ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Original Article

Prevalence of anaphylaxis among individuals with allergic diseases in the state of São Paulo, southeastern Brazil, through an online questionnaire

Prevalência de anafilaxia entre indivíduos portadores de doenças alérgicas no estado de São Paulo através de questionário online

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ABSTRACT

Introduction: Anaphylaxis is a severe, potentially fatal systemic reaction, making rapid and accurate diagnosis essential for adequate treatment. Despite the seriousness of the condition, studies focusing on its prevalence in Brazil are scarce, limiting the understanding of its real impact and hindering the planning of preventive measures for anaphylaxis in the country. This study aimed to contribute to the understanding of the prevalence of anaphylaxis in individuals with allergic diseases in the state of São Paulo, southeastern Brazil. **Methods:** The study was conducted using the digital platform Google Forms, with anonymous participation from residents of the state of São Paulo, and was previously approved by the Research Ethics Committees of the involved institutions. Two validated questionnaires were disseminated through social media, targeting individuals up to 7 years old and those older than that age. **Results:** A total of 309 questionnaires were collected from individuals aged 7 years or older who reported having an allergy. Based on suggestive anaphylaxis scores, 46 individuals (14.9%) were potentially anaphylactic. The reported causes were medications (56.5%), foods (47.8%), insect stings (26.0%), latex (4.3%), and undetermined (4.3%). Other diagnoses included rhinitis (60.8%), dermatitis or eczema (41.3%), asthma (30.4%), and isolated anaphylaxis (30.4%). Among children up to 6 years, 11 months, and 29 days, 84 questionnaires indicated allergies, with 21.4% showing suggestive scores of anaphylaxis. The causes in this group were foods (72.2%), insect stings (22.2%), and medications (22.2%). Dermatitis was reported in 38.8% of the questionnaires, asthma in 55.5%, rhinitis in 44.4%, and isolated anaphylaxis in

RESUMO

Introdução: Anafilaxia é uma reação sistêmica grave potencialmente fatal, sendo fundamental um diagnóstico rápido e preciso para que o tratamento seja realizado de forma adequada. Apesar da gravidade da doença, os estudos voltados para sua prevalência no Brasil são escassos, limitando o conhecimento do real impacto e dificultando o planejamento de medidas preventivas para a anafilaxia no país. Este estudo objetiva, assim, contribuir para o conhecimento da prevalência da anafilaxia em indivíduos portadores de algum tipo de doença alérgica no estado de São Paulo. **Métodos:** O estudo foi realizado através da plataforma digital Google Forms com envolvimento anônimo dos participantes residentes do estado de São Paulo, previamente aprovado pelos Comitês de Ética em Pesquisa das instituições envolvidas. Foram divulgados, através de mídias sociais, dois questionários validados direcionados a indivíduos com até 7 anos e acima dessa idade. **Resultados:** Foram obtidos 309 questionários de indivíduos com sete anos ou mais que referiam ter algum tipo de alergia. Através dos escores sugestivos de anafilaxia, obteve-se 46 pessoas (14,9%) possivelmente anafiláticas. Entre estas, as causas foram medicamentos em 56,5%, alimentos em 47,8%, ferroadas de insetos em 26,0%, látex em 4,3%, e indeterminado em 4,3%. Outros diagnósticos: rinite, 60,8%; dermatite ou eczema, 41,3%; asma, 30,4%; diagnóstico isolado de anafilaxia, 30,4%. Entre crianças de até 6 anos 11 meses e 29 dias, 84 questionários referiram alergia, sendo que 21,4% apresentaram escores sugestivos de anafilaxia, cujas causas foram: alimentos em 72,2%, insetos em 22,2%, e medicamentos em 22,2%. Dermatite apareceu em 38,8% dos questionários, asma em 55,5%, rinite em 44,4%, e anafilaxia

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5.55%. **Conclusion:** Anaphylaxis is not a rare condition among individuals with atopy, especially in young children. The causes of anaphylaxis reported were similar to those found in the medical literature, with medications predominating in the older population and foods being more common in children.

Keywords: Prevalence, epidemiology, anaphylaxis, precipitating factors, allergens.

isoladamente em 5,55%. **Conclusão:** A anafilaxia não é doença rara entre portadores de atopia, especialmente nas crianças pequenas, e as causas foram similares às referidas pela literatura médica, predominando medicamentos na população mais velha, e alimentos nas crianças.

Descritores: Anafilaxia, epidemiologia, fatores desencadeantes, prevalência, alérgenos.

Introduction

Anaphylaxis is a severe, acute, potentially life-threatening systemic reaction triggered by a hypersensitivity mechanism. Anaphylaxis is characterized by the sudden onset of systemic clinical symptoms, which may progressively or simultaneously affect multiple systems, including the skin, mucous membranes, respiratory and cardiovascular systems, central nervous system, and gastrointestinal tract.[1] A later study showed high sensitivity for these diagnostic criteria, with moderate specificity. This indicates that while the criteria are extremely useful, the diagnosis may be overestimated in nearly 20% of cases.[2] The World Allergy Organization (WAO) has recently defined new clinical criteria to help diagnose anaphylaxis in both adults and children.[3] The goal of simplifying these criteria is to allow faster recognition of anaphylactic reactions, as experts agree that the condition is becoming more common, especially in the pediatric population.[4]

The triggers of anaphylaxis vary depending on age group and population habits. Food is the most common cause in children, adolescents, and young adults, and it has been identified as the main factor responsible for the increase in incidence in recent years. In contrast, medications, insect venom, and idiopathic anaphylaxis are more frequently seen in older patients.[5]

In Brazil, research on the epidemiology of anaphylactic reactions is still limited. The causative agents appear to be similar to those reported in international medical literature, with medications, food, and insects being the most common triggers.6 Given the challenges of conducting epidemiological studies in the country, Gagete et al.[7] proposed a new tool for population-based studies on anaphylaxis and its potential causes.

Online surveys and social media are part of today's reality, especially in the post-COVID-19 world. The Internet is a powerful tool that brings people and ideas together and can be useful for gathering relevant data. Thus, the present study aimed to assess the prevalence of anaphylaxis and its main triggers among individuals in the state of São Paulo, southeastern Brazil, who have any diagnosis of "allergy." Data were collected using a standardized questionnaire distributed electronically through various social media platforms.

Methods

The validated and standardized questionnaire developed by Gagete et al.[7] was sent electronically to Internet users, without requiring participant identification. This tool separates individuals aged 7 years and older (Q.1 questionnaire) from children aged 0 to 6 years, 11 months, and 29 days (Q.2 questionnaire), with each version tailored specifically to the age group. The forms were created using the Google Forms platform. This platform allows respondents to view each question one at a time, with new questions appearing as previous ones are answered, while earlier ones are hidden. It also automatically organizes responses into an Excel spreadsheet, facilitating later data analysis. Each questionnaire contains multiple questions and subquestions based on anaphylaxis diagnostic criteria, which are described in greater detail in the original publication.[7] In summary, the questions address symptoms, symptom progression, whether the diagnosis was made by a specialist, and the triggering factors. Responses are assigned positive and negative scores, and the total score indicates the likelihood of an individual having experienced anaphylaxis. To avoid bias associated with the word "anaphylaxis," considering that many different terms are used to describe the condition (such as "glottic edema," "giant urticaria," "cow's milk protein allergy," etc.), the questionnaire does not mention anaphylaxis as the focus; instead, it uses the broader term

"allergy." This approach encourages a wider range of allergic individuals to respond. As a result, the questionnaire includes negatively weighted questions for the differential diagnosis between anaphylaxis and other conditions such as severe asthma and acute urticaria.

The link to the questionnaires, along with an explanatory letter, was distributed through the following channels:

– all email contacts registered by the project authors;
– social media platforms such as WhatsApp, Facebook, and Instagram belonging to the project authors;
– respondents were also asked to share the questionnaire with their own contacts.

The Prática Clínica platform was used for sample size calculation,[8] considering a 5% margin of error, a 95% confidence level, and a maximum estimated prevalence of 6%. The sample size was calculated based on the population of the state of São Paulo, which is approximately 44 million according to the 2022 census,[9] resulting in a required sample size of 87 individuals. However, for this study, we considered 87 to be the minimum sample size and included in the analysis all questionnaires collected over the 6-month study period (from June to December 2022). The study was approved by the Research Ethics Committee (CEP USP) of the Hospital das Clínicas, School of Medicine, University of São Paulo – HCFMUSP (CAAE 45043621.2.0000.0068).

Results

A total of 309 Q.1 questionnaires were collected from individuals who reported being "allergic," with ages ranging from 7 to 81 years. Additionally, 84 Q.2 questionnaires were completed for children whose respondents reported some type of allergy.

Regarding Q.1 questionnaires, 46 individuals (14.9%) scored within the range indicating a possible diagnosis of anaphylaxis. Of these, 36 (78.3%) were female. The reported triggers for these 46 individuals included: medications, 26 (56.5%); food, 22 (47.8%); insect stings (bee, wasp, or ant), 12 (26.0%); latex, 2 (4.3%); and unknown causes, 2 (4.3%) (Figure 1). The total number exceeds 46 because some respondents reported multiple reactions triggered by different agents. Other diagnoses reported among these individuals with possible anaphylaxis included: rhinitis, 28 (60.8%); dermatitis or eczema, 19 (41.3%); asthma, 14 (30.4%); and isolated diagnosis of

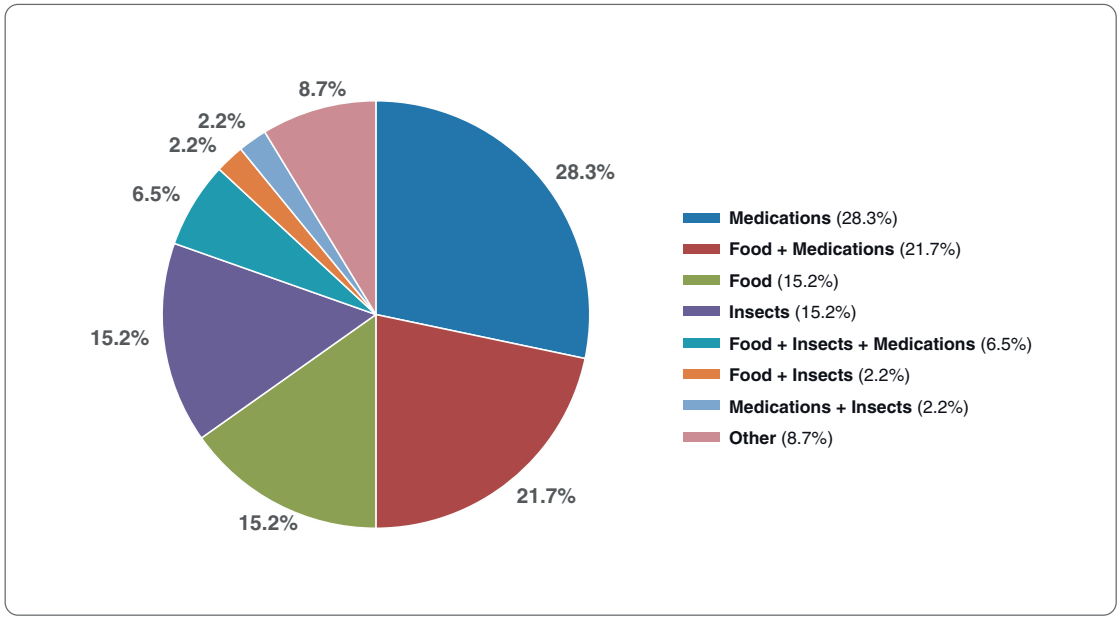

Figure 1
Reported causes of anaphylaxis in Questionnaire 1

anaphylaxis, 14 (30.4%). Among the 26 respondents who identified medications as the cause, nonsteroidal anti-inflammatory drugs (NSAIDs) were reported as the trigger in 18 cases (69.2%), antibiotics in 3 cases (11.5%), and muscle relaxant, vitamin, and vaccine in 1 case each (3.8% each). One respondent did not identify the medication involved (3.8%). Among the 22 respondents who identified food as a trigger, the breakdown was as follows: milk, 10 (45.4%); seafood, 6 (27.2%); egg, 4 (18.1%); fish, 2 (9.0%); and tree nuts, peanut, sesame, fruit, sunflower seed, and wheat, 1 each (4.5% each).

Among the 46 individuals with possible anaphylaxis, 33 (71.7%) reported that a physician confirmed the diagnosis through tests and/or examinations. Of these 46 patients, 5 reported that they had never received a medical diagnosis of the condition (or a related term such as "glottic edema" or "giant urticaria"). Regarding the number of episodes, 6 respondents reported only 1 episode; 8 had 2 episodes; 3 had 3 episodes; and 29 had 4 or more episodes.

Regarding Q.2 questionnaires, of 84 respondents indicating allergy, 18 had scores suggestive of anaphylaxis (21.4%). The reported triggers included: food, 13 (72.2%); insect stings, 4 (22.2%); and medications, 4 (22.2%). Asthma was reported in 10 questionnaires (55.5%), dermatitis in 7 (38.8%), rhinitis in 8 (44.4%), and an isolated diagnosis of anaphylaxis in 1 (5.55%). Of the 18 individuals with probable anaphylaxis, 9 were female (50.0%) and 9 were male (50.0%). For food-related causes of probable anaphylaxis, the following were reported: milk in 8 individuals (61.3%), egg in 3 (23.0%), tree nuts in 2 (15.3%), wheat in 1 (7.6%), food dye in 2 (15.3%), peanut in 4 (30.7%), fish in 2 (15.3%), and soy in 2 (15.3%). The number of reported causes is greater than the number of individuals because 5 of them indicated more than one trigger (Figure 2).

Among insect-related cases, 1 respondent reported a bee sting, 2 reported mosquito bites, and 2 reported ant stings. Regarding the 4 respondents who identified medications as the cause, 3 reported antibiotics. The respondents for all 15 children with probable anaphylaxis stated that a physician had confirmed the etiology. As for the number of episodes, the responses were as follows: 2 individuals (11.1%) reported only 1 episode; 4 (22.2%) reported 2 episodes; 2 (11.1%) reported 3 episodes; and 10 (55.5%) reported 4 or more episodes of possible anaphylaxis.

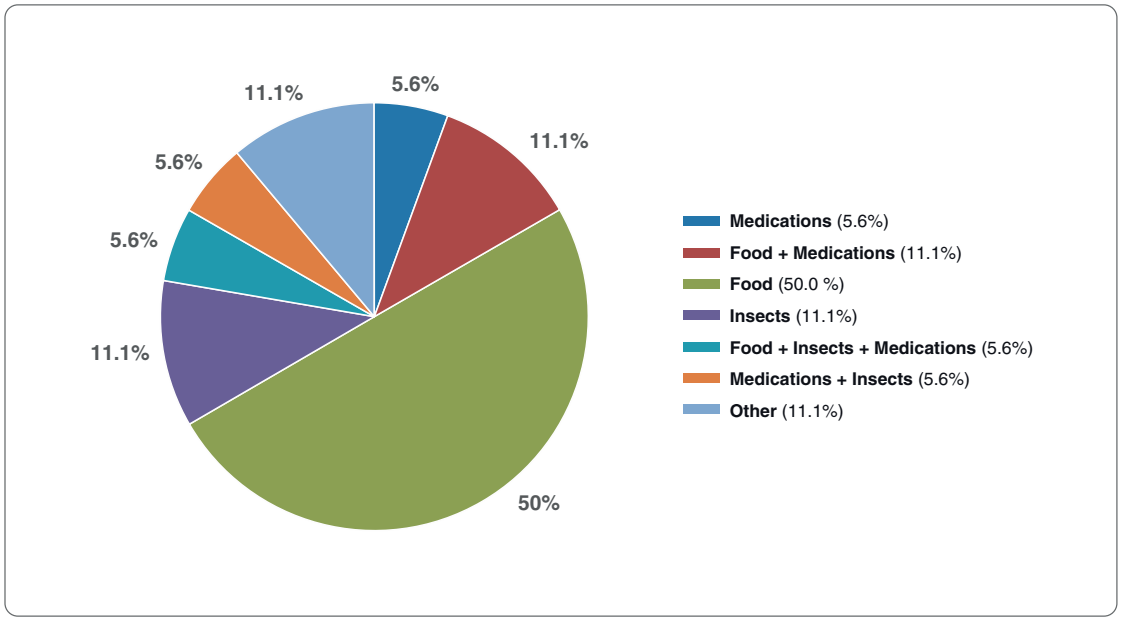

Figure 2
Reported causes of anaphylaxis in Questionnaire 2

Discussion

Anaphylaxis is a medical emergency where etiological diagnosis and patient guidance are the responsibility of allergist specialists. Anaphylactic reactions have been on the rise for reasons that are not yet fully understood,[10] making the study of this condition increasingly important. In Brazil, self-injectable epinephrine is still not available, despite being considered the cornerstone of self-management during an anaphylactic reaction while waiting for medical care. The reasons for the lack of approval of this device in the country remain unclear. However, one possible explanation may be the limited number of epidemiological studies demonstrating the need for such a resource in the Brazilian population.

Conducting epidemiological studies poses many challenges, especially concerning anaphylaxis, since the term "anaphylaxis" was not included in the International Classification of Diseases (ICD) until its 11th edition. Previous studies have shown that several ICD-9 codes suggestive of allergic reactions in the medical records of children treated in emergency settings — when later reviewed based on presented symptoms — were actually cases of anaphylaxis. However, these cases were recorded with diagnoses such as "unspecified allergic reaction" (999.3), "adverse food reactions" (995.7), and "allergic urticaria" (708.0), among others. This issue persists in ICD-10, which includes only codes such as "unspecified allergy" (T78.4), "personal history of allergy" (Z88.0 to Z91.0), and "anaphylactic shock" (T78.0, T78.2, T80.5, and T88.6).[11] However, ICD-11 explicitly includes the term "anaphylaxis," and once this new classification system is fully implemented, it will certainly facilitate epidemiological research.[12]

Questionnaires are widely used in epidemiological studies, despite challenges related to respondents' understanding of the content. These tools have proven useful in many areas of medicine, particularly in allergy and immunology. Well-known examples include the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire[13] and the online Latin American survey on anaphylaxis (OLASA).[14] The latter study, which involved several Latin American countries including Brazil, identified medications as the predominant triggers of anaphylactic reactions, especially NSAIDs and antibiotics. Food was the second most frequent cause, with common triggers including fish, milk, fruits, wheat, peanuts, egg, tree nuts, and cassava. Other causes reported were insect venom, immunotherapy, latex, exercise, and iodinated contrast agents. Other studies in Latin America have also used questionnaires to identify food-related anaphylaxis.[15-17] In Brazil, a recently published research protocol outlines a study that will use a questionnaire to investigate the prevalence of self-reported food allergies in older adults.[18] Additionally, Gagete et al., using a validated questionnaire, reported a 6.2% prevalence of anaphylaxis in the city of Botucatu, state of São Paulo, southeastern Brazil, where medications were the main cause, especially metamizole.[7] Sousa et al., using the same instrument in children and adolescents in the city of Imperatriz, state of Maranhão, northeastern Brazil, found a 5.78% prevalence of anaphylaxis.[19]

In this study, we used previously standardized questionnaires to investigate the prevalence of anaphylaxis among Internet users in the city of São Paulo who reported having some type of allergy. The prevalence rate was 14.9% with the Q.1 questionnaire and 21.4% with the Q.2 questionnaire. These rates are significantly higher than those previously reported in the general population using the same instruments. This may reflect a higher prevalence of anaphylaxis among individuals with preexisting allergic conditions, as these conditions may increase the likelihood of developing anaphylaxis.[20] There is also evidence supporting a positive correlation between anaphylaxis and a prior allergic condition.[21]

Our data also show that, among older children and adults (Q.1 questionnaire), medications were the most common triggers of anaphylactic reactions, followed closely by food. In contrast, among younger children (Q.2 questionnaire), food was clearly the leading cause of anaphylaxis, which is consistent with findings from previous studies conducted in Brazil and worldwide.[14,22] Another noteworthy finding is that 5 Q.1 respondents scored very high for symptoms, suggesting possible anaphylaxis even though no formal diagnosis of anaphylaxis had been made. While this could be a false positive, the lack of follow-up with respondents suggests that the study population may not have received proper guidance on when to seek specialist care for accurate diagnosis and treatment. This becomes even more evident considering that most respondents reported experiencing more than 1 episode, with 29 individuals indicating they had experienced 4 or more possibly anaphylactic reactions. It is likely that these individuals have not received proper guidance on how to prevent future episodes of anaphylaxis.

Questionnaire-based population studies face several challenges. A significant challenge is motivating individuals to respond to electronically distributed surveys, especially given the routine nature of such communications today. We should consider the potential for bias, as individuals with more severe allergies or those who have experienced more severe episodes may be more inclined to participate. However, the use of symptom scores and cutoff points for the diagnosis of possible anaphylaxis can help identify individuals who might otherwise remain undiagnosed, since many are mislabeled or do not consult specialists. Another challenge is ensuring respondents fully understand the questions. In a country where public education is increasingly inadequate, questionnaires are likely to be answered primarily by the more educated segment of the population, which can lead to results that do not represent all social classes. Moreover, conducting surveys online assumes that respondents have access to a mobile device and an Internet connection, which is still not a reality for the entire population.

Despite the challenges, epidemiological studies are essential to understand the true impact of anaphylaxis on the Brazilian population. Further research is needed to increase awareness of this important condition among the public, health professionals, and health authorities.

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