*-like bacteria reached the rates of vaginally delivered infants at 1 month and 10 days, respectively. Infants born by Caesarean deliveries were significantly less often colonized with bacteria of the *Bacteroides fragilis* group compared with infants born through vaginal deliveries.[14] At 6 months the rates were 36% and 76%, respectively (p=0.009). The balance between *Bifidobacterium* and *Clostridium* species may affect immuno-physiological development, with a heightened risk for disease associated with fewer *Bifidobacterium* and more *Clostridium*.[15]

Our search found seven articles that discussed the association between delivery mode and childhood allergies. Table 1 presented the risk of developing asthma, allergic rhinitis, atopic dermatitis, and food allergies among children born by C-section. The highest risk with significant association was found in childhood asthma, followed with food allergy. While the risk for

allergic rhinitis and atopic dermatitis were still unclear. The articles searched are listed in **Table 1**.

Nutritional intervention

Nutrients from mothers are transported to the fetus across the placenta, including food allergens.[23,24] There is assumption that maternal diet during pregnancy could affect fetal immune development. Intake of relevant dietary supplements, avoidance specific food allergens, and overall dietary pattern of pregnant mothers should be carefully considered. The World Allergy Organization guideline recommends the use of probiotics in pregnant women at high risk for allergy in their children.[25] However, guidelines from US National Institute of Allergy and Infectious Disease[26] and the European Society for Pediatric, Gastroenterology, Hepatology, and Nutrition (ESPHGAN) do not support this.[27] The Australasian Society of Clinical Immunology and Allergy (ASCIA) recommends the consumption of oily fish up to 3 serves per week during pregnancy to prevent eczema.[28]

We searched for articles that include any maternal diet to prevent further eczema or asthma or allergic diseases in the offspring. Various type of diet was analyzed to determine the association with risk of allergy, i.e. prebiotics, probiotics, omega-3-fatty-acid, vitamin D supplementation, and avoidance of food allergens. In Table 2, we presented the effect of food supplement or nutrition intervention during maternal pregnancy towards the risk of childhood allergy. Overall, positive association was found between the use of probiotics and reduction risk of eczema or atopic dermatitis, with RR/OR below 1 (protective effect) for all included studies. Other positive correlation was seen in the consumption of prebiotic, omega-3-polyunsaturated-fatty-acid with food sensitization, fish oil, Mediterranean diet, zinc, vitamin D and E supplementation with the reduction risk of allergy in children. No evidence shows vitamin B and C supplementation, and avoidance of antigenic foods can reduce risk of allergy in children. Nevertheless, our review did not provide a thorough assessment on the specific type and amount of these nutrients. There are still more rooms to be explored in this field.

An association between low serum Vitamin D levels and the development of allergic diseases had been reported but this may not be causal. Besides that, in terms of allergic prevention, vitamin D supplementation may have no role in the primary prevention of allergic diseases. Moreover, increased Vitamin D supplementation in pregnant women did not confer protection against allergic diseases in their children had been reported by two recent randomized trials.[45] The articles searched can be seen in **Table 2**.

Educational intervention

Understanding the risk of Caesarean delivery and its possible effects upon mother and child is one of the basic knowledges that pregnant women should know. There are various non-clinical interventions, with health education as the core intervention to reduce birth with C-section.[56] Risks and benefits of Caesarean delivery should be informed before decision on birth mode is taken. Chen et al noted that health education provided by Obstetrician could reduce the risk of elective C-section from 66.8% to 53.7%.[57] Numerous studies also found that effective prenatal education would lead to better preparation for childbirth, including to reduce unnecessary C-section.[57] Other factors that also need to be taken into consideration for future review and researcher are related to the population of working mothers.[58] Economic burden of C-section born babies were also other health related indicator that need to be consider as points to be further discuss and analyzed in the future researches and reviews.[59,60]

We acknowledge that there are limitations to this review. The knowledge and competency development among birth attendants, including midwives and obstetric gynecologist are points that need to be thoroughly reviewed in order to get the full perspective on how medical practitioners could also plays role in mother's decision making on delivery mode. The viewpoints, knowledge update as well as education retention were mandatory to be discussed in future research.[61,62] The articles were not identified through a systematic searching strategy. Useful information and unpublished studies might have been missed. Nevertheless, we aim for studies which have best methodology, i.e. systematic review and meta-analysis. Additionally,

we did not perform critical appraisal for the included articles, and thus, we did not know the quality of these studies.

Conclusion

This review presents the potential risks of C-section on childhood allergies. Obstetrician holds a key role in providing information on nutrition and health education for pregnant mothers. Childhood asthma and food allergy were found to have positive association with C-section delivery mode. Consumption of probiotics, prebiotic, omega-3-polyunsaturated-fatty-acid, fish oil, Mediterranean diet, zinc, vitamin D and E supplementation are considered to be effective in reducing childhood allergies. However, further research still need to be done to understand the complex mechanism of how C-section could induce childhood allergies, and more interventions could be explored to prevent them.

Table 1. Risk of Caesarean delivery on childhood allergy

Author	Publication Year	Study Design	Respondents	Outcome OR/RR (95% CI)
Asthma				
Chu S et al[16]	2017	Cross-sectional	17,571 children	1.63 (1.18–2.24)
Renz-Polster H et al[17]	2005	Retrospective cohort	8,953 children	1.24 (1.01–1.53)
Huang L et al[18]	2014	Meta-analysis	26 studies	Overall risk: 1.16 (1.14 –1.29) Elective CS: 1.21 (1.17–1.25) Emergency CS: 1.23 (1.19–1.26)
Darabi et al[19]	2019	Meta-analysis	37 studies	Overall risk: 1.20 (1.15–1.25) Elective CS: 1.23 (1.20–1.26) Emergency CS: 1.18 (1.07–1.29)
Bager P et al[20]	2008	Meta-analysis	26 studies	1.18 (1.05–1.32)
Allergic rhinitis				
Chu S et al[16]	2017	Cross-sectional	17,571 children	1.18 (1.00–1.40)
Loo EXL et al[21]	2017	Prospective cohort	1,237 pregnant mothers	Infant aged 18 months: Adjusted OR: 0.8 (0.4–1.4) Infant aged 36 months: Adjusted OR: 0.8 (0.5–1.2) Infant aged 60 months: Adjusted OR: 0.9 (0.6–1.5)
Bager P et al[20]	2008	Meta-analysis	26 studies	1.23 (1.12–1.35)
Atopic dermatitis				
Renz-Polster H et al[17]	2005	Retrospective cohort	8,953 children	0.94 (0.75–1.19)
Bager P et al[20]	2008	Meta-analysis	26 studies	1.03 (0.98–1.09)
Food allergy				
Renz-Polster H et al[17]	2005	Retrospective cohort	8,953 children	1.34 (0.54–3.29)
Bager P et al[20]	2008	Meta-analysis	26 studies	1.32 (1.12–1.55)
Koplin J[22]	2008	Systematic review	4 studies	Increased risk of IgE mediated sensitization to food allergy in children born by CS

Table 2. Effect of maternal diet during pregnancy to reduce allergy risk in children

Author	Publication Year	Study design	Respondents	Risk of eczema/ atopic dermatitis	Risk of asthma/wheeze	Risk of food allergy / sensitization	Risk of allergic rhinitis
Probiotics							
Garcia-Larsen V et al[29]	2018	Meta-analysis	89 trials and 92 observational studies	0.78 (0.68-0.90)			
Zuccotti G et al[30]	2015	Meta-analysis	17 studies, 4755 children	0.78 (0.69-0.89)			
Cuello-Garcia CA et al[31]	2015	Meta-analysis	29 studies	0.71 (0.60-0.84)	0.94 (0.72-1.23)	1.08(0.73-1.59)	0.86 (0.44-1.70)
Li L et al[32]	2019	Meta-analysis	28 studies	0.67 (0.54-0.82)			
Zhang G et al[33]	2016	Meta-analysis	17 trials, 2947 infants			1.01 (0.66-1.55)	
Azad MB et al[34]	2013	Meta-analysis	20 trials		Asthma: 0.99 (0.81-1.21) Wheeze: 0.97 (0.87-1.09)		
Dang D et al[35]	2013	Meta-analysis	14 studies	0.69 (0.62-0.78)			
Pelucchi C et al[36]	2012	Meta-analysis	14 studies	0.79 (0.71-0.88)			
Prebiotics							
Cuello-Garcia C et al[31]	2017	Meta-analysis	6 studies	0.68 (0.40-1.15)	0.37 (0.17-0.80)	0.28 (0.08-1.00)	
Dang D et al[35]	2013	Meta-analysis	3 studies	0.80 (0.54-1.18)			
Omega-3-polyunsaturated fatty acid (fish oil)							
Garcia-Larsen V et al[29]	2018	Meta-analysis	89 trials and 92 observational studies			Sensitization to egg: 0.55 (0.40-0.76) Sensitization to peanut: 0.62 (0.40-0.96)	
Best KP[37]	2016	Meta-analysis	10 cohorts and 5 RCTs	0.53 (0.35-0.81)		Sensitization to egg: 0.55 (0.39-0.76) Sensitization to any food: 0.59 (0.46-0.76)	
Gunaratne AW[38]	2015	Systematic review	8 trials	Risk of any allergy below 36 months: 0.66 (0.41-0.98)			

Author	Publication Year	Study design	Respondents	Risk of eczema/ atopic dermatitis	Risk of asthma/wheeze	Risk of food allergy / sensitization	Risk of allergic rhinitis
				Risk > 36 months: 0.96 (0.84-1.09)			
Vahdaninia M et al[39]	2019	Meta-analysis	10 RCTs			Sensitization to egg: 0.54 (0.32-0.90) Sensitization to peanut: 0.62 (0.40-0.96)	
Klemens CM et al[40]	2011	Meta-analysis	5 RCTs		0.35 (0.15-0.79)	Sensitization to egg: 0.33 (0.16-0.70)	
Mediterranean Diet							
Biagi C et al[41]	2019	Systematic review	5 cohort studies, 2 cross-sectional		Persistent wheeze: aOR: 0.22 (0.08-0.58) Atopic wheeze: aOR: 0.30 (0.10-0.90) Current wheeze: OR: 0.71 (0.53-0.97)		
Zhang Y et al[42]	2019	Meta-analysis	18 observational studies		Wheeze ≤ 12 months: 0.92 (0.88-0.95) Asthma: 1.01 (0.94-1.09) Current wheeze: 0.76 (0.45-1.29)		
Nurmatov U et al[43]	2011	Meta-analysis	62 studies		0.22 (0.08-0.58)		
Vitamin D							
Shen SY et al[44]	2018	Meta-analysis	4 studies		Asthma at ≤ 5 years: 0.89 (0.77-1.04) Wheeze: 0.66 (0.53-0.82)		
Yepes-Nuñez JJ et al[45]	2017	Systematic review	1 RCT	0.96 (0.57-1.61)	1.12 (0.50-2.54)	1.92 (0.57-6.50)	0.76 (0.31-1.85)
Beckhaus AA et al[46]	2015	Meta-analysis	5 cohort studies		0.58 (0.38-0.88)		
Li W et al[47]	2019	Meta-analysis	6,068 participants		0.68 (0.55-0.83)		
Venter C et al[48]	2020	Meta-analysis	17 RCTs, 78 observational studies		0.72 (0.56-0.92)		
Vahdaninia M et al[49]	2017	Meta-analysis	5 RCTs		0.81 (0.67-0.98)		

Author	Publication Year	Study design	Respondents	Risk of eczema/ atopic dermatitis	Risk of asthma/wheeze	Risk of food allergy / sensitization	Risk of allergic rhinitis
Nurmatov U et al[43]	2011	Meta-analysis	62 studies		0.56 (0.42-0.73)		
Fish consumption							
Zhang G et al[50]	2017	Meta-analysis	1 RCT, 13 cohort studies	0.88 (0.75-1.04)	Wheeze: 0.94 (0.83-1.07) Asthma: 0.94 (0.75-1.18)		0.95 (0.62-1.45)
Song H et al[51]	2017	Meta-analysis	15 prospective studies		0.87 (0.75-1.02)		
Avoidance of antigenic foods							
Kramer MS et al[52]	2012	Systematic review	2 trials	1.01 (0.57-1.79)	2.22 (0.39-12.67)		
Vitamin E							
Wu H et al[53]	2018	Meta-analysis	10 studies		Asthma: 0.97 (0.95-1.00) Wheeze: 0.65 (0.56-0.75)		
Beckhaus AA et al[46]	2015	Meta-analysis	7 cohort studies		0.54 (0.41-0.71)		
Nurmatov U et al[43]	2011	Meta-analysis	62 studies		0.68 (0.52-0.88)		
Vitamin A							
Beckhaus AA et al[46]	2015	Meta-analysis	7 studies	0.76 (0.46-1.26)	0.97 (0.68-1.37)		
Vitamin B							
Beckhaus AA et al[46]	2015	Meta-analysis	4 cohort studies	Folic acid (B9): 0.91 (0.76-1.09) Vitamin B2 0.86 (0.74-1.01)	Folic acid (B9) 0.91 (0.49-1.68)		
Crider KS et al[54]	2013	Meta-analysis	5 studies		Folic acid: 1.01 (0.78-1.30)		
Vitamin C							
Beckhaus AA et al[46]	2015	Meta-analysis	6 cohort studies	0.95 (0.69-1.31)	0.99 (0.48-2.04)		
Zinc							
Beckhaus AA et al[46]	2015	Meta-analysis	6 cohort studies		0.57 (0.40-0.81)		
Fruit intake							
Seyedrezazadeh E et al[55]	2014	Meta-analysis	2 cohort, 13 cross-sectional		Wheeze: 0.81 (0.74-0.88) Asthma: 0.84 (0.79-0.89)		
Vegetable intake							
Seyedrezazadeh E et al[55]	2014	Meta-analysis	1 cohort, 10 cross-sectional		Wheeze: 0.89 (0.81-0.98) Asthma: 0.88 (0.82-0.95)		

Conflict of Interest

Authors declared no conflict of interest regarding this article.

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