Original Research Report

PRELIMINARY INVESTIGATION OF RISK FACTORS FOR FOOD ALLERGIES IN THE PEDIATRIC POPULATION: OBSERVATIONS FROM A SURVEY UTILIZING A SIMPLIFIED QUESTIONNAIRE IN GRESIK, EAST JAVA, INDONESIA

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ABSTRACT

In Gresik, Indonesia, limited resources have led to challenges in accurately diagnosing food allergies. This study aimed to identify risk factors for food allergies among children in Gresik using a questionnaire-based approach. The study's ultimate goal was to develop a simple diagnostic tool in primary healthcare settings. Conducted at Petrokimia Gresik Hospital, this cross-sectional study enrolled children aged ≥6 months experiencing respiratory symptoms or atopic dermatitis for ≥1 week. The subjects (n = 247) underwent a two- to four-week restrictive diet for diagnostic purposes. The questionnaire demonstrated validity and reliability. Bivariate statistical analyses were performed to examine the correlations between risk factors and the incidence of food allergies ($p < 0.05$). A receiver operating characteristic (ROC) curve analysis was used to establish the cut-off values for the number of food allergies and atopic family members. The majority of the 247 children enrolled in this study were 6 to 12 years old. Respiratory symptoms (56.3%) were more common than atopic dermatitis (38.1%). The significant risk factors for food allergies included atopic dermatitis ($p = 0.001$; $R = 0.203$), previous history of suspected food allergies ($p < 0.001$; $R = 0.747$), and atopy in the family ($p = 0.013$; $R = 0.157$). The ROC curve analysis established the cut-off values for the number of atopic family members at 1.5 ($p = 0.005$; 95% CI 0.53-0.67) and the number of food allergies at 0.5 ($p = 0.000$; 95% CI 0.85-0.94). In conclusion, children are considered at risk of food allergies if they display persistent respiratory symptoms or atopic dermatitis, considering the history of suspected food allergies even to only one specific type of food.

Keywords: Food allergy; atopic dermatitis; chronic respiratory diseases; questionnaire; health risks

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Highlights:
1. A questionnaire, comprising various risk factors associated with food allergies, is anticipated to provide reliable indications for determining the necessity of restrictive diets for patients within primary healthcare settings.
2. Over time, the findings of this study can facilitate the development of a streamlined and cost-effective diagnostic tool, which will be particularly beneficial in remote regions due to its practical and efficient means of identifying food allergies.

INTRODUCTION

Food allergies are a significant health issue that is particularly prevalent in developed nations. These conditions encompass a spectrum of conditions triggered by adverse immune reactions to dietary antigens (Renz et al. 2018, Salsabila et al. 2021). Individuals of all ages can be affected by allergic diseases. However, food allergies are becoming more common in children, who also tend to have a more favorable prognosis (Halken et al. 2021, Putera et al. 2023, Putera & Ramadhianty 2023).

The prevalence of allergic diseases varies between

urban and rural areas, with differences observed in the risk and protective factors. In rural area, exposure to farm animals during pregnancy has been shown to have a protective effect against allergies for infants and their mothers (Allen & Koplin 2019, Botha et al. 2019, Levin et al. 2020). In urban areas, children born via caesarean section are linked to an increased risk of food allergies. Conversely, the consumption of fermented milk products is associated with a lower prevalence of asthma and atopic dermatitis. In both urban and rural cohorts, antenatal maternal smoking and exposure to environmental smoking are primarily associated with asthma, while the consumption of fast foods and fried meats is associated with allergies (Dzakiyyah et al. 2022, Putera et al. 2023).

Gresik, a major industrial estate in East Java, Indonesia, is renowned for its various industrial facilities. Two notable examples are Petrokimia Gresik, a leading fertilizer factory, and Semen Gresik, a prominent cement factory (Sulistyandari 2019). With around 1.3 million residents, Gresik exhibits disparities in terms of healthcare facilities, particularly in the field of allergy-immunology, when compared to metropolitan areas. Insufficient resources, such as the lack of specific immunoglobulin E (IgE) skin tests, have contributed to the misdiagnosis of food allergies in this area (Statistics Gresik 2023). Therefore, a study employing a straightforward questionnaire to identify significant risk factors for food allergies in children is essential. In clinical practice, identified risk factors can serve as valuable indicators to assess the need for implementing a restrictive diet for specific patients.

Food allergy screening has been lacking in primary healthcare, despite the fact that this could be remedied by asking relevant questions. Prior research reported that a particular center has created a standardized questionnaire covering medical history, family history of atopy, and dietary habits (Sacchetti et al. 2017). The current study is an early exploration of food allergy questionnaires to formulate a standardized national questionnaire to be implemented in primary healthcare facilities.

The assessment of food allergies requires an extensive medical history, concentrating on potential triggers (raw or cooked foods), onset, related symptoms, symptom consistency, and additional factors such as physical activity, medication use, or comorbidities. Symptoms of IgE-mediated allergies emerge quickly (within 2 hours of exposure), typically affecting the skin, respiratory system, and gastrointestinal tract (Renz et al. 2018). The objective of this study was to provide a comprehensive assessment of self-reported and expert-screened instances of food allergies within an unselected pediatric population. This study focused on identifying the risk factors for food allergies using a questionnaire in Gresik, Indonesia.

MATERIALS AND METHODS

A cross-sectional questionnaire-based survey was conducted at the Outpatient Department of Petrokimia Gresik Hospital in Gresik, Indonesia, from 1/2/2023 to 31/7/2023. This study consecutively recruited children aged six months and older who presented with respiratory symptoms and atopic dermatitis that had persisted for more than one week. Written informed consent was obtained from the subjects' parents, verifying that they fully understood and agreed to participate in the survey. Strict measures were implemented to safeguard the patients confidentiality (Wang & Cheng 2020).

The diagnosis of food allergies relied on a comprehensive assessment encompassing history taking, physical examination, and additional investigations conducted. This comprehensive assessment is required to eliminate differential diagnoses (Devdas et al. 2018). The subjects adhered to a two- to four-week period of dietary restriction, during which they excluded poultry, seafood, and dairy products from their daily meals. Respiratory and skin symptoms were evaluated through detailed history taking and routine physical examinations. For those with respiratory symptoms, Water's view X-ray and tuberculin tests were conducted to rule out other diagnoses. Participants were excluded if they had not been ingesting solid food for any reason or were unable to fulfill the requirements of the prescribed dietary restriction.

The questionnaire utilized in this study was a modified version of the history-taking list used at the Allergy and Immunology Division, Department of Pediatrics, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. The questionnaire design followed several principles. First and foremost, the questionnaire needed to be deemed valid by both parents and clinicians who contributed to its development. Additionally, it was necessary for the questionnaire to be appropriate for the children's developmental stages. Furthermore, the questionnaire was designed to be concise, straightforward, and easy for parents to fill out independently. A standard and anonymous questionnaire was crafted to gather personal histories and general information, specifically focusing on feeding practices, dietary patterns, and the co-existence of atopy in the family (Wu et al. 2012). Each parent of the participants received a self-administered questionnaire that they were required to complete.

It was crucial to assess the validity and reliability of the research instruments to ensure the accuracy of the study's hypothesis. Prior to data collection, a subset of 40 data points was chosen from a total of 247 for the purpose of testing validity and reliability. The research instrument was considered valid if the Pearson correlation analysis yielded a value of $p<0.05$. Additionally, it was deemed reliable if the Cronbach's alpha coefficient exceeded 0.6. These values indicated that the questionnaire could produce consistent responses across different respondents, making it suitable for data collection (Tsang et al. 2017). Table 1 outlines the validity and reliability of the questionnaire items.

Table 1. Assessment of the questionnaire items on food allergies.

Questionnaire items	Scores	
	p	α
Respiratory tract symptoms		0.793
Cold in the morning	0.000	
Stuffy nose	0.000	
Sneezing	0.000	
Runny nose	0.000	
Recurrent shortness of breath	0.000	
Recurrent cough every month	0.002	
Nagging cough at night or early in the morning	0.000	
Atopic dermatitis symptoms		0.836
Xerosis	0.000	
Recurrent rash and itching due to allergy	0.000	
Previously-suspected allergenic foods		0.836
Milk	0.000	
Egg	0.000	
Chocolate	0.000	
Poultry	0.000	
Seafood	0.000	
Noodles	0.000	
Fruits	0.000	
Chips	0.000	
Peanut	0.000	
Family history of atopy		0.723
Paternal	0.000	
Maternal	0.000	
Siblings	0.000	
Parents' siblings	0.000	
First-degree relatives	0.000	

Legends: The Pearson correlation value is denoted by the symbol "p"; the Cronbach's alpha correlation coefficient is denoted by the symbol "α".

IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, N.Y., USA) was used for the statistical analyses, which included descriptive, inferential, and path analyses. The significance level was established at $p<0.05$. The descriptive statistics provided an analysis of the study samples' characteristics, while the bivariate statistics assessed the correlations between symptoms, environmental factors, family history, and food allergy incidence (Zhang 2016). The receiver operating characteristic (ROC) curve analysis was conducted to determine the questionnaire accuracy and establish the cut-off values for food allergies and familial atopy. The analysis helped in identifying the development of food allergies. An evaluation was also performed to assess the sensitivity and specificity of the identified risk factors.

RESULTS

Figure 1 illustrates the sample enrollment process in this study. The age distribution of all respondents at the Outpatient Department of Petrokimia Gresik Hospital, Gresik, Indonesia, was as follows: 23.5% in the age group of 1–3 years, 30.4% in the age group of 3–5 years, and 40.1% in the age group of 6–12 years.

As shown in Table 2, respiratory symptoms (56.3%) were more common than atopic dermatitis (38.1%) among the respondents. Both family history of atopy (63.9%) and previously-suspected food allergies (45.8%) were higher in the group with food allergies. Respondents were suspected of having food allergies if they exhibited symptoms such as itching, sneezing, wheezing, or coughing after previously consuming certain foods.

Table 2. Clinical characteristics of the study population.

Clinical characteristics	Respondents (n=247)		p
	Food allergy (-) (n=124)	Food allergy (+) (n=123)	
Age			
Range	6 months–16 years	9 months–13 years	0.292
Mean±SD	4±3 years	5±3 years	
Sex			
Male	77	77	0.934
Female	47	46	
Respiratory tract symptoms	69	70	0.841
Atopic dermatitis symptoms	35	59	0.001*
Previous history of suspected food allergy	7	106	<0.001*
Family history of atopy	70	88	0.013*

Legends: SD=standard deviation; (*) signifies any statistical significance; the Chi-square test significance value is denoted by the symbol "p".

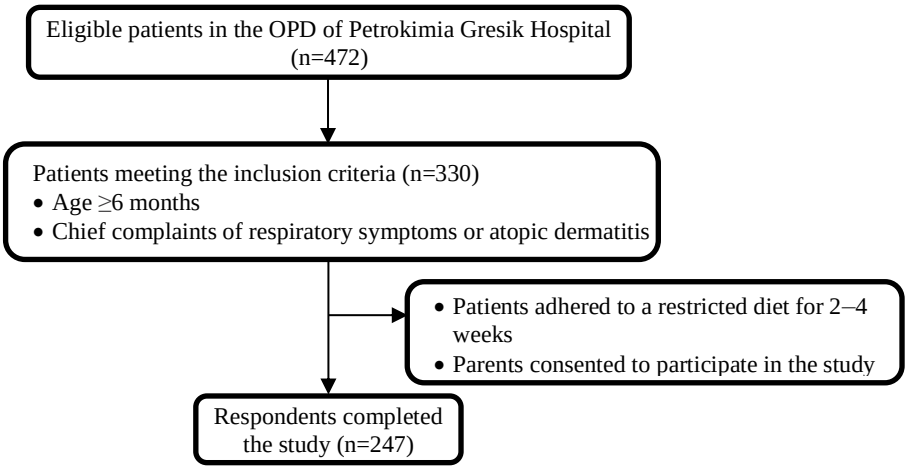

Figure 1. Study sample enrollment flowchart. Legend: OPD=Outpatient Department.

The incidence of food allergies was confirmed by a positive response to the restrictive diet. Specifically, the results exhibited several risk factors that were found to be significantly related to food allergies. These included atopic dermatitis (p = 0.001, R=0.203), previous history of suspected food allergy (p<0.001, R=0.747), and family history of atopy (p=0.013, R=0.157).

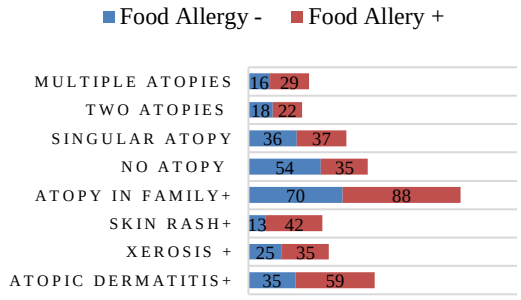

Figure 2. The prevalence and family history of atopies in both food allergy and non-food allergy groups.

In the food allergy group, xerosis (p=0.129) and skin rash (p<0.001) were shown to be more prevalent as symptoms of atopic dermatitis compared to the non-food allergy group (Figure 2). Skin rash emerged as the symptom significantly related to the incidence of food allergies. In addition, over 50% of the respondents in both groups were unable to articulate the onset of their symptoms.

Among the participants in the food allergy group (n=123), a significant proportion (n=106, 86.2%) had previously suspected that they might have food allergies. The participants could identify multiple suspected allergenic foods, but the majority only reported having one (28.5%) or two types of allergies (22.8%). The most frequently suspected allergens were chocolate, milk, and eggs (Figure 3).

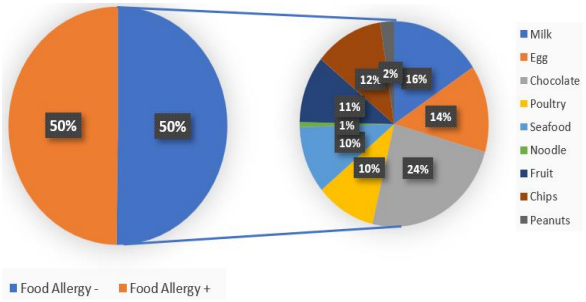

Figure 3. Types of food that are likely to cause allergies, as shown by the questionnaire results.

Out of the 123 respondents in the food allergy group, 88 respondents (71.5%) reported a family history of atopy. Among them, 30.1% specifically mentioned having only singular atopy. The most common family atopies were maternal (43.9%) and paternal (39.8%). The ROC curve analysis established a cut-off value for family history of atopy at 1.5 (p=0.005, 95% CI 0.53-0.67), with sensitivity and specificity of 71.5% and 43.5%, respectively. The quantification of the number of food allergies (Figure 4B) resulted in a cut-off value of 0.5, which was statistically significant at p<0.001, with a 95% CI of 0.85-0.94. The sensitivity and specificity were 86.2% and 94.4%, respectively. The results of this study could contribute insights into food allergy quantification, offering a robust diagnostic approach. In terms of the correlation between risk factors and the incidence of food allergies, children

were deemed at risk if they had two or more family members with atopy or if they had a history of at least one type of food allergy.

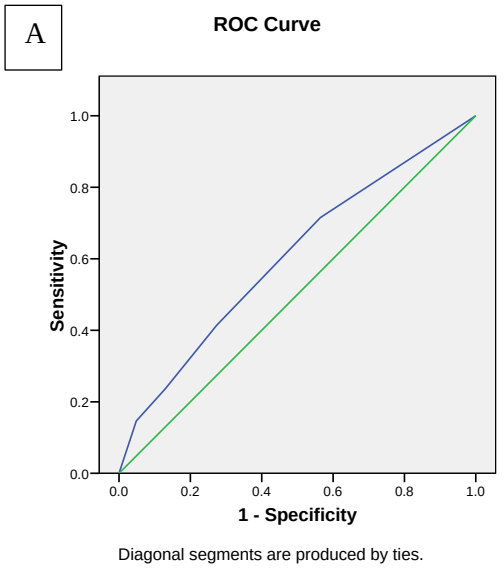

Figure 4. Receiver operating characteristic (ROC) curves of the cut-off values for the number of atopic family members (A) and the occurrence of food allergies (B).

This study identified three noteworthy risk factors correlated with food allergies: atopic dermatitis, a previous history of suspected food allergies, and a family history of atopy. However, the results of the Spearman's correlation test and ROC curve analysis revealed that a history of suspected food allergies exhibited the highest correlation coefficient (R) and a larger area under the curve compared to the other risk factors. The results demonstrated that a history of suspected food allergies had a substantial influence and accuracy in predicting the occurrence of food allergies.

DISCUSSION

Food allergies are a common allergic condition characterized by an adverse immune response to food allergens. The severity of symptoms and their increasing occurrence over recent years have led to the recognition of this issue as a significant pediatric health concern in Western countries. In children, the gastrointestinal tract is often the primary organ affected, followed by the skin and respiratory tract. Multiple systems can be implicated, with the potential for rapid progression to systemic anaphylaxis. An evaluation for children suspected of having food allergies typically involves a thorough history taking, physical examination, screening tests, and assessment of response to restrictive diets and oral food challenges (Baker & Nowak-Wegrzyn 2020).

IgE-positive food allergies often accompany atopic dermatitis during early childhood, representing one of the earliest indications of atopic march. In this study, atopic dermatitis was significantly correlated with food allergies. A total of 38.1% of the respondents had atopic dermatitis, and 62.8% of them were confirmed to have food allergies as well. Allergens, including food and aeroallergens, can permeate the skin via a compromised skin barrier. As a result, skin sensitization during early childhood is linked to a higher likelihood of sensitization during adolescence and an increased probability of developing food allergies at the ages of 12 and 18 years. The food allergy aspect is regarded as the biggest risk factor for atopic march (Mastrorilli et al. 2017, Yang et al. 2020). This study revealed a significant correlation between food allergies and atopic dermatitis, a family history of atopy, and a previous history of suspected food allergies. The most substantial correlation with food allergies was observed in cases where there was a previous history of suspected food allergies. This aligns with the findings of previous studies (Yang et al. 2020, Al-Adawiyah et al. 2021). The findings imply that if children exhibit persistent respiratory or atopic dermatitis symptoms and have a previous history of suspected food allergies, it is advisable to consider the possibility that food allergies may be the underlying cause of these symptoms.

A large number of children in a birth cohort from the Isle of Wight, England, had overcome their allergies to cow's milk and eggs by the age of ten. However, the occurrence of peanut allergies remained relatively constant during their first decade of life (Mastrorilli et al. 2017, Skjerven et al. 2022). In Indonesia, particularly in Surabaya, children tended to outgrow cow's milk allergy at a mean age of 50.32±31.19 months old. In contrast, those experiencing persistent cow's milk allergies had a mean age of 60.24±25.57 months old (Putera

& Ramadhianty 2023). In this study, most respondents were 6–12 years old. Nevertheless, this study found that allergy symptoms, such as respiratory tract or atopic dermatitis symptoms, could still be present in this age group. The earlier investigation affirmed that the predominant allergy symptoms associated with IgE, induced by cow's milk protein, primarily manifested in the respiratory tract.

A previous study conducted by Yang et al. (2020) examined 2,222 infants between the ages of 11.5 and 25.5 months old diagnosed with atopic dermatitis. Within three months of birth, 64% of the infants exhibited IgE-mediated sensitivity to milk, peanuts, or eggs. In infants under 12 months old, the severity of atopic dermatitis was found to be correlated with the proportion of those who showed sensitivity to eggs, milk, or peanuts. However, this correlation was not seen in children who were diagnosed with atopic dermatitis after turning one year old. In this study, half of the participants were found to have confirmed food allergies. The most suspected allergenic foods were chocolate (24%), milk (16%), and eggs (14%). It is important to note that chocolate often contains cocoa powder, milk, and sugar. Thus, milk has been identified as the most allergenic food among the Indonesian population, especially in Gresik, Indonesia.

A positive family history of atopy has been established as a significant risk factor for the development of allergies in children. This is corroborated by multiple previous studies, including those carried out by Baker & Nowak-Wegrzyn (2020) and Kalach et al. (2019). A separate study conducted by Saito-Abe et al. (2022) in the Japanese population found positive links between either or both parents having allergic diseases and their children's food allergies at the ages of 1.5 and 3 years old. The risk of developing food allergies was higher when both parents had a history of allergic diseases. In this study, a significant association was observed between a family history of atopy and the incidence of food allergies. The respondents who had atopic family members demonstrated a notable trend of food allergies, with most of them having one family member affected by atopy, mainly from either the paternal or maternal side. Children with a genetic predisposition to atopy, shown by having two or more family members with the condition, were found to have an increased susceptibility to food allergies. This validates the conclusions of previous research, such as the one conducted by Hoehn et al. (2016). Furthermore, specific lifestyle practices may correlate with atopy. In recent decades, researchers have focused on lifestyle changes, such as vaccination and antibiotic usage, smaller family sizes, and improved hygiene practices, all of which have been associated with atopy (Kummeling et al. 2006). These items should be considered to be added to the questionnaire for future studies.

Strength and limitations

This study has proven that the questionnaire is a simple, user-friendly, and cost-effective diagnostic tool suitable for all healthcare professionals, particularly in remote areas. However, the development of a more comprehensive food allergy questionnaire in the future can offer an alternative diagnostic approach in primary healthcare settings. However, the parents might struggle to accurately recall their children's dietary intake when filling out the questionnaire regarding the variability in food consumption. In order to address this challenge, future research should involve older children in independently completing the questionnaire. Moreover, this study was constrained by the lack of documented information on past medication history and limited details on symptom onset. The reliance on caregivers for symptom information, which is a consequence of many working parents in Gresik, Indonesia, poses challenges in obtaining accurate data.

CONCLUSION

Atopic dermatitis, a family history of atopy, and a previous history of suspected food allergies are identified as the notable risk factors for the incidence of food allergies. A history of suspected food allergies had the strongest correlation with the incidence of food allergies compared to other risk factors. Children are considered at risk of food allergies if they show persistent respiratory symptoms or atopic dermatitis along with a history of food allergies even to only one type of food.

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Conflict of interest

None.

Ethical consideration

This study received ethical approval from the Ethics Committee of Petrokimia Gresik Hospital, Gresik, Indonesia, under ethical clearance No. 1128/04/NK. 06.01/RSPG/2023 dated 28/4/2023.

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Author contribution

NEJ performed data analysis and interpretation, drafted the article, and secured funding while overseeing data collection and patient support. ZH aided in the study design and conception in addition to providing administrative, technical, and logistic support. AMP contributed to the drafting of the article. AE provided statistical expertise. Final approval and critical revision for important intellectual content were performed by ZH, AMP, and AE.

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