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Systematic Review
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Unveiling Atopic Dermatitis: Exploring Smoking, Obesity, and Fast Food as Pivotal Risk Factors - A Systematic Review

Faiz Nur Hibatullah[1,2], Elisabeth Chelsea Uma Kalada[2], Etina Noor Baita[2], Erlin Siauwono[2], Fabianus Yvan Marino Cahaya Putra[2], Ronald Pratama Adiwinoto[2,3], Hanung Prasetya[4]

[1]Magister Program in Public Health, Airlangga University
[2]Faculty of Medicine, Hang Tuah University
[3]Department of Public Health, Faculty of Medicine, Hang Tuah University
[4]Health Polytechnic of the Ministry of Health Surakarta

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ABSTRACT

Background: Atopic dermatitis (AD), also known as Eczema, is an inflammatory skin disease that causes dry, itchy skin. several risk factors for AD have been reported including demographics, socioeconomics, active and passive smoking, urbanization, diet, breastfeeding and timing of introduction of solid foods, obesity, physical exercise, fast food, and environmental air pollution. This study aims to better understand the effect of smoking, obesity, and fast food consumption as one of the risk factors of AD.

Subjects and Method: Systematic review with the help of PICOs to search for eligible articles. Articles were searched from 3 different databases (PubMed, ScienceDirect, and Google Scholar) with the help of a search engine application, Publish or Perish (PoP), using the following keyword: "smoking AND atopic dermatitis", "fast food AND atopic dermatitis", "obesity AND atopic dermatitis".

Results: 10 articles matched the specified inclusion and exclusion criteria for this study. Whether or not smoking causes AD is still conflicting, few studies reported there is no correlation between smoking and AD, whereas other studies said otherwise. In contrast to that, second-hand smoke was found to be affecting AD conditions more (up to 2.320). Most of our eligible articles reported that obesity did cause severe reactions of AD up to 1.62 times. Frequent fast food consumption was also found to be causing severe AD conditions (OR=1.580).

Conclusion: Obesity and fast food consumption are one of the causes of AD development and AD severity. The risk factor of cigarette smoking still conflicts with whether or not it affects AD conditions.

Keywords: Atopic dermatitis, eczema, smoking, obesity, fast food

Correspondence:
Faiz Nur Hibatullah, Magister Program in Public Health, Airlangga University. Jl. Dr. Ir. H. Soekarno, Mulyorejo, Surabaya, East Java 60115, Indonesia. Email: faiz.nur.hibatullah-2021@-fkm.unair.ac.id. Mobile: +6287855184186

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BACKGROUND

Atopic dermatitis (AD), also known as eczema, is an inflammatory skin disease that causes dry, itchy skin that severely affects a person's quality of life. AD is found in all age groups but commonly occurs during childhood (Chovatiya, 2023). Previous studies said the prevalence in children under two years old reaches up to 20% of the population (Page, Weston and Loh, 2016). According to the Phase III International Study of Asthma and Allergies in Childhood (ISAAC), the prevalence of AD ranges from 2.0% to 22.3% in children aged 6 to 7 years and 1.8%–19.0% in age group of 13 to 14. Meanwhile among adults, the prevalence is lower in ranges from 2.1 to 8.1% (Ng and Chew, 2020).

Atopic dermatitis is a complex familial skin disease and a that is still uncertain. Few studies reported that the triggering factor of AD is caused by interactions between genetic, immune and environmental risk factors (Robert Kantor, 2018). AD often found simultaneously with asthma, allergic rhinitis, and food allergies. With the formation of the ISAAC consortium, several risk factors for AD have been reported including demographics, socioeconomics, active and passive smoking, urbanization, diet, breastfeeding and timing of introduction of solid foods, obesity, physical exercise, fast food and environmental air pollution (Nutten, 2015).

Cigarette smoking has a numerous unhealthy effects on the body, it's found to have a harmful effect on humoral or cellular immunity. The exact effect is still uncertain, although, it is believed to impair skin-barrier function through process formed by reactive oxygen species (ROS) on keratinocytes (Acharya and Mathur, 2020). Obesity also now affects more than 2 million people worldwide. Obesity believes to be the risk factor of diseases, such as: hypertension, diabetes mellitus, etc., including allergic diseases such as atopic dermatitis (Li and Kan, 2023).

Diet playing a huge factors in allergic diseases. Previous study found that, children with a healthy diet or consume Mediteranian diet have a lower chance of developing asthma and other allergic reaction. Oxidative stress and inflammation are reported to be the cause of allergic reaction, thus type of food can lessen or worsen allergic condition (Cepeda et al., 2015; Antonogeorgos et al., 2022).

The intricate nature of Atopic dermatitis, which is closely connected to genetics, immunology, and the environment, presents a formidable obstacle. AD, which stands for atopic dermatitis, shares risk factors with asthma and allergies. These risk factors include various demographic characteristics, socioeconomic factors, and lifestyle decisions. The harmful effects of smoking on the immune system and the worldwide increase in obesity both contribute to the mysterious cause of Atopic dermatitis. The influence of dietary patterns, such as the Mediterranean diet, on allergic reactions highlights the importance of a comprehensive investigation. Understanding the many risk factors associated with AD is crucial for implementing specific management strategies and preventive actions. Therefore, the objective of this study is to reveal the subtle influence of smoking, obesity, and fast food consumption as significant risk factors for AD. The findings offer the potential for not only a more profound understanding of AD but also well-informed approaches for its management and prevention.

SUBJECTS AND METHOD

1. Study Design

This was a systematic review.

2. Eligibility of Articles

The original articles were chosen based on the PICOS (Population, Intervention, Comparator, Outcome) framework research design, which is described in full in Table 1. The research incorporated cross-sectional, case-control, and cohort studies, which consisted of control groups without any intervention conditions, as well as intervention groups. The exclusions included of reviews, study methods, and meta-analyses. The process of determining eligibility involves a thorough examination of titles, abstracts, and key texts in accordance with the stated PICOs criteria (see Table 1). In addition to the database search, the bibliographic references of eligible research were carefully examined to identify any articles that may have been missed. The additional inclusion requirements were that articles must be written in either English or Indonesian and must have been published from January 2019 to December 2023, in accordance with the final search timeframe.

3. Search Strategy

The systematic review was conducted and reported in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flowchart. Articles searched from 3 different database (PubMed, ScienceDirect and Google Scholar) with the help of search engine application, Publish or Perish (PoP). Relevance article searched using the following keyword: “smoking AND atopic dermatitis”, “fast food AND atopic dermatitis”, “obesity AND atopic dermatitis”. A total of 273 articles were found based on the following search strategy, with 10 articles left that met the specific inclusion and exclusion criteria as the final result (Figure 1)

4. Operational Definition of Variables

Smoking: active or passive tobacco smoking. Second-hand exposure or passive tobacco smoking also included, as it counted as environmental exposure.

Obesity: defines according to World Health Organization definition of obesity, BMI more or equal to 30. The levels of obesity wasn’t specified.

Fast Food Consumption: a habits of consuming fast food (burgers, pizza etc., not including instant foods) in the past weeks. Frequency were disregarded.

Atopic Dermatitis: most common inflammatory skin disease which causes repetitive eczema-like lesion, dry and intense itchy sensation. AD level of reaction were disregarded.

5. Study Instrument

The software application of Publish or Perish (PoP) was used to carried out articles search through out 3 different databases, ScienceDirect, Google Scholar and PubMed. PRISMA was also used for filtering chosen studies.

6. Bias Assessment

Risk of Bias was assessed using Newcastle-Ottawa Quality Assessment for cohort studies. And Newcastle-Ottawa Quality Assessment Scale modified for cross-sectional study was also used. Newcastle-Ottawa Scale consist of assessing the bias of selection, comparability and outcome of the articles. The overall score tallied and interpreted as: article scores of 8-9 star considered low risk of bias; 5-7 considered to have medium risk of bias; and score under 5 considered as high risk of bias

7. Data Extraction

Spreadsheet was used for data extraction for chosen eligible articles, consist of the following data: article tittle, author(s), year of publication, research location, and outcome/ result.

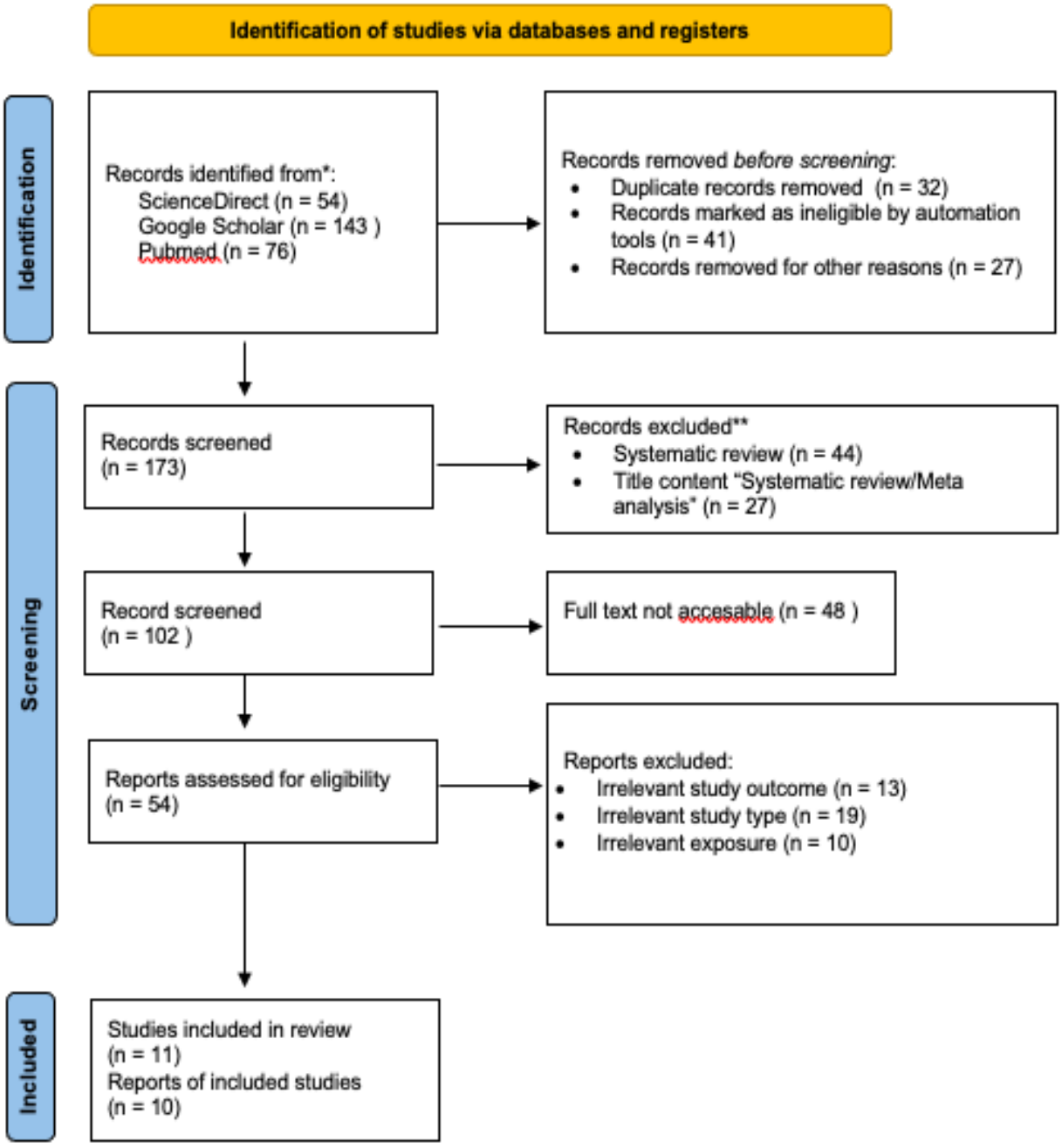

Figure 1 PRISMA flowchart and filtering result of the systematic review

RESULTS

Based on the article search study, we found 10 articles that matched the specified inclusion and exclusion criteria for this study (See Figure 1 for PRISMA Flowchart). 10 articles are using cohort, cross-sectional and case control as the study design, with 7 cross-sectional study, 2 cohort studies and 1 case control study. Most of the articles that we found are focused to the risk factor we picked (obesity, fast food consumption and smoking) on atopic dermatitis, excluding the 2 articles that focused on environmental impact and fat consumption.

Table 1. PICOs criteria of the unveiling atopic dermatitis: exploring smoking, obesity, and fast food as pivotal risk factors

Criteria	Description
Population	General population
Intervention	Inclusion: 1. Risk factor including: smoking (passive or active smoker), fast food consumption, and obesity. 2. The study contain population with risk factor both in intervention group and control group 3. Journals published in the last 5 years (2019-2023) 4. Original research Exclusion: 1. Other articles that did not mention nor contain the described risk factor in inclusion criteria. 2. Other articles that did not contain atopic dermatitis. 3. Other articles that mentioned other disease and other intervention.
Comparator	Absence of risk factor: smoking, fast food consumption, and obesity.
Outcome	Atopic dermatitis
Study design	1. Case control 2. Cohort 3. Cross-sectional.

Table 2. Risk of bias assessment of the unveiling atopic dermatitis: exploring smoking, obesity, and fast food as pivotal risk factors

No.	Authors	Selection	Comparability	Outcome	Total score
1.	Morra et al. (2020)	2	2	2	6
2.	Wang et al. (2023)	4	1	3	8
3.	Jing et al. (2020)	4	2	2	8
4.	Ascott et al. (2021)	5	2	2	9
5.	Smirnova et al. (2020)	5	1	2	8
6.	Vehapoglu et al. (2021)	4	1	2	7
7.	Cho et al. (2020)	4	2	3	9
8.	Lim (2023)	4	2	2	8
9.	Lim (2023)	4	1	2	7
10.	Liu (2022)	4	2	2	8

Table 3. Detailed result of eligible articles of the unveiling atopic dermatitis: exploring smoking, obesity, and fast food as pivotal risk factors

No	Author/Year	Location	Study Design	Result
1	Morra et al. (2020)	U.S	Cohort	Smoking were not significantly associated with AD. But, among smokers, partici-pants who smoke 25+ cigarette daily have higher risk of AD (HR= 1.18)
2	Jing et al. (2020)	China	Cross-sectional	Participant that exposed to second-hand smokers have higher risk of developing AD, Furthermore, participants exposed 1day/week have significantly higher risk (OR= 1.29)
3	Wang et al. (2023)	Chang Gung Memorial Hospital,	Cohort	Infant who got exposed with smoking in household environment have higher risk of developing eczema at age 6 months (RR=2.320)

No	Author/Year	Location	Study Design	Result
		Taiwan		
4	Ascott et al. (2021)	U.K	Cross-sectional	Participants with obesity have higher risk of developing AD than those with normal BMI (OR= 1.10). This study also shown that smoking only add a little different in AD condition (OR=1.07)
5	Smirnova et al. (2020)	Sweden	Cross-sectional	Participants with obesity at risk of developing AD, both mild and severe (OR= 1.33; OR=1.92). This study also shown that smoker have a higher chance of developing severe AD (OR=2.04)
6	Vehapoglu et al. (2021)	Istanbul, Turkey	Case control	Children age 3-10 with obesity have a higher risk of developing AD (OR= 1.71) compared to those with normal BMI.
7	Cho et al. (2020)	South Korea	Cross-sectional	Participants which frequently consume fast food have a higher risk of developing AD (OR=1.424). This study also found that participant with obesity at risk of developing AD (OR= 1.220)
8	Lim (2023)	Singapore and Malaysia	Cross-sectional	Participants with habits of consuming burgers/fast food are significantly related to AD severity (OR=1.920)
9	Lim (2023)	Singapore and Malaysia	Cross-sectional	Study shown that consuming high TFA (including fast food consumption) is significantly related to AD severity (OR=1.288).
10	Liu (2022)	Shenzhen, China	Cross-sectional	This study shown that, children diagnosed with eczema have a history/ habits of consuming fast food 4 times or more (OR= 1.581). Furthermore, smoking exposure shown have no significant relation with AD.

As it shows in Table 2, majority of our eligible articles have low risk of bias, with 3 articles have medium risk of bias. Our study found that, bias due to confounding factors was frequently found. Most of our studies also have not yet validated the measurement tool, although it is still described thoroughly.Despite the difference focus of this two articles, these studies still have the corelated bibliography references and in line with the risk factors that we decided to study on (See Table 3 for thorough result).

DISCUSSION

Smoking and Atopic Dermatitis

The particular mechanism of smoking effect on atopic dermatitis (AD) is still unclear. Eligible articles that we found also still conflicted. Self-reported studies using validated questionnaire by Smirnova *et al.* (2020) shown that, participants who smokes have a higher chance in having severe reaction of eczema (OR= 2.04). In contrast to that, studies conducted by Ascott *et al.*, (2021) and Morra *et al.* (2021) said that smoking is not significantly related to AD. In a large cohort studies among adult woman in the U.S conducted by Morra et al shown that there's no asso-

ciation of AD in participant that currently smoke nor to those that didn't smoke or a past smokers (OR=1.21; OR= 1.02). However, while compared with the quantity of smoking among smoker participants, smoking more than 25 cigarettes a day have a higher risk of developing AD (HR=1.18).

Among our eligible articles, two articles discussing the effect of second-hand or passive smoking on AD. Cross-sectional studies among first-year college students in five different universities in China conducted by Jing *et al.* (2020) shown that, second-hand smoking (SHS) is significantly associated with higher risk of AD. Furthermore, greater risk of AD is found in those with 1 day/weeks exposure of SHS (OR= 1.29, p= 0.010) and with the duration of exposure more than 6 years (OR= 1.50, p=0.010). Longitudinal cohort study conducted by Wang *et al.* (2023) also found that, infant that exposed to SHS have a higher chance of developing eczema around age of 6 months (OR= 2.320). Whereas, study conducted by Liu *et al.* (2022) found different result, children with environmental exposure of cigarette smoking in their household didn't have any significant relations with the development of AD.

Although the exact mechanism of smoking on atopic dermatitis still unclear, previous research hypothesized that smoking stimulates AD through an allergic reaction. Cigarette smoke stimulates the release of TNF-α, TNF-α receptor, interleukin (IL)-1, IL-6, IL-8 and granulocyte-macrophage colony-stimulating factor. Excessive production of TNF-α weakens the body's defences against contamination and causes the development of inflammatory skin diseases (Wang and Zhang, 2023).

Obesity and Atopic Dermatitis

Obesity is one of the risk factor of atopic dermatitis. Cross-sectional study of cohort of adult in U.K population conducted by Ascott *et al.* (2021) found that, adults with body mass index (BMI) of overweight or obese, according to World Health Organization (WHO) definition, have a higher risk of developing AD compared to those with normal BMI (OR= 1.10). However, overall of the study said that there is no association of overweight and obesity on atopic eczema status. Contrary to result study conducted by Smirnova *et al.* (2020), a self-reported using questionnaire among participants diagnosed with AD, obesity did affect AD condition. The study found that, people with BMI higher or equal to 30 prone to have mild or severe AD reaction (OR= 1.33; OR= 1.92). Study conducted by Vehapoglu *et al.* (2021) as well have the same result regarding the effect of obesity and AD development. Prepuberty children at age 3 to 10 years old with overweight (OR 1.71, 95% CI: 1.08–2.71, p=0.021) and obesity (OR 1.62, 95% CI: 1.06–2.50, p=0.026) have a higher risk in developing AD compared to those with normal BMI. Nationwide cross-sectional survey conducted by Cho *et al.* (2020) also found that, participant with BMI define as obesity is at risk of developing AD (OR=1.220).

The exact mechanism of obesity in causing AD is still unknown. However, recent research explains that obesity is associated with Th2 cell activation, which furtherly causes severe inflammation in AD. The role of TH17 cells is also prominent in obese people with allergic diseases. Previous research, using a previously collected targeted serum proteome dataset of AD patients, identified two skin TH17 inflammatory markers that correlate positively with BMI (Son *et al.*, 2019; Bapat *et al.*, 2022).

Fast food consumption and Atopic Dermatitis

AD is a complex disease that have multi-pathomechanism as a triggering factor,

dietary intake is one the risk factor leads to AD. Few studies believes that fast food consumption can increase the risk of AD (Wang *et al.*, 2018). Cho *et al.* (2020) conducted a nationwide cross-sectional study in South Korea, their study reported a significant association of fast food consumption and AD ($p < 0.001$). Participants whom consumed frequent fast food, frequently described as consuming fast food more than 5 times in the past week, have a higher risk of developing AD (OR= 1.424). Study conducted by Lim *et al.* (2023) reported the same thing. This two-staged cross-sectional sequential design study in Singapore and Malaysia found that, respondent with a habit of consuming burger/fast food prone to have a severe AD reaction. Another study conducted by Lim, Reginald, *et al.* (2023) also found that, respondent with high consumption of Total Fat Amount (TFA), which is commonly found in fast food, leads to severe AD reaction. Aligned with the other study, Liu *et al.* (2022) also found that eczema was found in children with history of consuming fast food more than 4 times a week (OR= 1.581).

Pathomechanism of fast food consumption in triggering AD reaction is still uncertain. Past studies hypothesized that carbohydrate intake from foods with a higher glycemic index is directly correlated with inflammation and increased inflammatory markers such as IL-6. IL-6 is a proinflammatory cytokine that causes Th17 differentiation in human skin. Foods with a higher glycemic index also increased plasma IL-6 concentrations in patients undergoing puberty and IL-6 expression was shown to be irregular and persistent in the skin and blood of AD patients. Many studies also reported that diets that consume excess fat can increase chronic inflammation and furtherly, promote atopic disease (Lim, Lim, *et al.*, 2023).

To summarize, this study aims to understand the effect of smoking, obesity and fast food consumption on AD. Among 10 articles that we found, majority of it reported that obesity and fast food consumption are one of the causes of AD development and AD severity. However, the risk factor cigarette smoking is still uncertain, as few of our eligible articles are conflicted whether or not to affect AD condition, whereas second hand smoking found to be one of the triggering cause of AD. Further study needs to be conducted to determine the effect of smoking on AD.

AUTHORS CONTRIBUTION

Author 1 lead researcher responsible for topic selection, search, and collection of research data. Author 1 - 6 analyzed the data, reviewed the research documentation, and interpreted the results.

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CONFLICT OF INTEREST

There are no conflict of interest.

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