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Climate change may impact appetite for fish and chips: Increasing *Scombroid* poisoning, a broad perspective from a multicenter study

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Abstract

Scombroid poisoning (SP) is one of the most common causes of morbidity associated with fish consumption. The condition is caused by elevated levels of histamine in dark-fleshed fish and fish products due to inadequate processing or storage temperatures. This multicenter study was conducted at four hospitals located in two major coastal cities in Türkiye: İstanbul and Trabzon. Patient records were retrospectively evaluated for 108 cases from January 1, 2014, to December 31, 2023. A total of 79 patients were included in the study. Demographics, clinical findings, and discharge outcomes are reported. The onset of complaints was 0-60 minutes in 72 cases (91.1%) and over 1 hour in 7 cases (8.9%). Most patients were admitted to the Emergency Departments in groups of three (36.7%), four (32.9%), and two (20.3%). The most common symptom was skin rash, observed in 78 SP cases (98.7%), followed by abdominal pain in 65 (82.3%), headache in 59 (74.7%), dizziness in 54 (68.4%), heartburn in 47 (59.5%), metallic taste in the mouth in 38 (48.1%), circumoral paresthesias in 34 (43%), nausea/vomiting in 20 (25.3%), and palpitations in 13 (16.5%) patients. This study emphasizes the importance of initial diagnosis based on symptoms and patient history. With accurate diagnosis and antihistamine treatment, the benefits are significant in terms of cost-effectiveness, quality of care, hospital crowding, and patient satisfaction. The significance is discussed from a broad perspective, spanning the disciplines of emergency medicine and public health. The practical clinical suggestions apply to cases on the rise worldwide.

Keywords: Histamine fish poisoning, food safety, emergency medicine, public health

Introduction

Scombroid poisoning (SP) is a significant cause of morbidity associated with fish consumption, resulting from elevated histamine levels in improperly stored or processed dark-fleshed fish, such as mackerel, tuna, and bonito [1,2]. SP is common during warmer months when outdoor consumption of frozen fish increases, presenting a substantial public health challenge. Despite its prevalence, SP can be easily prevented with standard precautions, and accurate diagnosis followed by antihistamine treatment can rapidly yield positive outcomes.

Epidemics have been reported globally, highlighting the need for detailed food safety guidelines. For example, an outbreak among elementary school students in Korea was linked to yellowtail fish with histamine levels exceeding safety limits [3] Another large outbreak occurred in Senegal due to yellowfin tuna at a military mass catering event and also mass histamine FP was reported from Japan and described as an anaphylaxis outbreak [4,5]. These incidents underscore the importance of rigorous food safety measures and public health education in preventing SP. Effective public health strategies, including proper seafood handling and storage, can significantly reduce the incidence of SP and its associated healthcare burden. To prevent further occurrences of SP, it is crucial that public health authorities be notified when outbreaks are suspected.

While previous studies have documented SP incidents, they often focus on isolated cases or specific regions, lacking a comprehensive perspective. This multicenter study evaluates SP

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cases from hospitals in İstanbul and Trabzon, Türkiye, providing a broader view of SP's clinical presentation and management. Our study emphasizes the importance of distinguishing SP from other conditions like allergies and bacterial infections to enhance patient outcomes and optimize resource use in emergency departments (EDs). The primary objective of this research is to evaluate the demographics, clinical findings, and discharge outcomes of SP patients in the ED. By analyzing patient data from multiple hospitals, we aim to provide evidence-based insights into the management of SP, highlighting the cost-effectiveness and benefits of accurate diagnosis and antihistamine treatment. This study underscores the importance of proper seafood handling and public health education to prevent SP and reduce its burden on healthcare systems. The findings and implications will be discussed, focusing on improving clinical care and patient satisfaction.

Material and Methods

The study was conducted as a multicenter, retrospective analysis at four different hospitals: Yeditepe University Faculty of Medicine-affiliated Koşuyolu and Kozyatağı Research and Training (R&T) Hospitals in İstanbul, Health Sciences University Trabzon Kanuni R&T Hospital, and Karadeniz Technical University Faculty of Medicine Farabi Hospital in Trabzon.

After obtaining approval with the registration number 2024/50 from the Scientific Research Ethics Committee of the Trabzon Medical Faculty, Health Sciences University, on January 16, 2024, administrative authorization was attained officially from all four hospital locations. Data was obtained from four hospitals, following Trabzon Medical Faculty, Health Sciences University Ethics Committee's official approval and the institutional consent attained from Hospital Chief Medical Officers in response to the petition to conduct research. Due to the retrospective nature of the study and the examination of hospital records, written consent from participants was not deemed necessary. Database records were reviewed and assessed by the researchers.

Patients who presented to the emergency departments of the included hospitals between January 1, 2014, and December 31, 2023, and were assigned ICD codes and subcodes for allergy, urticaria, and anaphylaxis were identified from hospital databases. After an analysis of electronic patient records by the researchers, all cases determined to be fish-derived SP were included in the study. Demographic characteristics, patient medical history, poisoning history (time from symptoms onset, fish consumed), symptoms, clinical findings (including vital parameters), medical interventions, and patient outcomes were recorded retrospectively through hospital medical records.

The statistical analysis of patient data was performed using IBM SPSS® 23.0 program. Frequencies, percentages, ordinal and nominal data are presented in numerical format and mean±standard deviation and minimum-maximum values (mean±SD, min-max).

Results

After analyzing the ED records of four hospitals in İstanbul and Trabzon over the 10-year period from 2014 to 2023, a total of 79 SP cases were identified and all of them included in the study. The demographics and other features of the SP cases were given in Table 1.

Among the cases, 42 (53.2%) were male and 37 (46.8%), were female. The ages of the patients ranged from 8 to 76.

Of the patients, 69 (87.3%) were Turkish citizens, while 4 (5.1%) were Georgian, 2 (2.5%) were Russian, 2 (2.5%) were Persian, 1 (1.3%) was British, and 1 (1.3%) was Japanese. The majority of the patients were university graduates (50.6%). In terms of occupations, most of the cases were found to be students. A total of 42 patients (52.3%) were identified as students. This was followed by 21 (26.6%) self-employed individuals, 9 (11.4%) housewives, 4 (5.1%) tourists, 2 (2.5%) retirees, and 1 (1.3%) teacher.

Patients had preexisting conditions of diabetes mellitus (DM) in 2 (2.5%), hypertension (HT) in 2 (2.5%), acute coronary syndrome (ACS) in 1 (1.3%), epilepsy in 1 (1.3%), and coronary artery disease (CAD) in 1 (1.3%) case.

In most SP incidents, patients presented to the ED in groups of three (36.7%), followed by those who arrived in groups of four (32.9%) and groups of two (20.3%). Most patients presented to the ED between 3:00 and 9:00 PM. Forty-five cases (57%) presented during these hours, indicating that most patients consumed the spoiled fish that caused the clinical picture at lunch, in the afternoon, or early evening.

The most common fish consumed by the patients was mackerel with 45 (57%) cases. Other fish species were bonito in 23 (29.1%), and tuna fish in 11 (13.9%) cases.

In most cases the onset of complaints was within the first hour, as in 72 (91.1%) of the patients. In 7 cases (8.9%), symptoms began after the first hour.

The most common complaints were skin rash (98.7%), abdominal pain (82.3%), headache (74.7%), dizziness (68.4%), heartburn (59.5%), metallic taste in mouth (48.1%), circuoral paresthesias (43%), nausea/vomiting (25.3%), and palpitations (16.5%) respectively. Diarrhea, vertigo, itchiness, facial rash, dysphagia, uvula edema, fever, generalized swelling, and hypotension were other symptoms that were relatively rare (Figure 1).

Upon evaluating the monthly distribution of cases, it was observed that the highest incidence occurred in June, accounting for 31.6% of the cases. Additionally, 30.4% of the cases were reported in May, 24.1% in April, 7.6% in March, and 6.3% in July (Figure 2).

Diagnosis was made through physical examination alone in 45 patients (57%), whereas a combination of physical examination and laboratory tests was employed in the evaluation of 34 patients (43%).

Physical appearance of one of our patients was shown in Figure 1 (by courtesy of F. Celikmen). This patient was a twenty-year-old female college student, and she presented to Kozyatağı R&T hospital ED with the complaints of widespread rashes on her body, headache and nausea. The patient stated that the symptoms progressed rapidly, and all the symptoms started in less than half hour, after she ate tuna fish salad in a restaurant. Symptoms regressed completely after in half an hour after antihistamine administration (Figure 3).

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Table 1. *Scromboid* poisoning cases, presenting features and demographics (*n*, %, mean±SD, min-max values)

Gender	**Female**	**Male**								
	37 (46.8%)	42 (53.2%)								
Age	**Female**	**Male**								
Fish consumed	**Mackerel**	**Bonito**	**Tuna fish**							
	45 (57%)	23 (29.1%)	11 (13.9%)							
Patient per incident	**One**	**Two**	**Three**	**Four**	**Five**					
	3 (3.8%)	16 (20.3%)	29 (36.7%)	26 (32.9%)	5 (6.3%)					
Education	**Primary school**	**Middle school**	**High school**	**University**	**Post-graduate**					
	6 (7.6%)	9 (11.4%)	18 (22.8%)	40 (50.6%)	6 (7.6%)					
Occupation	**Student**	**Self-employed**	**Housewife**	**Tourist**	**Retiree**	**Teacher**				
	42 (53.2%)	21 (26.6%)	9 (11.4%)	4 (5.1%)	2 (2.5%)	1 (1.3%)				
Citizenship	**Turkish**	**Georgian**	**Russian**	**Persian**	**British**	**Japanese**				
	69 (87.3%)	4 (5.1%)	2 (2.5%)	2 (2.5%)	1 (1.3%)	1 (1.3%)				
Time (appr.)	**12:00noon**	**1:00pm**	**2:00pm**	**3:00pm**	**4:00pm**	**5:00pm**	**6:00pm**	**7:00pm**	**8:00pm**	**9:00pm**
	8 (10.1%)	9 (11.4%)	2 (2.5%)	11 (13.9%)	14 (17.7%)	7 (8.9%)	13 (16.5%)	4 (5.1%)	10 (12.7%)	1 (1.3%)
Month	**March**	**April**	**May**	**June**	**July**					
	6 (7.6%)	19 (24.1%)	24 (30.4%)	25 (31.6%)	5 (6.3%)					
Onset of complaints	**0-1 hr**	**>1 hr**								
	72 (91.1%)	7 (8.9%)								
Complaints	**Skin rash**	**Stomach ache**	**Headache**	**Dizziness**	**Heartburn**	**Metallic taste in mouth**	**Circumoral paresthesias**	**Nausea, vomiting**	**Palpitation**	**Diarrhea**
	78 (98.7%)	65 (82.3%)	59 (74.7%)	54 (68.4%)	47 (59.5%)	38 (48.1%)	34 (43%)	20 (25.3%)	13 (16.5%)	5 (6.3%)
	Vertigo	**Itchiness**	**Facial rash**	**Dysphagia**	**Rhonchi**	**Edema of the uvula**	**Fever**	**General swelling**	**Hypotension**	
	4 (5.1%)	3 (3.8%)	2 (2.5%)	2 (2.5%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	
Comorbidity	**DM**	**HT**	**ACS**	**Epilepsy**	**CAD**					
	2 (2.5%)	2 (2.5%)	1 (1.3%)	1 (1.3%)	1 (1.3%)					
Vital signs*	**Body temperature**	**Pulse rate**	**Systolic BP**	**Diastolic BP**						
	36.8±0.4 (36-38.5)	77±14 (40-110)	116.8±13.3 (90-140)	73.6±10.2 (50-90)						
Diagnostic method	**Physical examination**	**Physical examination & laboratory testing**								
	45 (57%)	34 (43%)								
Treatment	**Antihistamine**	**Steroid**								
	79 (100.0%)	1 (1.3%)								
Recovery time	**0-30 min**	**31-60 min**								
	38 (48.19%)	41 (51.9%)								

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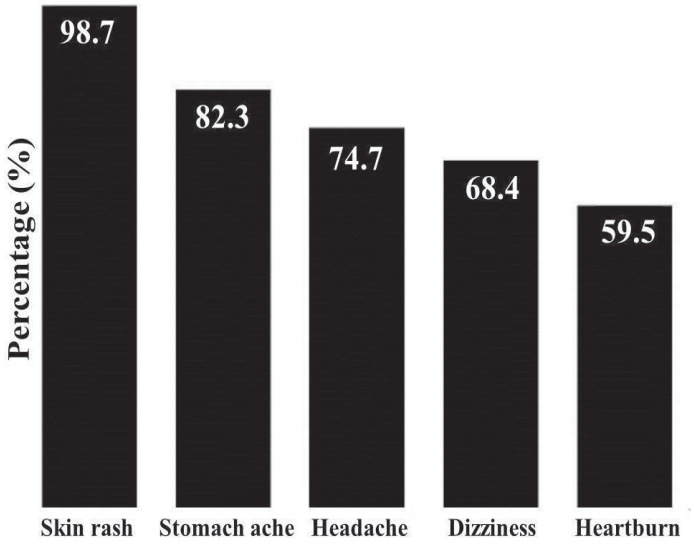

Figure 1. Scromboid poisoning, common complaints

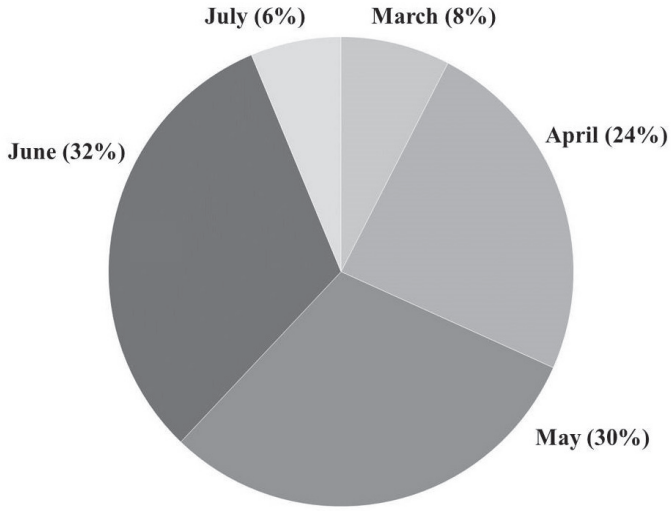

Figure 2. Incidents by month (%)

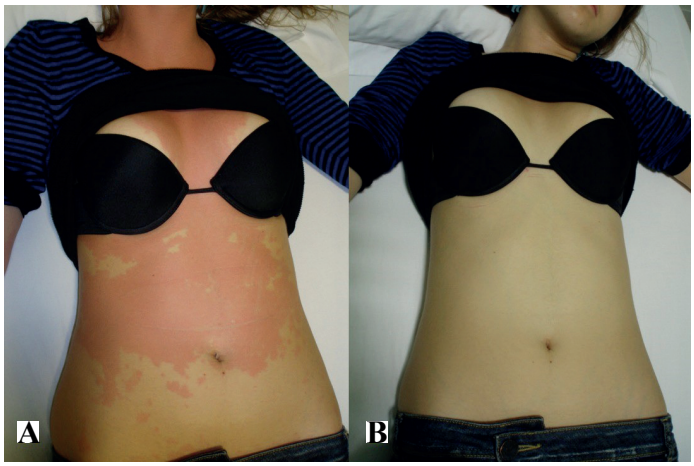

Figure 3. A: The image of the patient who ate tuna fish 1.5 hours ago in the ED, **B:** The image of the patient after antihistamine treatment

Discussion

In this study, data obtained from four hospitals in İstanbul and Trabzon, Türkiye, were meticulously analyzed to understand the demographic characteristics, clinical findings, and discharge outcomes of SP cases. By examining patient records from these diverse healthcare settings, we aimed to provide a nuanced and representative view of SP's impact on a varied population, contributing valuable insights to the field of emergency medicine and public health.

SP is a common cause of morbidity associated with fish consumption, resulting from elevated histamine levels due to inadequate processing or storage of fresh, canned, or smoked fish [1,2]. The causative agents are dense, dark-fleshed fish from the *Scombroidae* family, including mackerel, bonito, tuna, and yellowtail amberjack. During the seasonal fishing ban starting in March, there is an increased consumption of frozen fish, which continues to rise as the weather warms up. Fish sandwiches, popular street foods in Türkiye, similar to fish and chips in English-speaking countries, play a significant role in this trend.

Histamine in mishandled fish products is produced through the activity of decarboxylase enzymes from enterobacterial species, converting histidine to histamine in the fish muscles. These enzymes are mainly produced by enteric gram-negative bacteria such as *Morganella morganii, Escherichia coli, Klebsiella species*, and Pseudomonas aeruginosa. Histamine levels in fish must not exceed 10 mg per 100 g, as this heat-resistant compound cannot be inactivated by cooking [6,7].

In our study, the most common complaint was skin rash, followed by abdominal pain, headache, dizziness, and heartburn. Particular attention is drawn to erythema, which is present in almost every case and predominantly seen in the current study [1,3,8-10] (Table 1) (Figure 2).

In a 1986 publication, a total of twenty-five cases of SP from previous years were presented in a retrospective study conducted in the US and Yugoslavia. The clinical manifestations were very similar in most cases, consisting of alterations in taste, anxiety, hyperemia (particularly of the face and neck), nausea, pruritus, headache, and other symptoms and signs. Most patients responded to antihistamines, and all cases were self-limiting [6]. In a 1992 publication from South Africa, ten incidents from the year 1990 were reported, involving 22 patients. The symptoms and signs were suggestive of SP in the patients who had all consumed Cape yellowtail (Seriola lalandiz). The presenting symptoms and signs were skin rashes, diarrhea, palpitations, headache, nausea, abdominal cramps, paresthesia, unusual taste sensation, and breathing difficulties, in the order of frequency [9]. In a case of SP ichthyosarcotoxism from Brazil, a skin rash was first noted 10 minutes after the consumption of tuna fish. The patient presented with a 60-minute history of a burning and itching cutaneous eruption, headache, and metallic dysgeusia. Large areas of flushing were mainly over the face and trunk [11]. Three cases were reported from Türkiye. Two cases involved

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individuals who ate various fish, including mackerel, in the same environment and presented to the ED with complaints of flushing on the face and skin, hot flushes, abdominal pain, and nausea approximately one hour after eating. The third patient reported that about half an hour after a meal containing mixed seafood, others at the table also ate the fish, but only he became ill [2]. Two cases of SP in Singapore presented with signs and symptoms that could have easily been attributed to allergies. The article draws attention to the differences between *Scombroid* and allergic reactions [12]. A unique case presented in shock several hours after ingesting imitation crab meat sushi in the US. This was an atypical SP case with the uncommon concurrent pathogen Brevundimonas vesicularis septicemia in the blood cultures. The patient was discharged with recovery after comprehensive treatment in the ICU [13].

Cardiac involvement was reported in 1997 and remains a rare condition [14]. In 2020, a letter commented on worldwide emerging evidence of Ischemic *Scombroid* Syndrome (ISS), which apparently dates back to 1980 in Great Britain [15,16]. Cardiovascular *Scombroid* cases and SP leading to vasospastic angina with chest pain are increasing reported. Findings include gastrointestinal disorders, cutaneous reactions, ambiguous chest, non-ST-segment elevation myocardial infarction-like ECG patterns, following Scromboid fish ingestion [10,17,18]. Kounis syndrome and ISS appear as similar conditions with coronary vasospasm clinical presentation which is exclusively related to the histaminergic storm that are exclusively related to the histaminergic storm, with fundamental pathophysiological differences [9,16,18,19].

As stated earlier in this article and in previous scientific studies, the relatively rapid positive response to antihistamines is of great importance in confirming the initial diagnosis. In this respect, the importance of approaching SP cases adequately was emphasized, within the context of patient management in EDs and public health practices, including cost-effectiveness, the efficient use and allocation of human/financial resources, patient satisfaction, and disease burdens. In the current study, antihistamines were used in all 79 patients (100%), and steroids were added in only one patient (1.3%). Thirty-eight patients recovered in up to a half hour (48.19%), and the remaining 41 patients recovered within the first hour of treatment (51.9%). This is definitive for SP and confirms that the condition had been correctly diagnosed when first seen in the ED [1,6,9,13] (Table 1).

Previous studies have demonstrated similar findings. For example, the conditions of 22 SP patients from South Africa resolved within 12-24 hours, responding well to antihistamines [9]. An antihistamine was prescribed to a patient with SP ichthyosarcotoxism in Brazil, and the outcome was complete resolution within 24 hours, with no hypersensitivity reactions on subsequent ingestions of tuna [11]. All three SP patients reported from Türkiye received antihistamines, H2 receptor blockers, corticosteroids, and other symptomatic treatments in the ED. The complaints of all three patients subsided after a two-hour follow-up, and they were discharged [2]. An article from Singapore draws attention to the differences between *Scombroid* and allergic reactions, noting that antihistamines and supportive treatment are usually sufficient for SP, while adrenaline and corticosteroids are not routinely indicated [12].

Although the symptoms may resemble an IgE-mediated allergic reaction or fish allergies, SP is actually a reaction developed against histamine produced by bacteria, often leading to misdiagnosis [2]. Histamine fish poisoning is an often underrecognized infectious disease. Differential diagnosis is important to address the issue practically without wasting unnecessary time, effort, and expenditure.

We found that most patients presented to the ED between 3:00 and 9:00 PM. The question may come to mind that these are the relatively warmer hours of the day. Another consideration might be that eating out rather than at one's home may be a factor in the care/attention given to handling the fish. In this respect, as preventive medicine public health practices, transfer of knowledge and information to restaurants can come to the fore. Suggestions may further be made for improving the inspections.

It was found that in most cases, the onset of complaints occurred within the first hour. This is consistent with the literature, which reports that in SP, the onset of symptoms begins within the first hour after consuming fish [2,12].

Upon evaluating the monthly distribution of cases, it was observed that the highest incidence occurred in June, accounting for 31.6% of the cases. This pattern aligns with typical findings in seasonal patterns (SP) previously discussed. As the weather gets warmer, people tend to spend more time outdoors and consume more frozen fish that is often cooked and served without adequate attention to cold chain requirements.

From a public health perspective, SP is crucial because it can affect both individuals and larger groups, but it is preventable with standard precautions. Rapid and correct clinical evaluation and treatment yield positive results, reducing treatment costs and the disease burden. SP symptoms, resembling allergic reactions, arise from ingesting poorly preserved fish out of the cold chain, with scombrotoxin being a significant food safety hazard [20,21]. SP is predominantly a self-limited illness, with symptoms resulting from histamine toxicity [8,13].

A preventive public health approach to avert future *Scombroid* outbreaks will require that fishermen, public health officials, restaurant workers, and medical professionals work together to devise international safety standards and increase awareness. The disease is intimately linked with the global fish trade [7]. A 2022 article puts forth that *Scombroid* accounts for approximately 5% of food toxicities in the US [17]. Therefore, robust food safety measures and public health education are critical in preventing SP and reducing its associated healthcare burden. Effective public health strategies, including proper seafood handling and storage, can significantly reduce the incidence of SP.

From a broader public health perspective, the analysis has implications for food safety and health education. In order to determine the possible cause and prevent new cases, healthcare workers are asked to alert authorities when encountering outbreaks of suspected SP cases [9]. To prevent further reoccurrence of SP, public health authorities should be notified. Epidemics have been reported globally, highlighting the need for detailed food safety guidelines. For example, an outbreak among elementary school students in Korea was linked to yellowtail fish with histamine levels exceeding safety limits [3]. Another large outbreak of SP-associated was reported due to yellowfin tuna at a military mass catering event in Senegal [4]. A *Scombroid*-induced mass histamine FP was reported from Japan and described as an anaphylaxis outbreak [5]. These incidents underscore the importance of rigorous food safety measures and public health education in preventing SP.

Limitations

Despite the valuable insights gained from this multicenter study, several limitations must be acknowledged. First, the retrospective design of the study relies on the accuracy and completeness of medical records, which may vary between institutions and could introduce bias. Second, the sample size, while substantial, is limited to two coastal cities in Türkiye, potentially affecting the generalizability of the findings to other regions with different seafood consumption patterns and public health infrastructures. Third, the study focuses on cases presenting to emergency departments, possibly overlooking milder cases of SP that did not seek hospital care. Additionally, the reliance on ICD codes for identifying cases may have led to the exclusion of some patients who were misdiagnosed or whose conditions were not correctly coded. Lastly, environmental factors influencing histamine production in fish, such as specific handling practices or storage conditions, were not systematically investigated, which could provide a more comprehensive understanding of SP risk factors.

Conclusion

This multicenter study on SP underscores the critical importance of accurate initial evaluation and timely treatment with antihistamines for cost-effectiveness and patient satisfaction. Analyzing hospital records for 79 patients from four hospitals affiliated with three universities in two coastal cities provided valuable insights. Proper diagnosis is vital for effective SP management, preventing the wastage of time, effort, and resources in emergency departments (EDs) and reducing unnecessary expenses. Given the issue of overcrowding in EDs, minimizing the time spent is crucial. Accurate evaluation and diagnosis enhance care quality, patient safety, satisfaction, and overall clinical care. Key diagnostic indicators include recognizing facial or generalized skin redness, assessing the rash with patient history, noting seasonal patterns, and differentiating SP from allergies. Antihistamines lead to rapid symptom regression within 30 minutes if the diagnosis is correct. This study emphasizes the importance of public health initiatives to improve food safety practices and raise awareness about SP, preventing future outbreaks and mitigating the public health impact. The cost difference when SP is misdiagnosed highlights the significance of rapid and correct diagnosis and treatment, providing essential recommendations for emergency medicine and public health and serving as a reference for future SP research globally.

Conflict of Interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

The authors declare that they have received no financial support for the study.

Ethical Approval

Ethical approval with the registration number 2024/50 is taken from the Scientific Research Ethics Committee of the Trabzon Medical Faculty, Health Sciences University, on January 16, 2024.

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